CASE REPORT

Tuberculosis with Secondary Vasculitis Presenting as a Nasal Septal Perforation

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ABSTRACT

A 45 years old man with tuberculosis (TB) and secondary vasculitis presented with perforation of the nasal septum, involving skin and cranial nerves. Vasculitis is a recognized, tough rare complication of tuberculosis and has not been previously described in the literature as a cause of nasal septal perforation. It presents a diagnostic dilemma. The diagnostic challenges of this case are outlined, and the clinical implications are discussed.

Key words: *Tuberculosis. Vasculitis. Perforation. Nasal septum.*

INTRODUCTION

Tuberculosis may masquerade many diseases. Vasculitis is a recognized, though rare, complication of tuberculosis that can present a particularly difficult diagnostic dilemma. Though described in other conditions such as retinal vasculitis and peripheral vasculitis causing limb gangrene,[1,2] it has not previously been described as a cause for nasal septal perforation.

This case, therefore, has some uncommon features worth reporting.

CASE REPORT

A 45 years old Asian gentleman presented to the Rheumatology Department with fever, night sweats, weight loss, a rash on his legs and a blocked nose of several weeks' duration. He reported no cough, shortness of breath, chest pain or haemoptysis. His past medical history included chronic rhinosinusitis and a fully resolved Bell's palsy. He did not take any medications and was a non-smoker.

Examination revealed bilateral axillary lymphadenopathy. The rash on his legs involved his shins, and clinically seemed vasculitic in nature. The rest of the examination was normal.

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He was admitted for treatment and investigations. Blood tests revealed a raised CRP of 70 mg/L and an ESR of 57 mm/ first hour. His $_{Y}$GT level was 778 IU/L, and ALP level was 681 IU/L suggesting an intra-hepatic cholestasis. All other blood investigations were normal including rheumatological markers (ANA, ANCA, and ENA [extractable nuclear antibodies]), which were negative. His 24-hour urine collection and urinalysis were unremarkable and did not reveal casts. A chest X-ray showed patchy changes at the right heart border. A Heaf test was strongly positive. An axillary lymph node biopsy was arranged, histopathology of which showed epithelioid granuloma formation with central caseation necrosis in keeping with a diagnosis of tuberculosis (TB, Figure 1).

He was discharged having started TB chemotherapy (rifampicin, ethambutol, pyrazinamide) but his symptoms deteriorated. He complained of continued weight loss, listlessness, malaise, ongoing nasal blockage and developed double vision. Examination now revealed palsy of the right third and fourth cranial nerves, a right sided ptosis, and a mid-septal perforation of the cartilaginous septum with irregular edges that were granular in appearance. There was no bony septal involvement. The rash on his shins, however, was resolving. The rest of his neurological examination was normal. When further questioned, he denied any prior history of nasal or septal surgery.

He was re-admitted for further investigations and his immunoglobulin levels were found to be high but there was no evidence of cryoglobulins. His ALT and $_{Y}$GT remained high, but ALP had returned to normal. Hepatitis A, B and C serology and serum ferretin were all negative. ANA was repeated, which was positive, but the low level of the titres suggested a positive result due to TB rather than a connective tissue disorder. Smooth muscle markers were negative. Serum ACE was tested to exclude sarcoidosis and was negative. A CT of his chest showed no abnormality and an MRI of his orbits

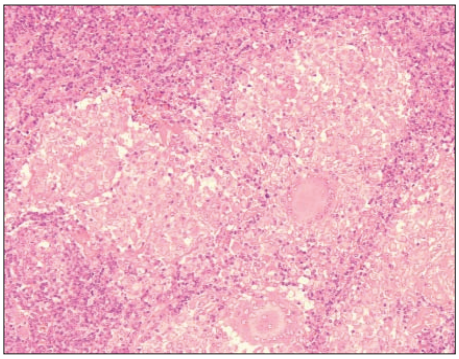

Figure 1: Lymph node biopsy showing epithelioid granuloma with central caseation (H&E stain, x 200 mag).

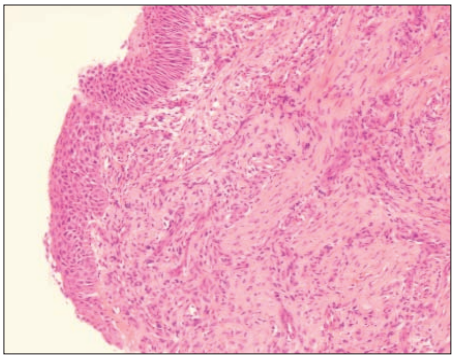

Figure 2: Nasal septal perforation biopsy showing chronic active inflammation (H&E stain, x 200 mag).

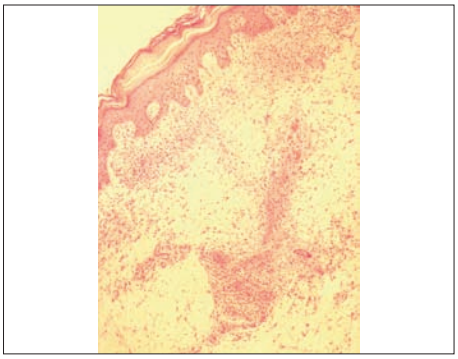

Figure 3: Low power view of skin showing widespread angiocentric inflammation and oedema in the dermis (H&E stain, x 40 mag).

showed them to be clear of granulomata, vasculitis or oedema. Lumbar puncture was attempted without success.

The ocular, nasal and skin findings raised the possibility of an undiagnosed underlying connective tissue disorder occurring simultaneously with his TB. He was reviewed by the ENT team. Besides his history of chronic rhinosinusitis, his ENT history was otherwise unremarkable. Examination revealed an anterior nasal septal perforation. The external nose, osteomeatal complexes, post-nasal space and turbinates were otherwise normal. As the cause of the septal perforation and cranial nerve palsies was not known, a biopsy of the edge of the septal perforation was performed to rule out Wegener's granulomatosis. It revealed chronic active inflammation only, with no evidence of granulomata (Figure 2).

At the same time a biopsy of the rash on his legs was performed and this revealed a necrotizing granulomatous vasculitis with no eosinophils, hence ruling out a connective tissue disorder as a cause of his rash (Figure 3). A final diagnosis of TB with secondary affecting the cranial nerves, nasal septum and skin was made. Prednisolone was added to his anti-TB medication. He continued to improve with resolution of his cranial nerve palsies. The septal perforation is being managed conservatively.

DISCUSSION

Vasculitis is a term used to describe a heterogeneous group of diseases that result in inflammation of both arteries and veins of any size, which may ultimately leads to ischaemic end-organ damage. Because the pattern of vessel involvement is highly variable, the clinical presentation of vasculitis is exceedingly broad. Often, a diagnosis is not reached until more specific organ damage has occurred.[3]

Vasculitis is generally classified by the size of blood vessel it affects. There are three main categories: large-vessel vasculitis (temporal and Takayasu arteritis), medium-vessel vasculitis (polyarteritis nodosa and Kawasaki disease) and small-vessel vasculitis (including Wegener's granulomatosis, Churg-Strauss syndrome and Henoch-Schönlein purpura).[3] TB vasculitis, or tropical vasculitis as it is also known, is one of the rarer infection-related vasculitides that affects large blood vessels, including the aorta, and does not seem to discriminate for age or gender.[4,5] When it affects blood vessels of the central nervous system, it can become exceedingly difficult to differentiate the presenting clinical manifestations from TB meningitis.

TB meningitis was high on the list of this patient's differential diagnosis, but it was ruled out for several reasons. A lumbar puncture was unsuccessful. In the light of the histological findings of the vasculitic leg rash, this patient's cranial nerve palsies were more in keeping with a vasculitic phenomenon as opposed to TB meningitis. Also, patients presenting with TB meningitis tend to develop neurological manifestations early on in the course of the illness as opposed to months after the initial presentation as was the case in this patient. The timing of the patient's response to medications also aided with the diagnosis: despite very atypical symptoms, he eventually became well with anti-tuberculosis chemotherapy. So, though a meningitis-type picture was eventually ruled out, there was enough clinical evidence to suspect the presence of tuberculosis. In addition, his rash responded well to oral steroids, suggesting its vasculitic nature.

The patient developed an intra-hepatic cholestasis, but an autoimmune cause was deemed unlikely due to his smooth muscle markers being negative, and ALT remaining normal. His anti-TB medication was not cited as a cause, as the cholestasis antedated its initiation. The cholestasis was eventually linked to the TB, a well documented, albeit uncommon, phenomenon of the disease.

Imaging may be useful in the diagnosis of a vasculitis, especially of that occurring in the central nervous system. MRI and angiography are the most common modalities employed.[6] This patient had an MRI of his orbits following the disturbance in his vision. This was negative. Ideally, an angiogram would have been

performed, but the diagnosis of TB vasculitis was made retrospectively, and hence there was no clear indication for an angiogram at that time.

The appearance of a nasal septal perforation or ulcer or its location does not predict the clinical diagnosis.[7] However, systemic disease may still be suspected in unclear nasal septal perforation. It has been shown that biopsy of the nasal septum does not seem to be useful in the diagnosis of systemic disease, except when granulomata or vasculitis are found, and is unlikely to contribute to the management of patients unless the supportive tests of ANCA and ACE are abnormal or unless malignancy is suspected.[4] This patient's ANCA and ACE were both negative, but because of the presence of his vasculitic rash, it was deemed reasonable to perform a biopsy of the perforation edge anyway in an attempt to rule out all other diagnoses and hence strengthen the clinical suspicion of a TB vasculitis. In searching for a cause, evidence suggests that taking a thorough history, performing a full examination and requesting relevant blood investigations may be more useful in gleaning the cause of the perforation than actually performing a biopsy of its edge, unless carcinoma is suspected.[7]

Management involves first addressing the causative disease process once identified, before undertaking specific treatment of the perforation. Many perforations are incidental findings and asymptomatic, requiring no intervention. Perforations that cause symptoms such as crusting or bleeding may require intervention. This may be in the form of conservative measures such as barrier creams and silver nitrate cautery to granulations arising at the edge of the perforation, or closure of the perforation. The use of silastic buttons has been described, as have a variety of surgical procedures, including the use of oral mucosal flaps, inferior turbinate grafts, composite cartilage grafts, titanium membrane and acellular human dermal allograft.[8-10]

TB vasculitis is a rare cause of septal perforation, but is one that may become increasingly relevant to the ENT surgeon with the number of TB cases rising annually. This paper aims to increase awareness about it. With increasing cases of TB, the ENT surgeon needs to be more vigilant for its occurrence by including TB vasculitis in the list of differentials in a patient presenting with nasal septal perforation. Its diagnosis can be challenging due to its non-specific presentation both clinically and diagnostically, and a high index of suspicion is needed, as it is ultimately a diagnosis of exclusion.

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