Cytowanie: Wong BL, Mohamad I, Marimuthu SG, Abu Bakar MN: Tak podobne, a tak różne: podobieństwo obrazu gruźlicy nosogardzieli i raka nosogardła.
Pediatr Med Rodz 2023; 19 (3): 251–254. DOI: 10.15557/PiMR.2023.0043.

Bao Ling Wong[1,2], Irfan Mohamad[1], Shashi Gopalan Marimuthu[2],
Muhammad Nasri Abu Bakar[2]

Otrzymano: 03.04.2023
Zaakceptowano: 01.06.2023
Opublikowano: 05.12.2023

Tak podobne, a tak różne: podobieństwo obrazu gruźlicy nosogardzieli i raka nosogardła

One world but miles apart: great mimicry of nasopharyngeal tuberculosis with nasopharyngeal carcinoma

[1] Department of Otorhinolaryngology, Head and Neck Surgery, Universiti Sains Malaysia, Malaysia
[2] Department of Otorhinolaryngology, Head and Neck Surgery, Sibu Hospital, Malaysia
Adres do korespondencji: Irfan Mohamad, Department of Otorhinolaryngology, Head and Neck Surgery, Universiti Sains Malaysia, Malaysia, e-mail: irfankb@usm.my

https://doi.org/10.15557/PiMR.2023.0043

ORCID iDs
1. Bao Ling Wong https://orcid.org/0000-0001-5455-1199
2. Irfan Mohamad https://orcid.org/0000-0001-8572-0514
3. Shashi Gopalan Marimuthu https://orcid.org/0000-0001-5536-6331
4. Muhammad Nasri Abu Bakar https://orcid.org/0000-0002-5750-3536

Streszczenie

Gruźlica nosogardzieli jest rzadką postacią gruźlicy, nawet na obszarach endemicznych choroby. Może występować pierwotnie lub wtórnie do gruźlicy płucnej albo układowej. Chociaż gruźlica jamy nosowo-gardłowej odpowiada za mniej niż 1% wszystkich przypadków gruźlicy, w ostatnim czasie odnotowuje się wzrost liczby zgłaszanych przypadków. Z uwagi na zróżnicowanie objawów gruźlica w obrębie jamy nosowo-gardłowej stanowi wyzwanie diagnostyczne, ponieważ często naśladuje inne schorzenia. W niniejszej pracy przedstawiamy doświadczenia własne związane z diagnostyką i leczeniem trzech przypadków rzadkiej pierwotnej gruźlicy nosogardzieli o różnej etiologii. Opisujemy objawy kliniczne, endoskopowe i radiologiczne, w przypadku których zasadne jest uwzględnianie tej postaci gruźlicy w diagnostyce różnicowej. Wskazujemy, że w procesie diagnostycznym przydatna jest biopsja jamy nosowo-gardłowej. Przedstawieni w pracy pacjenci dobrze zareagowali na chemioterapię przeciwgruźliczą. Zmienność obrazu choroby dowodzi, że w procesie diagnostycznym ważne jest zachowanie szczególnej czujności klinicznej. Takie podejście umożliwia sprawne stawianie diagnozy i wdrażanie prawidłowego leczenia.

Słowa kluczowe: gruźlica, radioterapia, nosogardziel, rak nosogardła

Abstract

Nasopharyngeal tuberculosis is rare, even in endemic areas. It can be primary or secondary to pulmonary or systemic tuberculosis. Although nasopharyngeal tuberculosis represents less than 1% of all tuberculosis cases, there has been an increase in cases reported recently. The variety of presenting symptoms in nasopharyngeal tuberculosis makes it challenging to diagnose because the condition commonly mimics other pathologies. In this paper, we would like to share our experience managing three cases of rare primary nasopharyngeal tuberculosis with different backgrounds. We provide a comparison in their clinical presentations, and endoscopic and radiological features, highlighting the situations when nasopharyngeal tuberculosis needs to be considered as a differential diagnosis. A nasopharyngeal biopsy is helpful to establish the diagnosis. The patients responded well to anti-tuberculosis chemotherapy. The variation in findings proves that it is important to have a high index of suspicion in order to get an accurate early diagnosis and initiate proper treatment.

Keywords: tuberculosis, radiotherapy, nasopharynx, nasopharyngeal carcinoma

INTRODUCTION

Tuberculosis (TB) is a globally widespread infectious disease caused by *Mycobacterium tuberculosis*, which often affects the lungs. All organs can be affected, with up to 10% of extrapulmonary TB involving the head and neck regions[1]. Upper respiratory tract involvement is uncommon, accounting for about 1.8% of all TB cases, and the involvement of the nasopharynx is rarer (0.1%), even in the endemic areas[2]. In the head and neck region, the presenting symptoms of TB might be the same as in other pathologies. Mimicry of other diseases, causing delayed diagnosis, is common[3]. Nasopharyngolaryngoscopy provides direct visualisation of the nasopharynx and larynx to rule out pathology such as malignancies, especially in regions with high incidence of nasopharyngeal carcinoma. Clinical, radiological, and endoscopic features of TB of the head and neck are not specific. Another limitation is the fact that endoscopic devices are only available in certain health care centres, and a trained person is needed to perform and obtain a biopsy. The diagnosis is even more challenging as it has a lower bacterial load compared to pulmonary TB[1,4].

CASE 1

A 70-year-old female complained of multiple painless swellings on the right side of the neck, persisting for two months. She denied any nasal symptoms, epistaxis or any constitutional symptoms. A few cervical lymph nodes were palpable over right level IV and V of the neck, about 1 cm in size, which were firm, non-tender and mobile. Chest radiography, and blood and sputum investigations were negative for acid-fast bacilli. On nasoendoscopy, the nasopharynx mucosa appeared normal (Fig. 1). Punch biopsy was taken from the right fossa of Rosenmüller (FOR) due to the presence of lymph nodes and high incidence of nasopharyngeal carcinoma (NPC) in the area of Sarawak. Meanwhile, computed tomography (CT) of the neck showed bilateral symmetrical FOR with no masses, thus ruling out submucosal NPC. Histopathology of the right nasopharyngeal tissue revealed caseating granulomatous lesions scattered throughout in multiple foci, exhibiting epithelioid cells and Langhans giant cells with occasional foci of pale eosinophilic necrosis. These features are indicative of TB infection. After the patient completed a course of anti-TB treatment for nine months, the neck swellings resolved, and she remained asymptomatic on the subsequent follow-up.

CASE 2

A 33-year-old female with a history of NPC completed chemotherapy and radiotherapy 20 years prior. She had been kept on a yearly follow-up at our otorhinolaryngology clinic. During a review in clinic, the patient complained of persistent yellowish nasal discharge over the past six months. There were no palpable cervical lymph nodes. Surveillance nasoendoscopy revealed a fullness over the left nasopharynx (Fig. 2). Left FOR tissue biopsy was obtained in view of the possibility of tumour recurrence. Histopathology revealed chronic granulomatous inflammation, but the Ziehl–Neelsen stain was negative and failed to demonstrate malignancy. CT of the neck revealed an ill-defined enhancing soft tissue mass over the left pharyngeal mucosa space with midline and basisphenoid invasion, which were highly suspicious of tumour recurrence (Fig. 3). In addition, there was no cervical lymphadenopathy. A deeper nasopharyngeal tissue biopsy was repeated under general anaesthesia. The repeat biopsy revealed granulomatous inflammation with the presence of acid-fast bacilli from Ziehl–Neelsen stain but without any evidence of tumour recurrence. Anti-TB therapy was commenced and showed good response after two months of treatment, with less yellowish nasal discharge and reduced fullness over the nasopharynx. The patient completed a nine-month course of treatment, with resolved

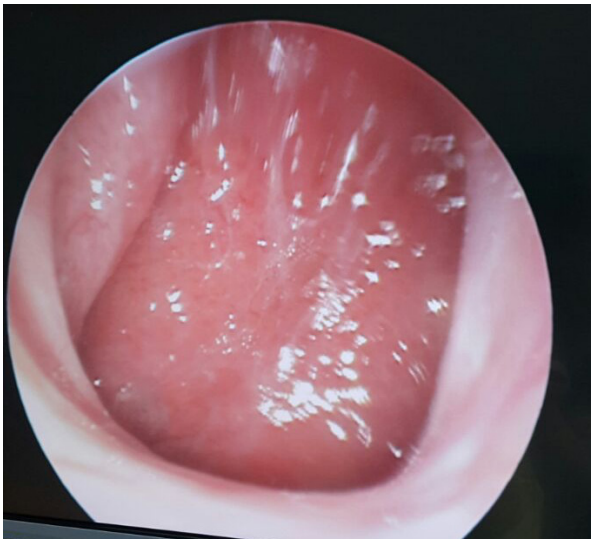

Fig. 1. Right nasopharynx with overlying normal appearing mucosa

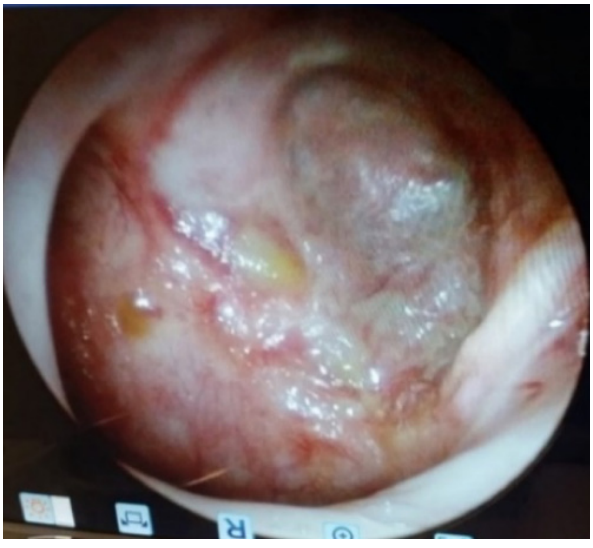

Fig. 2. Crust and fullness over left FOR

DOI: 10.15557/PiMR.2023.0043

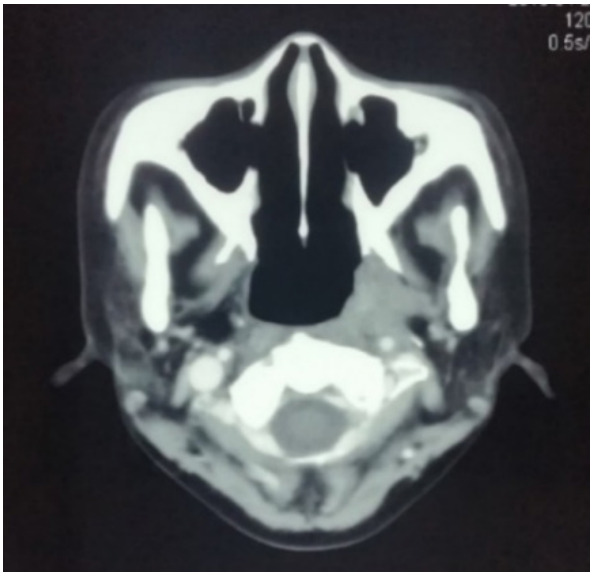

Fig. 3. Axial view of CT neck showing ill-defined enhancing soft tissue lesion over left nasopharynx

nasal discharge and surveillance nasoendoscopy showing fibrosis over the nasopharyngeal mucosa.

CASE 3

A 25-year-old female with no known medical illness presented with nasal blockage and rhinorrhoea for two months. Nasoendoscopy showed adenoid hypertrophy reaching the posterior choana. There were post-nasal drips with yellowish nasal discharge (Fig. 4 A). Otherwise, the turbinates and nasal cavity appeared normal. There were no palpable cervical lymph nodes. Bilateral nasopharyngeal tissue biopsy was obtained to rule out malignancy. Meanwhile, the patient was treated for rhinitis with adenoid hypertrophy, and was prescribed a nasal spray and decongestants. However, the nasal symptoms remained despite medical therapy. Histopathology revealed features of caseating granulomatous inflammation, but the Ziehl–Neelsen stain was negative and failed to demonstrate malignancy. The features were highly suggestive of tuberculous infection. Anti-TB therapy was initiated and continued for nine months. Her nasal symptoms, particularly nasal blockage and discharge, improved considerably. Nasoendoscopy after treatment showed resolved mucopus and much smaller adenoids with post-nasal drip (Fig. 4 B).

DISCUSSION

Tuberculosis (TB) is one of the top 10 causes of death worldwide. The latest WHO Global Tuberculosis report (2016) showed that 10.4 million people are infected with TB, with a reported mortality of 1.8 million. Nasopharyngeal carcinoma (NPC) was the fifth common cancer in Malaysia, with the highest incidence reported in Sarawak[5]. Both NPC and TB are common diseases in this part of the region. Nasopharyngeal tuberculosis (NPTB) represents less

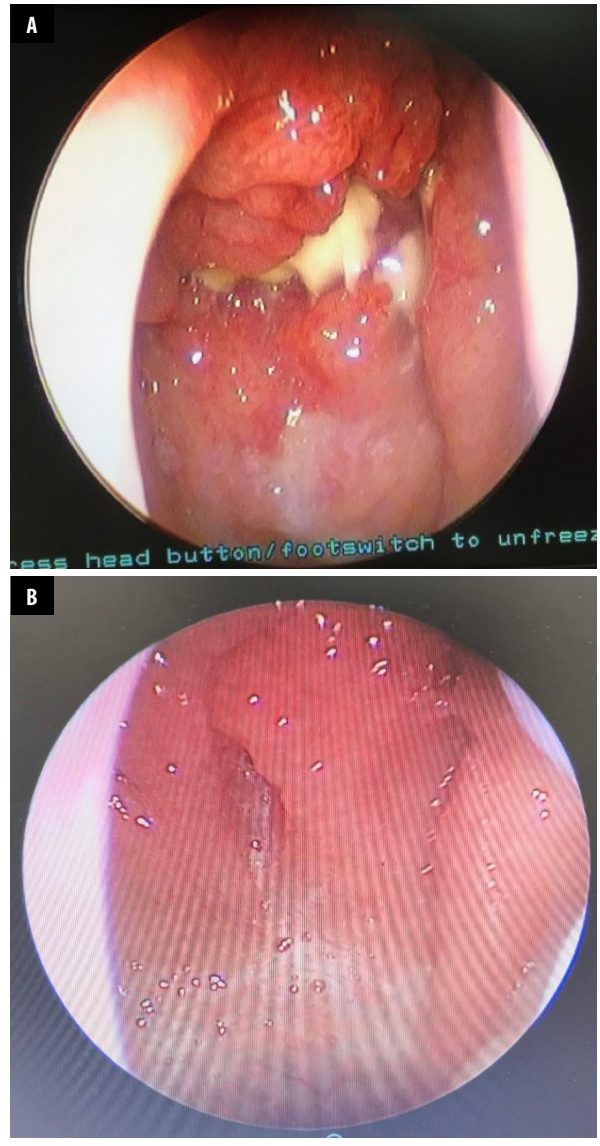

Fig. 4. **A.** *Nasoendoscopy showing enlarged erythematous adenoids and mucopus over left nasopharynx.* **B.** *Much smaller adenoids post anti-TB treatment*

than 1% of cases of head and neck TB, with 95% presenting as cervical TB lymphadenitis. It is even rarer to have a patient affected by both pathologies. NPTB seems to be more predominant in women, with two peaks of frequency, between the ages of 15 and 30, and between the ages of 50 and 60, which corresponds to the age group of our patients[6]. Our report showed that patients infected by NPTB may appear completely healthy, without any underlying disease, or may happen in a treated NPC case. Very rare cases of NPTB following radiotherapy have also been reported. NPTB may mimic NPC or tumour recurrence, or coexist with other conditions in the head and neck, such as laryngeal TB, oropharyngeal TB, and post-radiation NPC[7,8]. The most common symptom is high jugular cervical lymphadenopathy (50 to 90%), followed by nasal obstruction, snoring, rhinorrhoea, otorrhoea, reduced hearing, tinnitus, and otalgia[9].

 DOI: 10.15557/PiMR.2023.0043

Case 1 had no nasal or otological symptoms other than enlarged cervical lymph nodes. We considered NPC first, as the occurrence rate is high in Sarawak[5]. Conversely, Case 2 presented with nasal discharge, with no evidence of enlarged cervical lymph nodes. Endoscopy in NPTB can present a varied range, from an apparently normal mucosa (like in Case 1) to an evident mass, mucosa with adenoids or swollen appearance, post-nasal discharge, ulcers, and leukoplakic areas[1,6,9].

NPTB can be caused by direct inoculation from pulmonary TB, hematogenous dissemination, or initial infection from the Waldeyer ring. The Waldeyer ring has a dense lymphatic network, which explains lymphatic nasopharyngeal contamination[6,10]. The major location of the bacillus is typically the roof of the nasopharynx, where direct infection and inhalational reactivation of dormant acid-fast bacilli in the adenoids or mucosa might occur. Alveolar macrophages engaged in phagocytosis when the respiratory epithelium was exposed to the bacteria, but because they were unable to digest them, the bacteria multiplied as a result[11]. Moreover, high doses of radiotherapy used to treat NPC may have contributed to the development of NPTB in patients after treatment. As a result, the mucosal barrier breaks down, and a localised immunodeficiency or vulnerability occurs[8].

In NPTB, CT and magnetic resonance imaging (MRI) have been reported as useful imaging modalities in head and neck TB. Radiological imaging may demonstrate the sites, pattern, and extension of the disease. Previously, two radiological patterns have been described, which are polypoid masses and diffuse thickening of the mucosa[6,9,12]. Here, we report a case of NPTB which may show completely normal nasopharynx on CT. On the contrary, there was an ill-defined enhancing soft tissue mass on CT, highly suggestive of tumour recurrence, which turned out to be NPTB.

NPTB has similar clinical features as NPC, including cervical lymphadenopathy. The association of cancer and TB has already been reported[13]. Therefore, tissue sampling plays an important role in establishing a correct differential diagnosis between these diseases. The gold standard for TB diagnosis is positive mycobacterial smear and culture but it is difficult in certain cases due to low concentrations of the bacilli[1,12]. Histopathology has also been suggested as a helpful diagnostic tool. The typical histopathological features of NPTB include caseating granulomatous inflammation with multinucleated giant cells of Langhans type and foreign body giant cells, either with or without necrosis[8,13]. Furthermore, tissue biopsy can also demonstrate chronic granulomatous inflammation with positive Ziehl–Neelsen staining for acid-fast bacilli or bacteria. In cases which are strongly suspicious for TB but negative for bacterial culture, bacterial stain and polymerase chain reaction (PCR) analysis for *M. tuberculosis* DNA are helpful, but is the examination is quite time-consuming. It has been suggested that Ziehl–Neelsen staining for acid-fast bacilli is more sensitive, reliable, less costly, and makes it possible to arrive at a diagnosis faster than with bacterial culture and PCR analysis[1,2,8].

Our patients were initiated with standard anti-TB therapy for a duration of nine months. Based on the literature, most patients diagnosed with NPTB show good treatment outcomes, which was noted in our patients as well.

CONCLUSION

Chronic granulomatous changes in the nasopharynx after radiotherapy can be caused by tuberculosis. Misdiagnosis may lead to NPC diagnosed as NPTB, or vice-versa. Hence, high index of suspicion and tissue biopsy are important, especially in regions with high incidence of TB, to obtain an accurate and early diagnosis in order to initiate anti-TB treatment promptly, which increases the chances of a favourable outcome.

Conflict of interest

The authors have no funding, financial relationships, or conflicts of interest to disclose.

Author contributions

Writing of manuscript: BLW. Critical review of manuscript: IM, SGM, MNBAB. Final approval of manuscript: IM.

Piśmiennictwo

1. Darouassi Y, Chihani M, Elktaibi A et al.: Association of laryngeal and nasopharyngeal tuberculosis: a case report. J Med Case Rep 2015; 9: 2.
2. Rohwedder JJ: Upper respiratory tract tuberculosis. Sixteen cases in a general hospital. Ann Intern Med 1974; 80: 708–713.
3. Mohamad I, Nik Hassan NFH, Nik Othman NA: Head and neck tuberculosis: the great mimic. Malays Fam Physician 2016; 11: 38.
4. Ministry of Health Malaysia, Academy of Medicine Malaysia, Malaysian Thoracic Society, World Health Organization: Clinical Practice Guidelines – Management of Tuberculosis (3rd Edition). Malaysia Health Technology Assessment Section (MaHTAS) 2012; 5: 4–7.
5. Azizah Ab M, Nor Saleha IT, Noor Hashimah A et al.: Summary of Malaysian National Cancer Registry Report 2007–2011. National Cancer Institute, Ministry of Health 2015; 1: 44–45.
6. Sawada N, Inokuchi G, Komatsu H et al.: Nasopharyngeal tuberculosis. J Infect Chemother 2013; 19: 1158–1160.
7. Chua BL, Tan H, Yang ETL: Tuberculosis of the nasopharynx following radiotherapy. Clin Oncol (R Coll Radiol) 1998; 10: 59–61.
8. Chan ABW, Ma TKF, Yu BKH et al.: Nasopharyngeal granulomatous inflammation and tuberculosis complicating undifferentiated carcinoma. Otolaryngol Head Neck Surg 2004; 130: 125–130.
9. Martínez A, Lede Á, Fernández JA: Primary rhinopharyngeal tuberculosis: an unusual location. Acta Otorrinolaringol Esp 2011; 62: 401–403.
10. Patil C, Kharat Patil R, Deshmukh P et al.: Primary tuberculosis of nasopharynx (adenoid) – a rare presentation. Asian Pac J Trop Med 2013; 6: 246–248.
11. Handler EB, Quinn K, Wen A et al.: Pediatric laryngeal tuberculosis: a case with significant diagnostic challenges. Int J Pediatr Otorhinolaryngol Extra 2012; 7: 36–38.
12. Tachibana T, Orita Y, Fujisawa M et al.: Factors that make it difficult to diagnose cervical tuberculous lymphadenitis. J Infect Chemother 2013; 19: 1015–1020.
13. Cai PQ, Li YZ, Zeng RF et al.: Nasopharyngeal tuberculosis: CT and MRI findings in thirty-six patients. Eur J Radiol 2013; 82: e448–e454.