Nocardiosis diseminada

Disseminated nocardiosis – a case report

Tiago Guimarães Costa, Luís Rocha, Luciana Silva, Inês Rato, Sara Pinto
Internal Medicine. Centro Hospitalar de Vila Nova de Gaia/Espinho. Vila Nova de Gaia (Portugal)

ABSTRACT

Nocardiosis, caused by various species of *Nocardia*, poses diagnostic and therapeutic challenges due to its diverse clinical presentations that often mimic other infections and malignancies. We present the case of a 72-year-old woman with a history of autoimmune hepatitis and diabetes *mellitus* (DM) who initially presented with fever, headaches, and confusion. Extensive investigations revealed an ischemic lesion in the central nervous system (CNS) attributed to vasculitis.

Two months later, returned with literal paraphasia, ocular symptoms (red eye and retro-orbital pain), and fever. Despite negative blood cultures, *Nocardia cyriacigeorgica* was isolated from vitreous humour and lung tissue, confirming the diagnosis of disseminated nocardiosis. Treatment included trimethoprim/sulfamethoxazole (TMP/SMX), Meropenem, and Linezolid, led to significant improvement.

This case underscores the diagnostic complexity of Nocardiosis, emphasizing the need for early and precise diagnosis, multidisciplinary care, and prolonged treatment in severe cases. Further research is required to optimize therapeutic protocols, particularly in CNS-involved nocardiosis.

Keywords: Nocardia, immunodepression, CNS infection, vasculitis.

RESUMEN

La nocardiosis, causada por varias especies de *Nocardia*, plantea retos diagnósticos y terapéuticos debido a sus diversas presentaciones clínicas que a menudo imitan otras infecciones y neoplasias. Presentamos el caso de una mujer de 72 años con antecedentes de hepatitis autoinmune y diabetes *mellitus* (DM) que inicialmente presentó fiebre, cefaleas y confusión. Investigaciones exhaustivas revelaron una lesión isquémica en el sistema nervioso central (SNC) atribuida a vasculitis.

Dos meses después, regresó con parafasia literal, síntomas oculares (ojo rojo y dolor retro-orbital) y fiebre. A pesar de los hemocultivos negativos, se aisló *Nocardia cyriacigeorgica* del humor vítreo y del tejido pulmonar, lo que confirmó el diagnóstico de nocardiosis diseminada. El tratamiento, que incluyó trimetoprim/sulfametoxazol (TMP/SMX), Meropenem y Linezolid, condujo a una mejoría significativa.

Este caso subraya la complejidad diagnóstica de la Nocardiosis, haciendo hincapié en la necesidad de un diagnóstico precoz y preciso, una atención multidisciplinar y un tratamiento prolongado en los casos graves. Es necesario seguir investigando para optimizar los protocolos terapéuticos, especialmente en la nocardiosis con afectación del SNC.

Palabras clave: Nocardia, inmunodepresión, infección del sistema nervioso central, vasculitis.

CASE PRESENTATION

A 72-year-old woman, living independently, with a medical history of autoimmune hepatitis managed with a daily dose of 50 mg azathioprine, as well as DM, was admitted to the hospital for an evaluation of her fever, headaches, and confusion. Extensive analytical, immunological, and cerebrospinal fluid (CSF) studies did not reveal any significant abnormalities (Table 1). Cultures of her blood, urine, and CSF all came back negative (Table 2). Brain magnetic resonance imaging (MRI) revealed small ischemic lesions in partial territory of the middle cerebral artery (Figure 1), due to a vascular stenosis involving this vessel, shown in the angio-MR. Digital subtraction angiography of the cerebral vessels confirmed the vascular stenosis and it was immediately treated with angioplasty (Figure 2).

However, her hospitalization became complicated when she experienced a seizure and developed literal paraphasia. Subsequent MRI showed progression and new multiple ischemic lesions in the same territory (Figure 3). A new angiography was performed, which confirmed the patency of the previously dilated vessel. A "vessel-wall" MRI study revealed contrast uptake suggestive of inflammatory etiology. Based on clinic and imaging findings, it was presumed that CNS vasculitis was the underlying cause, and she was discharged with a prescription for azathioprine 75mg and prednisolone at a dose of 1 mg/kg/day (60 mg prednisolone), which was maintained for one month, before starting tapering.

Two months later, she returned to the hospital due to worsening previous language deficits, a red eye (Figure 4), retro-orbital pain, and persistent fever. Laboratory tests revealed anemia, leukocytosis, elevated erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels (Table 1). Although she had no respiratory symptoms, the septic focus investigation included a chest x-ray that demonstrated hypotransparency in the right apex, better characterized by chest CT (Figure 5). Additionally, she had a granulomatous lesion in her left eye, leading to a diagnostic vitrectomy. During her hospitalization, she remained febrile and experienced another seizure, accompanied by a decreased level of consciousness. A repeat lumbar puncture showed CSF findings suggestive of a bacterial infection (Table 2). A contrast-enhanced MRI unveiled multiple new lesions consistent with supratentorial and posterior fossa abscesses (Figure 6). Despite extensive bacteriological, mycobacteriological, and mycological examinations of blood, sputum, bronchial wash, bronchoalveolar lavage, and CSF, no pathogens were identified. However, *Nocardia cyriacigeorgica* was isolated from the vitreous humor, and a lung biopsy confirmed the diagnosis of pulmonary nocardiosis (Figure 7). Antibiogram showed sensibility to amikacin, ceftriaxone, cotrimoxazole, imipenem and linezolid, and resistance to ciprofloxacin.

She was promptly initiated on a treatment regimen consisting of TMP/SMX, Meropenem, and Linezolid for disseminated nocardio-

Correspondencia: 12484@chvng.min-saude.pt
Cómo citar este artículo: Guimarães T, Rocha L, Silva L, Rato I, Pinto S.
Disseminated nocardiosis – a case report. Galicia Clin 2024; 85-3: 31-33.
Recibido: 29/09/2023 ; Aceptado: 09/11/2023 // https://doi.org/10.22546/75/4162

Figure 1. Brain MRI showing acute small ischemic lesions in partial left middle cerebral artery territory.

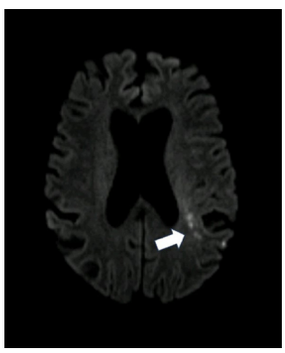


Figure 2. Digital subtraction angiography confirming a sub-occlusive stenosis involving a proximal branch of the left middle cerebral artery (arrow on the left); angioplasty was performed successfully (arrow on the right).

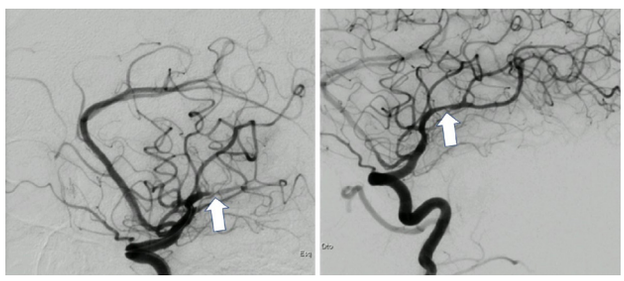
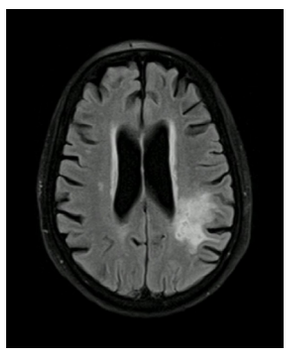


Figure 3. Brain MRI showing progression and new ischemic lesions in the same arterial territory.



sis affecting her lungs, CNS, and eyes. After completing a six-week course of treatment, she displayed significant improvement and was discharged on TMP/SMX and Amoxicillin/Clavulanic Acid which she kept doing for another 12 months.

Her recovery was closely monitored, and she received ongoing care and rehabilitation at a Continuity of Care Unit. After more than a year of follow-up under the Internal Medicine department's care and six months of rehabilitation, she achieved an impressive level of autonomy. Importantly, there were no recurrences of seizures or any new symptoms during this period.

Figure 4. Red eye demonstrating ocular involvement of nocardiosis.

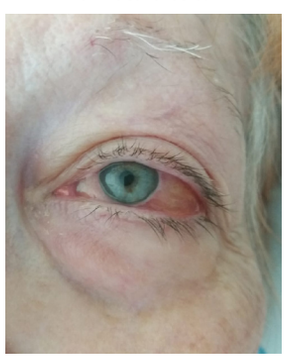
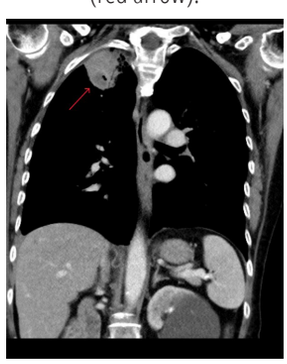


Figure 5. Chest CT scan showing right apical mass (red arrow).



DISCUSSION

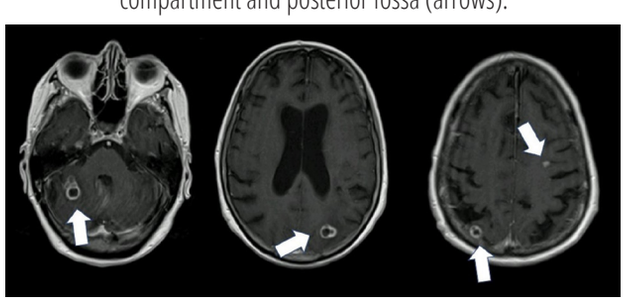
The presented case highlights the complexities and challenges associated with Nocardiosis. These infections can manifest in diverse clinical presentations, often resembling other infections and even malignancies.

The lungs serve as the primary site of *Nocardia* infection due to the inhalation of airborne pathogens. However, *Nocardia* also displays a unique affinity for neural tissue, leading to parenchymal abscess formation within the CNS.[3]

A key observation in this case is the neurological manifestation of Nocardiosis, which can make it difficult to distinguish from other diseases. The patient's language deficits were initially due to a likely vasculitic stroke. However, during her second hospitalization, the worsening of these deficits was probably due to CNS involvement from *Nocardia*. Therefore, these neurological signs could have been neglected and not investigated with MRI and lumbar puncture, which later demonstrated CNS infection and brain abscesses. This emphasizes the critical importance, particularly in immunocompromised patients, of ruling out infectious complications and considering less typical causative agents.

Corticosteroid therapy initiation may be linked to nocardial infection. The patient, already immunocompromised from prior azathioprine use for autoimmune hepatitis, began high-dose corticosteroids (60 mg prednisolone). As indicated by Margalit *et al.*, treatment with any immunosuppressive agent, particularly systemic corticosteroid therapy, was strongly linked to an elevated risk of nocardiosis.[4]

Figure 6. Contrast-enhanced MRI unveiled multiple new ring-enhancing lesions consistent with abscesses both in the supratentorial compartment and posterior fossa (arrows).



This raises the question of whether the patient should have undergone prophylaxis with TMP/SMX at the time of initiating a high dose of corticosteroids, which would be primary prophylaxis for *Nocardia* and *Pneumocystis jirovecii* infection. TMP/SMX prophylaxis is protective against nocardiosis in certain populations, as demonstrated in a study by Goodlet *et al.*[5]

Effective *Nocardia* infection treatment requires combination antimicrobial therapy due to varying resistance patterns in clinical isolates. Empiric therapy typically employs two or three agents, especially in severe cases. Since all disseminated nocardiosis cases are considered severe, a three-drug regimen was used. Meropenem was preferred over imipenem for its lower seizure risk, and linezolid was chosen for its lower nephrotoxicity risk compared to amikacin. TMP-SMX is com-

Table 1. Evolution of analyses.

	First hospitalization	Second hospitalization	Hospital discharge	After 1 year of follow-up	Normal range
Hemoglobin	12,6 g/dL	8.2 g/dL	9.6 g/dL	12.3 g/dL	12.0-16.0
Leucocytes	7300/µL	12470/µL	6800/µL	9500/µL	3.6-11.0
CRP	0.15 mg/dL	7.18 mg/dL	0.06 mg/dL	0.04 mg/dL	0-0.5
ESR	29 mm/h	92 mm/h	6 mm/h	10 mm/h	0-20

CRP (C-Reactive Protein), ESR (Erythrocyte Sedimentation Rate)

Table 2. Evolution of cerebrospinal fluid.

		First hospitalization	Second hospitalization		Normal range
Colour		colorless	colorless		colorless
Erythrocytes		100/µL	200/µL		0
Leucocytes		2/µL	1567/µL	Polymorphonuclear 90%	0-5
				Mononucleates 10%	
Glucose		81 mg/dL	69 mg/dL		40-70
LDH		22 U/L	102 U/L		0-40
Proteins		53 mg/dL	136 mg/dL		15-45
Syphilis	VDRL	non-reactive	non-reactive		non-reactive
	TPHA	< 1/20	< 1/20		< 1/20
ADA		0.6	3		0-9

ADA (Adenosine Deaminase), LDH (Lactate Dehidrogenase), TPHA (Treponema Pallidum Hemagglutination), VDRL (Venereal Disease Research Laboratory)

monly recommended as a first-line therapy, but the optimal treatment duration is debated, with most experts advocating a prolonged course to prevent *Nocardia* infections from relapsing. In certain cases, treatment may extend for several months to over a year, especially when the CNS is involved[6]. In this case, after six weeks of intravenous antibiotics, a two-drug oral scheme was preferred over TMP-SMX alone, due to the severity of the clinical condition. Although *N. cyriacigeorgica* is often resistant to amoxicillin/clavulanate, resistance was not reported in the antibiogram, as it wasn't tested, and it was used in association with TMP-SMX. Furthermore, susceptibility test results don't always correlate with treatment outcomes for *Nocardia*[7], and the patient was closely monitored, displaying favorable clinical progress.

This case underscores the importance of early and accurate diagnosis, the necessity for a prolonged treatment regimen in severe nocardiosis and the critical role of rehabilitation in achieving favorable outcomes, as demonstrated by the patient's remarkable recovery.

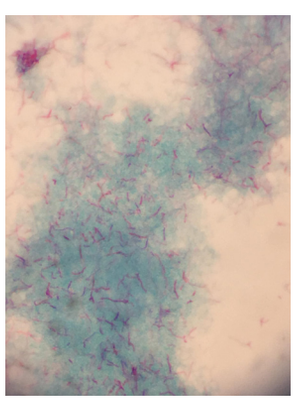


Figure 7. *Nocardia* colony culture smear stained by modified ziehl neelsen at 1000x magnification.

CONFLICT OF INTEREST
The authors declare that they have no conflict of interests.

SOURCE OF FUNDING
This research had no funding sources.

ETHICAL ASPECTS
All participants submitted a consent form to be included in this study.

BIBLIOGRAPHY

1. Duggal SD, Chugh TD: Nocardiosis: A Neglected Disease. Med Princ Pract. 2020, 29:514-523.
2. Jain S, Duggal S: Nocardial Infections: An Under-Diagnosed Malady of Immunocompromised Hosts. J Immunol Tech Infect Dis. 2013, 2:4.
3. Branco L, Rodriguez-Nava V, Boiron P, Pinheiro D: Disseminated nocardiosis: report of five cases. JMM Case Rep. 2015, 2:1-6.
4. Margalit I, Goldberg E, Ben Ari Y, et al.: Clinical correlates of nocardiosis. Sci Rep. 2020, 10:14272.
5. Goodlet KJ, Tokman S, Nasar A, Cherrier L, Walia R, Nailor MD: Nocardia prophylaxis, treatment, and outcomes of infection in lung transplant recipients: A matched case-control study. Transpl Infect Dis. 2021, 23:e13478.
6. Wilson JW: Nocardiosis: Updates and Clinical Overview. Mayo Clin Proc. 2012, 87:403-407.
7. Yagi K., Ishii M., Namkoong H. et al.: Pulmonary nocardiosis caused by Nocardia cyriacigeorgica in patients with Mycobacterium aviumcomplex lung disease: two case reports. BMC Infect Dis. 2014, 14:684.