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Índice
Summary

Galicia Clinica de ayer y hoy: un viaje al futuro, desde el pasado

Dr. José López Castro

Director de Galicia clínica
S. de Medicina Interna. Hospital Público de Monforte (Lugo, España).

Queridos amigos y compañeros,

Tras pasar 5 años disfrutando del enorme privilegio de afrontar la Dirección de Galicia Clínica, quisiera hoy hacer una breve reseña de las alegrías que han sido muchas y los sinsabores, que también han existido, durante este ilusionante periplo. Cuando en junio de 2015 me hice cargo de la organización de la revista, percibí nítidamente como mis predecesores más directos (Dres. Héctor Meijide y Fernando de la Iglesia) llevaban con enormes dificultades la mayor parte del peso organizativo y científico de la misma lo cual les generaba una sobrecarga considerable. Por otra parte pienso que las revistas médicas deben abrirse a la participación de sus lectores por lo que se ampliaron enormemente en estos últimos 5 años los comités científicos y editorial, nutriéndose de revisores de talla internacional sin perder la riqueza de los grandes talentos gallegos, que también los hay… La necesidad de abordar la confección y maquetación de cada número hizo necesaria la labor del Dr. Manuel Fernández Muinelo que con absoluta firmeza y minuciosidad tenía montado el número correspondiente siempre antes de la fecha programada, para él mi agradecimiento al igual que para los compañeros de las empresas RUBINE y LUGONET por su aportaciones técnicas y buenhacer. No debemos olvidar la contribución callada pero imprescindible de Dña Yolanda Carbajales, artista y esposa del Dr. Julio Montes, que materializó las portadas de la edición en papel de Galicia clínica hasta que dicha edición se eliminó.

La visibilidad de una revista es fundamental sobre todo en la era digital presente, por tanto para ello se sacrificó la edición en papel en pro de una página web más visitable y con mayores opciones de búsqueda, lo cual incrementó el movimiento de internautas que entraron a ver nuestra revista on line. Se renovaron algunas licencias de bases de datos como DOAJ o DULCINEA y se consiguió entrar en otras más exigentes como MIAR (con 7.5 puntos) o ESCI (Emerging Sciencie Citation Index) antesala de la WOS. Se ha quedado en el tintero la posiblidad de entrar en SCOPUS y MEDLINE entre otras cosas por aspectos como el tipo de página web o la exigencia imperiosa de internacio-

Correspondencia: jose.lopez.castro@sergas.es

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"no podía dejar de mencionar la importancia de nuestra revista como vehículo de expresión de ideas y pensamientos de los médicos internistas que tanto hemos luchado para que esta nueva enfermedad no cercene las ilusiones, esperanzas y a veces la vida de tantos enfermos que atendemos diariamente"

nalización de las colaboraciones de la revista que en nuestro caso son mas bien escasas.

Una traba muy importante a la indexación de una revista en bases de datos internacionales de prestigio, además de la calidad de los artículos publicados y de la reputación científica de los miembros de sus comités científico y editorial es que sea una revista de ámbito internacional y publicada íntegramente en lengua inglesa. Tras haber sometido a la opinión de la Junta directiva la posibilidad de cambio de nombre de la revista por uno que no sea localista o eliminar el castellano como lengua opcional de publicación, la Junta se ha mantenido tajante, prefiriendo mantener el nombre original y su identidad (gallega) así como la posibilidad de enviar trabajos en castellano, lo cual hace prevalecer las raíces de la revista frente a otros intereses del tipo de índices bibliométricos y demás. Y como escribo estas líneas en plena pandemia de COVID19, no podía dejar de mencionar la importancia de nuestra revista como vehículo de expresión de ideas y pensamientos de los médicos internistas que tanto hemos luchado para que esta nueva enfermedad no cercene las ilusiones, esperanzas y a veces la vida de tantos enfermos que atendemos diariamente aquejados de esta nueva enfermedad.

En resumen, durante esta etapa hemos intentado que los lectores de Galicia clínica sientan que aportamos información relevante y veraz para su práctica médica diaria. Si lo hemos conseguido, sería para nosotros el mejor regalo.

Muchas gracias a todos.

Covid 19 and venous thromboembolic disease. Review on a series of patients

Manuel Jesús Núñez-Fernández[1], Emilio Manuel Padín-Paz[1], Beatriz Suárez-Rodríguez[2], Beatriz Pombo – Vide[3], Carmen Mella-Pérez[4], Cristina Barbagelata-López[5], José Antonio Díaz-Peromingo[6], Rubén Puerta-Louro[7], Alberto Rivera-Gallego[8], en representación del Grupo de Enfermedad Tromboembólica de la SOGAMI.

[1]Servicio de Medicina Interna. Complejo Hospitalario Universitario de Pontevedra, [2]Complejo Hospitalario Universitario de Ourense, [3]Hospital Universitario Lucus Augusti, [4]Hospital Arquitecto Marcide, [5]Complejo Hospitalario Universitario de A Coruña, [6]Complejo Hospitalario Universitario de Santiago de Compostela, [7]Hospital POVISA, [8]Hospital Álvaro Cunqueiro.

INTRODUCTION

In December 2019, the first cases of an atypical pneumonia named COVID-19 (the acronym in English for "Coronavirus Disease 19") by the World Health Organization, and caused by the SARS-CoV2 virus (severe acute respiratory syndrome coronavirus-2), appeared in Wuham, China [1]. Currently the infection is considered a pandemic which has caused more than 300,000 deaths worldwide in less than 6 months.

Over the weeks and given the magnitude of the problem, several series of cases of patients infected with SARS-CoV2 have been published in different countries, including ours, basically describing clinical characteristics, laboratory data, and radiological findings [1-9].

COVID-19 and coagulopathy

Three of the publications of the Ning Tang group of Huazhong University [10-12], caused the medical community to turn their attention to the existence of inflammatory and coagulation disorders very characteristic of patients with COVID-19, and some of them related to the worst prognosis. Increments on factor VIII, fibrinogen, ferritin, interleukin-6, and especially D-dimer (DD) were described. In the group of patients with D-dimer elevation receiving heparin treatment, the mortality was lower compared to the group that hadn´t been treated [10-11]. Tang et al, conclude that patients with sepsis-associated coagulopathy, or significant elevations in DD levels, could benefit from an anticoagulant treatment [10-11].

After performing a meticulous study of the publication by Tang et al., some authors wonder if the elevation of the D-dimer, in the patients provided, could be due to the existence of pulmonary embolisms in many of them, since only 99 of the 449, had received thromboprophylaxis with heparin [13].

Since then, a large number of publications have appeared showing the importance of the thrombotic phenomena, especially venous, in patients infected with SARS-CoV2. Thus venous thrombosis has been described related to acute coronary events [14], with aortic thrombosis [15], in pregnant women [16], causing hypokinesia of the right ventricle [17], in travellers[18], etc.

However, both the incidence and prevalence of a venous thromboembolic disease (VTE) in COVID-19 infected patients, are unknown. The high risk of contagion associated with the moving of these patients in different hospital areas, as well as the fact that many of them are under an invasive ventilation at the time of the suspicious diagnosis[19], these are some of the situations that prevent us from knowing exactly the VTE in these patients. Some authors even recommend starting an anticoagulant treatment under the suspicion of VTE, and postponing diagnostic tests for pulmonary embolism (PE) and deep vein thrombosis (DVT).

With all the above, it was necessary to publish series of patients, to see if the clinical cases described above were simple anecdotes or on the contrary, if there was a close relationship between COVID-19 and venous thrombotic phenomena.

COVID-19 and VTE: case series

Until the presentation date of this work (June 17), and after an exhaustive bibliographic search, we have been able to find 26 series with three or more patients diagnosed with acute infection by COVID-19 and VTE[20-46], simultaneously. The analysis was performed on a total of 667 patients, 357 with PE and 287 with DVT (Table 1). As a whole, the publications present a very noticeable heterogeneity, so drawing conclusions on aspects such as what may be the best thromboprophylaxis treatment would be inappropriate given that in some series do not provide information in this regard.

Most of them agree in highlighting that a high incidence of VTE exists in admitted patients with COVID-19, both in the conventional ward, but mostly in those who required admission in Intensive Care Unit (ICU) 21-25, reaching a percentage between 13-85% of patients [31,34].

In some centres, the presence of COVID-19 is clearly related to a greater number of VTE cases in connection with the same period of the previous year; and even this year, patients who are COVID-19 negative have a lower incidence of VTE compared to those infected with SARS-CoV-2 [22,29,32].

The performance of diagnostic tests for VTE, CT angiography and venous Doppler echo is not uniform. There is a predominance of a greater number of authors who perform both[21-25,31,36,] the rest perform either only CT angiography [28-30,33], or only venous Doppler echo[26,27,32,34,35]. Despite the practical equality between the performed diagnostic tests, there is a greater number of patients with the diagnosis of PE. The Cattaneo series stands out, which, after performing a venous ultrasound on 64 patients infected with COVID-19, asymptomatic for VTE, did not diagnose any case of DVT [47]. In opposi-

Correspondencia: majenu@cmpont.es

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Table 1. Series of patients

	References	Total VTE	PE	DVT	PE-group1	PE-group2	Proximal-DVT	Distal-DVT	Thromboprophylaxis
Klok et al.	21	68	65	3	0	25	1	0	Yes
Poissy et al.	22	27	22	5	2	11	ND	ND	Yes
Helms et al.	23	28	25	3	17	8	ND	ND	Yes
Middeldorp et al	24	33	11	22	0	11	12	9	Yes
Llitjos et al.	25	24	6	18	ND	ND	ND	ND	Yes
Spiezia et al.	26	5	0	5	0	0	ND	ND	Yes
Cui et al.	27	20	0	20	0	0	ND	ND	No
Franco-López et al.	28	8	8	0	3	4	0	0	ND
Leonard-Lorant et al.	29	32	32	0	18	14	0	0	ND
Grillet et al.	30	23	23	0	ND	ND	0	0	ND
Lodigiani et al.	31	16	10	6	3	4	4	1	Yes
Marone et al.	32	16	0	16	0	0	7	4	Yes
Griffin et al	33	3	3	0	1	ND	0	0	Yes
Ren et al.	34	41	0	41	0	0	5	36	Yes
Demelo-Rodríguez et al.	35	23	0	23	0	0	1	22	Yes
Beun et al.	36	23	20	3	4	16	ND	ND	Yes
Bompard et al.	37	32	32	ND	10	22	ND	ND	Yes
Poyiadji et al.	38	72	72	ND	41	31	ND	ND	Yes
Nahum et al.	39	27	ND	27	ND	ND	9	23	Yes
Tveita et al.	40	3	3	ND	ND	ND	ND	ND	Yes/ Not all
Zhang et al.	41	66	1	66	ND	ND	23	43	Yes/Not all
Voicu et al.	42	26	ND	ND	ND	ND	13	13	Yes
Thomas et al.	43	5	5	ND	1	4	ND	ND	Yes
Tavazzi et al.	44	10	2	8	0	2	ND	ND	Yes
Gervaise et al.	45	13	13	ND	6	7	ND	ND	No
Grandmaison et al.	46	23	4	21	ND	ND	7	21	Yes
		667	**357**	**287**	**106**	**159**	**82**	**172**	

Abbreviations: ND, Not documented; VTE, venous thromboembolism; PE, pulmonary embolism; DVT, deep vein thrombosis.

tion, we find the results of Ren et al., who diagnosed 85% patients admitted in ICU with COVID-19 as DVT[34].

We have divided the anatomical distribution of PE into two groups: group 1-proximal, which includes PE with central-trunk-lobar location; and 2-distal group, which are segmental and sub-segmental PE. Some series, such as that of Llitjos et al., and Grillet et al., do not specify the distribution [25,30]. In the rest, we found almost twice as many cases in the group 2-distal (159 cases) as in the 1-proximal group (106 cases). The anatomical location of DVTs is wide (proximal, distal, superficial, upper limb, thrombosis of the inferior cava, associated with a catheter, etc.), with a clear predominance of distal DVT over the others.

The timing of the VTE diagnosis is also variable. Generally, in patients admitted to the ICU, it is diagnosed up to the 5th day on average [23]; in the series by Grillet et al., the diagnosis of PE is 12 days after the onset of COVID-19 symptoms [30]. Lodigiani et al., describe that half of thromboembolic events in their 36 patients occur within 24 hours of hospital admission[31].

The anticoagulant treatment prior to the diagnosis of SARS-CoV2 infection, prevented the appearance of VTE in all 19 patients who received it in Middeldorp et al., series [24]. Something different ocurred to a total of 11 anticoagulated patients in the Poissy et al., Llitjos et al., and Leonard-Lorent et al [22,25,29]. In most series, patients were receiving treatment for ETV thromboprophylaxis with the correct doses, even at higher doses, and a small group were anticoagulated, as previously stated. To be highlighted in the series described by Cui et al., of 81 patients admitted to the ICU, the absence of thromboprophylaxis in all is described, including the 20 patients who developed DVT [27].

Anatomo-pathological findings

The first descriptions of the biopsies obtained from cadavers deceased from COVID-19, at a pulmonary level predominated diffuse alveolar damage (DAD) to different degrees, with hyaline membranes and interstitial thickening[48,49]. In Carsana et al., and Dholnikoff et al., minimally invasive autopsies in 48 deaths from COVID-19, in addition to the diffuse alveolar damage, the existence of fibrin thrombi in small pulmonary arterioles is evident in most patients [50,51]. The complete autopsies of 35 deceased patients with COVID-19 have been published, in which the existence of thrombi in the small pulmonary arterial vessels, with small haemorrhages, is revealed again, all of which is compatible with microangiopathy associated to SARS-Cov-19[52-55]. In addition to prostate and pulmonary micro vascular thrombosis, Wichman et al., and Menter et al., confirm the existence of bilateral DVT and fresh pulmonary embolisms, which are identified as the cause of death in a high percentage of patients[54,55].

It should be noted that a third of those who died in the series from Wichmann et al., were receiving anticoagulant treatment before their death. In short, there is data on hypercoagulability, mainly with pulmonary microangiopathic involvement and macrovascular thromboembolic disease, both in the lung and in the lower extremities.

SUMMARY

1. Based on the data provided in the series of clinical and autopsy cases, VTE is a frequent pathological process in patients with COVID-19. It affects two possible non-exclusive forms, a "microvascular" with micro thrombi in lung areas affected by DAD, in relation to microangiopathy, which can progress into the form of local pulmonary thrombosis[56,57]. This form would be consistent with a greater number of cases of segmental-

sub segmental involvement, and even in those cases in the absence of DVT and presence of PE demonstrated by CT angiography. The second is a "macrovascular" form of venous thrombosis, demonstrated both in radiological studies, and especially in necropsies, which causes PE with significant repercussions in right heart chambers, causing death. Prospective series will be published shortly, such as that of the RIETE group with data from 592 patients with VTE and COVID19 infection (Fernández-Capitán et al., pending publication) that will increase our knowledge about these pathologies.

2. The decision to increase thromboprophylaxis doses, or to directly initiate a full-dose anticoagulant treatment to prevent coagulopathy associated with COVID-19, as well as the VTE that may develop, are not based on the results of any clinical trial. However, some guidelines recommend increasing thromboprophylaxis doses based on the results of Ning Tang publications, clinical data from patient series, and information obtained from autopsies. The posture of starting anticoagulant treatment at the time of hospital admission is proposed by some authors based on the significant increase in the number of cases of VTE related to COVID-19 detected in their hospital centres[32]. The guidelines of different scientific societies recommend continuing thromboprophylaxis with the usual doses, justifying its increase based on weight or added risk factors (such as previous VTE or cancer)[58-61]. Vivas et al, recommend increasing the dose or even anticoagulation in those patients with a high thromboembolic risk established by clinical and analytical parameters [62]. Several clinical trials are ongoing, evaluating the suitability of increasing the thromboprophylaxis dose [63].

3. There are discrepancies in regard to the drugs to be used in the treatment of coagulopathy associated with COVID-19 with a clear tendency to thrombotic phenomena. The controversy is established by some authors, considering patients with elevated fibrinogen, factor VIII, and DD, together with anti-thrombin III in the normal range, as components of a pro-coagulant state, which would cause a therapeutic resistance to LMWH [36,64]. Therefore, they recommend a treatment with unfractionated Heparin (HNF) adjusted to anti-Xa levels, and even if there is a clinical worsening, with systemic fibrinolysis [36,64]. The group by Barrett et al., established as the main measure, to anticoagulate with HNF those infected with COVID with severe forms of coagulopathy and clinical deterioration from their admission [64].

4. With the data observed in the autopsies of patients with COVID-19, it becomes evident that there is both a macrovascular and microvascular involvement, preferably venous. Underlying microvascular injury there is a notable impact on the endothelium caused by a tremendously complex inflammatory process and variable in intensity, with mechanisms in which platelets, neutrophils, mast cells, NETs, cytokines, interleukins, haemostasis factors, and complement are involved, among others[65-69]. After seeing the complexity in the pathophysiology of thrombosis caused by COVID-19, it is appropriate to call the process "immunothrombosis" since both processes are linked. We therefore believe that, in addition to trials that would evaluate different anticoagulation modalities and doses for the prevention of coagulopathy and VTE, trials should be launched to study different therapeutic targets [68], as to avoid the inflammatory cascade, in which the thrombotic phenomena are a fundamental part, but not the only one, and probably the final stage of the entire inflammatory process triggered by SARS-CoV2.

CONCLUSIONS

The association between SARS-CoV2 infection and VTE is frequent, as evidenced in the clinical case series, and also in the necropsies of those who died from COVID-19. The incidence and prevalence of COVID-19 associated with VTE are highly variable, due to the difficulty in diagnosing VTE in these patients, caused by their high contagiousness and their clinic situation, mainly in intubated patients. There is a venous microvascular and a macrovascular involvement, with peripheral and central lung embolisms, as well as proximal and distal deep vein thrombosis. The relevance of thromboembolic disease within COVID-19 is due to the fact that its responsibility has been proven in the deaths of a significant number of people infected with SARS-CoV2. The multiple pathological analysis show damage to the vascular endothelium with thrombosis at the pulmonary level, which was initiated by viral infection and with pathophysiological mechanisms involving a large number of elements, therefore the process has been called "immuno-thrombosis". The clinical trials publication on thromboprophylaxis in these patients is essential, given the great controversy that exists on the subject. We believe that venous thrombosis is multifactorial and the final consequence of the entire process which begins with SARS-Cov2 infection. It is necessary to achieve the neutralization of the virus, and also to study possible targets in the immunological process, which would prevent reaching the end in the form of thrombosis.

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Sepsis – Retrospective Observational Study of Sepsis and Septic Shock treated in internal medicine wards

Sepsis – Estudo Observacional Retrospectivo de Sépsis e Choque Séptico na enfermaria de medicina interna

Sónia Santos[1], Ana Ponciano[1], Joana Raquel Monteiro[1], Fernanda Pinhal[2], José Leite[2], Célio Fernandes[3]

[1]*Internal Medicine Resident, Department of Internal Medicine II, Centro Hospitalar de Leiria, Leiria, Portugal.*
[2]*Internal Medicine Specialist, Department of Internal Medicine II, Centro Hospitalar de Leiria, Leiria, Portugal.*
[3]*Internal Medicine Specialist and Department Director, Department of Internal Medicine II, Centro Hospitalar de Leiria, Leiria, Portugal*

ABSTRACT

Introduction: Sepsis and septic shock are very relevant in clinical practice. Most studies focus on the treatment in Intensive Care Units. Outside these units, the reality is largely unknown. The aim of this study is to epidemiologically characterize sepsis and septic shock patients admitted at internal medicine wards.

Material and Methods: Retrospective observational study, involving patients admitted to internal medicine wards with the diagnosis of sepsis/septic shock during a year

Results: A total of 308 patients were included in the study. 53% were female, with higher levels of comorbidities. Almost 40% were in septic shock, at admittance. Mortality rate was 29,87%. Overall, microbiologic documentation was possible in 92.2% of the cases, with higher prevalence of infection in the urinary (52.6%) and respiratory (34.8%) systems. Initial antibiotic therapy was appropriate in 50% of cases.

Previous antibiotic therapy (OR 3.84; IC95% 2.4-6.2; p<0.0001) and bedridden status (OR 3.15; IC95% 1.7-5.8; p<0.0002) were independent risk factors to antimicrobial resistance.

Discussion: Sepsis outside intensive care units is an escalating reality with high rates of morbidity and mortality. Timely diagnosis and collecting cultures to appropriate treat are primordial to best results.

Conclusion: This study provides data regarding sepsis/septic shock treated outside intensive care units, that allow a better knowledge of this reality so that it is possible to plan strategies to best attend these patients. Prospective analysis to consolidate criteria for diagnosis, follow-up and prognosis of these patients, as well as review of protocols of action are needed.

Keywords: Infection; Sepsis; Septic Shock; Internal Medicine Ward; Portugal

RESUMO

Introdução: A sépsis e o choque séptico apresentam grande relevância na prática clínica. A maioria dos estudos abordam o tratamento em Unidades de Cuidados Intensivos. A realidade fora destas unidades é amplamente desconhecida. O objectivo deste estudo é caracterizar epidemiologicamente doentes com sépsis/choque séptico internados na enfermaria de medicina interna.

Material e Métodos: Estudo observacional, retrospectivo, dos doentes admitidos no serviço de Medicina Interna com o diagnóstico de sépsis/choque séptico durante um ano

Resultados: Foram incluídos 308 doentes, 53% do sexo feminino, com maior grau de comorbilidades. Cerca de 40% apresentavam choque séptico à admissão. A taxa de mortalidade foi de 29,87%.

Globalmente, foi possível documentação microbiológica em 92.2% dos casos, sendo as infecções dos aparelhos urinário (52.6%) e respiratório (34.8%) as mais prevalentes. A antibioterapia inicial foi adequada em 50% dos doentes.

Antibioterapia prévia (OR 3.84; IC95% 2.4-6.2; p<0.0001) e o estado de dependência (OR 3.15; IC95% 1.7-5.8; p<0.0002) foram factores de risco independentes para a presença de resistência antimicrobiana.

Discussão: A sépsis fora das unidades de cuidados intensivos constitui uma realidade crescente com elevada morbimortalidade. O diagnóstico precoce e a colheita de exames culturais para tratar de forma dirigida são primordiais para melhores resultados.

Conclusão: Este estudo fornece dados de sépsis/choque séptico tratados fora de unidades de cuidados intensivos, que permitem um melhor conhecimento desta realidade para planear estratégias para melhor tratar estes doentes. Análises prospectivas para consolidar critérios de diagnóstico, seguimento e prognóstico destes doentes, bem como a revisão de protocolos de actuação são necessárias.

Palavras-chave: Choque Séptico; Enfermaria Medicina Interna, Infecção, Portugal, Sépsis

INTRODUCTION

Sepsis can be defined as the systemic response to an infectious disease, caused by bacteria, virus, fungus or protozoa. Its incidence is increasing[1] due to best emergency attendance, larger elderly population and larger number of immunosuppressed patients. More, the growing of bacterial resistance has also contributed to that increase[2]. Although the real numbers aren't known and probably are underestimated, it is estimated 17 million cases all over the world[3].

According to the *Center for Disease Control and Prevention*, sepsis incidence has duplicated from 2000 to 2008, and the number of hospitalizations has raised 70%[4]. Additionally, elevated mortality rates are observed, between 18% and 40%[4] in patients with sepsis and septic shock. SOAP study (The European Sepsis Occurrence in Acutely Ill Patients), that included patients admitted with sepsis and septic shock in 198 intensive care units from different countries, estimates mortality rates from 32% for sepsis and 54% for septic shock[5].

In Portugal, hospital mortality for sepsis after a community acquired infection was estimated to be 38% in the SACiUCI study (community-acquired sepsis in intensive care unit). National data available at INFAUCI study (Impact of infection on admission and of the process of care on mortality of patients admitted to the Intensive Care Unit) indicate high mortality rates as 48,8% in septic shock patients[6].

Sepsis can be associated with any infectious focus, with the

Correspondencia: soniacmsantos.mail@gmail.com

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most common infections being pneumonia, intra-abdominal infection and urinary tract infections. Pneumonia, in most epidemiologic studies is the responsible focus for half of all cases. Other frequent focus are catheter infection related, soft tissue abscess, meningitis, endocarditis among others[7].

Not all patients with sepsis or septic shock are admitted to intensive care units. According to guidelines[8], admission to intensive care units should be evaluated according to curability of the disease and effective utility of intensive care. It is important to recognize that overloading of hospital beds, makes its management difficult, and in the real world severe patients may stay in medicine wards or emergency department[9,10].

The reality of sepsis treated outside intensive care units is widely unknown, so this study aims to ascertain sepsis/septic shock data at internal medicine wards of a non-tertiary hospital by quantifying and epidemiology characterize patients admitted during a year. This study also aims to identify and characterize antibiotics used, most common infections and microorganisms associated with these patients.

MATERIAL AND METHODS

This is retrospective observational study, using a selection of patients that were discharged from internal medicine wards at a non-tertiary hospital, with sepsis and/or septic shock diagnosis between January and December 2015.

During the study period, were included all patients over 18 years old that were discharged from internal medicine wards. Patients transferred from other hospitals were excluded. Discharge notes that were codified with the diagnostic sepsis and/or septic shock in accordance with International Statistical Classification of Diseases and Related Health Problems, 9th Revision (ICD-9) were selected and sepsis/septic shock criteria were confirmed according to sepsis-2 definitions[11] (the definition in force when the patients were admitted to hospital).

Nosocomial and community acquired infections were defined according to the Center for Disease Control and Prevention (CDC) definitions for nosocomial infections[12].

Organisms were defined as multiresistant if resistant to three or more antimicrobial classes[13].

All the patients were evaluated taking in account its clinical files from the emergency department and hospital admission. Demographic data, diagnosis at admission, comorbidities present, as clinical and laboratorial data, including microbiologic data. Microbiologic product where agent was isolated was registered, initial antibiotic therapy and its appropriation (according sensibility tests). Length of stay and discharge status were also collected data.

General descriptive statistical analysis was realized for each study variable. Continuous variables are presented as medium ± standard deviation according to its distribution. Groups comparison was realized using chi square (categorical variables) and Student's T or Mann-Whitney (continuous variables).

For independent risk factors associated with infection was elaborated a model of logistic regression. Was evaluated appropriated antibiotic therapeutics with bacteria resistance, length of stay and hospitality mortality.

A p values inferior to 0.05 was considered as sufficiently low so that a significant difference is considered. Statistical analysis was done with software SPSS, version 22, IBM, New York, USA.

RESULTS

During the study period, 308 patients were included. Mean age was 79.6±12 years old, 53% were female. 26% of the patients were resident in nursing home and 24.7% had a high grade of dependence (17% bedridden). 105 patients had been in a hospital ward the 3 months before the index case.

Female population presented more prevalence of diabetes *mellitus* (58.3% vs. 41.7%, p=0.004), heart failure (53.3% vs. 46.7%, p= 0.25) and dementia (56.8% vs. 43.2%, p=0.02). Global mortality rate was 30%, and the mean length of stay was 12±11 days.

Population characteristics are presented at Table 1.

Urinary tract infection (52.6%) and respiratory infection (34.8%) were the most common. 0.6% (2 patients) had catheter-related infection and 1 patient (0.3%) had a central nervous system infection. In 5.2% was not possible to identify the infection focus (Graphic 1).

Globally, it was possible to document microbiology agent in 92.2% of the cases. 50% by urine culture, 27.4% by blood culture and around 17% by sputum culture. The other 2 cases (0.6%) concern catheter culture and wound exudate culture.

Gram negative agents were the ones more prevalent (80.1%), mostly *Escherichia coli* (92.3%), followed by gram positive (14.5%). Almost 5.4% *Candida* spp was isolated.

When microorganism was isolated in catheter culture or wound exudate culture, 56% was *S. aureus* and it was also registered one case of fungal infection by *Candida* spp.

The prevalence of multiresistance[14] was of 43.2%, in which *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Staphylococcus aureus* methicillin-resistant and *Acinectobacter* spp were the most widely found.

Graphic 2 presents agents distribution by sample.

Initial empiric antibiotic therapy was proper in 50% of the patients, being the most frequent antibacterial used a beta lactam with beta lactamase inhibitor (71.1%). Length of antibacterial therapy was of 5.86±3 days. Inappropriate antibiotic therapy was due in 84.7% of all cases to the presence of antibiotic resistance.

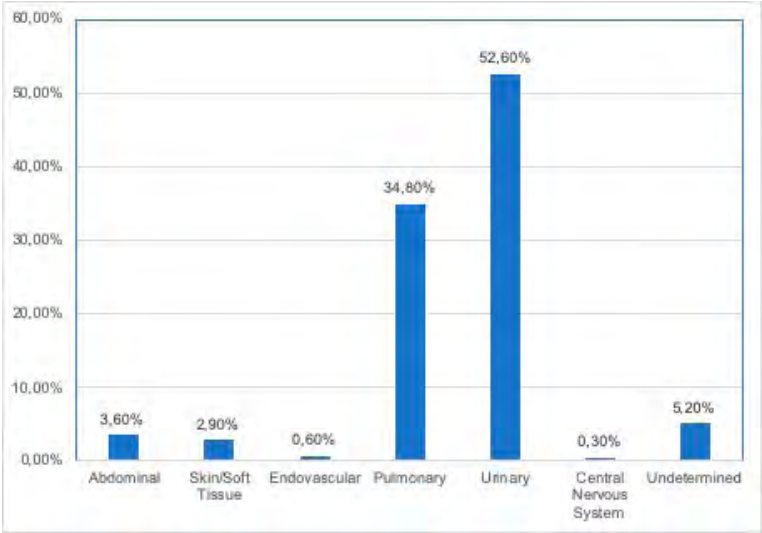
Multivariate analysis, after adjusting for comorbidities, mortality was associated with illness severity (OR 1.95, IC95% 1.2-3.2, p 0.008) and functional status (OR 4.74, IC95% 2.7-8.2, p <0.0001). Early introduction of antibiotic therapy

Table 1. Population demographic characteristics

	Female (n=162; 53%)	Male (n=146; 47%)	Total (n=308)	*p*
Age (years), min-max	79±12	80±12	79.6±12	0.4658
Length of stay (days) medium	12±11	13±11	12±11	0.4263
Functional status Dependent Bedridden	 61.8% 60.4%	 38.2% 39.6%	 24.7% 17.2%	 <0.0001 0.0003
Mortality	58.7%	41.3%	92 (29.9%)	0.0023
Septic shock at admission	90 (54.1%)	56(45.9%)	122(39.6%)	0.1513
Diabetes *mellitus*	58.3%	41.7%	33.4%	0.0037
Chronic Kidney Disease	48.9%	51.1%	30.5%	0.7003
Heart failure	53.3%	46.7%	14.6%	0.2481
Chronic pulmonary Disease obstructive disease	45.2%	54.8%	13.6%	0.0930
Dementia	56.8%	43.2%	24%	0.0173

Community acquired infection was identified in 74,03% of the patients.

Graphic 1: Source of infection



Graphic 2. Multiresistant agents distribution

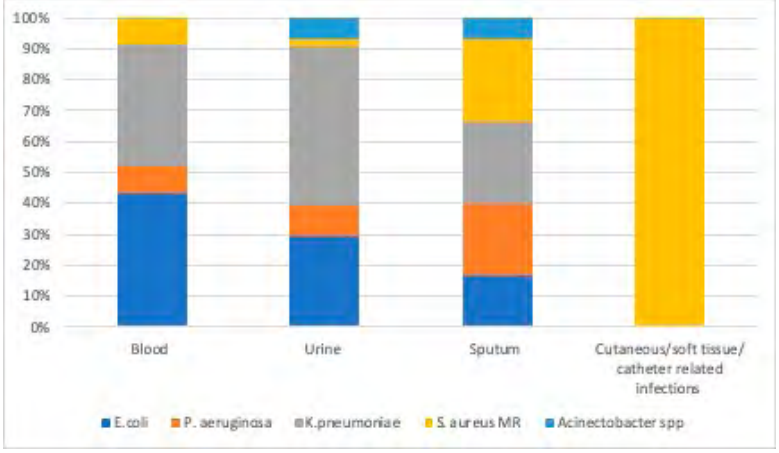


Table 2. Risk factors at admission and mortality – multivariate analysis

	Total	Survival	Non – survival	Odds ratio	Confidence Interval 95%	p
Functional Status Dependent Bedridden	 24.7% 17.2%	 21.6% 33.5%	 56.6% 54.7%	 4.74 3.61	 2.7335-8.2298 1.9585-6.6399	 p<0.0001 p<0.0001
Multiresistant agent	32.1%	39.5%	15.1%	0.27	0.1443-0.5093	p<0.0001
Previous antibiotic therapy (AT)	51.6%	22.8%	37.1%	1.99	1.2105 – 3.2899	p 0.007
Inappropriate initial AT	34.1%	27.9%	30.5%	1.13	0.6241 – 2.0594	p 0.68
Beginning AT <3hours	38.3%	31.6%	27.9%	0.14	0.6195-1.2659	p 0.5
AT changed	33.4%	33.9%	23.3%	0.59	0.3242 – 1.0795	p 0.085

was considered a protective factor with a 86% reduction in mortality. Table 2 presents mortality risk factors in our cohort.

Previous antibiotic therapy (OR 3.84, IC95% 2.4-6.2, p <0.001) and extreme dependence status (OR 3.15, IC95% 1.7-5.8, p 0.0002) were independent risk factors to the presence of antibiotic resistance. (Table 3)

DISCUSSION

This study presents a contemporary analysis of the epidemiology and prognosis of sepsis patients admitted to internal medicine wards. So far, we do not have knowledge of other national studies with this population, so it is a pioneer study regarding the population that doesn't gather criteria to admission in intensive care units.

Almost a quarter of patients presented septic shock at admission with higher mortality associated as well as comorbidities in accordance with national reality[6].

Community-acquired infections and Gram-negative bacteria predominated. This study also presents high prevalence in microbiological documentation in line with international epidemiological studies[14].

The urinary tract has been identified as the main source of infection in more than half of the cases, contrary to the tendency of previous national series in which respiratory tract infections predominate, which we associate with the increasing use of invasive devices and urological procedures.

There is an elevated number of sputum cultures without microbiology isolation and an elevated number of urine cultures positive with microbiology documented which explains the high rate of gram negative isolated.

In this study, it was not possible to determine the focus of infection in 5.2%, stressing the risk of antimicrobial resistance by the use of broad spectrum empirical antibiotics. A multidisciplinary and cooperative approach between emergency and inpatient services can contribute to an improvement not only in the procurement of biological products but also in microbiological documentation, which are crucial for the rational use of antimicrobials.

The presence of multiple risk factors is significantly associated with the presence of bacterial resistance to antimicrobials. Among them, the use of antibiotics in the previous 3 months was the most significant risk factor.

This retrospective analysis allowed to establish the general characteristics of patients with sepsis in the internal medicine wards as well as prognostic analysis. However, because it is a retrospective analysis, there are some limitations, namely the selection of patients diagnosed with sepsis/septic shock based only in medical records and the methodology of product harvesting. These limitations imply a prospective analysis to consolidate criteria for diagnosis, follow-up and prognosis of these patients, as well as review of protocols of action, with a view to reducing mortality.

Table 3. Multivariate analysis – antimicrobial resistance

	Odds ratio	Confidence interval 95%	p
Functional status Dependent Bedridden	 3.12 3.15	 1.7946 – 5.3804 1.7165 – 5.8093	 p 0.0001 p 0.0002
Age (per year)	0.99	0.99-0.99	p 0.9
Previous antibiotic therapy	3.84	2.3900 – 6.1592	p<0.0001

CONCLUSION

This study calls to attention the significant prevalence of sepsis/septic shock treated in internal medicine wards, particularly in specific high-risk populations, with marked prevalence in elderly, dependent and with many comorbidities patients. It also serves to highlight the importance of soon diagnose and the value of collection of cultures to appropriately treat.

These records would also be useful in providing reliable, quantifiable data regarding sepsis/septic shock treated outside intensive care units numbers in regards to plan strategies to best attend these patients.

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Enfermedad de Forestier-Rotés Querol: un proceso continuo desde la Atenas de Pericles hasta el mundo de Almodóvar

Forestier-Rotés Querol disease: a continuous process from the Athens of Pericles to the world of Almodóvar

Julio Montes-Santiago

Servicio de Medicna interna. Complejo Hospitalario Universitario de Vigo.

RESUMEN

Se presentan 2 casos, separados por un intervalo de más de 2500 años, de Enfermedad de Forestier – Rotés-Querol, uno de ellos procedentes de un enterramiento de la Atenas de Pericles y el otro actual para ejemplificar su presencia continua en la historia de la patología humana. Se realiza una sucinta revisión histórica sobre su separación de las espondilopatías inflamatorias anquilosantes, se revisan sus posibles manifestaciones clínicas y radiológicas y se menciona su importante papel en el desarrollo de la última película de Pedro Almodóvar, Dolor y Gloria.

Palabras clave: Enfermedad de Forestier-Rotés Querol.

ABSTRACT

We present two cases of Forestier-Rotés-Querol disease, separated by an interval of more than 2500 years, one of them coming from a burial in the Athens of Pericles and the other from the present. This exemplify its continuous presence in the history of human pathology. A brief historical review of their separation from ankylosing inflammatory spondylopathies is carried out their possible clinical and radiological manifestations are reviewed, and it is mentioned an important role in the development of the latest film by Pedro Almodóvar, Dolor y Gloria.

Key words: Forestier-Rotés Querol disease.

INTRODUCCIÓN

En 1950 Jaume Rotés Querol, que hacía una estancia en Aix-les-Bains, Francia, junto al afamado reumatólogo Jacques Forestier, revisaba junto con otro colaborador de Forestier, François Jaqueline, la historia de 200 casos de pacientes con Espondilitis anquilosante (EA). Descubre 9 casos "rarísimos, porque todos son viejos – media de 65 años-, no tienen dolor, no tienen sacroileitis y tienen unas formaciones muy particulares"[1]. Ello llamó inmediatamente la atención de Forestier, con lo que descubren nuevos casos procedentes de necropsia. Estos hallazgos son comunicados y revisaron los hallazgos de autopsia, añadiendo nuevos pacientes. Estos estudios son presentados en la Reunión de la *Ligue Française contre le Rhumatisme* y publicados en el mismo año 1950 en *Annals of the Rheumatic Diseases*[2]. Con ello adquiría carta de naturaleza en el ámbito científico, como diferente de la EA, la "hiperostosis vertebral anquilosante senil" – enfermedad de Forestier-Rotés-Querol (EFRQ)-, aunque más tarde perderá el apelativo senil por descubrirse también en pacientes entre 40 y 50 años.

En 1975, Resnick y colbs.[3] la denominan hiperostosis esquelética idiopática difusa (DISH) y fijan sus criterios radiológicos definitorios. 1) Osificación de la porción anterolateral de al menos 4 cuerpos vertebrales. 2) Preservación de la altura discal del nivel afectado. 3) Ausencia del fenómeno del vacío o de esclerosis marginal en los cuerpos vertebrales. 4) Ausencia de anquilosis de las articulaciones interapofisarias o de alteraciones en las sacroilíacas.

Presentamos 2 casos separados por más de 2500 años, uno que data del siglo V aC., y otro actual.

CASOS

Caso 1. Excavaciones realizadas en 1891 en el antiguo cementerio ateniense de Kerameikos (Fig. 1A) desvelaron un sarcófago de mármol con el esqueleto en buenas condiciones de un hombre maduro, junto con restos de parras de vino y 2 lekythoi (vasos funerarios) procedentes del taller del pintor Tymbos, según la tradición de enterramiento frecuente en la Grecia clásica. No existen más datos sobre dicho personaje, pero su inspección a traves de las vitrinas de cristal del Museo Arqueológico Nacional de Atenas muestra en columna y costillas inequívocos signos de osificación "en manto céreo" del ligamento vertebral anterior dorsal (Fig. 1B). No hay afectación sacroilíaca. Además presentaba cálculos y carencias de piezas dentales. Dicho sarcófago (T35), datado entre 460-450 aC es, pues, contemporáneo de Pericles (495-429 aC).

Caso 2. Varón de 70 años, calderero jubilado, remitido a nuestra consulta por parestesias nocturnas en miembros inferiores. Refería además dolores lumbares y cervicales que empeoraban con los cambios climáticos. El paciente era hipertenso y tenía diabetes mellitus (DM) con HbA1c actual: 6,2%. Presentaba dolor a la motilidad cervical y percusión lumbar, con reflejos y sensibilidad conservados. El electromiograma mostró datos compatibles con polineuropatía sensitivo-motora con predominio axonal y distal, sin afectación radicular, y que fue atribuida a la DM. En Rx. y TAC se observan osteofitos dorsolumbares anterolaterales compatibles con DISH, con espacios intersomáticos conservados (Fig. 2A y fig. 2B). Había estenosis de canal L4-L5 y foraminal L5-S1. Fue tratado con AINES, pregabalina y fisioterapia.

DISCUSIÓN

La DISH o EJRQ es un proceso no inflamatorio idiopático en el que se produce osificación de las entesis y ligamentos vertebrales anterolaterales. No obstante, a diferencia de las descripciones iniciales se ha comprobado que pueden ser

Correspondencia: julio.montes.santiago@sergas.es

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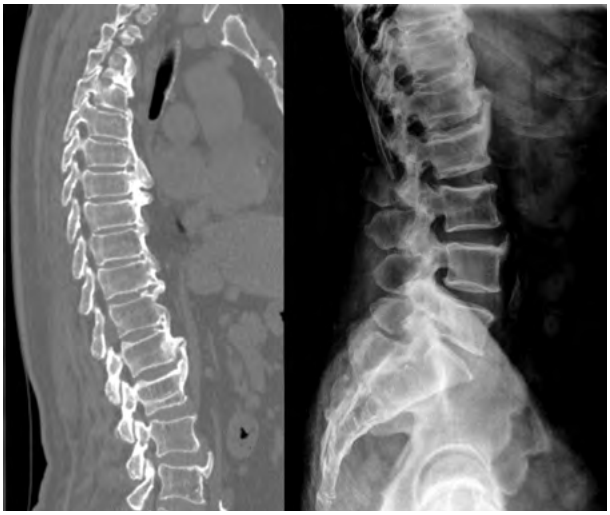
Fig. 1A: Vista del cementerio de Kerameikos en Atenas. Fig. 1B: Varón enterrado en sarcófago T35 con el característico manto "cereo" óseo (flecha), sugestivo de enfermedad de Forestier-Rotés Querol. Museo Arqueológico Nacional de Atenas (Fotografías. cortesía de Y. Carbajales).

Fig. 2 A: Rx. de columna lumbar. Fig. 2B: TAC dorso-lumbar con las hiperostosis del ligamento vertebral anterior.



también afectados los ligamentos de articulaciones periféricas como los rotulianos, tendón de Aquiles, fascia plantar, etc[4].

Aunque diferenciada sólo a partir de 1950 de la EA y otras espondilopatías inflamatorias, se ha documentado su existencia en investigaciones arqueológicas realizadas sobre distintas poblaciones medievales en zonas de Grecia, Inglaterra, Suiza, Francia, etc[5,6].

Actualmente se considera un proceso común, afectando hasta el 10% de la población, sobre todo varones a partir de 60 años. Puede ocasionar pocos síntomas o, por el contrario, dolor y rigidez dorso lumbares y en casos más graves las excrecencias óseas pueden comprimir mecánicamente el esófago produciendo síndromes obstructivos[7]. Se ha relacionado con factores mecánicos, exceso de flúor en el agua o de vitamina A, uso prolongado de isotretinoína y hábitos nutricionales y en asociación frecuente con síndrome metabólico y diabetes.

Desde el punto de vista fisiopatológico, se supone que todos estos procesos – mecánicos, metabólicos, genéticos, de inmovilidad, ambientales o dietéticos, etc – podrían estimular varios factores de crecimiento como el IGF1, o el NFkappa B y otros, que activarían la actividad osteoblástica y ocasionarían la proliferación ósea[4]. Su tratamiento es conservador con antiinflamatorios, fisioterapia, pero los casos graves de disfagia pueden requerir resección de los segmentos hiperostóticos[8].

En su última película, *Dolor y Gloria*, (nº 21), probablemente la más personal de Pedro Almodóvar, el personaje de Antonio Banderas – que representa un director de cine inmerso en una esterilidad creativa agobiante – sufre quejas mal caracterizadas, entre ellas disfagia y algún aparatoso episodio de broncoaspiración[9]. Sus médicos creen que es cáncer, pero cercano el final le revelan que sus síntomas se deben a la "Enfermedad de Forestier", le muestran en la radiografía las características hiperostosis dorsales que comprimen su esófago y le proponen una intervención…

Aunque solo reconocida como entidad separada de la EA en 1950, los dos casos aportados sirven para ilustrar la continuidad histórica de este proceso, que ha merecido la atención de uno de nuestros más universales cineastas.

Derecho a la privacidad y consentimiento informado. El autor ha obtenido consentimiento informado del paciente nº 2 referido en el artículo. Dicho paciente autorizó que las imágenes de su proceso pudieran ser utilizadas con fines científicos.

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Botulism – A brief review based on a case

Fernando Rocha Correia; João Andrade

Unidade Local de Saúde do Alto Minho

ABSTRACT

Foodborne botulism is a serious, acute disease with digestive and neurological symptoms. It results from ingestion of food, containing toxins formed by Clostridium botulinum. There has been an increase in the incidence in Portugal and Spain. The authors report a case of botulism that culminated in the identification of a common origin for four other cases.

It was a patient of 47 years with a clinical picture of diplopia, dysphagia, fever, dizziness, blurred vision, dry mouth and constipation and gastrointestinal complaints. He ingested smoked product 48-72h before resorting to the emergency room. He was interned for study. Changes in EMG compatible with presynaptic neuromuscular block were found. Serum toxin and suspicious food product were isolated and identified. He recovered completely from the clinical picture with support therapy and physiotherapy.

The authors intend to alert to a disease that although not rare, presents difficulties in the diagnosis, being this one essentially clinical with suggestive epidemiological context, confirmed by electromyographic changes and identification of the toxin.

INTRODUCTION

Botulism is a flaccid neuroparalytic disease induced by a potent toxin produced by the bacterium Clostridium botulinum. Justinus Kerner, in 1820, recognized for the first time the association between the occurrence of paralytic disease and the ingestion of sausages, in an outbreak that affected 230 people[1].

Six epidemiological types are described: food botulism, wound botulism, infant botulism, botulism of indeterminate classification, inhaled botulism, and iatrogenic botulism.

Some strains (A and B) produce proteolytic enzymes that spoil contaminated food leaving an unpleasant appearance, odor and taste. Eight types of toxins are described: A – H. Toxins A, B, E and, rarely, F, G, H cause disease in humans. Unlike the spores (destroyed if T.ª> 120ºC), the toxin is sensitive to the heat, being destroyed at temperatures ≥ 80ºC[2,3].

CLINICAL CASE

A 47-year-old caucasian man recurred to the emergency room (ER) due to nausea, food vomiting, diarrhea and fever (Tª: 38ºC). He was discharged with the diagnosis of acute gastroenteritis and medicated with ciprofloxacin (750mg, 12 / 12h) and *Saccharomyces boulardii*. The next day he started with blurred vision, diplopia, dysphagia for liquids and sensation of abdominal distension, resorting again to the ER. He presented without nausea, vomiting, diarrhea or fever. He had intaked smoked products ("alheiras" and chorizo) in the previous weekend (48-72 hours before admission).

In the ER, he was hemodynamically stable and afebrile. He presented conscious, cooperative and oriented; with mydriatic pupils, poorly reactive to light; he was closing the left eye to avoid the discomfort caused by diplopia; he had no changes in facial sensitivity, no facial paresis. He had symmetrical elevation of the palate, dysphonia, but without aggravation of dysphonia with fatigability maneuvers. He had no change in sternocleidomastoid muscles and trapezoids. No deviations of the tongue in the protrusion were seen or motor deficits or changes in limb or trunk sensitivity. He presented flexion in the cutaneous-plantar reflex, bilaterally. No dysmetria was seen. The gait was normal and had no dysphagia for liquids and solids. He was stained and hydrated; without signs of respiratory distress; Abdomen was soft and depressible, painless to palpation, with no defense; without peripheral edema.

The analytical study had no significant abnormalities. The LCR from lumbar puncture was rock water type and values were in the normal range. Chest X-ray, abdominal ultrasound, brain-CT and brain MRI were also performed and showed no significant changes.

He was evaluated by Ophthalmology that diagnosed bilateral paresthesia of the third cranial nerve. He was also evaluated by Neurology who placed the diagnostic hypothesis of Miller-Fisher Syndrome. Human immunoglobulin was administered for three days. He was then admitted to the Internal Medicine Service. An electromyography was performed and revealed alterations compatible with presynaptic neuromuscular block. He was transferred to UCIM for respiratory monitoring. Due to the suspected botulism the "Instituto Ricardo Jorge" was contacted and the serum was sent for toxin research. The case was signed to health delegate for attempted recovery of suspect food samples. Despite the strong suspicion of food botulism, it was decided not to administer botulinum antitoxin (evolution of symptoms greater than 24-48 hours). Four days after admission the diagnosis of Botulism was confirmed, with a positive type B botulinum toxin in serum.

The patient recovered from paresis of the third pair, with resolution of dysphagia for liquids or solids and progressive improvement of dyspnea with kinesitherapy. He was discharged after 21 days of hospitalization oriented to the external consultation of Internal Medicine.

Five cases of food botulism were reported by the "Direção Geral da Saúde de Portugal" in the same month, laboratory confirmed, without death records. A common origin associated with the ingestion of smoked food products ("alheiras") was identified. Shortly thereafter, they were withdrawn from the market.

DISCUSSION

All forms of botulism result from the absorption of botulinum toxin into the circulation. It binds irreversibly to synaptotagmin II at the neuromuscular junction, preventing the release of acetylcholine, conditioning dysfunction both in the muscle

Correspondencia: fernandomiguelrochacorreia@gmail.com

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Analyses	1.ª vinda ao SU	2.ª vinda ao SU
Hb (g/dl)	16.7	14.9
VGM (fL)/ CHGM (g/dl)	87.1/34.8	84.8/ 35.6
Leucocytes (10^9/L)/ Neutrophils (%)	10.00/ 87	5.13/ 51
Platelets (10^9/L)	193	191
Glucose (mg/dl)	107	84
Urea / creatinine (mg/dl)	70/0.99	35 / 0,84
Sodium/ Potassium (mmol/L)	142/ 4.6	141/ 4.7
PCR (mg/dl)	0.67	1.22
Total bilirrubin (mg(dl)	1.13	0.99
FA/ GGT (UI/L)	43/ 67	42 /91
AST/ ALT (UI/L)	27/ 48	26 / 40

and in the autonomic nervous system. The recovery of synaptic function requires the regeneration of a new presynaptic terminal, a process that may take as long as 6 months. The adrenergic synapses are not affected by the toxin and the blood-brain barrier does not allow its passage[4,5].

Epidemiology

Although considered to be rare and serious, there has been an increase in incidence in Portugal since 1970. In 2004, four cases associated with the consumption of ham and one case of canned tuna were identified. In 2009, one case related to canned sausages was reported and finally in 2015, five cases were confirmed, by consumption of "alheiras" (includes case described)[5].

In Spain, in the period from 1997 to 2015, 154 cases of botulism were identified, most of them associated to food-borne botulism[6].

Clinical manifestations

The incubation period is variable, from 12-36h up to one week. The clinical picture can range from mild complaints to death within the first 24 hours. It is associated with prodromes: nausea and vomiting, abdominal pain, diarrhea, dry mouth and dysphagia, which may remain throughout the evolution of the disease. The involvement of the cranial nerves is frequent: blurred vision (secondary to fixed dilation of the pupils and paralysis of the cranial nerves III, IV, VI); diplopia; nystagmus; ptosis eyelid; dysphagia; dysarthria and weakness of the facial mime muscles. There is a decreasing and symmetrical muscle weakness that usually progresses to the trunk and upper limbs and subsequently to the lower limbs. Respiratory difficulty due to diaphragmatic paralysis and / or upper airway compromise is often seen and also urinary retention, constipation and hypotension[7-11].

Electromyography may suggest the diagnosis: low amplitude M waves; short low-voltage explosions in motor units; excessive potential for action; repetitive nerve stimulation is associated with a significant increase in the M. wave amplitude. Leukocyte count, cytobacterial study of CSF and VS are generally normal. The lumbar pucture for the exclusion of meningitis or encephalitis is not generally indicated [2,5,9].

Differential diagnoses should include: Myasthenia Gravis, Lambert-Eaton myasthenic syndrome, Guillain-Barré, Neuroborreliosis, Poliomyelitis, heavy metal poisoning and stroke.

The presence of toxin in the blood confirms the diagnosis and is detectable up to twelve days after ingestion. Samples of feces, vomit, and suspect foods may also reveal the toxin, which together with clinical manifestations, can establish the diagnosis. In Portugal, the samples are sent to "Instituto Ricardo Jorge" (anaerobic culture medium).

Treatment

All patients with signs, symptoms and suspected botulism should be hospitalized and monitored, monitoring signs and symptoms of respiratory failure, which is the main cause of death. Early intubation and mechanic ventilation drastically reduces the risk of death. Orotracheal intubation is recommended if there is respiratory insufficiency / loss of airway patency or vital capacity <30% of predicted value.

Heptavalent equine antitoxin is used in children > 1 year and adults (human immunoglobulin for infant botulism, children <1 year). It contains antibodies to seven of the eight toxins identified. If botulism is suspected and symptoms are progressing, it should be administered as soon as possible (24-48 hours), and should not be delayed by the lack of analytical results. It may cause sensitization and anaphylaxis and should only be given to patients at high risk of disease.

CRL	10/09
Total cell count(mm^3)	0,0
leucocyts and others	0,0
erithrocyts	0,0
glucose	54
proteins (15-45mg/dl)	43
Capsular atg search	neg
Bacteriological	neg

In Portugal, most of the cases described are associated with the ingestion of type B toxin and were associated to mild symptoms. The use of antitoxin was not necessary[2,5,7].

Prevention

Appropriate techniques for preparing homemade preserves allow the spores to be destroyed: cooking times, pressure (using "pressure cookers") and temperature. Damaged conserved products should be avoided. The botulinum toxin is highly thermolabile, so it is recommended to cook the homemade preserves at 100 °C for 10 minutes before being consumed.

Prognosis

Botulism usually requires hospitalization for one to three months. The mortality ranges from ≤5-8% and <1% in infant botulism and <4% in food. Wrong/late diagnosis and toxin A are factors of worse prognosis. Patients precociously hospitalized and under respiratory monitoring usually recover completely. If the patient has moderate illness, the symptoms usually resolve within the first 3 months. Those who have severe disease and require prolonged mechanical ventilation, may sustain neurological deficits for years[10-11].

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Mujer de 41 años con lesiones cutáneas

41 Year old woman with skin lesions

Liroa Romero MF[1], García Trincado B[1], Loureiro Martínez M[2], Rabuñal Rey R[3]

[1]Servicio de Medicina Interna, Hospital Universitario Lucus Augusti. [2]Servicio de Dermatología, Hospital Comarcal de Monforte de Lemos
[3]Unidad de Enfermedades Infecciosas, Hospital Universitario Lucus Augusti

RESUMEN

La lepra o enfermedad de Hansen, es una entidad nosológica infecciosa producida por Mycobacterium leprae. No se conoce exactamente su mecanismo de transmisión. Es más frecuente en hombres y aparece habitualmente entre la segunda y tercera década de la vida. El diagnóstico de lepra es clínico, sin embargo la presencia de los bacilos en frotis y biopsias cutáneas y la detección de su ADN permiten su confirmación. El tratamiento es largo y la curación se consigue tras varios años sin enfermedad. Presentamos un caso de lepra autóctono atendido en nuestro centro. Mujer de 41 años de edad, española, agricultora que consulta por presentar lesiones cutáneas redondeadas, con centro deprimido, eritematodescamativas en el borde y acompañadas de unas lesiones cutáneas nodulares en miembros inferiores. Se decidió biopsiar las lesiones nodulares que confirmaron el diagnóstico de lepra. Se inició tratamiento y las lesiones cutáneas evolucionaron favorablemente hasta su resolución. Actualmente existen dos casos de lepra activos y tres en vigilancia tras el tratamiento. En Galicia es poco habitual, y casi siempre está en relación con población inmigrante.

ABSTRACT

Leprosy or Hansen's disease is an infectious nosological entity produced by Mycobacterium leprae. Its transmission mechanism is not known exactly. It is more common in men and usually appears between the second and third decade of life. The diagnosis of leprosy is clinical, however the presence of bacilli in smears and skin biopsies and the detection of their DNA allow their confirmation. The treatment is long and the cure is achieved after several years without disease. We present a case of autochthonous leprosy attended in our center. A 41-year-old Spanish woman, a farmer who consulted due to rounded skin lesions, with a depressed center, erythematodescampathetic on the edge and accompanied by nodular skin lesions on the lower limbs. It was decided to biopsy the nodular lesions that confirmed the diagnosis of leprosy. Treatment was started and the skin lesions evolved favorably until their resolution. Currently there are two cases of active leprosy and three in surveillance after treatment. In Galicia it is unusual, and it is almost always related to the immigrant population.

Palabras claves: Lepra, lesiones cutáneas, autóctono, Galicia.

Keywords: Leprosy, skin lesions, autochthonous, Galicia

INTRODUCCIÓN

La lepra o enfermedad de Hansen, es una entidad nosológica infecciosa producida por *Mycobacterium leprae.* No se conoce exactamente su mecanismo de transmisión, sin embargo para llegar a contagiarse de la misma es necesario mantener un contacto muy íntimo y prolongado. El periodo de latencia de la enfermedad es variable y suele durar entre 3 y 10 años. Cuando se manifiesta la enfermedad afecta principalmente a la piel, a los nervios periféricos y a las vías aéreas superiores[1].

Es más frecuente en hombres y aparece habitualmente entre la segunda y tercera década de la vida. El diagnóstico de lepra es clínico (lesiones cutáneas hipopigmentadas o rojizas, afectación de nervios periféricos con pérdida de sensibilidad fundamentalmente), sin embargo la presencia de los bacilos en frotis y biopsias cutáneas y la detección de su ADN en la reacción en cadena de la polimerasa (PCR) permiten su confirmación[2].

El tratamiento recomendado por la OMS es prolongado; 6 meses para casos paucibacilares y 12 meses los multibacilares. La curación se determina tras dos años libre de enfermedad en los paucibacilares y 5 años en los multibacilares[3].

Presentamos un caso de lepra autóctono atendido en nuestro centro.

CASO CLÍNICO

Mujer de 41 años de edad, española, agricultora, bebedora de una unidad de bebida estándar diaria. Se intervino en 2003 de un quiste sacro. Estaba en tratamiento con Anticonceptivos orales.

Consultó en Dermatología en julio de 2016 por presentar lesiones cutáneas de 15 días de evolución en la mitad superior del cuerpo, de características redondeadas, con centro deprimido, eritematodescamativas en el borde y acompañadas de unas lesiones cutáneas nodulares en miembros inferiores. En la analítica se observó una velocidad de sedimentación globular (VSG) de 68 y ligera leucocitosis con neutrofilia. La biopsia demostró un patrón anatomopatológico compatible con dermatosis neutrofílica. Se diagnosticó de eritema nodoso en probable relación con anticonceptivos orales y se indicó tratamiento con corticoides orales durante 25 días en pauta descendente.

En la revisión al mes persistió la clínica; se realizó una segunda biopsia donde se objetivó un infiltrado inflamatorio linfocitario de predominio perivascular e intersticial, en la dermis papilar con extensión a la dermis reticular y algunos neutrófilos aislados. La epidermis mostraba espongiosis y degeneración hidrópica de la capa basal focal y leve como únicas alteraciones significativas. No había vasculitis ni extravasación de hematíes. Se mantuvo el diagnóstico previo y se pautó otro ciclo de esteroides durante 20 días.

Dos meses después consultó de nuevo por empeoramiento de las lesiones (figura 1 y 2). Se reinició tratamiento con prednisona y se añadió colchicina. Una nueva analítica objetivó un discreto aumento de los reactantes de fase aguda. Se decidió biopsiar nuevamente una de las lesiones nodulares de la cara interna de la rodilla con el siguiente resultado: epidermis conservada; en la dermis se observó un importante infiltrado inflamatorio histiocitario rodeando los vasos, nervios y también perianexial. La tinción de Ziel-Neelsen mostró bacilos ácido-alcohol-resistentes. La tinción de Wade-Fite-Faraco mostró asimismo estructuras compatibles con micobacterias. Los hallazgos descritos fueron compatibles histológicamente con lepra.

Se remitió a nuestro centro para completar estudio. La exploración

Correspondencia: manlirrom@gmail.com

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Figura 1a, 1b y 1c: lesiones nodulares eritematosas en piernas.

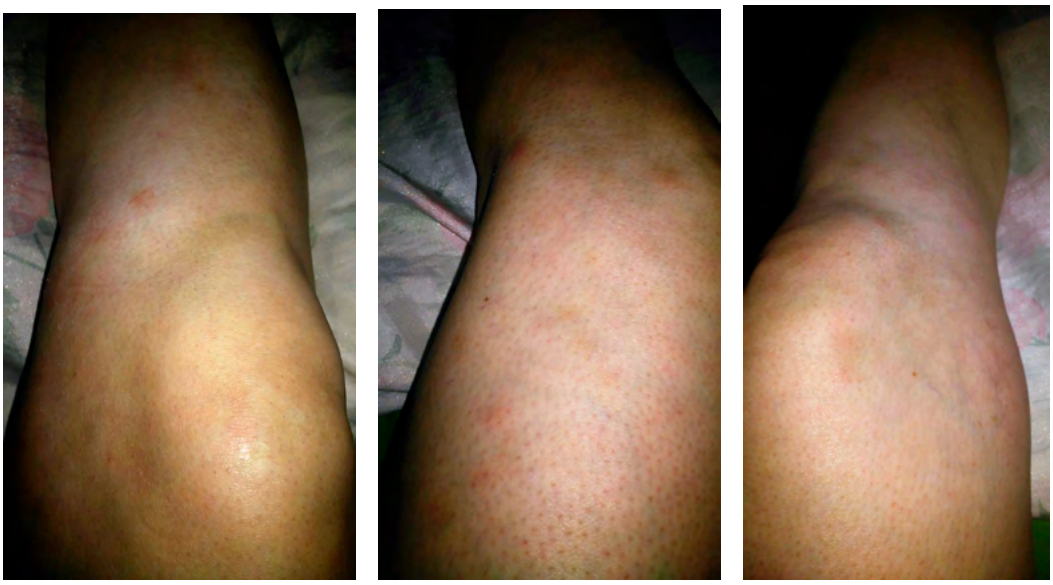

Figura 2a y 2b: lesiones eritematodescamativas de dorso de las manos.

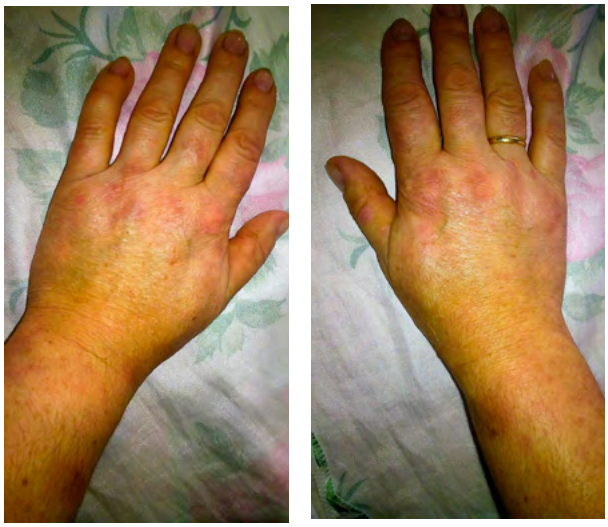

Figura 3a y 3b. Blister de tratamiento.

neurológica fue normal y el electromiograma no objetivaba lesiones nerviosas a ningún nivel. Se realizó serología de Virus de hepatitis B y C, VIH, Lúes y Borrelia, las cuales fueron negativas. Las baciloscopias y PCR para micobacterias en orina fueron negativas. Se decidió practicar una tercera biopsia de una lesión nodular de las extremidades inferiores confirmándose los hallazgos de la biopsia previa, aunque la baciloscopia, cultivo y PCR para micobacterias (tuberculosis y lepra) fueron negativas. Se tomó un frotis nasal donde se observaron escasos bacilos ácido-alcohol-resistentes, y otro de linfa en lóbulo de oreja que fue negativo.

Con el diagnóstico de lepra probablemente lepromatosa se instauró tratamiento según pauta OMS de doce ciclos (un año) con: Rifampicina 600 miligramos una vez al mes y clofazimina 300 miligramos una vez al mes, continuándose posteriormente con clofazimina 50 miligramos diarios y dapsona 100 miligramos diarios[4]. Antes del inicio del tratamiento se solicitó los niveles de glucosa-6-fosfato-deshidrogenasa que fueron normales.

Durante el tratamiento las lesiones cutáneas evolucionaron favorablemente hasta su resolución.

Se realizó exploración dermatológica a los contactos (hijos y esposo) sin encontrarse lesiones relevantes.

DISCUSIÓN

La lepra es una enfermedad infecciosa que cursa con una evolución crónica causada por *Mycobacterium Leprae*[1]. Afecta fundamentalmente a la piel y el sistema nervioso. El desarrollo de la enfermedad, de sus manifestaciones clínicas y de la evolución dependen fundamentalmente de la respuesta inmune del individuo, condicionada por sus características genéticas además de otros factores como los socio-económicos, geográficos, sexo y edad[2]. El diagnóstico de la enfermedad se basa en las manifestaciones clínicas, confirmándose definitivamente con los resultados positivos de las baciloscopias, la histopatología y PCR para micobacterias.

En nuestro caso, la clínica, y las pruebas complementarias (baciloscopia y biopsia) confirman el diagnóstico. La nega-

tividad de la PCR podría explicarse por la escasa cantidad de ADN en las muestras analizadas, habitualmente paucibacilares y la falta de estandarización de esta prueba en nuestro medio.

El tratamiento es prolongado y complejo, por lo que para mejorar la adherencia al tratamiento se han desarrollado una serie de blísteres en los que se especifica el fármaco y la dosis a tomar cada día (figura 3). Una vez completado el tratamiento, los pacientes deben realizar una consulta de revisión anual con estudio de baciloscopia de lesiones cutáneas y PCR de linfa durante 5 años en casos de lepra multibacilar y durante 2 años en caso de lepra paucibacilar[5-6].

En España, en 2016 se identificaron 11 casos nuevos de lepra, en 2017, 8 casos de los cuales 1 consta España como país de contacto7. Concretamente en Galicia se notificaron 23 casos de lepra entre el 1993-2012. Desde entonces hasta el 2017 se han notificado 5 casos; 4 en La Coruña, 1 en Orense. Tres de los cinco eran mujeres y todos tenían entre 25-55 años de edad. Se conoce que todos eran importados originariamente de Brasil. Sólo un caso, en 2013, fue de nueva aparición y el resto fueron recidivas. Actualmente dos casos siguen activos y tres en vigilancia tras el tratamiento.

En Galicia el diagnostico de lepra es poco habitual, y casi siempre está en relación con población inmigrante. De ahí el interés de nuestro caso, en una paciente autóctona y sin foco de contagio conocido.

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Mantle Cell Lymphoma – a less frequent presentation

Tiago Alves, Inés Coelho, Mário Santos, Teresa Inés

Serviço de Medicina II, Hospital de Abrantes. Centro Hospitalar do Médio Tejo. Tomar. Portugal
Servicio de Medicina Interna I, Hospital de Abrantes. Centro Hospitalar do Médio Tejo. Tomar. Portugal

ABSTRACT

The clinical manifestations of non-Hodgkin's lymphomas (NHL) are unspecific and may vary with their location, growth rate or organs involved. Chylothorax consists of an accumulation of chyle in pleural space. Lymphoproliferative diseases represent the main non-traumatic aetiology. The authors report the case of an 81-year-old woman admitted with right pleural effusion and lower limbs oedema, initially interpreted as decompensated heart failure. The thoracocentesis revealed a chylothorax and the aetiological study exposed a mantle cell lymphoma. The authors aim to alert to a less frequent presentation of NHL and remind that a low suspicion may delay the diagnosis.

Keywords: Chylothorax, Mantle, Lymphoma

INTRODUCTION

The chyle is formed by chylomicrons and very low density lipoproteins absorbed in small intestine and secreted to intestinal lymphatics. Approximately a total of 2.4 litres of chyle are transported every day through the lymphatic system. Chylothorax results from a rupture, laceration or obstruction of the thoracic duct that leads to a large accumulation of chyle in the pleural space[1]. This condition was first described in 1633 by Bartolet[2]. The aetiology of the chylothorax can be traumatic or non-traumatic. In the group of non-traumatic, malignancy is the main cause, and lymphomas are found in 70% of the cases[1]. The diagnosis of chylothorax is made through pleural fluid analyses. The fluid usually has a milky appearance and present a level of triglyceride >110mg/dl and cholesterol <200mg/dl. A triglyceride level <50mg/dl with a cholesterol >200 mg/dl is found in pseudochylothorax usually associated with old exudative effusion that remains in pleural space[1].

CLINICAL CASE

The authors report a case of an 81-year-old woman who presented to the emergency department due to dyspnea, orthopnea, easy fatigue and worsening of lower limb oedema with 3 weeks of evolution. The patient had history of arterial hypertension treated with lisinopril plus hydrochlorothiazide 20+12.5mg id.

At the physical examination, the patient was conscious and oriented, apyretic with tympanic temperature of 37.2ºC, blood pressure: 142/86mmHg, heart rate: 89bpm, tachypnoeic with respiratory rate of 24cpm with oxygen saturation of 89% with FiO2: 21%. Skin and mucous membranes had normal colour, and didn't present jugular vein engorgement. Pulmonary auscultation with abolished vesicular murmur at the base of the right hemithorax. Cardiac auscultation without changes. The abdominal exam was normal, without organomegaly or ascites. Bilateral malleolar oedema with Godet sign +.

The laboratory study revealed leukocytosis:9.400/ul with 93% neutrophilia, C-reactive protein: 4.3mg/dl, creatinine: 1.3mg/dl, urea: 35mg/dl, LDH: 732UI/L.

The chest radiography showed bilateral pleural effusion moderate at right and slight at left with an increased cardiothoracic index.

The condition was interpreted as decompensated heart failure, and the patient was admitted for hospitalization for therapeutic optimization. At the medical nursery, a thoracentesis was performed, which revealed a milky pleural fluid, with the following biochemical analyses: total leukocyte count: 2.500/mm3 (98% lymphocytes), triglycerides: 1899mg/dl, cholesterol: 123mg/dl, LDH: 452 IU/L, pH:7.0, Proteins: 2.8g/dl, glucose:155mg/dl, adenosine deaminase:16.0U/L. Pleural fluid was negative for acid-fast bacilli and sterile on culture.

Due to the absence of recent surgery or trauma, to exclude a malignancy aetiology a thoraco-abdomino-pelvic computed tomography was performed, which revealed bilateral pleural effusion, with medium volume on the right hemithorax, with slight cardiomegaly, without pericardial effusion. Normal pulmonary parenchyma and no mediastinal, hilar or axillary adenomegalies. In the abdominal cavity was observed a voluminous adenopathic inter-aortic-cava conglomerate, where a mass with around 7cm stood out. Multiple adenopathies in the celiac trunk and hepatic hilus were also visible.

The patient underwent a biopsy of the mesenteric adenopathy, whose histological result revealed Mantle Cell Non-Hodgkin's Lymphoma, classified as stage IV with serous involvement. The Oncologist was contacted and, considering the characteristics of the patient, started chemoimmunotherapy with R-mini-CHOP scheme (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone). During hospitalization, as a result of respiratory worsening a chest drainage was perform along with a low-fat diet (medium chain triglycerides), with significant improvement. After 6 cycles of R-mini-CHOP chemoimmunotherapy the patient achieved complete response and is currently on remission on Rituximab therapy.

DISCUSSION

The clinical manifestations of non-Hodgkin's lymphomas (NHL) are unspecific and may vary with their location, growth rate or organs involved. The typical manifestation that include the B-symptoms[3] (fever, weight loss exceeding 10% of body weight in 6 months, drenching night sweats), adenomegalies or splenomegaly aren't always present, and their presence might be associated with aggressive behaviour lymphomas or advance stage disease. The mantle cell lymphoma represents less than 10% of all NHL and has a heterogeneous clinical behaviour ranging from indolent to very aggressive[3]. In this case, the patient didn't have any B-symptom or suspect adenomegalies or organomegaly at the physical examina-

Correspondencia: tiago.pereira.alves88@gmail.com

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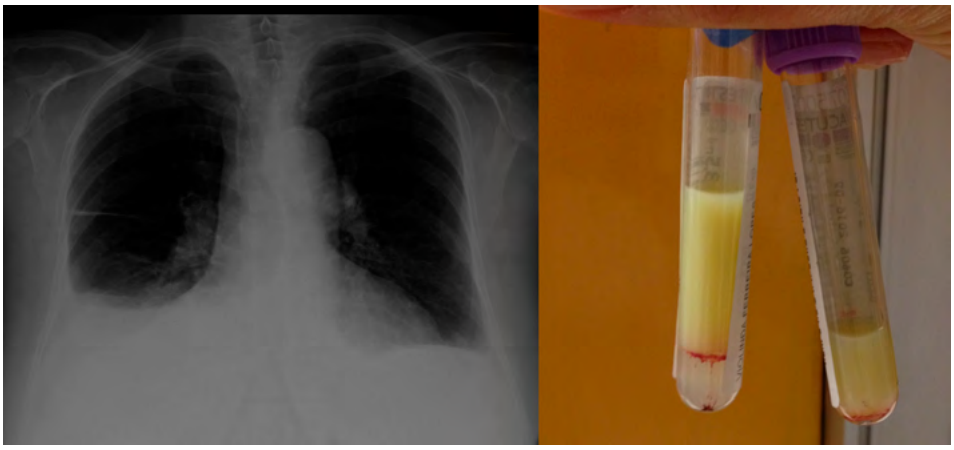
Figure 1. Posterior-anterior chest radiograph with bilateral pleural effusion (left), pleural effusion sample (right)



tion. The dyspnea and orthopnea caused by the chylothorax were the principal symptoms that drove the patient to the emergency department. In fact, these symptoms associated with oedema of the lower limbs, right pleural effusion and increased cardiothoracic index may fit in a context of decompensated heart failure. Thoracentesis was essential for the patient's diagnostic. In the presence of non-traumatic chylothorax it's mandatory to exclude malignancy, in which lymphoproliferative diseases represent 70% of the situations. Less frequent non-traumatic aetiologies are metastases, sarcoid or tuberculosis[2].

Considering the age, comorbidities of the patient and toxicity of the chemoimmunotherapy, it was decided to initiate R-mini-CHOP (reduced doses of cyclophosphamide and doxorubicin) followed by rituximab maintenance, that has been shown to be a good compromise between efficacy and safety in older patients[4,5].

The chylothorax treatment can be complex and differs according to the aetiology. The first principle approach is to treat the underlying disease. However, in the case of lymphomas, chemotherapy may improve the disease burden, but sometimes it doesn't translate into an improvement in chylothorax. Other strategies include low-fat diet with medium chain triglycerides, total parenteral nutrition, somatostatin or analogues drugs. The need for invasive procedures such as chemical or surgical pleurodesis should be evaluated on a second phase, depending on the patient's evolution and characteristics[2]. Our patient presented a very good response to chemotherapy, maintaining complete remission under Rituximab therapy, without exacerbation of the chylothorax.

With this case the authors aims to alert to an uncommon presentation of Non-Hodgkin's Lymphoma and remind that sometimes the low suspicion and the unspecific symptomatology may delay the correct diagnosis and jeopardise the patient's prognosis.

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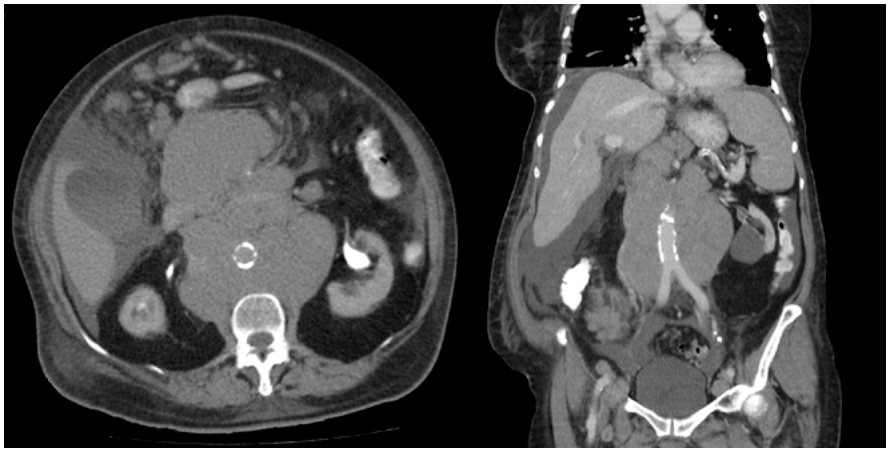
Figure 2. CT-scan of adenopathic inter-aortic-cava conglomerate in transerval plane (left) and coronal plane (right)



Complicated Malaria caused by Plasmodium ovale, Salamanca, Spain

María Paz Vaquero-Herrero[1], Jesús Martín Centellas[2], Verónica Temprado Moreno[3], Hugo Guillermo Ternavasio-de la Vega[1, 3, 4]

[1]Department of Internal Medicine. University Hospital of Salamanca. Spain. [2]Department of Nephrology. University Hospital of Salamanca. Spain. [3]Institute for Biomedical Research of Salamanca (IBSAL). Spain. [4]Department of Medicine. University of Salamanca. Spain.

ABSTRACT

Background: Monomicrobial imported infection by Plasmodium ovale is very rare. Case presentation: We report a case of complicated imported malaria by Plasmodium ovale in a man who suffered from subacute recurrent fever, thrombocytopenia and splenomegaly. Conclusion: Both the patient history and a search of epidemiological medical history were fundamental for confirming the suspicion.

Keywords: Imported malaria, Plasmodium ovale, paludism.

BACKGROUND

Plasmodium ovale is distributed mainly in tropical Africa, South America, and Asia, but cases of *P. ovale* malaria have been reported outside endemic areas[1]. Monomicrobial imported *P. ovale* infection is very rare, being found in about 5% of malaria cases worldwide[2] and 1–2% of malaria cases in Spain[3, 4]. It usually presents as a co-infection with *P. falciparum* or *P. vivax*[4].

CASE PRESENTATION

The patient, a 36-year-old man sought care in our emergency department for intermittent fever up to 40 ºC, accompanied by chills, asthenia, diaphoresis, left pleuritic pain, and vomiting that had evolved over 3 weeks. Between febrile episodes, he maintained good general health. He denied having travelled recently and had no animals or risky sexual contacts. On physical examination, he presented with a blood pressure of 103/71 mm Hg, a heart rate of 99 beats per minute, an ambient air oxygen saturation of 99% by pulse oximetry, a respiration rate of 14 breaths per minute, an axillary temperature of 36.4 ºC, and pain in the left hypochondrium. Laboratory tests showed anemia (hemoglobin 10.5 g/dL), a normal white blood cell count (6.34 × 10^3/mm^3) and normal leukocyte formula, thrombocytopenia (80 × 10^3/mm^3), acute renal failure (estimated glomerular filtration rate 58,2 ml/min/1,73 m^2), hyperbilirubinemia (total bilirubin 2.6 mg/dL, indirect bilirubin 1.6 mg/dL), elevated lactate dehydrogenase (553 U/L), elevated C-reactive protein (10.0 mg/dL), elevated procalcitonin (14.0 ng/mL), and a decrease of haptoglobin (7.7 mg/dL). Additionally, an abdominal ultrasound revealed splenomegaly.

Upon initial suspicion of bacterial sepsis, empirical antibiotic treatment was started with ceftriaxone (2 g/day IV) and a single-dose of gentamicin (5 mg/kg IV). A computerized axial tomography showed two lesions compatible with splenic infarctions and signs of minimal perisplenic hemoperitoneum secondary to splenic fissure (figures 1 and 2). The surgery unit suggested observation of the hemoperitoneum. Therefore, the patient was re-interrogated and reported that he had undergone dental implant placement 15 days before the onset of symptoms. Given the suspicion of an endovascular focus, the antibiotic treatment was changed to daptomycin (10 mg/kg/day IV), cloxacillin (2 g every four hours IV), and gentamicin (3 mg/

Figure 1. Splenic Fissure in axial computerized tomografy (arrow)

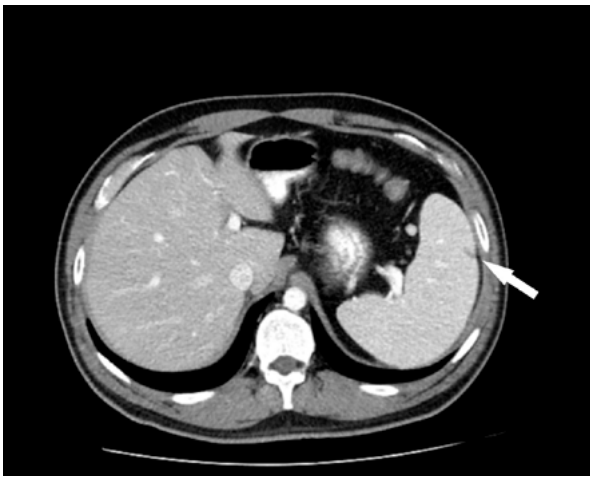
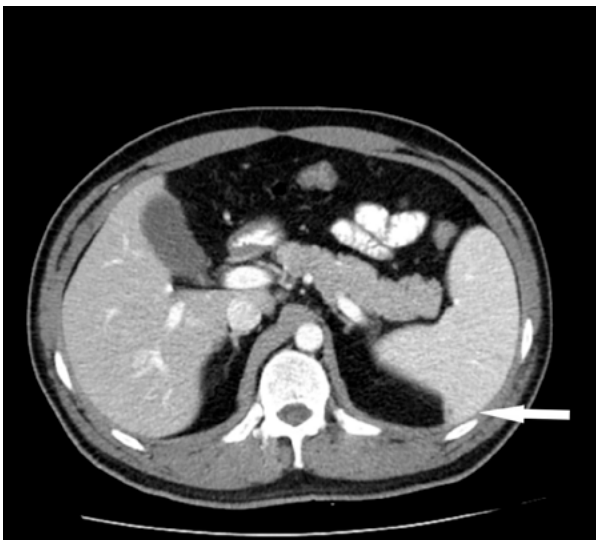


Figure 2. Perisplenic hemoperitoneum in axial computerized tomography (arrow)



Correspondencia: hgternavasio@saludcastillayleon.es

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kg/day IV). Infective endocarditis was ruled out by transthoracic and transesophageal echocardiography. Serial blood cultures were also negative.

On the fifth day of admission the patient persisted febrile. Then, he reported having worked in Ghana and Equatorial Guinea for 18 months without antimalarial prophylaxis, two years before the date of admission. He asserted that he had not considered this data due to the long time that had elapsed since his return to Spain. In Africa he had presented a self-limiting febrile syndrome of unknown cause for which he did not receive any specific treatment. Studies to rule out *Plasmodium spp.* infection (peripheral blood smears and immunochromatography Binax NOW® twice), were negative. Nevertheless, serum polymerase chain reaction (PCR) for *Plasmodium* was ordered (the sample was processed at a centralized reference center in Spain, with results to be received later). Treatment with systemic artesunate (2,4 mg/kg/dose initially, followed by 1,2 mg/kg at 12 hours, 24 hours, then 1,2 mg/kg /day for five days) was followed by oral atovaquone proguanil (Malarone® 250/100 mg, four tablets per day for three days). After the change of antibiotic therapy and start of antimalarial treatment, the patient experienced clinical, biochemical, and radiological recovery and was discharged. A week later, a positive PCR result or *P. ovale* was received.

DISCUSSION AND CONCLUSIONS

P. ovale hypnozoites can persist in the hepatocytes of infected patients producing a malarial relapse, months or even years after the initial infection[5]. Latency periods of up to 60 weeks in length have been described[6, 7]. Therefore, we emphasize the importance of thorough patient history to rule out malaria in every traveler coming from an endemic area who presents with fever, despite a long delay since returning[5]. In the current case, the patient had returned more than 80 weeks prior.

The belief that *P. ovale* can cause benign malaria with a low level of parasitemia should be cautiously considered because it is also able to produce complicated infections like those caused by *P. falciparum*, although it occurs less often[8, 9]. In fact, mortality associated with complicated malaria caused by *P. ovale* is about 30%, with 70% of patients developing respiratory distress syndrome, 30% developing splenic rupture or infarction, and 10% developing acute renal failure[9]. In this case, the patient presented signs of splenic infarction and fissure, and renal failure.

Due to the potential severity of *P. ovale* infection, a correct diagnosis is critical[10]. In such infections, frequent false negatives have been described in studies of peripheral blood smears, and a sensitivity of 25–30% in immunochromatography[7, 11]. PCR provides enhanced detection sensitivity and allows for the identification of the species, conforming the World Health Organization recommendations for the early diagnosis of imported malaria in non-endemic areas[11, 12].

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Transurethral Resection of the Prostate Syndrome: a Case Report

Síndrome pós Ressecção Transuretral da Próstata: Caso Clínico

Cristina Martins, Pedro Ribeiro

Serviço de Medicina Interna, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

ABSTRACT

Transurethral resection of the prostate syndrome is a systemic complication caused by excessive absorption of hypotonic electrolyte-free irrigation fluids, that results in hypervolemia, acute dilutional hyponatremia and consequent neurologic and cardiovascular disturbances, that can range from nausea, vomiting, altered mental status and hypertension, to convulsions, visual disturbances, hypotension, pulmonary edema, cardiac arrest, coma and death. It may occur as early as 15 minutes after resection starts or as late as 24 hours after surgery. The majority of cases published describe the occurrence of the syndrome during surgery, in patients under general anesthesia, being the neurologic manifestations masked and the cardiovascular signs predominant. We describe a case diagnosed in the emergency room, that occurred several hours after surgery and presented mostly with neurologic signs. Immediate and aggressive treatment of acute hyponatremia is a major cornerstone of this syndrome management.

Key Words: Acute Hyponatremia; Transurethral Resection of the Prostate; TURP Syndrome

RESUMO

O síndrome pós-ressecção transuretral da próstata é uma complicação sistémica deste procedimento, secundário à absorção excessiva de fluidos de irrigação hipotónicos utilizados, com desenvolvimento consequente de hipervolémia e hiponatrémia dilucional aguda que, por sua vez, conduzem a distúrbios neurológicos e cardiovasculares: desde náuseas, vómitos, alterações da consciência e hipertensão arterial, até convulsões, alterações visuais, hipotensão, edema pulmonar agudo, paragem cardiorespiratória, coma e morte. Pode desenvolver-se logo após os primeiros 15 minutos da cirurgia ou até 24 horas da mesma. A maioria dos casos publicados descrevem a ocorrência do síndrome ainda durante a cirurgia, em doentes anestesiados, motivo pelo qual se verifica um predomínio da clínica cardiovascular, estando os sintomas neurológicos mascarados. Os autores descrevem um caso diagnosticado no serviço de urgência, que ocorreu diversas horas após a cirurgia e com manifestações predominantemente neurológicas. O tratamento imediato e agressivo da hiponatrémia aguda é primordial na abordagem deste síndrome.

Palavras-chave: Hiponatrémia aguda; Ressecção Transuretral da Próstata; Síndrome Pós-RTU

INTRODUCTION

Transurethral resection of the prostate (TURP) Syndrome is a systemic complication caused by excessive absorption of electrolyte-free irrigation fluids[1]. Though it is called TURP Syndrome, it can occur during other procedures that also require the use of great amounts of irrigating fluids to dilate the mucosal spaces (uretero-renoscopy, percutaneous nephrolithotomy, transcervical resection of endometrium)[2,3]. Being these fluids hypotonic, their absorption results in hypervolemia and acute dilutional hyponatremia, with consequent neurologic and cardiovascular disturbances, that constitute the TURP Syndrome[4,5]. The clinical spectrum may range from nausea, vomiting, altered mental status and hypertension, to convulsions, visual disturbances, hypotension, pulmonary edema, cardiac arrest, coma and death[4,6]. TURP Syndrome has become a rare event in recent years, with incidence rates between 0.78% and 1.4%[7]. Severe TURP syndrome is even rarer, but there are a few cases published, all describing patients that developed a severe form of this syndrome, during surgery, while anesthetized[1,4,6,8]. We report a rare case of a patient that presented to the Emergency Room (ER) with severe manifestations of TURP Syndrome, 24 hours after surgery.

CLINICAL CASE

A 76-year-old man, with arterial hypertension and type 2 diabetes, medicated with Telmisartan and Metformin, is referred to the ER, from a private practice (where an emergency support system is nonexistent), with a history of a single tonic-clonic seizure, that lasted approximately 1 minute and had spontaneous resolution. 24 hours before, he had been submitted to a TURP, due to benign hyperplasia, with no peri or post-operative complications. On admission, the patient was afebrile, hemodynamically stable, but confused, somnolent, agitated, with a Glasgow coma scale of 11 (E4M5V2). The remaining neurological and physical exams were normal. A blood gas analysis was performed revealing a sodium (Na) concentration of 115 mmol/L. Being the pre-operative Na level of 138 mmol/L, a diagnosis of acute severe hyponatremia was made and assumed as the most probable cause of the seizure. A Na correction with hypertonic (3%) saline was initiated, at a rate of 25 ml/h. Laboratory tests confirmed the results (Na 119 mmol/L and serum osmolality 253 mOsm/Kg) and showed no other major alterations. A head CT and an electroencephalogram (EEG) were still performed, to exclude other potential diagnosis. CT was normal and EEG showed a slow generalized activity, compatible with a diffuse encephalopathy (secondary to the acute hyponatremia). The patient was admitted for observation. Six and twelve hours after the beginning of hypertonic saline, the patient's Na levels were 123 and 125 mmol/L (Table 1), respectively, and a progressive improvement of his neurological status was observed with the Na progressive ris-

Correspondencia: anacristinapm@hotmail.com

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Table 1. Temporal variations of relevant analytical parameters

Admission				6 h	12 h	24 h	48 h	72 h
Blood Gas		Biochemistry		Biochemistry				
pH	7.40	Urea	30	24	22	17	16	16
pCO2	35.2	Cr	1.30	1.18	1.12	1.09	1.00	0.98
pO2	79.2	Na+	119	123	125	130	134	137
HCO3-	21.7	K+	3.8	4.1	4.0	4.3	3.8	3.8
Lactate	3.5	Glucose	221	139	122	100	144	110
Na+	115	Osm	253	254	256	273	282	283
K+	4.1	LDH	323	541	411	500	380	190
Glucose	235	CPK	410	1519	3036	2857	1365	487
Units of measure: pCO2, pO2 in mmHg; HCO3 – mmol/L; Lactate in mmol/L; Na+, K+ in mmol/L; Glucose, Urea, Cr in mg/dL; Osm in mOsm/Kg; LDH, CPK in U/L								

ing. No causes of acute hyponatremia were identified, except for the surgical procedure, so a TURP Syndrome was assumed as the most probable cause. The patients Urologist at the private practice later informed that glycine was the irrigation fluid used during the procedure, which reinforced the TURP Syndrome diagnosis. After 72 hours of admission, the patient was discharged, with a serum Na of 137 mmol/L, a normal neurological exam, and oriented back to his Urologist.

DISCUSSION

TURP Syndrome is a clinical condition characterized by neurologic and cardiovascular disturbances, that results from excessive absorption of electrolyte-free irrigation fluids, through the opened prostatic venous channels (intravascular) and the perforated prostatic capsule (extravascular)[1,4,5]. The rate of fluid absorption depends on a number of factors, but the average is 20 ml/min[6]. Given that a regular TURP procedure lasts at least 45-60 minutes, a patient can easily absorb over 1L of hypotonic fluid in a small amount of time, leading to hypervolemia, acute dilutional hyponatremia and, ultimately, TURP Syndrome. This may occur as early as 15 minutes after resection starts or as late as 24 hours after the operation[8]. The majority of cases published describe the occurrence of the syndrome during surgery, in patients under general anesthesia, being the neurologic manifestations masked and the cardiovascular signs predominant: usually an unexplained rise in blood pressure followed by a fall associated with refractory bradycardia[1,4,6,8]. We describe a rare case of TURP Syndrome diagnosed in the ER, that occurred several hours after surgery and presented mostly with neurologic signs.

Acute hyponatremia is an electrolyte imbalance capable of causing seizures. Differential diagnosis includes metabolic disturbances, drug toxicity, central nervous system infectious, tumors or trauma, and must be excluded[9]. Potential causes of acute hyponatremia must also be identified: recent thiazides or terlipressin prescription, polydipsia, exercise, colonoscopy preparation, use of methamfetamine, post-TURP[9-10]. Within our case, the overall work-up was unremarkable, except for severe acute hyponatremia, being TURP Syndrome the most logical cause. Treatment depends on the severity and clinical manifestations[2]. Patients with severe manifestations (coma, cardiac arrest, pulmonary edema, severe hypotension, bradycardia) often need intubation, mechanical ventilation and vasopressor support, and should be managed by an intensive care team[2-3]. Patients with moderate symptoms may be treated more conservatively with close monitoring, oxygen and fluid restriction[4]. Despite that, all patients should initiate immediate and aggressive correction of acute hyponatremia with 3% saline. This will increase serum Na concentration, reduce brain edema and improve symptoms, avoiding their progression[5-6]. The suggested treatment regime is 1.2-2.4 ml/kg/h. This should produce a rise in serum Na of 1-2 mmol/h. Correction of hyponatremia should not be faster than 1.5-2 mmol/L/h for 3-4 hours then 1 mmol/L/h until symptomatic improvement or Na greater than 125 mmol/L. Maximum rise of Na should not exceed 12 mmol/L in 24 hours8. In this case, despite the final successful recovery of our patient, we should have been more aggressive with our initial fluid regime (> 25 ml/h), since he presented with important neurological manifestations.

The irrigation fluids most commonly used are sorbitol, mannitol and glycine[2-3].Glycine may contribute to neurologic symptoms in TURP Syndrome, due to direct intravascular toxic effect and indirect effect of metabolites (ammonia)[2,5,8]. Glycine and ammonia levels can be measured in blood and although their excess does not require a treatment change, it may explain why a specific patient have a more indolent

clinical course[8]. In this case, we should have measured our patient's glycine and ammonia blood levels.

Even though severe TURP Syndrome is rare, its mortality rate can be as high as 25%. In the setting of acute hyponatremia, presenting in the ER, TURP Syndrome is usually forgotten as a potential cause, due to its rarity, since it is usually diagnosed during surgery or during immediate surgical and anesthetic recovery. However, clinicians should be aware of this possible cause of acute hyponatremia, to allow an adequate management and avoid extensive and inadequate etiological investigations. Besides, in a time where we assist to a rise in private practice facilities, in Europe, possibly lacking holistic medical resources, especially in the emergency field, it is only logical that more cases like this may reach medical professionals in this setting. In the light of this, the authors believe that only through the description of such rare cases can the clinicians be aware of its existence and improve its recognition and adequate management.

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Unintentional weight loss as presenting form of Whipple's disease. Role of PET-CT scanning and review of the literature

Páez-Guillán E, García-Villafranca A, Lazaré-Iglesias H (*), Díaz-Peromingo JA.

Department of Internal Medicine and (*) Department of Pathology. Hospital Clínico Universitario. Santiago de Compostela. Spain.

INTRODUCTION

Whipple's disease (W.D.) is a multisystemic chronic infectious disorder first described in 1907 by Dr. George Hoyt Whipple[1]. The disease is very rare, with an annual incidence of 1 per 1.000.000 inhabitants[2]. It not only involves malabsorption from gastrointestinal involvement but also affects other systems like the joints, cardiovascular system and central nervous system[3]. The etiological agent, *Tropheryma whipplei* (*T. whipplei*) was first described in 1992. It is a gram-positive actinomycete, periodic acid-Schiff-positive (PAS) and acid-fast negative[4]. It contains polysaccharides that stain positive with PAS. The foamy rosy appearance of macrophages inside the intestinal mucosa determines an extensive involvement of the lamina propria[2] and, in this sense, the name of the etiological agent comes from the Greek "Trophy" (food), and "Eryma" (barrier), that means obstacle to absorption of food[5].

The authors describe a case of W.D. presented as isolated weight loss and review the literature focusing on the role of PET-CT scanning as a diagnostic tool.

CASE REPORT

A 68 years old man was referred to the outpatient consultation because of unintentional weight loss. He had lost 10 kg in a period of three months. The patient tried to lose weight on a diet and doing some exercise. He stopped both after suffering an influenza infection, but the weight loss continued. He was a retired man and referred a history of hypertension, hyperuricemia, and atrial fibrillation. There was no history of fever, arthralgia, nausea, vomiting, abdominal pain, diarrhea, or bleeding.

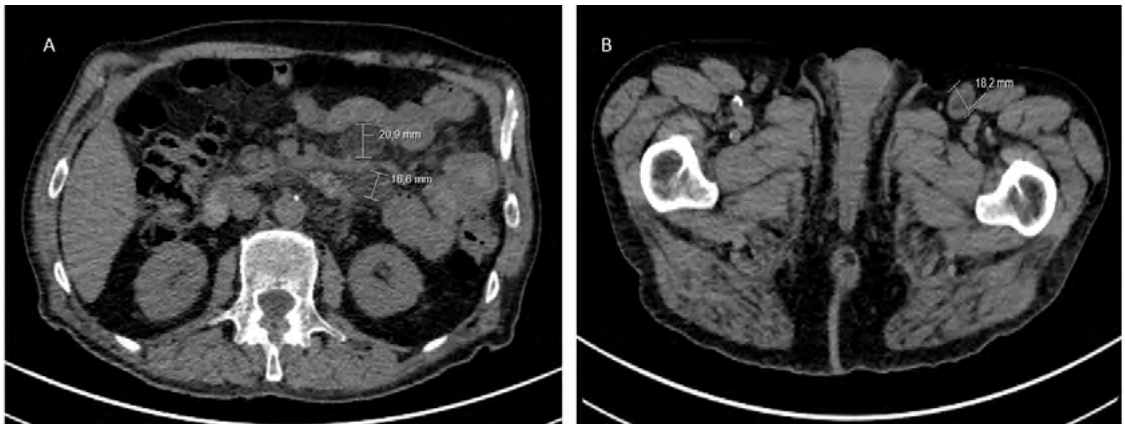
On physical examination, the patient was afebrile and vital signs were normal. Neurological examination, digestive system and joints were normal.

Serum biochemistry, leucocyte count, platelet count, as well blood coagulation was normal. Mild anemia (Hb 12.8 g/L) was found with normal serum ferritin level, and iron level. Anti-tissue transglutaminase antibodies (ATGT) were negative. An abdominal ultrasonographic study, upper endoscopy and colonoscopy were normal.

After this initial evaluation the patient referred no associated symptoms but continued losing weight. A positron emission tomography/computed tomography (PET-CT) scan was performed (Figure 1) showing enlargement of several abdominal and inguinal hypodense lymph nodes suggesting the radiologic appearance of the cavitating mesenteric lymph node syndrome. A core needle biopsy from the inguinal lymph node was reported as normal. Duodenal biopsy with investigation of coeliac disease and W.D. was performed showing thickening of the intestinal villi and foamy macrophages containing numerous granular intracytoplasmic inclusions PAS positive (Figure 2). Special staining for acid-fast bacilli and fungi were negative. There was no evidence of malignancy. Polymerase chain reaction (PCR) assay targeting the 16S rRNA gene of *T. whipplei* showed a positive result in the duodenal biopsy.

Antibiotic treatment using ceftriaxone (2 g/day intravenously at home) was given for 2 weeks. This initial therapy was followed by long term trimethoprim-sulfamethoxazole (TMP-SMZ; 160/800 mg twice a day). Currently he continues to take TMP-SMZ on a regular basis.

Figure 1. PET-CT scan. Panel A shows enlarged mesenteric lymph nodes and Panel B an inguinal enlarged lymph node. Biopsy of the inguinal lymph node was made showing no pathological findings.



Correspondencia: jose.antonio.diaz.peromingo@sergas.es

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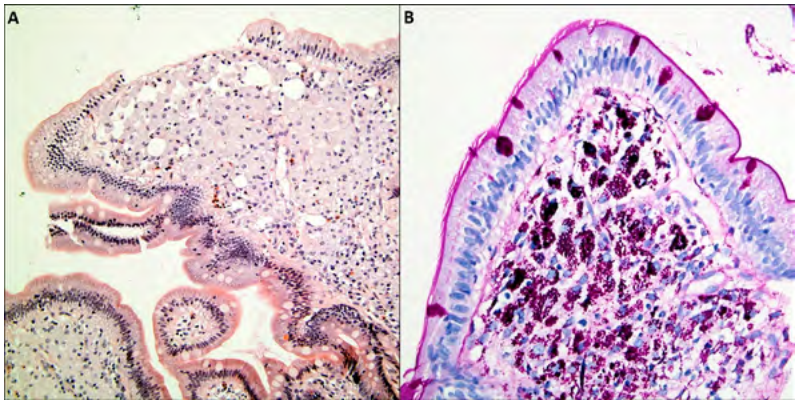
Figure 2. Duodenal biopsy. Panel A shows thickening of the intestinal villi and foamy macrophages (H&E, original magnification x 20). PAS stain (Panel B) reveals the presence of numerous granular intracytoplasmic inclusions PAS positive, diastase resistant (PAS-D, original magnification x 40).



DISCUSSION

This case deals with a rare disease presenting with unexplained unintentional weight loss. Non-malignant organic disorders, mainly digestive diseases are the most frequent cause of unintentional weight loss[6]. Malabsorptive diseases like W.D. are a possible underlying etiology.

Epidemiologically, W.D. is linked to a fecal-oral transmission, particularly in male patients that work with animals[7] affecting mainly patients from Europe and North America. It is very rare in the native African and Asian populations[8]. After introducing PCR testing as a tool for diagnosis of W. D., the annual incidence rate has been estimated to be between 1 and 6 new cases per 10.000.000 persons per year worldwide[9].

Asymptomatic carriers of *T. whipplei* represent a large reservoir from which other humans might be colonized. Most carriers develop protective response that prevents spread of the bacterium through the body, but carriage can last for several years[10]. *T. whipplei* has been found in numerous biological samples including urine, blood, saliva, stool, skin, lymph node, synovial fluid, skeletal muscle, myocardium, cardiac valve, lung, bronchoalveolar fluid, liver, spleen, stomach, small bowel, colon, larynx, maxillary sinus, aqueous humor, brain, and cerebrospinal fluid[11,12].

Relatives of chronic W.D. patients have a higher chance of carrying the bacterium either because of human to human transmission or because they are infected by the same environmental source[13]. Although it is assumed that the bacterium is acquired during childhood[14], only a limited number of carriers develop W.D. In this sense, it seems that host, bacterial, and environmental factors may all contribute to the pathogenesis[14]. Probably, subjects who do not develop a protective immune response are prone to development of classical W.D.[1].

The most frequent and common symptoms involve the gastrointestinal system (75-95%)[2,16]. Diarrhea is the most common complaint in patients affected from W.D.[17] frequently associated with malabsorption[18]. Weight loss is the second most important manifestation[17] commonly associated with other symptoms but isolated weight loss is very rare. A patient with W.D. associated weight loss can lose up to 15 Kg in one year. Weight loss is less common in patients under 40 years. It is most common in males 40-50 years old[7,19]. When weight loss is a predominant feature of the disease, cachexia may result both from anorexia and nutritional deficiency due to malabsorption[16].

Clinical presentation is highly polymorphic. There has been described four commonly recognized patterns: classic W.D., localized chronic infections, acute infections, and carriage[13,20]. Symptoms tend to develop in three phases. An early phase with symptoms of infection such as fever, arthritis or arthralgia. A middle phase with diarrhea and weight loss, and a late phase where almost every organ can be involved, mostly the eyes, heart, and central nervous system[21]. Pathophysiology of gastrointestinal affectation is due to bacterial overgrowth and diffuse edema and exudates inside the intestinal wall and mucosa[22].

Polyarthralgia due to chronic polyarthritis with migrant involvement of distal joints is common (65-90%) and can evolve to spondylitis[5,23]. The cardiovascular system is affected in 17-55% of the cases being endocarditis the most frequent feature[2,22]. The central nervous system can be involved around 10-43% in patients with W.D. Neurological manifestations can be the result of a relapse of previously treated classic W.D., neurological involvement in untreated W.D., or an isolated neurological symptom[24].

Important diagnostic support is provided by the molecular diagnosis with PCR giving a determination of the nucleotide sequence of the 16S RNA gene of *T. whipplei*. This test have a high sensitivity (59-95%) but low specificity (45-71%), depending from the PCR assay performed[11,16]. PCR also allows to evaluate the degree of patient response to antibiotic therapy and perform a differential diagnosis with other bacteria such as *Mycobacterium complex*, *Corynebacterium spp*, *Rhodococcus equi*, or *Histoplasma sp*[16].

Both diagnostic tests, PCR and PAS positive, allow also the differentiation with malabsorptive disorders such as celiac disease, lymphoma, Crohn's disease or amyloidosis[25]. Never-

theless, histology (PAS positive) and PCR may show discordant results especially because PCR sensitivity is higher than histology. A possible explanation for this discrepancy has been related to an uneven distribution of the bacterium within the gut[26]. Although intestinal tissue PCR has been traditionally ordered as a confirmatory test after PAS staining in classical disease, it can be also performed in non digestive samples such as synovial fluid, cerebrospinal fluid, cardiac tissue or blood[27]. Of note, some authors have proposed a strategy for diagnosing W. D. using PCR in stool or saliva samples. When positive, more invasive samples such as blood, or others according to clinical findings should be preformed[28].

PET-CT scanning is commonly used in the assessment of patients with suspected occult inflammation, primary malignancy, or in the evaluation of metastatic disease. Cavitating mesenteric lymph node syndrome (CMLNS) is a complication of celiac disease (chronic enteropathy characterized by intolerance to gluten ingestion) that is documented but poorly understood. Patients with CMLNS often present with weight loss that is refractory to treatment, fatigue, and diarrhea associated to clinical signs and laboratory findings of hyposplenism. Computed tomography shows multiple cystic mesenteric masses with a central low attenuation area caused by the presence of fluid and/or adipose material in the central cavity of the mesenteric lymph node[29]. Differential diagnosis should be made with cystic lymphangiomas, mesenteric lymphangiomas, tuberculosis, metastatic germ cell tumors, or lymphomas[16,25,30].

Peripheral lymphadenopathy is frequent in W.D. ranging from 40 to 60% of cases[31]. From a clinical point of view, they are indistinguishable from lymphadenopathy due to sarcoidosis, lymphoma or other infectious diseases such as tuberculosis. Mesenteric lymphadenopathy is also common and can evolve to chronic constipation and eventually intestinal obstruction[22]. The mesenteric and retroperitoneal lymphadenopathy can aggravate the lymphatic stasis and associated edema of the intestinal mucosa leading to malabsorption and diarrhea[31].

Diagnostic tools include upper endoscopy with duodenal biopsy that evidences thickening of the intestinal wall, lymphatic occlusion of vessels, lipid deposit in the lamina of the wall, and foamy macrophages with vesicles PAS-positive that can contain bacteria or remnants of bacteria. PCR testing can be positive for *T. whipplei* DNA.

Treatment with parenteral ceftriaxone, 2 gr daily, followed by prolonged antibiotic therapy with Trimethoprim and Sulfomethoxazole for 1 to 2 years guarantees the remission of the disease and prevents relapse[5.] Antibiotic treatment reduces clinical symptoms in 1-4 weeks. Regarding to follow up, gastroscopy with duodenal biopsy within 6 to 12 months from the onset of therapy should be made. When the PAS-positive macrophages research is negative, antibiotic treatment can be stopped.[16,25]

In patients with mesenteric or retroperitoneal lymphadenopathy and unintentional weight loss, a possible underlying W.D. should be investigated.

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Subcorneal Pustular Dermatosis of Sneddon-Wilkinson

Subcorneal pustular dermatosis is a rare, chronic, relapsing pustular eruption that strikes the corneal layer of the skin and presents with a neutrophilic infiltrate on histopathological examination[1-4]. It was first described by Sneddon and Wilkinson in 1956 and affects mainly middle-aged and elderly women. Its coalescing vesiculopustular eruptions typically involve the flexion sites of the trunk and proximal extremities[1-4].

Its etiology is not fully understood, presenting several pathophysiological mechanisms, one of them being increased tumor necrosis factor-α. It is frequently related to systemic pathologies, particularly hematological (gamopathies, multiple myeloma) and inflammatory diseases (rheumatoid arthritis)[1-4].

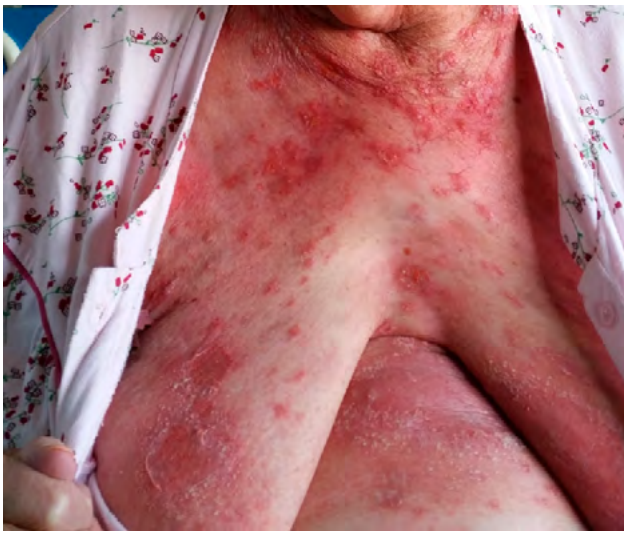
In this report is described the clinical case of a 74-year-old woman with metabolic syndrome who was hospitalized due to an extensive rash involving trunk and upper limbs associated with constitutional symptoms for a month.

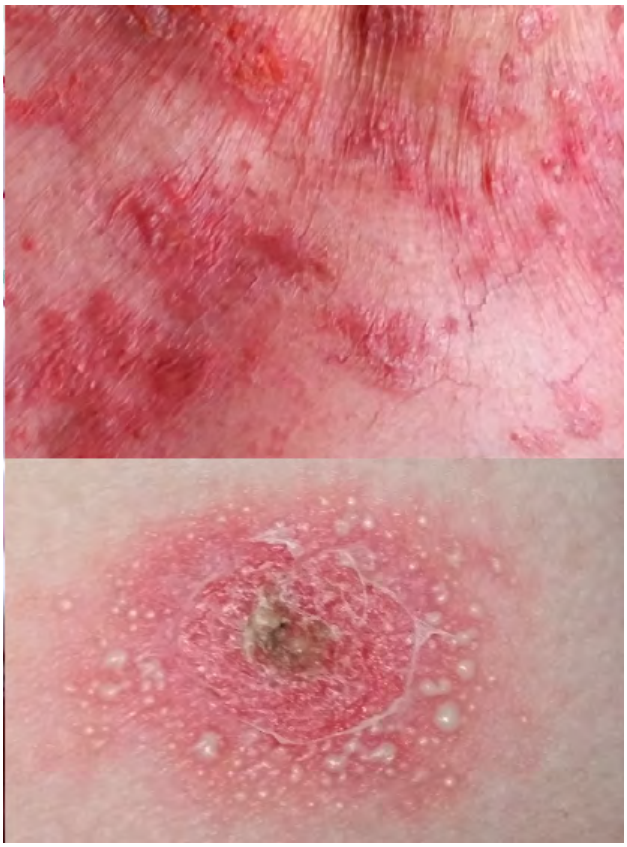
Dermatology collaboration was requested, and solitary by clinical observation and attending to the presence of classical signal which consists of superficial pustules arranged in annular and serpiginous pattern (see picture) classified the eruption as a Sneddon-Wilkinson dermatosis. This diagnosis, has indication to further study associated systemic pathologies and medical therapeutic intervention with *dapsone* and local wound disinfection.

Of the complementary diagnostic tests performed, an increased sedimentation rate of 30 mm and an IGA gammopathy, serum values of 1118 mg / dl confirmed in immunofixation and protein electrophoresis, and were considered as positive findings. With normal hematological formula and without other focusing clinic the patient was discharged from the hospitalization for follow-up in outpatient internal medicine and dermatology.

Despite a notorious improvement in investigation techniques, the pathogenesis of this dermatosis is still controversial. It was found that some patients with Sneddon and Wilkinson´s disease show epidermal intercellular immunoglobulin A (IgA) deposits on direct and indirect immunofluorescence, which places them in the group of IgA pemphigus[1-4].

The diagnosis is still established if the classic signal is present (see picture), or if there is confirmatory histology. Disease without cure, dermatological control´s treatment and prognosis is dependent on systemic associations[1-4].





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DIAGNOSIS

Subcorneal pustular dermatosis

Costelha J, Barros A

Unidade Local de Saúde do Alto Minho

Correspondencia: jpcostelha@gmail.com

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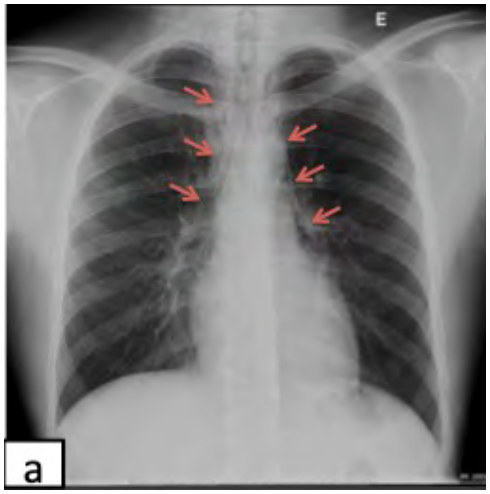
Spontaneous pneumomediastinum

Neumomediastino espontáneo

Pneumomediastinum is defined as the presence of air in the mediastinal cavity. Can be classified into two categories: secondary pneumomediastinum, when there is a causative etiological factor and spontaneous pneumomediastinum, without a clear etiology. Spontaneous pneumomediastinum is a rare disease in adults and most often affects young adults males in a relation to females of 8:1. Is usually benign, self-limited and just recurred in rare cases. Sometimes the diagnosis on chest radiography can be difficult [1-5].

The authors describe a case of a young men, 19 years old, crew ambulances worker, occasional smoker (less than one packet per year), with no relevant medical history or usual medication that appealed to the emergency department with central chest pain with pleuritic characteristics associated with dyspnea that started on resting. The patient denied recent trauma, physical exertion or invasive medical examinations. The objective examination showed cervical subcutaneous emphysema without any other changes. Electrocardiogram and blood tests including hemogram, renal and hepatic parameters, C reactive protein, D-dimers and troponin were normal. Chest radiography (Figure 1a) and computed tomography (Figure 1b) showed the presence of pneumomediastinum and emphysema that dissected the lower cervical plans without further changes. The patient was admitted to the Pulmonary Department for 4 days where he had rest, oxygen therapy and symptomatic relief. The patient presented clinical improvement without presenting recurrence until the present time.

Figure 1A. Thoracic radiography (postero-anterior and lateral view) with linear hypertransparencies covering the mediastinal structures (see arrows).



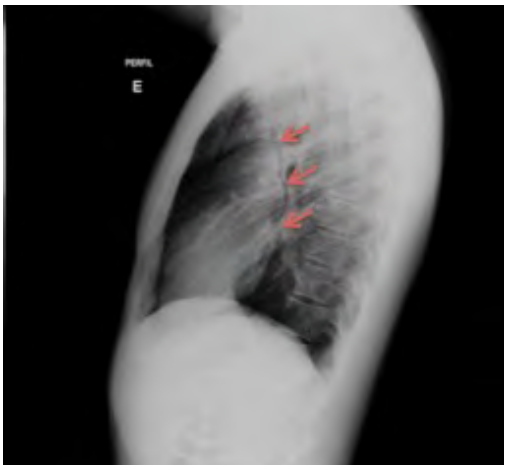
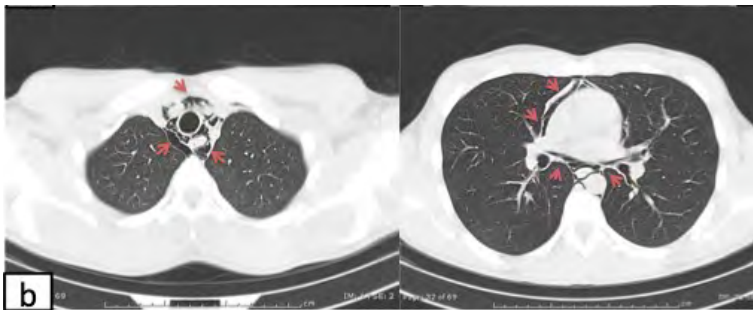


Figure 1B. Computed tomography of the lung (pulmonary window) with two cross-sections (tracheal and segmental bronchi level) showing air at inferior cervical plan and mediastinal structures (see arrows).



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Spontaneous pneumomediastinum

Lucas S[1], Ramos H[2]

[1] Serviço de Pneumologia, Hospital de Faro, Centro Hospitalar Universitário do Algarve, Portugal.
[2] Assistente de Pneumologia, Serviço de Pneumologia, Hospital de Faro, Centro Hospitalar Universitário do Algarve, Portugal

Correspondencia: susana.i.lucas@gmail.com

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Spontaneous Hemotorax Secondary to Rivaroxabano treatment

INTRODUCTION

Hemothorax corresponds to any pleural effusion with a hematocrit greater than 50%. More oftenly results from trauma or invasive thoracic procedures. Spontaneous hemothorax is rare and may be observed mainly in association with malignancies, pulmonary infarction and spontaneous pneumothorax. Massive hemothorax refers to a blood loss greater than 1500mL[1-4].

Anticoagulation is part of the therapeutic strategy of certain thromboembolic events. Previously the only available anticoagulants were vitamin K antagonists (VKA), with their well-known plasma concentration lability and increased haemorrhagic risk. The emergence of direct oral anticoagulants (DOACs) brought a therapeutic weapon effective as AVK and with a significant reduction in the risk of hemorrhage. Nevertheless some authors argue that hemorrhagic complications in this cases may be worse than those seen with VKA[2]. There are few cases of spontaneous hemothorax secondary to DOACs reported in the literature[1,2,4].

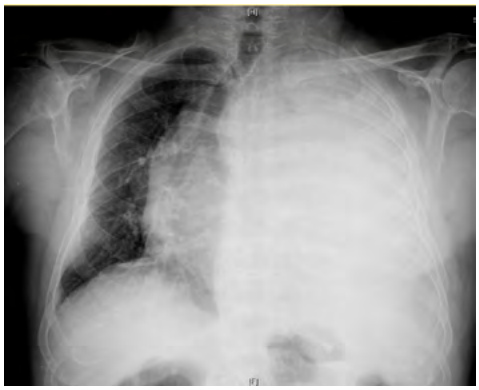
CLINICAL CASE

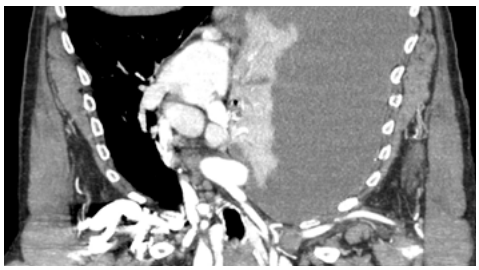
73 year old man, treated with rivaroxaban 20mg per day due to atrial fibrillation. He came to emergency department complainting of dyspnea and easy fatigue worsened in the last two days. He denied any trauma. Chest radiograph (Figure 1) showed an extensive opacity of the left hemithorax, with contralateral mediastinal deviation. Thoracic CT (Figure 2) revealed the presence of massive left pleural effusion with adjacent lung collapse. A thoracic drain was placed with an immediate outflow of 2 liters of bloody pleural fluid. Analytically, the prothrombin time and the activated partial thromboplastin time was increased, thus vitamin K and fresh plasma were administered with the purpose of normalizing coagulation times. Due to septation of the effusion, the adopted measures were not enough to completly drain the effusion, so patient was transferred to the thoracic surgery department for surgical drainage of the effusion and pleural descortication. Chest x-ray two months later (Figure 3) shows complete resolution of the effusion.

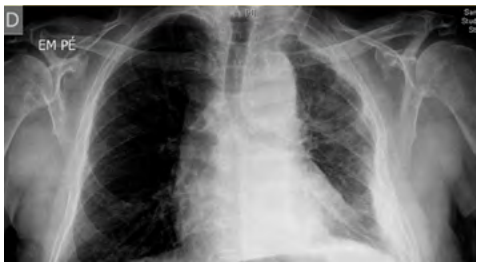
DISCUSSION

Spontaneous hemothorax as a complication of anticoagulant therapy with DOACs usually is not an expected occurrence but it should be taken into account by all clinicians when approaching a hypocoagulated patient with de novo pleural effusion[1-3]. To our knowledge there is only one published case of spontaneous hemothorax secondary to rivaroxaban[2]. In the presenting case, chest drain placement and reversion of anticoagulation were not sufficient to solve hemothorax, and the patient underwent video-assisted thoracic surgery for drainage and pleural descortication.

There are no formal indications for resuming oral anticoagulation following an iatrogenic hemorrhagic event. Continuity of the anticoagulant should always be questioned, taking into account the thromboembolic risk versus the risk of further hemorrhage, especially if the hemorrhagic focus is not controlled. It may be licit to stop anticoagulation definitly, replace the initially chosen anticoagulant, or adjust the dose of DOAC according to renal function[5].







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Spontaneous hemotorax

Carbalho A, Antunes A

Centro Hospitalario de Leiria. Portugal

Correspondencia: anajocarvalho@gmail.com

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Hyperbaric oxygen therapy: a key role in the treatment of cerebral gas embolism

ABSTRACT

Stroke is an important cause of morbidity and mortality. The etiologies are varied. Gas embolism is a known complication of invasive procedures, which may complicate with cerebral embolization and ischemia. Benefits of hyperbaric oxygen therapy are recognized in cerebral gas embolism when started in the first hours after the event, which are fundamental for the vital prognosis.

Keywords: cerebral gas embolism; hyperbaric oxygen therapy; stroke; patent foramen ovale

CASE REPORT

Introduction: Stroke is an important cause of morbidity and mortality. Early diagnosis and rapid etiological identification are fundamental for a timely treatment, in order to minimize possible neurological sequelae.

Clinical Case: A 63-year-old man, smoker, with lung injury under study was admitted for transthoracic aspiration biopsy (TAB). After the procedure, he suddenly had a cardiorespiratory arrest with electrical activity without a pulse. Immediatly advanced life support are started with recovery at the end of the first cycle. He was transported to the emergency room under invasive mechanical ventilation (IMV), but hemodynamically stable. Neurologically, he presented a conjugate deviation of the eyes to the right, a motor response in bilaterally extension, paratonia of the lower limbs and indifferent cutaneous-plantar reflexes. The etiological investigation concluded that it was a gas embolism (GE) in the territory of the right middle cerebral artery in a patient with an unknown patent foramen ovale (PFO). The patient was immediately transferred to the Hyperbaric Medicine Unit for treatment. He manteined IMV and intensive care hospitalization for 24 hours. At the time of discharge, he had left hemiparesis with face and grade 4+ muscle strength.

Discussion: GE is an uncommon, potentially catastrophic event secondary to air entering the blood vessels (venous or arterial)[1,2]. The most common causes are surgeries, trauma, vascular procedures, barotrauma, and TAB[2].

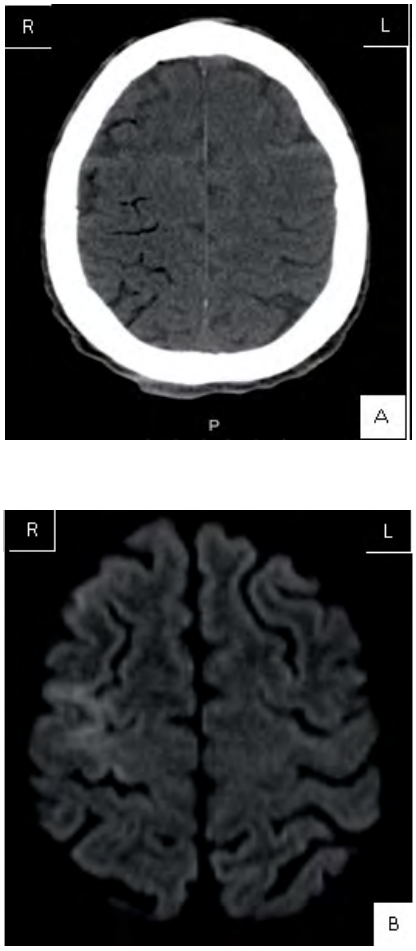
Smokers and patients with chronic obstructive pulmonary disease are risky groups.

PFO is a congenital anomaly with high prevalence in the adult population (20-25%)[3] and the association with cryptogenic stroke (40%) [3] has been demonstrated.

Hyperbaric oxygen therapy is recommended in cases of GE with cardiorespiratory compromise, neurological deficits and / or target organ damage, and its benefit are described in the literature, mostly when initiated within the first 6 hours after the event[4]. It provides oxygen pressures above atmospheric pressure and 100% oxygen concentrations, leading to a "supra-physiological" systemic hyperoxia level, allowing large nitrogen gradients to be displaced from the interior of the air bubble, which, in turn, reduces its size (Boyle's Law)[4]. At pressures of 282 kPa, the diameter of the gas bubble is reduced to 82%, resulting in a 45% decrease in volume and resolution of embolic phenomena[4].

Conclusion: In this case, airflow occurred in the systemic venous system, resulting from TAB, which is a rare complication (0.02 to 0.06%)[2], migrating to the arterial system through PFO, with embolization to the vasculature causing ischemia.

Figure 1. A: Cerebral CT with GE located in the cortical branches of the right middle cerebral artery. B: Cerebral MRI with small foci of acute ischemia at the pre-central, right frontal and right frontal gyri.



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DIAGNOSIS

Cerebral gas embolism

Fernandes AM[1], Fonseca T[1], Paixão AI[2], Castelões P[2]

[1] Resident of Intensive Medicine, Intensive Care Service, Centro Hospitalar Vila Nova Gaia/Espinho.

[2] Intensivist, Intensive Care Service, Centro Hospitalar Vila Nova Gaia/Espinho

Correspondencia: amargaridafernandes03@gmail.com

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Giant Pneumatocele

ABSTRACT

A 83-year-old woman presented to the Emergency Department with a 1-week history of dyspnea by a bulky pneumatocele. Pneumatoceles are more frequent post infectious, may be solitary or multiple and they are typically transient.

CASE REPORT

A 83-year-old woman, with heart failure, atrial fibrillation, hypertension, diabetes, chronic kidney disease and pulmonary emphysema presented to the Emergency Department with a 1 – week history of dyspnea. In the past, she was hospitalized for community acquire pneumonia. On auscultation of the chest reveals decreased breath sounds in right lung field. Laboratory was not compatible with infection. On image studies the thoracic radiography (Image 1) showed a hyper transparent circular area with well defined delimitation in the right lung field. The thoracic CT (Image 2) was performed to rule out abscess and has revealed in the posterior portion of the right lung a bulky pneumatocele measuring 13cm of greater diameter and a left pleural effusion. The patient has acidemia by hypercapnic respiratory failure. The pleural effusion was transudate from heart failure. Despite she has hypercapnic respiratory failure, because the large volume pneumatocele, was decided to do not start non – invasive ventilation by the risk of increase volume and tension of pneumatocele. The patient died during hospitalization.

DISCUSSION

Pneumatocele are thin-walled parenchymal cyst, typical asymptomatic. Pneumatocelescommonly occurs after acute bacterial pneumonia, in two thirds of the cases staphylococcal pneumonia and related to delayed therapy. They also result from chest trauma and barotrauma from mechanical ventilation. Although pneumatoceles are typically asymptomatic and often disappear following resolution of the inciting event, they can cause symptoms as dyspnea and contribute to respiratory failure[1,2].

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Keywords: pneumatocele, abscess, respiratory failure.

DIAGNOSIS

Giant pneumatocele

Image 1. Thoracic radiography showing a hyper transparent circular area with well – defined delimitation in the right lung field, corresponding to a pneumatocele.

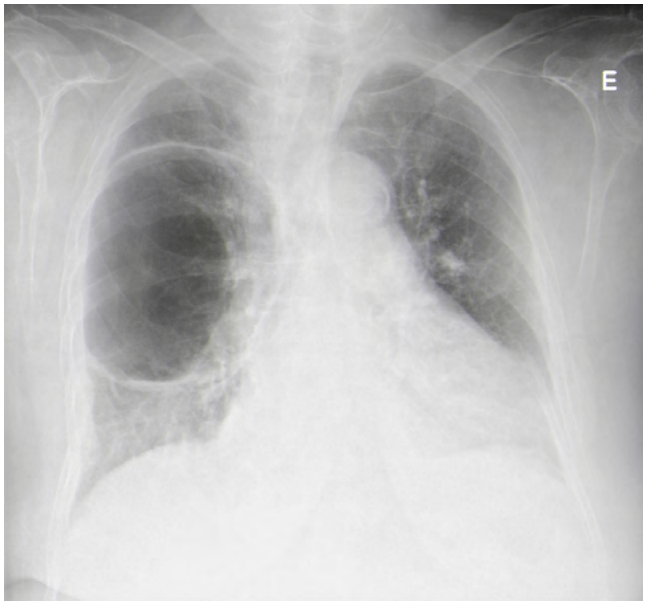
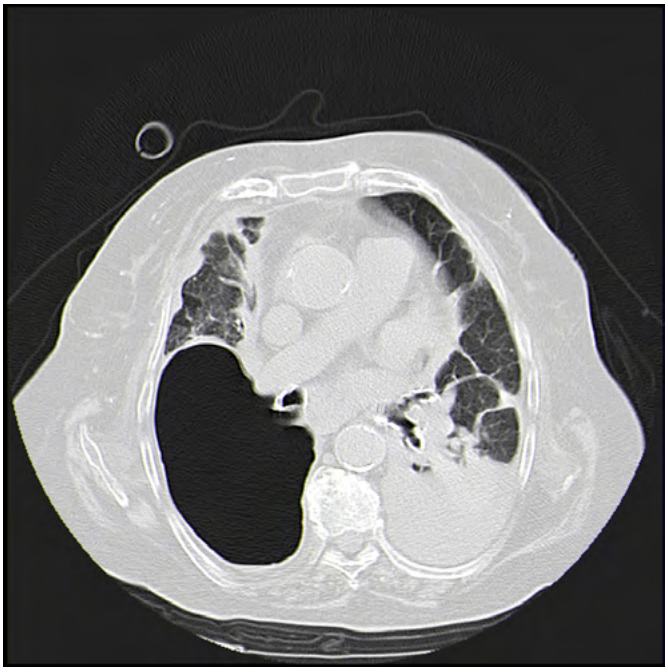


Image 2. Thoracic CT showing in the posterior portion of the right lung a bulky pneumatocele measuring 13cm of greater diameter and a left pleural effusion.



Zarcos Palma N, da Cruz M

Internal Medicine Department of Centro Hospitalar Tâmega e Sousa

Correspondencia: nzarcospalma@gmail.com

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Necrotizing fasciitis. ¿How fast can it develop?

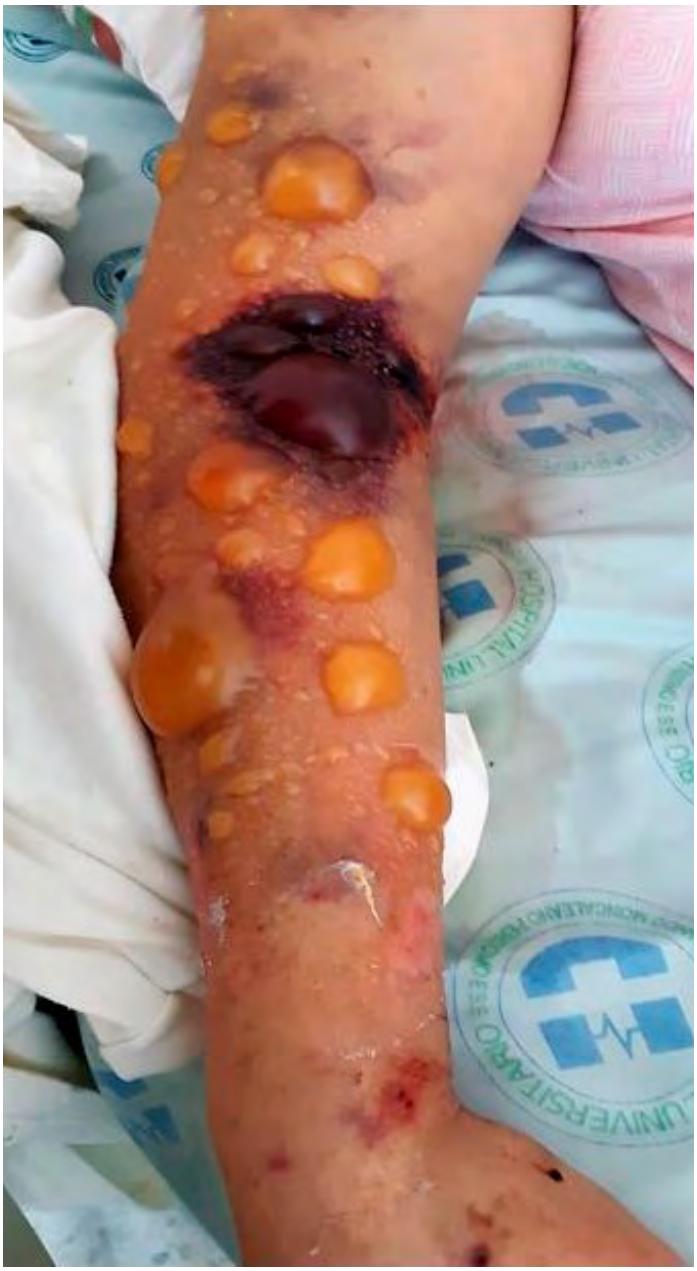
A 76-year-old woman with heart failure history and with no other relevant condition presented to the emergency department for evaluation of 6 hours of pain in right upper limb associated with small vesicles without systemic symptoms.

On physical examination, serous content vesicles with erythematous base, edema, crepitus and intense pain on palpation were identified on distal right upper extremity. No systemic inflammatory response (white blood cells 9750 mm3, lactate 1.7 mmol/L and c-reactive protein 4.6 mg/dL) or hemodynamic instability (blood pressure 140/75 mmHg and heart rate 82 beats per minute) were reported.

Antibiotic coverage was started with oxacillin 2 gr/4h. On the first 6 hours it progressed rapidly (Figure 1) with the presence of fever and ecchymosis, suspecting necrotizing fasciitis, vancomycin 15mg/kg and piperacillin tazobactam 4.5 gr dose were indicated. Emergency surgical debridement was carried out and wide necrotic tissue were identified on forearm muscles. Leukocytosis (white blood cells 15.000 mm3), positive c-reactive protein of 15mg/dL and negative blood cultures were reported. Despite prompt treatment 48 hours later the patient dies.

Necrotizing fasciitis is a deep tissue infection and it's a surgical emergency, where early diagnosis and treatment are essential[1,2]. Diabetes, cirrhosis and trauma are well known risk factors[3]. Findings like disproportionate pain, bullae or ecchymosis, tense edema, subcutaneous emphysema, systemic toxicity and rapid progression should rise suspicious about this entity[4].

The definitive diagnosis can only be made by surgical exploration and should not be delayed by diagnostic studies[1] like magnetic resonance, although inflammatory infiltration of the deep fascia and subcutaneous air could be identified, which is very specific on early stages. Despite early treatment mortality rises upon 30%, mainly associated with dissemination, comorbidities, extreme ages and delay in treatment[2].



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Keywords: Fasciitis, Necrotizing; Bacterial Skin Diseases; Gas gangrene

DIAGNOSIS

Necrotizing fascitis

Buitrago-Toro K, Jiménez-Salazar S

Department of Internal Medicine, Faculty of Health Sciences, Universidad Surcolombiana, Neiva, Colombia.
Department of Internal Medicine, Hospital Universitario Hernando Moncaleano Perdomo, Neiva, Colombia.
MI Dneuropsy research group Universidad Surcolombiana, Neiva, Colombia

Correspondencia: silvana1212@gmail.com

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Para el envío de originales se ha habilitado un formulario en la pagina web www.galiciaclinica.info. El sistema confirmará la entrega y permitirá consultar el estado del manuscrito. No se aceptaran originales enviados por otros métodos.

El comité editorial, eventualmente con la ayuda de revisores externos, evaluará los trabajos enviados decidiendo si procede su publicación, si es necesario realizar correcciones o si se desestima la publicación. Una vez aceptado, se enviarán al autor las pruebas de imprenta para la corrección de posibles erratas.

Los trabajos reunirán los requisitos de uniformidad habituales en revistas biomédicas. Dichos requisitos se pueden consultar en "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, Updated April 2010", disponible en http://www.icmje.org. Se recomienda encarecidamente leer en especial la sección "Preparing a Manuscript for Submission to a Biomedical Journal" (http://www.icmje.org/recommendations/browse/manuscript-preparation/) y seguir fielmente sus indicaciones a la hora de redactar el trabajo a enviar.

Se recomienda el empleo de los programas más habituales de edición de texto (Ej., Word) tanto para el texto como para las tablas. Dado que la mayoría de las páginas se imprimen en blanco y negro, se aconseja evitar en tablas y figuras en la medida de lo posible el uso de colores o tramas que no tengan el adecuado contraste para su identificación. Las figuras o imágenes se enviaran en archivo aparte, como archivo de imagen (jpeg o similar) o como PDF con una resolución de 300 ppp. a tamaño de impresión definitivo.

Todos los trabajos deben remitirse con el título en el idioma nativo y en inglés y con al menos 3 keywords.

La bibliografía será referenciada según las normas del ICMJE https://www.nlm.nih.gov/bsd/uniform_requirements.html

Correcciones: Los autores, tras realizar las correcciones sugeridas por los revisores, deben enviar una carta de respuesta al revisor, es decir, deberán remitir el manuscrito corregido y acompañado de una carta respondiendo a los comentarios del revisor punto por punto.

La revista presenta las siguientes secciones:

Editoriales: Habitualmente encargados por la dirección de la revista. Su extensión máxima será de 8 paginas de 30 líneas y se admitirá una figura o una tabla y quince citas bibliográficas. El número máximo de firmantes será de dos.

Revisiones: Habitualmente encargadas por la dirección de la revista. La extensión máxima recomendada del texto es de 30 páginas de 30 líneas, a las que se podrán añadir 6 figuras y 6 tablas, y un máximo de 50 citas bibliográficas. El número máximo de firmantes será de tres.

Originales: Trabajos de investigación sobre cualquier aspecto medico. La estructura general de los trabajos será la tradicional: Título: en el idioma original y en inglés, Resumen, Palabras clave (que deben corresponder a las materias médicas encabezadas -MESH- del Index Medicus), Introducción, Material y métodos, Resultados, Discusión, Bibliografía. La extensión máxima recomendada del texto es de 20 páginas de 30 líneas, a las que se podrán añadir 5 figuras y 5 tablas, y un máximo de 30 citas bibliográficas. El número máximo de firmantes será de ocho. El resumen debe estar estructurado en los siguientes epígrafes: objetivos, material y métodos, resultados y conclusiones.

Originales breves: Trabajos de investigación que por sus características no precisan un mayor espacio. Estructura similar a la de los originales. Su extensión máxima será de 10 páginas de 30 líneas, 3 figuras, 3 tablas y 20 citas bibliográficas. El número máximo de firmantes será de seis.

Notas clínicas: Descripción de casos clínicos de excepcional interés. Constarán de una breve introducción, caso clínico, y discusión correspondiente. Su extensión máxima será de 6 páginas, 2 figuras y dos tablas y 15 citas bibliográficas. El número máximo de firmantes será de cuatro.

Cartas al director: Comentarios, opiniones u observaciones sobre los diversos trabajos publicados con anterioridad en la revista. La extensión máxima será de 4 paginas de 30 líneas y se admitirá una figura o una tabla y diez citas bibliográficas. El número máximo de firmantes será de dos.

Preguntas clínicas: En esta sección se tratará de responder de forma concreta y sucinta a preguntas clínicas concretas que, bien han motivado una controversia, o cuestionan actitudes arraigadas en la práctica diaria. La extensión máxima será de 6 páginas de 30 líneas, dos figuras y dos tablas y 15 citas bibliográficas. El número máximo de firmantes será de dos.

Imágenes médicas: Imágenes curiosas, insólitas o demostrativas. Se acompañarán con un texto breve, como máximo 1 pagina de 30 líneas, en el que se explique el caso clínico, con una breve discusión acerca de la importancia de la imagen. El número máximo de firmantes será de dos.

Resúmenes de Tesis doctorales: Elaborados por el autor, describirán el trabajo realizado; su extensión máxima será de 2 paginas de 30 líneas. Debe incluirse un apéndice con los datos correspondientes a Universidad, departamento, director de la tesis y fecha de presentación.

Otros: La dirección de la revista considerara para su publicación cualquier artículo relacionado con la medicina en cualquier aspecto, aunque no se incluya exactamente dentro de los supuestos anteriores. En este caso se recomienda antes de su envío contactar con la dirección para acordar las características del mismo.

Todas las opiniones o afirmaciones expresadas en los artículos corresponden a los autores de los mismos. Tanto el comité editorial como la SOGAMI declinan cualquier responsabilidad a este respecto.

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Los trabajos reunirán los requisitos de uniformidad habituales en revistas biomédicas. Dichos requisitos se pueden consultar en "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, Updated April 2010", disponible en http://www.icmje.org. Se recomienda encarecidamente leer en especial la sección "Preparing a Manuscript for Submission to a Biomedical Journal" (http://www.icmje.org/recommendations/browse/manuscript-preparation/) y seguir fielmente sus indicaciones a la hora de redactar el trabajo a enviar.

Referencias: Indique las referencias en el texto con un número en superíndice de forma correlativa según el orden de aparición. Las referencias irán numeradas de esta forma en la lista final después del manuscrito de acuerdo al formato recomendado por el ICJME. El listado completo puede encontrarse en este enlace: https://www.nlm.nih.gov/bsd/uniform_requirements.html, siendo las referencias más habituales las siguientes:

- Artículo de revista:

  Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002;347:284-7.

  Rose ME, Huerbin MB, Melick J, Marion DW, Palmer AM, Schiding JK, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935:40-6.

- Libro de autores individuales:

  Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4ª ed. St. Louis: Mosby; 2002.

En relación con los artículos de revista, se incluirán los seis primeros autores seguidos por "et al" y se utilizarán las abreviaturas de las revistas del catálogo de Pubmed/Medline (http://www.ncbi.nlm.nih.gov/nlmcatalog/journals).

Los autores deben incluir las referencias a las fuentes primarias siempre que sea posible, evitando las fuentes secundarias o las referencias a trabajos no publicados, comunicaciones en congresos, etc. Es responsabilidad de los autores asegurar la exactitud de las referencias citadas.


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