Disseminated Nocardiosis with Ocular Involvement in a Patient with Anca-associated Vasculitis

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ABSTRACT

A 62-year male patient, diagnosed with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), developed proptosis and decrease in visual acuity while on rituximab treatment. As the ophthalmological examination and imaging studies could not exclude tumour of the orbit, enucleation of the orbit was performed. The histopathology displayed necrosis and inflammation. Because the clinical, laboratory and pathological findings of the patient suggested a vasculitis exacerbation, the immunosuppressive treatment was continued. However, the patient developed confusion and hemiplegia with cerebral mass lesions on imaging. The subsequent report of the pathology revealed a nocardial infection of the eye. The patient was diagnosed with nocardiosis with ocular and cerebral involvement. Despite efficient antimicrobial therapy, the disease progressed rapidly causing death. This case is unique as it describes disseminated nocardiosis with ocular and cerebral involvement in an AVV patient.

Key Words: *Immunosuppression, Nocardiosis, ANCA-associated vasculitis, Proptosis.*

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INTRODUCTION

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a rare heterogenous group of diseases that are characterised by necrotising inflammation in small and medium-sized vessels.[1] While the outcome of the disease is improved with immunosuppressive drugs, some patients develop side effects such as life-threatening infections. Nocardiosis is a rare opportunistic infection caused by gram-positive, aerobic, acid-fast stained filamentous bacterium species *Nocardia*.[2] Its most frequent clinical presentation is pulmonary infection.[3] Ocular nocardiosis is extremely rare.[4] It presents with insidious, painless vision loss and is associated with poor outcomes.[5]

Herein, a fatally presenting disseminated nocardiosis with ocular and cerebral involvement that occurred in a patient who received long-term immunosuppressive treatment due to AAV will be discussed. As far as we know, this is the first case of AAV complicated with ocular and cerebral nocardiosis.

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CASE REPORT

A 62-year male patient with no relevant past medical history was admitted to the hospital with complaints of cough, night sweats, and weight loss. The laboratory tests showed an elevated erythrocyte sedimentation rate (ESR) of 109 mm/1st h and C-reactive protein (CRP) of 111 mg/L. Thoracoabdominal computerised tomography (CT) showed extensive diffuse ground-glass density in both lungs with nodular areas. Meanwhile, hyperemic nodular lesions emerged on the right leg of the patient and the skin biopsy showed leukocytoclastic vasculitis and findings compatible with necrotizing vasculitis. Antinuclear antibody (ANA) and ANCAs (anti-proteinase-3, anti-myeloperoxidase) were negative. In the bone marrow biopsy, there was no evidence of lymphoproliferative or infectious disease. In the follow-up of the patient, episcleritis developed in his left eye. The patient was diagnosed with AAV and cyclophosphamide with concomitant methylprednisolone was initiated. After six months of induction treatment, regression of complaints and inflammatory markers were observed.

Therefore, the maintenance phase by azathioprine (AZA) and corticosteroid dose reduction was initiated. While on AZA treatment, new nodular lesions on the lower extremities and in the lung emerged with an increase in inflammatory markers. On the development of these a findings, relapse of vasculitis was suspected and his treatment was switched to rituximab (RTX). Six months after RTX initiation, he started having complaints of redness, increased lacrimation, and decreased visual acuity in the right eye. Initial ophthalmological examination revealed neovascular glaucoma, vitreal haemorrhage and choroidal detachment of the right eye. The diffusion magnetic resonance imaging (MRI) of the right orbit revealed diffuse contrast in the sclera, an increase in

the vitreal intensity, choroidal detachment, and focal diffusion restriction in the posterior part of the bulb (Figure 1).

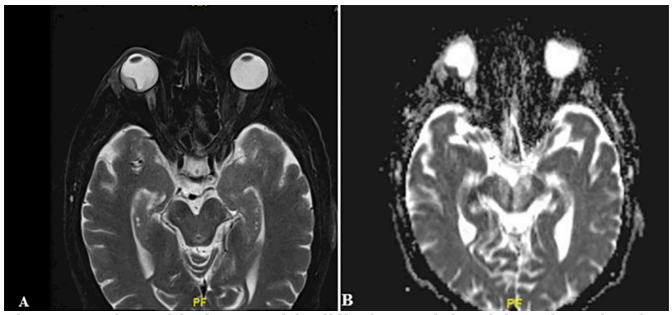

Figure 1: The orbital MRI with diffusion-weighted imaging showing orbital mass of the right eye (A) with abnormal diffusion restriction (B) Axial T2-weighted image showing right orbital mass.
Axial Diffusion-weighted Imaging (DWI) showing abnormal focal diffusion restriction.

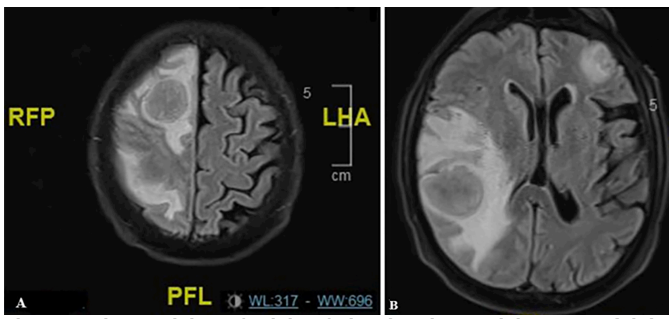

Figure 2: The cranial MRI (Axial, T2) showing the cranial masses of right frontal (A), right parietal (B) and left frontal (B) lobes.

As the findings of the ophthalmological examination, orbital MRI, and laboratory findings were compatible with vasculitis relapse, a second dose of RTX was given. However, the visual acuity of the right eye continued to decrease progressively with newly developing proptosis. Thus, a second orbital diffusion MRI was performed four months after the first evaluation which showed diffuse contrasting of the right sclera, choroid and ciliary body and a contrasting focal area of 5 mm diameter at the posterior superior aspect of the eye bulb. These findings were reported as progressive when compared with the previous imaging and vasculitis flare, infectious or neoplastic processes were suggested to be considered in the differential diagnosis. As an intraorbital tumour could not be excluded, enucleation surgery was carried out by ophthalmologists. The initial report of the eye pathology was described as a diffuse and severe destructive suppurative inflammatory lesion in the eye bulb with occasional areas of necrotic tissue without signs of a neoplastic process. Therefore, the patient received his third RTX dosage. After a few weeks, the patient was admitted to the hospital with mental confusion and hemiplegia on his left side. The cranial diffusion MRI showed cystic mass lesions of 3.5×3 cm in the right frontal, 4×3 cm in the right parietal and 1.3×1.0 cm in the left frontal lobes with peripheral contrast enhancement in the postcontrast series (Figure 2). In the differential diagnosis, primary tumours of central nervous system, metastatic lesions, and vasculitis relapse were suspected. Meanwhile, the subsequent report of the eye pathology reported thin filamentous microorganisms that had features compatible with *nocardia* in areas with intense inflammation. Therefore, the cerebral mass lesions on MRI were suspected to be due to cerebral nocardiosis. As a result, the patient was diagnosed with disseminated nocardiosis with ocular and cerebral involvement and treatment with Trimethoprim/sulfamethoxazole (TMP/SMX) and imipenem was started. However, a refractory septic shock developed during his follow-up and death was confirmed after unresponsiveness to resuscitation.

The incidence of nocardiosis in immunosuppressive patients is reported between 0.4% and 3.6% with a mortality rate of 77%.[6] Patients with the highest risk of infection are those who have been using steroids or drugs suppressing cellular immunity. Even though nocardia infections are well-defined, due to the rarity of the disease, diagnosis is often delayed. As in this case, Nocardia infections mimic features of vasculitis which may cause misdiagnosis, diagnostic delay and treatment failure. Therefore, opportunistic infections should always be considered in the differential diagnosis of cases of vasculitis.

PATIENT'S CONSENT:

The authors state that informed consent has been obtained from the legal representatives of the patient to publish the data concerning this case.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

ABKD, SS, MEY, GK: Interpretation of data, drafting of the work, final approval, and agreement for all aspects of the work.

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