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CASE SERIES

Extrapulmonary Tuberculosis in Otorhinolaryngology: A Case Series Describing the Challenges in their Management

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ABSTRACT:

Background: In Otorhinolaryngology, tuberculosis (TB) though uncommon is not a rare clinical problem. HIV-TB co-infection, multidrug resistant tuberculosis (MDR TB), and Extrapulmonary tuberculosis (EPTB) continue to be major public health threats. The success of the WHO, "END TB" strategy requires their effective management. In this article we look into the challenges while dealing with cases of EPTB in otorhinolaryngology.

Case Series: The clinical presentations & epidemiology of patients with extra pulmonary tuberculosis in otorhinolaryngology highlight the challenges in their management. Patients with laryngeal TB and TB of oral cavity and oropharynx are cases where the diagnosis can be easily delayed owing to lack of awareness and the need to exclude the other commoner lesions. The early diagnosis can be challenging with symptoms that mimic malignancy with subsequent hurdle being obtaining the histopathology report and confirmation of diagnosis. As elimination of this disease is the target which needs to be met there is need to ascertain features that will help accomplish the goal.

Discussion: Laryngeal tuberculosis is an area that demands high index of suspicion with technical expertise in obtaining positive yield on histopathology which can at times be challenging. Dysphagia is a symptom where the diagnosis of tuberculosis in our patient came as a surprise rather than the norm which required the histopathological report to retrospectively think on the likely pathology.

Conclusion: Extrapulmonary tuberculosis in otorhinolaryngology can have varied and atypical presentations responsible for delay in diagnosis. Awareness of this entity especially when the clinical signs are out of proportion to the symptoms among patients presenting to ENT OPD and emergency is necessary for prompt treatment. The features of carcinoma co-existing and confusing the diagnosis; along with paucibacillary nature of the specimens resulting in negative cultures makes histopathological examination mandatory, which is one among the challenges to be addressed for early diagnosis of EPTB cases in ENT. The timely initiation of anti tubercular treatment (ATT) can help avoid unnecessary surgery and morbidity

Keywords: Extrapulmonary TB(EPTB), laryngeal tuberculosis, Vocal cord palsy, dysphagia

Introduction:

Extrapulmonary tuberculosis (EPTB) poses a challenge to the clinicians not only in diagnosis but also in treatment as well as prevention and control. Although overall TB cases have been following a downward trend for the last years, proportion of EPTB cases compared to pulmonary tuberculosis (PTB) have increased in a study done, denoting a lack of effectiveness in control programs regarding EPTB.[1] One of the reasons for failure of TB control programme is the failure to timely diagnose and treat cases of EPTB. EPTB becomes more important as chances of developing it in immunocompromised patients are higher than their immunocompetent counterparts. Studies have suggested that the site of EPTB may vary according to geographic location, population groups and a wide variety of host factors. According to The Global TB Report 2020[2], Extrapulmonary tuberculosis (EPTB) constituted 16% of the 7.5 million reported TB cases globally and 19% in South-East Asia. However, these estimates may be the tip of the iceberg, as a considerable proportion remains undiagnosed or not notified.[4]

Tuberculosis in ENT is an uncommon but not rare clinical problem. Most physicians do not consider TB in the differential diagnosis of various otorhinolaryngeal symptoms, resulting in misdiagnosis and improper treatment. Despite the decline in the incidence of tuberculosis worldwide, there has been a re-emergence of the disease in various subspecialties of otolaryngology.[2]Symptoms and signs of tuberculosis of this region can mimic malignancy, and; hence, an early diagnosis is essential. HIV-TB co-infection, multidrug resistant tuberculosis (MDR TB), and EPTB continue to be major public health threats which require high index of suspicion, meticulous evaluation and timely appropriate treatment for control. In many cases of EPTB the challenge is in tissue diagnosis as at times even if symptoms and signs are suggestive obtaining sufficient sample as deemed necessary may become difficult. Usually, the extrapulmonary sample obtained by fine-needle aspiration or biopsy is used for microscopy, histopathology, culture, biochemical/immunological, and molecular testing, including drug susceptibility, to start an effective treatment. The sensitivity and specificity of various tests used to diagnose EPTB are highly variable; in most cases, clinical disease presentation should be considered in choosing and interpreting a specific diagnostic test. The treatment regimen for EPTB is the same as that for PTB for drug-sensitive and resistant cases; however, brain or bone involvement prompts a more extended treatment than PTB. In this regard tertiary care centres appear to be an excellent place for medical education & operational research. Just as in oncological practice the EPTB cases many a times require a multidisciplinary approach with a consensus to initiate therapy in challenging cases.

In view of the clinical significance of EPTB, this case series aims to highlight the varied clinical presentations and likely challenges in diagnosis and treatment of patients with EPTB of otorhinolaryngeal regions.

Case Series:

CASE REPORT 1

A 20 year old male MBBS student presented with hoarseness of voice for 2 weeks. The patient had cough without expectoration for over one year for which he had sought treatment from various doctors. The symptoms improved with medications but there was recurrence after a week or two. He had no history of fever, loss of appetite or loss of weight. There was no history of tuberculosis or tuberculous contact. On clinical examination indirect laryngoscopy revealed bowing of the left vocal cord which was in paramedian position with impaired mobility. There was left vocal cord paralysis which was confirmed on video laryngoscopy. (Fig 1) All his routine blood investigations were normal except for his ESR which was 29mm/hr. A contrast enhanced computed tomography scan from base of skull to diaphragm done to identify the etiology showed enhancing soft tissue lesion in the subcarinal location with discrete lesions in the paratracheal and hilar stations. (Fig 2) The diagnosis now required a histopathological confirmation from the lymph nodes which was challenging in view of the site and requirement of technical expertise to obtain it. Endobronchial ultrasound done, confirmed necrotic mass in the subcarinal region extending to the left hilar region. A transbronchial needle aspiration was done and microscopy showed necrotizing granulomatous inflammation with suppuration and the CBNAAT of the aspirate was positive. The patient was started on Anti tuberculous treatment (ATT) with improvement in symptoms. This case highlights the need for high index of suspicion of EPTB among young patients with unilateral vocal palsy with no co-morbidities. The need for confirmation of diagnosis with histopathology is imperative to initiate treatment as early as possible.

Fig 1: Video laryngoscopy picture showing left vocal cord palsy (Case report 1)

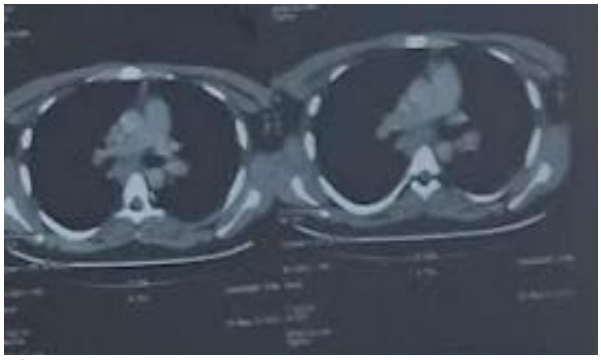

Fig 2: CECT Scan neck and thorax revealing the hilar lymphadenopathy (Case report 1)

CASE REPORT 2

A 52-year-old male patient, a driver, presented with pain on the right side of the neck for 3 months and hoarseness of voice for 2 months. He had no history of fever, sore throat, dysphagia, difficulty in breathing, loss of appetite or loss of weight. He was a smoker and occasional alcoholic. On clinical examination indirect laryngoscopy showed a hyperemic left vocal cord with thickening of the posterior two thirds of the cord. (Fig 3) Both the vocal cords were mobile with adequate glottic space. All blood investigations were normal except ESR of 32mm/hr. The Chest X-ray was normal and sputum AFB negative. The patient underwent direct laryngoscopy with biopsy and the histopathological report showed multiple giant cells, few Langerhans's cells and foci of caseous granulomatous lesions suggestive of tuberculosis. The patient was started on ATT with symptomatic improvement in 3 months and resolution of signs in 6 months. Laryngeal tuberculosis requires high index of suspicion among patients in places where TB is endemic, and features of laryngeal tuberculosis must be confirmed with biopsy. The biopsy in this area is of importance with need of adequate specimen and positive clinicopathological co-relation.

CASE REPORT 3

We had a 54-year-old male patient, a manual labourer who presented with foreign body sensation throat with no improvement with medications or treatment. On clinical examination indirect laryngoscopy revealed hyperemia of the left arytenoid with a granulomatous lesion obliterating the left pyriform sinus. There were no palpable neck nodes and the patient gave no history of use of tobacco in any form. The video laryngoscopy confirmed the findings with edema and hyperemia of the arytenoid and lesion obliterating left pyriform sinus. (Fig 4) In view of persisting symptom patient underwent direct laryngoscopy with biopsy which showed necrotizing granulomatous inflammation and CBNAAT positive. The patient was started on ATT with improvement clinically at 6 months.

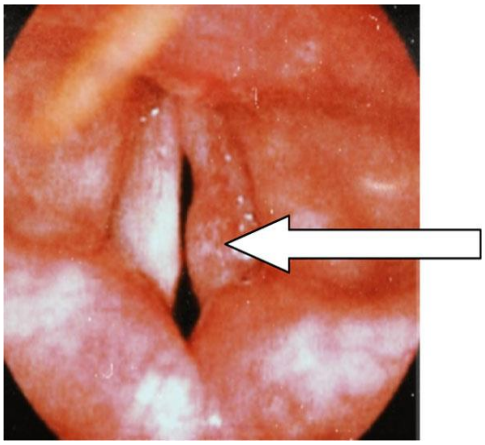

Fig 3: Video laryngoscopy picture of patient with laryngeal TB with single red cord (Case report 2)

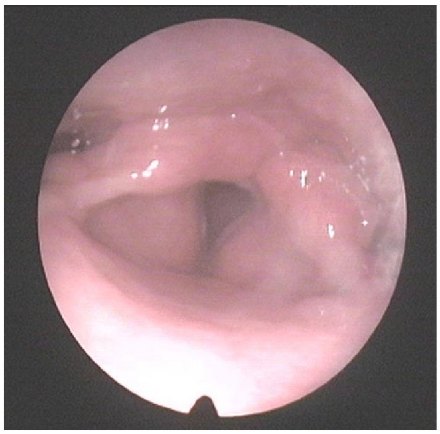

Fig 4: Video laryngoscopy showing edema left arytenoids with obliteration left pyriform fossa (Case report 3)

CASE REPORT 4

A 30-year-old male, a painter, presented with neck pain aggravated on movements of the neck and difficulty on swallowing for 3 months. There was no history of trauma, fever, neck swellings or loss of appetite and loss of weight. On clinical examination there was a bulge seen on the posterior pharyngeal wall left side (Fig 5) with indirect laryngoscopy normal. An MRI cervical spine done revealed an ill-defined T1 isointense; T2, STIR hyperintense lesion measuring 3.3 x 1.5 x 3.4 cm noted involving left lateral mass of C1 vertebra extending anteriorly in front of the anterior tubercle to the prevertebral space on left side behind the longus capitus muscle. (Fig 6) A differential diagnosis of Giant cell tumor or osteoblastoma was to be considered. The FNAC revealed abundant myxoid material with few small lymphoid cells. A trans oral excision of the cyst under general anesthesia was planned. (Fig 7) The lesion was excised with histopathology revealing necrotizing granulomatous lesion with multinucleated giant cells suggestive of tuberculosis. The histopathology came as a surprise with significant improvement post ATT. In patients with dysphagia when symptom persists despite treatment a thorough investigation to rule out tuberculosis must be carried out.

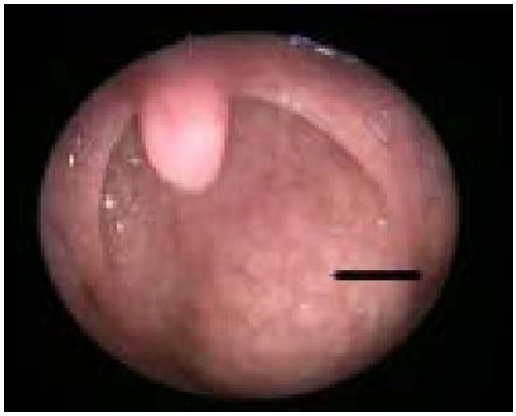

Fig 5: Oropharyngeal examination of patient with dysphagia revealed a bulge in the posterior pharyngeal wall left (Case report 4)

Fig 6: MRI Cervical spine showing T2 hyperintense lesion extending anteriorly in front of the anterior tubercle to the prevertebral space on left side behind the longus capitus muscle.

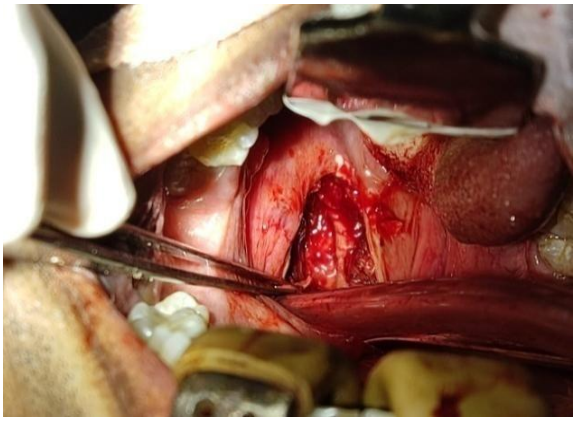

Fig 7: Transoral excision biopsy under GA being done

CASE REPORT 5

We had a 58-year-old male patient, a manual labourer who presented with a lesion in the oral cavity on the inner surface of his left cheek for over 4 months. He had no co-morbidities and was a nonsmoker and an occasional alcoholic. On clinical examination there was a pale well circumscribed, round ulcer with a diameter of about 1.2 cm on the left buccal mucosa with surrounding erythema. (Fig 8) There was no tenderness or induration. There was a single level II lymph node approximately 2 x 1.5 cm, mobile and non-tender. AFB smear microscopy and culture from the lesion was negative with FNAC from the lymph node showing diffuse reactive hyperplasia with abundance of lymphocytes. An excisional biopsy from the edge of the lesion with further histopathological examination showed classical necrotizing granulomatous lesions with epitheloid cells. The application of trichloroacetic acid on the raw surface with initiation of ATT helped in resolution of the lesion and the symptoms within 3 to 4 months.

In our case series, patients with laryngeal tuberculosis presented with change in voice, neck pain or persistent sore throat and foreign body sensation throat not responding to the usual line of management. All our patients were males with two of them in 2nd and 3rd decade of life. A raised ESR could help in raising the suspicion of tuberculosis especially in young or adolescent patients. A biopsy from the site with CBNAAT helped confirm the diagnosis and initiate treatment with ATT. Dysphagia, however is one symptom where a meticulous evaluation is necessary and lesions in oral cavity and oropharynx must be biopsied to help reach the appropriate diagnosis as early as possible.

Fig 8: Ulcerative lesion over buccal mucosa left (Case report 5)

Discussion:

Extrapulmonary tuberculosis (EPTB) includes tuberculosis affecting any organ other than the bronchopulmonary regions but there is a school of thought where the division of the lung and their covering pleura into two separate organs is felt incorrect and therefore they ascribe both organs to pulmonary tuberculosis, and instead of extrapulmonary tuberculosis use the terms extra thoracic tuberculosis (ETTB) or extra respiratory tuberculosis, which merge the tuberculosis of all organs except thoracic ones.[3] EPTB affecting the otorhinolaryngeal areas though uncommon is not rare. India is one among the 8 countries harbouring half the population with tuberculosis. Every year, 10 million people fall ill with tuberculosis (TB). Despite being a preventable and curable disease, 1.5 million people die from TB each year – making it the world's top infectious killer.[4]

Cervical lymphadenopathy, the most common clinical presentation of EPTB in the otorhinolaryngeal regions; is known to affect the posterior triangle lymph nodes, upper deep cervical group of lymph nodes and the submandibular lymph nodes. Laryngeal TB accounts for around 1% of all cases of tuberculosis and approximately 2-5% of extrapulmonary tuberculosis cases worldwide (Gupta et al., 2014).[5]The aetiology is the dissemination via the blood stream, of bacillary pulmonary foci or from the bacilli gaining entrance via the tonsils, dental or pharyngeal foci. However, any lymph node may be affected but this most prevalent form of TB in the head and neck region presents itself insidiously with a gradual increase in the lymph node and evolution to caseation.[6] No gender difference was found among those suffering from TB in cervical lymph nodes. However, what was verified is that there was greater prevalence in the 35–44 years old age group.[7] However in our case series we had patients in 2nd and 3rd decade of life which is significant as younger patients with symptoms too must be evaluated to rule out EPTB. The diagnosis was confirmed by USG neck and FNAC. It has been suggested by Chakravorty et al[8] that the paucibacillary nature of tissue other than sputum compromises the diagnosis rate in TB. In cases where FNAC is inconclusive a biopsy is necessary to confirm diagnosis. Transbronchial biopsy is an effective, safe and minimally invasive method for diagnosing endobronchial tuberculosis, particularly when mycobacterial culture of respiratory specimens is slow or has low sensitivity.[9]

The presented case series highlights the significance of considering extrapulmonary tuberculosis (EPTB) as a potential aetiology in patients with atypical symptoms such as hoarseness of voice, neck pain, dysphagia, and oral lesions. These cases emphasize the importance of maintaining a high index of suspicion for EPTB, particularly among young individuals without comorbidities. Early recognition and diagnosis of EPTB are crucial for initiating prompt treatment and preventing potential complications. The most common sites of tuberculosis in the larynx are, respectively, the interarytenoid region, the arytenoid cartilages, the posterior surface of the true vocal cords and the laryngeal surface of the epiglottis.[10]Two of our patients with laryngeal tuberculosis had involvement of the mentioned sites with one patient having a single hyperaemic cord and the other having involvement of the arytenoid. Vocal cord paralysis is rare among patients with pulmonary TB, occurring in less than 1% of cases.[11] The mechanism involved includes recurrent laryngeal nerve involvement by the inflammatory process in the lung apex or extrinsic compression by a mediastinal lymph node. The young male who presented with unilateral vocal cord paralysis in our case series too had

involvement of the hilar and subcarinal lymph nodes which was missed resulting in delay in diagnosis.

In the case of laryngeal tuberculosis, the symptoms often mimic other more common conditions, leading to delayed diagnosis and treatment. Therefore, it is essential for healthcare professionals to consider tuberculosis in differential diagnosis, especially in areas where TB is endemic. In these cases, laryngeal tuberculosis is confirmed using various diagnostic techniques, including indirect laryngoscopy, direct laryngoscopy with biopsy, and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). These approaches allowed the visualization of characteristic findings such as unilateral vocal cord paralysis, granulomatous inflammation, and necrotic lesions, helping to confirm the diagnosis and initiate appropriate anti-tuberculous treatment.

In addition to laryngeal tuberculosis, this case series also highlights the importance of considering tuberculosis in patients presenting with other manifestations such as neck pain, dysphagia, and oral lesions. In these cases, investigations including imaging studies (CT scan, MRI) and fine-needle aspiration cytology (FNAC) were instrumental in confirming the diagnosis. Radiological investigations play a crucial role in the early and correct identification of EPTB. Imaging modalities of choice are computed tomography (CT; lymphadenopathy and abdominal TB) and magnetic resonance imaging (MRI; CNS and musculoskeletal TB).[12] In our patient with lesion in the oropharynx; MRI done revealed the lesion with extension to the prevertebral space. The biopsy is of particular importance in the diagnosis of EPTB. It not only provides histopathological evidence but also enables clinicopathological correlation, which is crucial for accurate diagnosis. However, obtaining an adequate specimen from the larynx for histopathological examination can be challenging due to the anatomical location from where appropriate representative sample must be obtained and need for technical expertise with appropriate setting for successful outcome. These findings emphasize the necessity of a comprehensive evaluation when patients present with symptoms suggestive of tuberculosis, even if they do not have respiratory symptoms or a history of tuberculosis exposure.

On confirmation of diagnosis Anti tubercular therapy (ATT) is started as per Revised National Tuberculosis Control Programme guidelines (RNTCP). Quadritherapy with Isoniazid (INH), Rifampicin (RIF), Ethambutol (EMB) and Pyrazinamide (PZA) for 2 months, followed by INH and RIF for 4–7 months, is generally accepted. Role of surgery is limited only in obtaining samples for histopathology. The main stay in treatment is by anti- tubercular (ATT) treatment according to RNTCP guide- lines. If compliant, majority of symptoms decrease by 3 months after starting ATT.[15]In all our patients on initiation of therapy with ATT the symptoms resolved by 3 months and on follow up improvement was confirmed by 6 months. The patients with oropharyngeal lesion required surgical excision for diagnosis and the procedure was a blessing in disguise as it confirmed the diagnosis with prompt initiation of treatment.
Extrapulmonary tuberculosis (EPTB) still contributes to a substantial TB incidence, and under-diagnosis of EPTB is also likely to cause life-long sequelae and fatal complications.[11] Despite the large number of existing reports, the patient risk of medical injury and occupational exposure caused by a delayed diagnosis of head and neck tuberculosis does not seem to have decreased over the past decade.[13] Therefore the need to apprise on increased awareness of cases with EPTB affecting head and neck regions with stress on a multidisciplinary approach involving otolaryngologists, pulmonologists, radiologists and pathologists to ensure proper sampling and interpretation of biopsy specimens is a mandate. Early diagnosis and treatment can greatly enhance the therapeutic effect and patients' quality of life.[14]The greater access to diagnostic services could improve diagnosis, increase the number of diagnosed EPTB and improve clinical management of EPTB as well as treatment outcomes.[16]

Conclusion:

Extrapulmonary tuberculosis (EPTB) in otorhinolaryngology poses a challenge to the clinicians not only in early diagnosis but also in prompt initiation of treatment as well as prevention and control. The success of TB control programme mandates appropriate management of all these cases of EPTB. Tuberculosis in ENT is an uncommon but not rare clinical problem hence awareness of this entity especially when the clinical signs are out of proportion to the symptoms among patients is necessary. The features of carcinoma co-existing and confusing the diagnosis; along with paucibacillary nature of the specimens resulting in negative cultures makes histopathological examination mandatory, which is one among the challenges to be addressed for early diagnosis of EPTB cases in ENT. Laryngeal TB and TB of oral cavity and oropharynx require high index of suspicion with use of radiology and biopsy to confirm the same and initiate ATT at the earliest. Timely initiation of treatment with ATT can avoid unnecessary surgery and morbidity.

Consent: The patients provided written informed consent held in the electronic medical record. The approval is obtained from Institutional Research Committee (IRC) vide IRC/2023/Protocol/405 dated 20/01/2024

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Conflict of interest: The authors have no conflict of interest to declare.

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