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Nasopharyngeal tuberculosis

J. Percodani, M.D.*, F. Braun, M.D.*, P. Arrue, M.D.†, E. Yardeni, M.D.*, M. Murris-Espin, M.D.‡, E. Serrano, M.D.*, J. J. Pessey, M.D.*

Abstract
Rhinopharyngeal tuberculosis is a rare pathological condition. It is most often associated with lymph node and pulmonary lesions, but it may be an isolated finding. The authors report a recent case of an isolated rhinopharyngeal tuberculosis in a 64-year-old female. A review of the literature is presented. They emphasize the clinical presentation, that, in all aspects, may resemble a malignant tumour of the nasopharynx, as well as the difficulty of obtaining a pathological and bacteriological diagnosis.

Key words: Tuberculosis; Nasopharynx

Introduction

The diagnosis of rhinopharyngeal tuberculosis is often difficult. It is a rare pathological condition that may be difficult to distinguish from a malignant nasopharyngeal tumour. Repeat biopsies are sometimes necessary, as much for eliminating the diagnosis of a malignant tumour as for confirming tuberculosis. We report a case which illustrates these diagnosis difficulties.

Case report

A 64-year-old Caucasian female of French origin, retired secretary, was referred with symptoms suspicious of a nasopharyngeal tumour.

There was a past medical history of a stay in a sanitorium for five years (35 years ago), a hysterectomy in 1969, a cholecystectomy in 1983, a mastectomy followed by external radiotherapy for a malignant breast tumour in 1991, and a partial colectomy for diverticulosis in 1994. The family history was remarkable for non-treated tuberculosis in a grandmother and the father.

The present medical history began two months prior to admission, with left lateral pharyngeal pain, associated with left nasal obstruction, post-nasal drip, and left-sided hearing loss. No general health alteration, night sweats, or fever were noted.

A nasal fibre-optic examination showed nasopharyngeal bulging, with localized mucosal inflammation. An otoscopic examination revealed a left serous otitis media. A nasopharygneal examination using a rigid endoscope confirmed the previous finding, and multiple biopsies showed an inflammatory infiltrate suggestive of a non-specific infection. The cultures were sent to test for tuberculous bacilli, and were found to be negative.

A broad spectum antibiotic treatment was prescribed. No improvement was noted, and the patient was readmitted for further work-up.

On admission, the symptomatology was identical, having now been present for three months. The nasal fibre-optic examination again revealed an asymmetrical nasopharynx, but with an ulcerated lesion covered with fibrin deposits on the left lateral wall, probably secondary to the preceding biopsies. No cervical lymphadenopathy was noted on palpation.

A computed tomography (CT) scan, centred on the nasopharynx, showed heterogenous tissue formation of the left lateral wall, with filling of the pharyngeal recess, without bone extension (Figure 1). The CT scan confirmed the absence of cervical lymphadenopathy. Magnetic resonance imaging (MRI) centred on the nasopharynx, showed a left nasopharyngeal hyposignal on the T1-weighted sequence, with uptake after gadolinium injection, and a hypersignal on the T2-weighted sequence. These images were more suggestive of an inflammatory process than of a tumour. No bone extension was noted (Figure 2).

Nasopharyngeal biopsies, at a repeated examination using a rigid endoscope, with general anaesthesia, showed non-specific granulomatous lesions, without signs of malignancy, evoking the possibility of a fungal or atypical mycobacterial infection. The cultures remained negative.

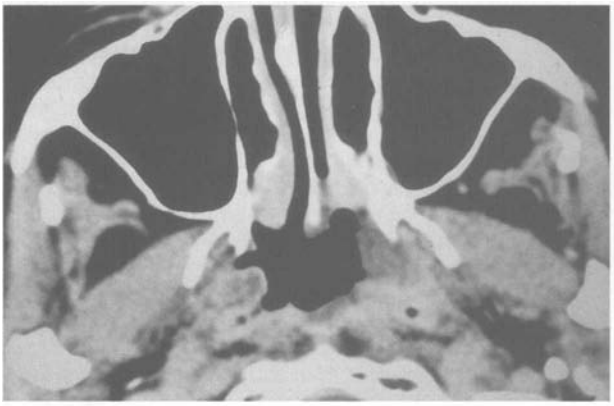

Fig. 1
Axial CT scan: Heterogenous tissue formation of the left lateral wall with filling of the pharyngeal recess.

From the Service d'ORL et de Chirurgie Cervico-Faciale*, the Service de Neuro-Radiologie†, and the Service de Pneumo-Allergologie‡, CHU de Rangueil, 31403 Toulouse, France.
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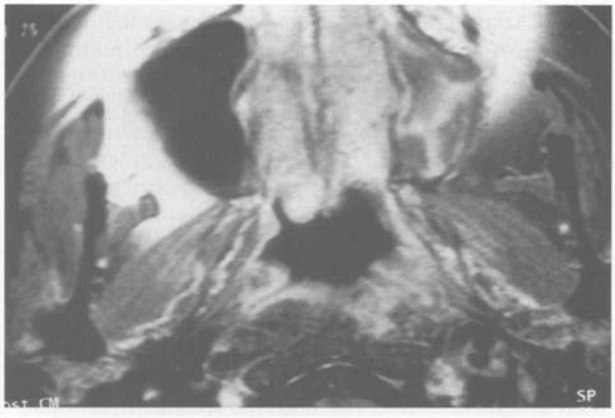

FIG. 2

Axial T1 MRI after gadolinium injection: left mass with posterior extension to the longus capitis.

The general physical, and particularly the pulmonary examination, were normal. The skin test, using 10 units of tuberculin, showed a vesicular reaction of three cm diameter, and no preceding anti-tuberculosis vaccination was elicited. The pathology results, having again excluded a nasopharyngeal tumour, led us to prescribe a macrolide antibiotic effective against atypical mycobacteria and an anti-fungal agent (Fluconazole).

In light of the inefficacy of this second treatment regimen, a third rigid endoscopic nasopharyngeal examination was undertaken, with biopsies for pathological, bacterial (particularly tuberculous bacilli), parasite, and virology studies. The pathological examination showed giant epithelioid cell granulomas without malignant cells. A direct examination after Ziehl-Nielsen staining was negative.

With the appearance of a vesicular intradermal reaction and the presence of giant epithelioid cell granulomas, suggestive of a pharyngeal tuberculosis, a pulmonary work-up was repeated, as the chest X-ray showed a sequelar mediastinal lymph node calcification. Gastric washings over a three-day period did not find any bacilli on direct examination. A thoracic CT scan showed parenchymatous micronodules, compatible with tuberculosis. A calcified mediastinal lymphadenopathy was seen in the inter-aorto-pulmonary and precarinal regions. Tracheo-bronchial endoscopy was normal. Tuberculous bacilli were sought in the bronchoalveolar washings; the direct examination was negative, and staged bronchial biopsies showed no granulomas. A liver work-up showed no sign of granulomatous hepatitis. An anti-tuberculosis treatment was thus prescribed, combining isoniazid, rifampicin, ethambutol, and pyrazinamide, after a negative pre-therapeutic work-up.

One month after beginning the treatment, cultures from nasopharyngeal biopsied tissue, grown in a Lowenstein medium, became positive for tuberculosis bacilli. Identification of *Mycobacterium tuberculosis* was confirmed by the molecular hybridization technique. No resistance to the prescribed antibiotics was demonstrated on culture. On the other hand, cultures from the gastric and bronchoalveolar washings remained negative.

The patient was seen two months after beginning the treatment: no functional symptoms were elicited and the nasopharyngeal examination had normalized. The absence of symptoms and a normal physical examination was corroborated at a three-years post-treatment consultation.

Discussion

The incidence of tuberculosis varies from country to country; in France it is 17.2 cases per 100 000 compared to 120 cases per 100 000 in Morocco (El Amine El Alami *et al.*, 1993; Begue *et al.*, 1995). The worldwide increase in tuberculous disease and its association with human immunodeficiency virus (HIV) infection should be underlined (Cleary and Batsakis, 1995).

In countries where tuberculosis is endemic, particularly in the Maghreb, pharyngeal tuberculosis is relatively common (Ennouri *et al.*, 1990; Marrakchi *et al.*, 1990; El Amine El Alami *et al.*, 1993; Raji *et al.*, 1995). Most cases reported in France occur in patients of North African origin (Lecointre *et al.*, 1980; Buffe *et al.*, 1984; Ennouri *et al.*, 1990; Marrakchi *et al.*, 1990; Bassoumi *et al.*, 1992; Raji *et al.*, 1995). Nevertheless, several studies show an underestimation of a pharyngeal localization in cases of pulmonary or lymph node tuberculosis (Graff, 1936; Lau *et al.*, 1991; Raji *et al.*, 1995).

Graff in 1936, carried out a systematic clinical and histological study of the nasopharynx in 120 patients presenting with pulmonary tuberculosis. Physical abnormalities were found in 36 per cent of the cases, and histological lesions in 82 per cent of the nasopharyngeal biopsies.

According to Lau *et al.* (1991), in a study of 75 patients presenting with tuberculous lymphadenopathy: 29 patients (36 per cent) had pulmonary localizations, with four of these presenting an associated nasopharyngeal lesion, 46 patients (61 per cent) did not have a pulmonary lesion, and only one patient in this group had a nasopharyngeal lesion.

In a series described by Ruaux *et al.* (1995), no clinical nasopharyngeal signs nor symptoms were noted in 33 patients with tuberculous lymphadenopathy, but no systematic nasopharyngeal histology was studied.

Rhinopharyngeal tuberculosis seems to be more frequent in women than in men (Marrakchi *et al.*, 1990; El Amine El Alami *et al.*, 1993; Raji *et al.*, 1995). It occurs in adults, with two peaks of frequency: between 15 and 30 years of age (Buffe *et al., 1984;* Ennouri *et al.*, 1990; Marrakchi *et al.*, 1990; Raji *et al.*, 1995) and between 50 and 60 years of age (Bath *et al.*, 1992; El Amine El Alami *et al.*, 1993). A Maghrebin origin is an accepted epidemiological factor, and most of the recent series come from studies carried out in the Maghreb (Buffe *et al.*, 1984; Ennouri *et al.*, 1990; Marrakchi *et al.*, 1990; Bassoumi *et al.*, 1992; Raji *et al.*, 1995). Tobacco use and a low social level are also risk factors found in some series (Ennouri *et al.*, 1990; Zanaret *et al.*, 1992). However, our patient was a 64-year-old Caucasian female, with no past tobacco use, of a middle-class social level.

Two modes of contamination are described (Ennouri *et al.*, 1990; Marrakchi *et al.*, 1990; Lau *et al.*, 1991; Zanaret *et al.*, 1992; El Amine El Alami *et al.*, 1993; Raji *et al.*, 1995; Al Serhani *et al.*, 1997).

(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 the rich lymphatic network of the Waldeyer ring.

This double mode of contamination explains how nasopharyngeal lesions may be primary (primitive nasopharyngeal tuberculosis), 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 or already healed, and, therefore, remains infraclinical. Isolated, primary cavitating forms are rare (Lecointre *et al.*, 1980; Lau *et al.*, 1991; Bath *et al.*, 1992; Raji *et al.*,

1995; Al Serhani *et al.*, 1997). Raji *et al.* (1995) and Lau *et al.* (1991) have each reported one isolated primary form in five cases of cavitary tuberculosis, Lecointre *et al.* (1980) report one case in three, and Bath *et al.* (1992) describe one isolated case. In fact, nasopharyngeal tuberculosis is generally associated with cervical lymphadenopathy or with a pulmonary localization.

In the case we present, the patient had no cervical lymphadenopathy, and the general physical examination was normal. Chest X-rays showed sequellar calcified mediastinal lymph nodes. A thoracic CT scan showed signs compatible with a pulmonary tubercular localization, but were not specific. Brondoscopy with bronchoalveolar washings did not become positive on cultures. In our view, this is not a case of an isolated and primary nasopharyngeal tuberculosis, since an endogenous reinfection cannot be formally ruled out in this immunocompetent patient with pulmonary signs.

Nasopharyngeal tuberculosis is most often discovered during a work-up for cervical tuberculous lymphadenopathy (Mahindra *et al.*, 1981; Lau *et al.*, 1991; Bath *et al.*, 1992; Chopra *et al.*, 1994) and rarely during a work-up for pulmonary tuberculosis (Graff, 1936). The clinical presentation can be the same as a nasopharyngeal tumour (Buffe *et al.*, 1984; Zanaret *et al.*, 1992).

Some elements of the medical history may offer clues to the diagnosis: contamination from a contact, absence of vaccination, alteration of general health, night sweats, and associated pulmonary signs and symptoms. The rhinological symptomatology may include: uni- or bilateral nasal obstruction, rhinorrhoea, nasal bleeding, as well as rare otological symptoms (hearing loss and/or unilateral otorrhoea (Bath *et al.*, 1992).

The physical examination shows a nasopharyngeal mass of variable appearance (Buffe *et al.*, 1984; Ennouri *et al.*, 1990; Marrakchi *et al.*, 1990; Zanaret *et al.*, 1992; Chopra *et al.*, 1994; Raji *et al.*, 1995): polypoid, ulcerated, ulcerovegetative, or sub-mucosal. Sometimes, the appearance is suggestive of ordinary adenoids. The otoscopic examination may reveal serous otitis media. Alternatively nasopharyngeal tuberculosis, in the course of lymph node or pulmonary tuberculosis, may be totally asymptomatic, as witnessed in purely histological forms (Graff, 1936; Lau *et al.*, 1991).

The diagnosis of nasopharyngeal tuberculosis is difficult, and the principal problem is that of a differential diagnosis from a malignant nasopharyngeal tumour. The standard biological work-up looks for a non-specific inflammatory syndrome. The tuberculin intradermal reaction is of value only when it is positive, in the absence of a known anti-tuberculous vaccination or when a preceding negative result is elicited. Nasopharyngeal puncture for cytology is used by some authors, searching for acid-alcohol-resistant bacilli on direct examination after Ziehl-Nielsen staining or on Lowenstein medium cultures (Weiner *et al.*, 1994). A rigid nasendoscopy with multiple biopsies is indispensable for the diagnosis. It allows a pathological study in order to eliminate a malignant tumour, as well as a bacteriological examination. Nevertheless, a pathological study is sometimes difficult. Typical giant cell epithelioid granulomas with caseous necrosis are found. Repeat biopsies are sometimes necessary, as much for eliminating a malignant tumour as for confirming tuberculosis (Lecointre *et al.*, 1980; Marrakchi *et al.*, 1990).

Treatment is either an anti-tuberculous triple therapy, for nine to 18 months according to the authors El Amine El Alami *et al.* (1993), Lecointre *et al.* (1980), Raji *et al.* (1995), combining isoniazid, rifampicin, and ethambutol, or a quadritherapy, including pyrazinamide, for nine months (Marrakchi *et al.*, 1990; El Amine El Alami *et al.*, 1993). According to a recent consensus, the minimal duration of an extra-pulmonary tuberculosis treatment is six months (Bégué *et al.*, 1995). With adequate medical treatment, nasopharyngeal tuberculosis carries a good prognosis; no cases of resistance to anti-tuberculosis drugs or therapeutic failure has been noted in the literature.

In conclusion, nasopharyngeal tuberculosis is a rare condition in Europe. It is often associated with pulmonary or lymph node tuberculosis, but may occur as an isolated pathology. In the absence of a pulmonary localization, it is essential to eliminate a malignant nasopharyngeal tumour. Biopsies are indispensable for diagnosis, but interpretation may be difficult, and repeated biopsies may be necessary. With a well-conducted anti-bacterial treatment, nasopharyngeal tuberculosis carries a good prognosis, where a cure without sequelae is the rule.

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Address for correspondence:
Professor E. Serrano,
Service d'ORL et de Chirurgie Cervico-Faciale,
CHU de Rangueil,
31403 Toulouse,
Cedex 4, France.

Fax: 33 5 61 32 20 78