Primary nasopharyngeal tuberculosis

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TITLE OF CASE

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SUMMARY

No part of human body is immune to tuberculosis, the most common site being the lungs. We report a rare case of primary nasopharyngeal tuberculosis without cervical lymphadenopathy nor pulmonary involvement. The only presenting symptom was an intermittent discomfort in the neck and throat. Several biopsies were performed to exclude nasopharyngeal carcinoma and to reach the final diagnosis of tuberculosis. The patient made full recovery following six months treatment with antibiotics. A multidisciplinary approach by Ear, nose and throat (ENT), Radiology, Pathology, and Infectious disease colleagues was crucial in reaching the diagnosis and managing the patient.

BACKGROUND

Tuberculosis (TB) has a global presence.[1] It is resurging in developed countries due to acquired immunodeficiency syndrome (AIDS), wide administration of immunosuppressive agents and immigration.[2] The patients may be asymptomatic and healthy, without underlying disease and no history of a positive contact.[1,2]

No part of human body is immune to it, the most frequent site being the lungs.[1,3] TB involving organs other than the lungs is termed as 'extra pulmonary tuberculosis' (EPTB).[4] Up to 10% of TB cases have some manifestation in the head and neck region.[1,3] Its most common manifestation in head and neck region is cervical lymphadenopathy, frequently involving posterior triangle and supraclavicular region.[3–5] Other ear, nose and throat (ENT) areas that TB may affect are pharynx, larynx, middle ear, oral and nasal cavity and submandibular glands.[3,4]

Nasopharyngeal TB comprises less than 1% of TB found in the upper respiratory tract.[1,3,6] Nasopharyngeal TB is a rare entity, even in endemic TB areas.[4,5,7] TB can involve nasopharynx primarily without affecting any other system or secondary to pulmonary or extrapulmonary involvement.[1] Primary nasopharyngeal TB is very unusual and only a few cases have been reported in the literature.[3] Nasopharyngeal TB has many presentations; subtle signs and symptoms may be missed.[8] TB should be a differential diagnosis of nasopharyngeal lesions. A biopsy and histologic study should be performed in every patient to avoid misdiagnosis.[1,7] Repeat biopsies are sometimes necessary, as much for eliminating the diagnosis of a malignant tumour as for confirming TB.[9]

When treated properly, nasopharyngeal TB carries an excellent prognosis, and complete resolution of the disease is the rule.[1]

CASE PRESENTATION

A male in his early 40's presented to ENT outpatient department with 2-month history of intermittent pain on the right side of his throat and neck. At the time of presenting to ENT he did

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not complain of hearing loss, odynophagia, dysphonia, cough, fever, night sweats nor weight loss.
He is a smoker for many years. He has not been on foreign travel for last 4 years. His only medication is topical clobetasol propionate ointment for alopecia areata of the scalp.
His father died of TB thirty years ago. The patient himself has never been treated for TB.
On examination with a flexible nasendoscope a postnasal mass was identified, more prominent on the right side, with no overlying discharge. Examination of both ears was normal. No cervical lymph nodes were palpable. At the time of these findings the most concerning differential diagnosis was nasopharyngeal carcinoma.

INVESTIGATIONS

A biopsy under local anaesthetic was taken and sent for histopathology which revealed no evidence of malignancy but did show granulomas without overt caseation (Figure 1). Ziehl-Neelsen (ZN), periodic acid-Schiff (PAS) and Grocott (or Gomori) methenamine silver (GMS) stains were performed but no Mycobacteria or fungal organisms were identified.
Serum angiotensin converting enzyme (ACE) and blood calcium were within the normal range. Anti-proteinase 3 (anti-PR-3) and anti-myeloperoxidase (anti-MPO) blood tests were also normal. Other routine blood tests showed no abnormal findings of red blood cells, white blood cells, C-reactive protein, plasma viscosity, electrolytes, liver and kidney function.

Following initial biopsy and blood tests another set of biopsies from the postnasal mass were taken for microbiology and histopathology. Microscopy revealed similar well-formed granulomas but no genuine caseous necrosis on a background of normal lymphoid tissue. Again, no acid fast bacilli or fungal organisms were identified on ZN, PAS and GMS stains.

Magnetic resonance imaging (MRI) of the sinuses and neck revealed a 12 mm mildly asymmetrical thickening of the posterior nasopharyngeal wall/adenoid area with no cervical lymphadenopathy (Figure 2). Computed tomography (CT) of the chest was normal, with no pulmonary lesions nor mediastinal lymphadenopathy.

After 7 weeks microbiology cultures revealed *Mycobacterium tuberculosis* (*M. tuberculosis*) sensitive to isoniazid, ethambutol, rifampicin and pyrazinamide.

DIFFERENTIAL DIAGNOSIS

The most concerning differential diagnosis was nasopharyngeal malignancy. This was excluded on histopathological examination of the biopsies.
As granulomas were found on histopathological examination, sarcoidosis, granulomatosis with polyangiitis and TB were among differential diagnoses. Sarcoidosis was excluded with normal serum ACE, calcium blood tests and plasma viscosity, as well as normal CT chest imaging. Granulomatosis with polyangiitis was excluded with normal anti-PR-3 and anti-MPO, as well as normal plasma viscosity. TB was only confirmed after 7 weeks of microbiology culture growth, as initial stains had not demonstrated any acid fast bacilli. As his dad died of TB this was the most likely diagnosis once malignancy was excluded.

TREATMENT

The patient was referred to Infectious disease colleagues for TB treatment. During their work-up HIV, hepatitis B and hepatitis C tests were all negative. He was started on daily rifampicin 720mg, isoniazid 300mg and pyrazinamide 1800mg and pyridoxine hydrochloride 10mg (prophylaxis to protect from isoniazid-induced neuropathy) for two months. Following that, he was started on daily rifampicin 600mg and isoniazid 300mg and pyridoxine hydrochloride 10mg for 4 months.

OUTCOME AND FOLLOW-UP

The total TB treatment course lasted six months. During this period routine liver tests were checked twice which were normal. Two months in the treatment course he was complaining of intermittent pain in the left side of his throat and neck region, as well as left sided facial paraesthesia and tenderness over the left eye. As the symptoms were progressing, one month before the end of the treatment an MRI brain and neck was performed. It revealed no abnormal findings and marked reduction of the previously noted soft tissue thickening in the nasopharynx (Figure 3). As the *M. tuberculosis* culture was sensitive to the antibiotics used in the treatment no further tests or treatment were necessary.

DISCUSSION

Nasopharyngeal TB seems to be more frequent in women than in men. It occurs in adults, with two peaks of frequency: between 15 and 30 years of age and between 50 and 60 years of age.[2,7,9]

Several known risk factors for TB have been reported. The most common ones are immunosuppression, history of TB exposure and ethnic origin.[3,5] In some case series, tobacco use and a low socioeconomic status have also been reported as risk factors.[2,3,9]
Some parts of the world have been accepted as an epidemiological risk factor for TB such as origin of Northwest Africa (Maghrebin) area.[9] Therefore, a thorough history must include information on travel, contact and immune status to identify at-risk individuals and plan investigations and management.[2,10]

Two modes of nasopharyngeal contamination of TB have been described: 1. airway: either directly through nasal ventilation, or secondarily through canalized bacillary expectoration; 2. haematogenous or lymphatic, from a primary site, most often pulmonary. Lymphatic nasopharyngeal contamination is explained by rich lymphatic network of the Waldeyer ring.[6,7,9] This double mode of contamination explains how nasopharyngeal lesions may be primary or secondary to lesions most often of pulmonary origin. Tuberculous lymphadenopathy is always secondary to a pulmonary or nasopharyngeal localization, but the inoculation site is sometimes too small to identify or already healed.[9]
TB of the upper respiratory tract and nasopharynx has been observed mainly in patients with active pulmonary TB.[2]

Nasopharyngeal TB is generally associated with cervical lymphadenopathy or with a pulmonary localization.[1,2,9] The clinical presentation can be the same as a nasopharyngeal tumour.[9] The most common presentation of TB in the head and neck is cervical lymphadenopathy which is

present in ~90% of cases of head and neck TB.[4,10] During a work-up for cervical tuberculous lymphadenopathy nasopharyngeal TB may be discovered.[2]
Some elements of patient's medical history may offer clues to the diagnosis: contamination from a contact, absence of vaccination, declining general health, night sweats, and associated pulmonary signs and symptoms. The rhinological symptomatology may include: uni- or bilateral nasal obstruction, rhinorrhoea, postnasal drip, nasal bleeding, and rare otological symptoms such as otalgia, hearing loss or unilateral otorrhoea.[1,5,7,9] Nasopharyngeal TB is a difficult diagnosis to confirm on clinical suspicion alone.[10]

Endoscopic examination may reveal a polypoidal mass, ulceration, plaque, or diffuse mucosal thickening of the nasopharynx.[1,2,7,9] At times, the appearance can be suggestive of ordinary adenoids.[9]

ZN staining is commonly used to detect acid-fast bacilli in histopathology specimens. However, modified staining methods such as the Fite-Faraco method or alternative techniques such as immunohistochemistry, whilst perhaps not as widely used, have been shown to provide greater sensitivity in identifying mycobacteria.[11] After four to six weeks of appropriate microbiological culture, the drug sensitivities of the infecting strain may become apparent.[7]

A rigid nasendoscopy with multiple biopsies is absolutely necessary for the diagnosis. It allows a pathological study in order to eliminate a malignant tumour, as well as a bacteriological examination.[1,5,9,10] Nevertheless, a pathological study is sometimes difficult.[9] The diagnosis of mycobacterial infections can be hampered by low organism load, making the organisms difficult to find using histochemical techniques. Typically, giant cell epithelioid granulomas with caseous necrosis are seen on histological examination.[7,9] When granulomatous inflammation is confirmed by tissue biopsy, TB should also be one of the differential diagnosis.[4]
Repeat biopsies are sometimes necessary, both for eliminating a malignant tumour and for confirming TB.[7,9]
Although the definitive diagnosis is based on microbiological culture, treatment is often commenced based on histological examination. This is because smear and culture tests take up to two months to provide a result and are difficult to perform in EPTB due to the low number of bacilli in the specimen.[3,5] In our patient's case treatment was started after microbiology culture revealing *M. tuberculosis* with sensitivities to antibiotics as the patient was stable and did not have severe symptoms and signs of TB. Modern laboratory methods such as polymerase chain reaction (PCR) are proving ever more useful in aiding the diagnosis.[3] Tuberculin skin tests, on the other hand, are not specific and often misleading.[3,12]

CT images usually show either a large or lobulated mass, or irregular soft tissue thickening of the nasopharynx. On MRI nasopharyngeal TB is seen as either a polypoid mass of the adenoids or diffuse thickening of the mucosal wall of the nasopharynx.[7]
It is important to investigate the thorax for evidence of old or new TB.[7,10] A chest X-ray is generally obtained at the time of diagnosis to exclude pulmonary TB, although chest CT scan is twice as sensitive in the detection of pulmonary cavities.[12] In our patient pulmonary TB was excluded by CT chest, although the first line recommended investigation is X-ray.

TB patients should be treated with multidisciplinary input, primarily lead by Infectious disease colleagues.

Involvement of the nasopharynx by TB may be underdiagnosed because it may not produce obvious symptoms or physical signs in all cases. Although rare, it is important to consider TB in the differential diagnosis of nasopharyngeal lesions and take biopsy specimens for histological and bacteriological studies.[2,4]

LEARNING POINTS/TAKE HOME MESSAGES *3-5 bullet points*

- TB should be one of the differential diagnosis of nasopharyngeal lesions.
- Repeat biopsies are sometimes necessary, as much for eliminating the diagnosis of a malignant tumour as for confirming TB.
- A multidisciplinary team approach including ENT, radiology, pathology, and infectious disease doctors should be followed during the diagnostic and treatment periods.

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FIGURE/VIDEO CAPTIONS

Figure 1. Microscopic images of postnasal biopsy specimen, haematoxylin and eosin stained sections.

a) Respiratory type epithelium (green arrowheads) overlies a lymphoid stroma (blue asterisk) containing multiple well-formed granulomas (black arrows) (10x magnification).
b) A focus of central degeneration can be seen within a large granuloma (red arrow), with associated acute inflammation (20x magnification).

c) The granulomas, predominantly composed of epithelioid histiocytes, lack the amorphous pink centre of caseous necrosis that is typical of tuberculous granulomas (100x magnification).

Figure 2. Axial views of MRI head scan. a) T1-weighted and b) T2-weighted images. White arrows pointing to symmetrical thickening of the posterior nasopharyngeal wall/adenoid area measuring up to 12mm in anterior to posterior dimension.

Figure 3. Axial views of MRI head scan. a) T1-weighted and b) T2-weighted images. White arrows highlighting reduced size of previously thickened posterior nasopharyngeal wall/adenoid area.

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