Tuberculosis ocular: un retrato portugués de este problema raro y desafiante

Ocular Tuberculosis – A Portuguese Portrait of This Rare and Challenging Problem

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ABSTRACT

Objectives: Although threatening there is not enough awareness for ocular tuberculosis, hence we intend to study and characterize the ocular tuberculosis observed on a Portuguese specialized pulmonology diagnostic center.
Materials and Methodologies: Retrospective study of individuals diagnosed with ocular tuberculosis and followed up from 1st January 2016 until 31th December 2018.
Results: We studied 38 patients with presumed ocular tuberculosis, with mean age 53,315,7 years old, whose 55,3% were females. Only one patient had known immunosuppression, seven patients had history of previous tuberculosis and only two patients reported a known risk contact. None had extraocular disease. All patients had at least one positive immunologic test, either tuberculin skin test (63,2%) or Interferon Gamma Release Assay test (86,8%).
Most patients presented bilateral ocular tuberculosis (44,7%). The standard four-drug regimen was the treatment of choice and corticosteroids were administered to 55,3% patients with no differences in treatment outcomes. The mean length of treatment was 8,6 months and among the patients who completed treatment, 72,4% presented clinical improvement or remission of the ocular manifestations.
Conclusions: Ocular tuberculosis, despite a rare condition, carries a huge burden in health care centers. Delay in starting proper treatment can result in permanent blindness and impairment of life's quality. This condition is probably underdiagnosed and, to our knowledge, there are no recent studies characterizing the latest trend of ocular tuberculosis in Portugal.

Keywords: ocular tuberculosis, tuberculosis, uveitis, mycobacterium, *mycobacterium tuberculosis*.

RESUMEN

Objetivos: Aunque amenazante, no hay suficiente conciencia sobre la tuberculosis ocular, por lo que pretendemos estudiar y caracterizar los casos de tuberculosis ocular observados en un centro portugués de diagnóstico especializado en neumología.
Materiales y Metodologías: Estudio retrospectivo de individuos con tuberculosis ocular seguidos desde 1 de enero de 2016 hasta 31 de diciembre de 2018.
Resultados: Se estudiaron 38 pacientes, con una edad media de 53,3±15,7 años, de los cuales el 55,3% eran mujeres. Solo un paciente tenía inmunosupresión iatrogénica, siete pacientes tenían antecedentes de tuberculosis previa y dos pacientes reportaron un contacto de riesgo conocido. Ninguno tenía enfermedad extraocular. Todos los pacientes tenían al menos una prueba inmunológica positiva, ya sea prueba cutánea de tuberculina (63,2%) o prueba de interferón gamma (86,8%).
La mayoría de los pacientes presentaron patología bilateral (44,7%). El régimen de cuatro fármacos fue el tratamiento de elección y se administraron corticoides al 55,3% de los pacientes sin diferencias en los resultados. La duración del tratamiento fue de 8,6 meses y entre los que completaron tratamiento, 72,4% presentó mejoría clínica o remisión.
Conclusión: La tuberculosis ocular, aunque una condición rara, sobrecarga los centros de salud. El retraso en el inicio del tratamiento puede provocar ceguera y deterioro de la calidad de vida. Esta condición probablemente está subdiagnosticada y, hasta donde sabemos, no hay estudios que caractericen su evolución en Portugal.

Palabaras clave: tuberculosis ocular, tuberculosis, uveítis, micobacteria, *mycobacterium tuberculosis*.

INTRODUCTION

Tuberculosis is a worldwide endemic and transmissible disease that, despite the existence of an effective treatment, remains a growing problem and one of the leading causes of sickness and death all around the world, the second after COVID-19 when considering infectious etiology[1].

The annual incidence of tuberculosis in Portugal has been consistently decreasing and since 2017 our country has been considered a country with low incidence of tuberculosis. However, this is not the picture of the whole country and tuberculosis continues to show a higher incidence in some regions, namely in the large urban centers of Oporto and Lisbon, where 25.3 and 23.7 cases per 100,000 inhabitants are reported, respectively[2]. In Portugal, all tuberculosis patients are referred to specialized pulmonology diagnostic centers, according to their place of residence, for treatment and appropriate surveillance of risk contacts.

Extrapulmonary tuberculosis represents 20-25% of notified tuberculosis cases[1,3] and a rare organ that may be affected is the eye, often leading to serious impairment in visual acuity and quality of life. The incidence and prevalence of this complex disease is variable, according to both individual risk factors and the tuberculosis burden of the region, ranging between 3.5 and 5.1 %[4].

In 2017 a Portuguese consensus on the management of diagnosis and treatment of ocular tuberculosis was published[5], which recommends the screening for tuberculosis in any uveitis of unknown etiology that recurs or not responds to conventional therapy. Moreover, it

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Table 1. Ocular tuberculosis proposed classification[5]

Confirmed ocular tuberculosis (both 1 and 2)	1. At least one clinical sign suggestive of ocular tuberculosis 2. Microbiological confirmation of Mycobacterium tuberculosis from ocular fluids/ samples
Probable ocular tuberculosis (1, 2, and 3 together)	1. At least one clinical sign suggestive of ocular tuberculosis (and other etiologies excluded) 2. Evidence of chest X-ray consistent with tuberculosis infection or clinical evidence of extraocular tuberculosis or microbiological confirmation from sputum or extraocular sites 3. At least one of the following: a. Documented exposure to tuberculosis b. Immunological evidence tuberculosis infection
Possible ocular tuberculosis (1, 2, and 3 together) or (1 and 4)	1. At least one clinical sign suggestive of ocular tuberculosis (and other etiologies excluded) 2. Chest X-ray not consistent with tuberculosis infection and no clinical evidence of extraocular tuberculosis 3. At least one of the following: a. Documented exposure to tuberculosis b. Immunological evidence tuberculosis infection 4. Evidence of chest X-ray consistent with tuberculosis infection or clinical evidence of extraocular tuberculosis but none of the characteristics given in 3

states that when there is suggestive ocular manifestations[6-8], together with evidence of tuberculosis exposure, either a positive Tuberculin Skin Test (TST) and/or Interferon gamma release assay (IGRA) test, ocular tuberculosis can be presumed and these patients should be treated for active tuberculosis. They also proposed a classification divided into confirmed ocular tuberculosis, probable ocular tuberculosis or possible ocular tuberculosis, as shown in Table 1[5,7]. The proposed treatment comprise the standard four drug anti-tuberculosis regimen with Isoniazid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E), over a period of 6-9 months and with regular follow-up reviews[5, 9-11].

Although a threatening disease, there is still not enough awareness for ocular tuberculosis. To better understand the epidemiology of ocular tuberculosis and sensitize health practitioners for this treatable disease, we intend to study and characterize the ocular tuberculosis population observed in a Portuguese specialized pulmonology diagnostic center.

MATERIALS AND METHODOLOGIES

Study Design

We conducted a retrospective study of individuals diagnosed with ocular tuberculosis, referred to and followed up in *Centro de Diagnóstico Pneumológico Dr. Ribeiro Sanches* (CDP-RS) (Lisbon) from 1st January 2016 until 31th December 2018.

Data were collected using their medical records and were documented and processed anonymously.

Setting

Although ocular tuberculosis has been recognized as a growing problem, its prevalence is unclear, since it depends not only upon individual factors but mostly on tuberculosis pervasiveness in each region and studies characterizing these patients' populations are scanty.

In Lisbon district CDP-RS is the diagnostic center of reference for tuberculosis, with an influence area of about 1.400.000 inhabitants. Hence, all cases of suspected ocular tuberculosis are referred to CDP-RS for exclusion of active pulmonary tuberculosis and treatment of ocular tuberculosis as indicated.

Patients and data collection

All patients with ocular tuberculosis evaluated in CDP-RS during the period of study were included and their medical records were assessed and reviewed.

Data included: sex, age, history of prior tuberculosis defined as two or more years before ocular tuberculosis diagnosis, known risk contact with tuberculosis, alterations on chest image, immunologic test results such as TST and/or IGRA (*QuantiFERON-TB Gold test*), location of ocular manifestation and anatomic classification of ocular tuberculosis (according to Standardization of Uveitis Nomenclature working group)[13], treatment duration and its adverse effects and clinical outcome. All data were processed anonymously and approval by the ethics committee of *Administração Regional de Saúde de Lisboa e Vale do Tejo* was obtained (6336/CES/2021).

Statistical analysis

A descriptive statistical analysis was performed using the Microsoft

Corporation (2013), Microsoft Office Excel 2013® software program and Fisher's exact test was performed using IBM SPSS Statistics for Windows v25.0 for statistical association analysis.

Continuous variables were presented as mean and standard deviation (SD), whereas categorical variables were expressed as frequency (percentage).

RESULTS

During the period of study there were 38 patients diagnosed with ocular tuberculosis and evaluated in CDP-RS, which is about 1,8% from the total number of registered cases of tuberculosis in CDP-RS in that period.

The clinical-demographic characteristics of patients with ocular tuberculosis are presented in Table 2. The mean age at time of diagnosis was 53,3 ± 15,7 years old (range 16-85) and there was a slightly higher percentage of females (55,3% vs 44,7% males). Screening for HIV was undertaken and none patient was positive for HIV infection. Regarding other comorbidities the most frequent reported were cardiovascular diseases like hypertension (n=13) and dyslipidemia (n=8), but there were also patients with hypothyroidism (n=6), depression (n=6), non-insulin dependent type 2 diabetes (n=4), benign prostatic hypertrophy (n=3), rheumatoid arthritis (n=2), including one patient under biological anti-TNF treatment, and epilepsy (n=1). Seven patients (18,4%) had history of previous tuberculosis, three (7,9%) were previously treated for latent tuberculosis, two (5,3%) had prior Lymph Node tuberculosis and one patient had prior Pulmonary tuberculosis. Of note, one patient was treated for presumed Ocular tuberculosis in the past and presented as a relapse. All of these patients were previously treated with a six months scheme of either HRZE in the cases of active tuberculosis or H in the cases of latent tuberculosis. The time elapsed until developing ocular tuberculosis ranged between 5 years, in the patient with previous ocular tuberculosis, 30 years in the case of previous pulmonary infection, and more than 50 years in the cases of the 2 patients who had had lymph node tuberculosis in their childhood. Among the patients with previous active tuberculosis disease there were no resistances reported.

Only two patients (5,3%) had a known history of risk contact with tuberculosis. All patients were screened for active tuberculosis disease by symptom questionnaire and chest image and none had suggestion of tuberculosis on a location other than ocular tuberculosis.

It was not possible to obtain a confirmed ocular tuberculosis diagnosis in any patient, because of the associated sample collection risk, therefore the majority of ocular tuberculosis diagnosis were possible (76,3%) and in nine cases the diagnosis was probable (23,7%).

None patient presented with a chest radiography suggestive of active pulmonary tuberculosis. However, at time of ocular tuberculosis diagnosis, three patients (7,9%) showed fibrotic changes on chest radiography and nine patients (23,7%) had a chest tomography showing sequels or residual signs of previous infection.

Positive TST was seen in 24 patients (63,2%) and the mean size of induration was 23,2 ± 9,3mm, whilst IGRA test were positive in 33 patients (86,8%) and negative in two patients (5,3%). In three patients it was not possible to access the IGRA result and it was classified as unknown IGRA result.

Table 2: Clinical and demographic characteristics of patients with ocular tuberculosis

Sex – n (%)		
Male	17	(44,7)
Female	21	(55,3)
Age – mean ± SD (years)	53,27 ± 15,72	
Prior tuberculosis – n (%)	7	(18,4)
Latent TB	3	(7,9)
Lymph Node	2	(5,3)
Pulmonary	1	(2,6)
Ocular	1	(2,6)
Tuberculosis contact – n (%)	2	(5,3)
Tuberculin Skin Test		
Positive TST – n (%)	24	(63,2)
Size of induration – mean ± SD (mm)	23,2 ± 9,3	
IGRA – n (%)		
Positive IGRA	33	(86,8)
Negative IGRA	2	(5,3)
Unknown result	3	(7,9)
Ocular tuberculosis classification – n (%)		
Confirmed	0	(0)
Probable	9	(23,7)
Possible	29	(76,3)

SD – standard deviation; TB – Tuberculosis; TST – Tuberculin Skin Test; IGRA – Interferon gamma release assay

The ocular manifestations as shown in Table 3 were bilateral in the majority of patients (44,7%). In unilateral cases of disease there was a tendency for right eye ocular tuberculosis, as seen in 31,6% cases, over the left eye, as seen in 23,7% cases. According to SUN (Standardization of Uveitis Nomenclature) working group anatomic classification, 14 patients (36,8%) presented with anterior uveitis, nine presented with posterior uveitis (23,7%) and two with intermediate uveitis (5,3%). Panuveitis was present in 13 patients (34,2%).

All patients were first proposed for a standard initial treatment regime with Isoniazid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E), however two patients had to undergo therapeutic change (Table 4). One patient experienced severe liver toxicity with Pyrazinamide and completed the two month initiation phase treatment with HRE, and another patient had hypersensitivity reaction to Rifampicin and had underwent HZE for the first two months of treatment and Isoniazid alone for continuation phase of treatment. The continuation phase for all other patients consisted of the standard regimen with Isoniazid and Rifampicin (HR). Noteworthy, in five patients Ethambutol was discontinued earlier due to concerns with ocular neuropathy. As for the other adverse effects, they were mostly mild and self-limited, such as arthralgia, paresthesia, gastrointestinal symptoms and hyperuricemia. Systemic corticotherapy was administered to 21 patients

Table 3: Ocular manifestations

Laterality of lesions – n (%)		
Bilateral	17	(44,7)
Unilateral – right eye	12	(31,6)
Unilateral – left eye	9	(23,7)
Anatomic Classification* of ocular tuberculosis – n (%)		
Anterior uveitis	14	(36,8)
Intermediate uveitis	2	(5,3)
Posterior uveitis	9	(23,7)
Panuveitis	13	(34,2)

* SUN working group anatomic classification

Table 4. Treatment scheme and outcomes of ocular tuberculosis

Treatment regime – n (%)		
HRZE	36	(9,5)
HRE[+]	1	(2,6)
HZE[++]	1	(2,6)
Systemic corticotherapy – n (%)	**21**	**(55,3)**
Completed treatment – n (%)	**29**	**(76,3)**
Clinical visual improvement – n (%)	21	(72,4)
Mean duration of treatment (months)	8,6 ± 2,1	

E – Ethambutol; H – Isoniazid; R – Rifampicin; Z – Pyrazinamide
[+]severe liver toxicity with Pyrazinamide; [++]hypersensitivity reaction to Rifampicin

(55,3%), according to ophthalmologist judgment and taking into account the inflammatory extension of ocular manifestations. Of note, no statistical significance in outcome was found when patients were under corticosteroids (p=0.525).

Nine patients (23,7%) dropped out of treatment and the mean duration of treatment was 8,6 ± 2,1 months. Among the 29 patients who had completed treatment, the majority (72,4%) presented clinical improvement or remission of the ocular manifestation, five patients had no improvement in their visual acuity probably related to other causes than ocular tuberculosis, namely glaucoma and ocular syphilis, and there was only one case of relapse.

DISCUSSION

Ocular tuberculosis is a rare extrapulmonary manifestation of tuberculosis and a challenging diagnosis. Since the variable clinical presentation and the difficulty in obtaining tissue samples, the diagnosis is frequently presumptive, which praises ophthalmologists' role to be aware of this hypothesis. That being said, all of our patients were referred by ophthalmologists for chronic inflammatory ocular diseases not responding to treatment and after exclusion of other common etiologies.

To our knowledge, there are no recent published studies characterizing the ocular tuberculosis population in Portugal. The last reports refers to 2011-2013[12] and 2012-2015[13], lacking studies about the epidemiology of this disease after Portugal had become a low incidence tuberculosis' country.

Albeit some ocular tuberculosis cases may present together with pulmonary tuberculosis[14], our study, similar to other published data[9, 12-15], showed that most cases occur in absence of systemic or respiratory manifestations. It must be noted that even though only seven patients had known history of previous tuberculosis and just two patients had known history of risk contact with tuberculosis, all of our studied patients had at least one positive immunologic test for tuberculosis exposure, either TST or IGRA, suggesting that a larger proportion of patient may have had previous unknown contact with the disease.

Apart from one patient who was immunosuppressed due to biological treatment for rheumatoid arthritis, all other patients had no relevant medical conditions that may impair their immune system.

A small proportion of patients had history of previous tuberculosis many years before and all had completed the 6 months treatment scheme, without any evidence of resistances. The reason for occurrence of a second infection is still unclear, but given the time lapsed and the high incidence of the tuberculosis in Lisbon we presumed they may have experienced a new infection rather than a reactivation of their previous infection.

The gold standard for ocular tuberculosis diagnosis relies on identification of *Mycobacterium tuberculosis* on a tissue sample or ocular fluid[10-11], however, the risk of that sample collection procedures and its low sensibility leads to a presumption diagnosis in the majority of cases[10,16], reflecting what was seen in our study, where all cases had a presumptive diagnosis.

Noteworthy, the exact mechanisms of disease is still unclear, which may comprise secondary hematogenous spread of *Mycobacterium* through ocular vasculature, or direct inoculation and entry into ocular surface, or even a hypersensitivity reaction to bacteria antigens[10,17].

The most common manifestations of ocular tuberculosis includes granulomatous uveitis, choroiditis, retinitis, blepharitis, vitritis and more rarely it may present as mucopurulent conjunctivitis[4,18]. Our patients presented mainly with anterior uveitis and panuveitis, but we could not clarify which specific form of ocular manifestation included in this anatomic classification they presented, since this specific information is lacking on their medical records. As opposed to other published reports[18], but interestingly similar to other Portuguese results[12-13], the ocular manifestations we found were most often bilateral, which may be explained by a potential hematogenous spread causing secondary ocular infection.

The standard four-drug treatment was proposed to all patients which they took for a mean of 8,6 ± 2,1 months, as stated by Portuguese consensus[5] and according to clinical evolution reported by their ophthalmologist. The majority of them had good tolerance to therapy with only minor adverse effects, whereas two patients had to undergo an alternative treatment because of severe liver toxicity and hypersensitivity reaction. Although some authors advocate longer courses of treatment[9], others state that a minimum of six months treatment comes up with good visual outcomes[19] and the clinical improvement noted in 72,4% patients in our study supports this 6-9 months period of treatment. Another controversial point about ocular tuberculosis treatment is the concomitant use of corticotherapy[9-11,20], and whilst some studies support its use others had shown no benefit or

even a major risk of relapse when corticotherapy was used. In our study 55,3% patients underwent systemic corticosteroids along with the anti-tuberculosis drugs, as by ophthalmologist judgment, whose decision criteria we could not retrospectively elucidate because of different ophthalmologic institutions and different ophthalmologists referred the patients. We did not find any differences in outcome when patients were under corticosteroids and there was only one case of relapse in the whole study, therefore, our study could not clearly enlighten whether or not corticosteroids may be beneficial.

What might limit our study is that it comprises a retrospective analysis including only patients from Lisbon district, howsoever, it has the influence of a huge area of population and we believe it may portray the national situation. Another limitation is that all ocular tuberculosis were presumed cases which means we cannot perform microbiology analysis, nevertheless, taking into account the restrictions implied in obtaining a confirmed diagnosis, this may reflect the reality in most centers worldwide. In addition, it must be noted that it was stated that a good response to treatment also supports the diagnosis and we attended a remarkable clinical improvement in most of our patients. It should also be mentioned that all patients were referred from ophthalmologists of outside institutions, which limited the characterization of patient's specific ocular manifestations.

Our study intended to show that ocular tuberculosis, despite being a rare condition, is probably underdiagnosed and carries a huge burden in health care centers, aside from restricting people's quality of life. Likewise, while ocular tuberculosis diagnosis is hard to achieve, the delay in starting proper treatment can result in permanent blindness, which can be distressing for clinicians. For that matter, we consider that the publication of a national consensus was a turning point clarifying diagnosis criteria and guiding management treatment.

Ultimately, we believe it is important to know the latest epidemiologic trend of ocular tuberculosis and by doing that our study may help understand and increase awareness among clinicians about this disease.

CONFLICT OF INTEREST
The authors declare that there is no conflict of interest in this work.

ETHICAL DISCLOSURE
This study was conducted in accordance with the Helsinki Declaration of the World Medical Association and was approved by the Ethics Committee for Health of Administração Regional de Saúde de Lisboa e Vale do Tejo (6336/CES/2021). Nevertheless, all data were processed anonymously.

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REFERENCES

1. Global tuberculosis report 2021. Geneva: World Health Organization; 2021. Accessed on November 13, 2021: https://www.who.int/publications/i/item/9789240037021
2. Programa Nacional para a Tuberculose. Tuberculose em Portugal 2018 (dados provisórios). Direção Geral da Saúde SVIG-TB 2019. Accessed on November 18, 2021: https://www.dgs.pt/paginas-de-sistema/saude-de-a-a-z/programa-nacional-para-a-tuberculose.aspx
3. Ramírez-Lapausa M, Menéndez-Saldaña A, Noguerado-Asensio A. Extrapulmonary tuberculosis: an overview. Rev Esp Sanid Penit. 2015;17:3–11.
4. Abdisamadov A, Tursunov O. Ocular tuberculosis epidemiology, clinic features and diagnosis: A brief review. Tuberculosis. 2020; 124:101963.
5. Figueira L, Fonseca S, Ladeira I, Duarte R. Ocular tuberculosis: position paper on diagnosis and treatment management. Rev Port Pneumol. 2017;23(1):31-38.
6. Gupta A, Bansal R, Gupta V, Sharma A, Bambery P. Ocular signs predictive of tubercular uveitis. Am J Ophthalmol. 2010;149(4):562-70.
7. Gupta A, Sharma A, Bansa lR, Sharma K. Classification of intraocular tuberculosis. Ocul Immunol Inflamm. 2015;23:7-13.
8. Jabs DA, Nussenblatt RB, Rosenbaum JT (Standardization of Uveitis Nomenclature (SUN) Working Group). Standardization of uveitis nomenclature for reporting clinical data. Results of the first international workshop. Am J Ophthalmol. 2005;140(3):509-16.
9. Agrawal R, Gupta B, Gonzalez-Lopez JJ et al. The role of anti-tubercular therapy in patients with presumed ocular tuberculosis. Ocul Immunol Inflamm. 2015;23(1):40-6.
10. Shakarchi FI. Ocular tuberculosis: current perspectives. Clin Ophthalmol. 2015; 9:2223-7.
11. Gupta V, Gupta A, Rao NA. Intraocular tuberculosis – an update. Surv Ophthalmol. 2007;52:561-87.
12. Portelinha J, Picoto M, Marques A, Isidro F, Guedes M. Tuberculose ocular presumida. Oftalmologia. 2013;37:227-235.
13. Teixeira-Lopes F, Alfarroba S, Dinis A, Gomes MC, Tavares A. Ocular tuberculosis – a closer look to an increasing reality. Pulmonology. 2018; 24(5):289–93.
14. Lara LPR, Ocampo Jr V. Prevalence of presumed ocular tuberculosis among pulmonary tuberculosis patients in a tertiary hospital in the Philippines. J Ophthalmic Inflamm Infect. 2013;3(1):1.
15. Krassas N, Wells J, Bell C, Woodhead M, Jones N. Presumed tuberculosis-associated uveitis: rising incidence and widening criteria for diagnosis in a non-endemic area. Eye. 2018; 32: 87–92
16. Ang M, Vasconcelos-Santos DV, Sharma K et al. Diagnosis of ocular tuberculosis. Ocul Immunol Inflamm. 2018;26(2):208-216.
17. Agarwal M, Shrivastav A. An update on tubercular uveitis. J Clin Exp Ophthalmol. 2017;8.
18. Shahidatul-Adha M, Zunaina E, Liza-Sharmini AT et al. Ocular tuberculosis in Hospital Universiti Sains Malaysia – A case series. Ann Med Surg. 2017; 24: 25–30.
19. Manousaridis K, Ong E, Stenton C, Gupta R, Browning AC, Pandit R. Clinical presentation, treatment, and outcomes in presumed intraocular tuberculosis: experience from Newcastle upon Tyne, UK. Eye. 2013; 27(4):480-6.