



Nontuberculous Mycobacterial Adenitis Of The Neck – An Intriguing Case Report With Literature Review

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Abstract

Here, we present a very intriguing case report of a young patient who presented to the out patient department of our institute with complain of neck nodule and was later diagnosed as a case of extrapulmonary tuberculosis identified further as Non-Tuberculous Mycobacteria (NTM). Timely initiation of therapy not only halted the disease progression but also led to significant symptomatic relief in the patient.

Keywords: neck nodule; extrapulmonary; tuberculosis; Non-Tuberculous Mycobacteria; therapy; progression

Introduction

The Indian subcontinent is a tuberculosis endemic zone owing to malnutrition, poverty, poor hygienic and sanitary conditions. Tuberculosis (TB) is a chronic pulmonary disease which primarily infects the lungs and is characterized by granulomatous inflammation [1]. The causative agent being an acid fast bacilli known as “Mycobacterium tuberculosis (M.tb)” It is a complex disease with a variety of clinical features and complications which poses a challenge to the treating physicians in diagnosing the disease. One-fifth of the patients with pulmonary infections can manifest the disease as extrapulmonary TB, which can affect a myriad of organs starting right from lymph nodes, bone, kidneys, etc. [1]. Diagnostic dilemma leads to either untreated cases for a longer time or late initiation of therapy. This leads to significant impact on the overall mortality and morbidity rates of the cases [2]. The cases of head and neck TB are relatively rare, and lack of fever, signs of inflammation makes the scenario even worse to diagnose and can be very easily left undiagnosed [2]. Majority of the extrapulmonary TB patients who present to the OPD with neck nodules or

cervical tuberculous lymphadenitis have absence of systemic symptoms as was seen in our patient. [3] In these case scenarios, Nontuberculous mycobacteria is implicated in substantial numbers and the cases is on a rise in the current times.

Nontuberculous mycobacteria (NTM), is also known as environmental mycobacteria, atypical mycobacteria and mycobacteria other than tuberculosis (MOTT). They are widely distributed in the environment, particularly in wet soil, marshland, streams, rivers and estuaries. Human disease is believed to be acquired from environmental exposures.

NTM have been categorized into 4 groups by Runyon (1959) based on pigment production and the growth rate: 1. *Photochromogens* - produce pigment only in light. 2. *Scotochromogens* - produce pigment in dark. 3. *Non-photochromogens* - do not produce pigment. 4. *Rapid growers* - growth occurs within 7 days.

Here, we report a very interesting and intriguing case of an extrapulmonary tuberculosis caused by a Non-Tuberculous Mycobacteria; *Mycobacterium abscessus*. Timely diagnosis and prompt initiation of therapy not only halted the disease progression but also led to significant symptomatic relief in the patient.

Case Report :

A 21-year-old healthy male visited the ENT OPD (out-patient department) of our institute with chief complaints of left cervical lymphadenopathy with multiple neck nodules from last 7 months. He gave the present history of progressive increase in the size of swelling over past two months with slight pain and redness. According to him, the swelling was initially only single in number but now, he could appreciate the development of another swelling over past two months in the same region. There was no associated dysphagia or odynophagia. There was no significant past history of any fever, rash, upper respiratory tract infection, weight loss, myalgia or any chronic disease. He had neither any recent travel history, nor any contact with animals or pets. Past history of the patient was negative for any drug or alcohol intake, and was a non-smoker and tobacco chewer. Family history also suggested no chronic illness or ailment in any of his blood relatives. In the treatment history, patient recalled multiple visits to different clinics in the past three months where he was prescribed antibiotics and steroids for the same. He completed the course of prescribed medicines but there was no relief in the neck swelling.

On clinical examination, the patient was non-febrile, no signs of sepsis or any septic manifestations were seen. Local examination of the neck region revealed two swellings in the left supraclavicular region measuring 5×6 cm and 4 x 6 cm respectively. The swellings were fluctuant in feel with no visible punctum, was tender and erythematous with blackish discoloration in one of them (figure 1). Multiple matted, firm, non-erythematous lymph nodes corresponding to level II of the neck were palpated. No lymphadenopathy or hepatosplenomegaly was seen. On auscultation of the Chest area, it was clear and bilaterally equal.

Patient was advised Routine baseline blood investigations which was unremarkable with slightly raised erythrocyte sedimentation rate (ESR). Liver

and Kidney function tests were also normal. Fine - needle aspiration was done in the department of Pathology and frank pus was drawn. This was later sent for culture and sensitivity in the bacteriology lab to rule out bacterial etiology and acid-fast bacilli (AFB) to rule out tuberculosis the department of Microbiology. The pus AFB staining revealed the presence of multiple acid fast bacilli (figure 2), suggesting the presence of Mycobacterium species. TrueNat or real time PCR for the above showed result as “Mycobacterium TB -not detected” on two separate occasions. However, Solid culture on Lowenstein-Jensen (L-J) media showed the characteristic growth of Mycobacterium colonies on 7 days of incubation. (Figure 3) Further speciation of these mycobacterial colonies was done by special biochemical reactions and interpreted as: Niacin test negative, Aryl Sulfatase test positive, Nitrate reduction negative, Tween 80 negative, Growth in presence of PNB was positive. This gave the presumptive diagnosis as *M. abscessus* which was later confirmed by Line probe assay. Sputum microscopy for AFB was negative and the chest radiography was unremarkable. Antibiotic sensitivity was performed for *M. abscessus* which revealed sensitivity to Amikacin, Azithromycin, Clarithromycin and Cefoxitin.

Finally, the patient was diagnosed as a case of extrapulmonary tuberculosis due to *M. abscessus* and was referred to the ENT department for further management. The patient was later started on an initial combination antimicrobial therapy with azithromycin 500 mg daily plus amikacin (25 mg/kg 3×/wk) with cefoxitin (up to 12 g/d given in divided doses) intravenous agents for two months followed by oral azithromycin 500 mg daily for a month. Routine Follow-up was planned and at his subsequent visit after a month, the patient did not report of any new symptoms, while redness and tenderness of the swelling had subsided and neither there was development of any new neck nodule. The patient was advised for monthly follow ups in the OPD, strict compliance with the therapy and good dietary habits. After two months of initiation of therapy and with good patient compliance, complete resolution of nodule was seen in the above case.

Discussion :

Neck nodules or mass usually comes with a variety of differential diagnosis depending on the age groups of patients attending the physicians. With an exhaustive list of etiologies ranging from benign to serious infections, the tertiary level centres should play a key role in diagnosing and managing these undiagnosed cases. Early initiation of therapy will not only result in better patient outcome but will also help to reduce the overall disease burden. 'Scrofula' or more precisely cervical tuberculous lymphadenopathy is the tuberculosis affecting the neck lymph nodes. The disease usually manifests as a result of a primary infection of the lymph nodes with the acid fast bacilli or a secondary one with foci in other sites of the body. Lymphatogenous or hematogenous route from the primary foci is the cause of dissemination of this bacilli to these extrapulmonary sites. Causative agent for cervical tuberculous lymphadenopathy is usually *M. tuberculosis* (*M.tb*) in adults and nontuberculous mycobacteria (NTM) like *M. avium*, *M. abscessus* and *M. kansasii* in children [4].

Jones and Campbell have described five stages involving the progression of tuberculous lymphadenitis. They are as follows: Stage 1: enlarged, firm, mobile, discrete nodes showing non-specific reactive hyperplasia. Stage 2: large rubbery nodes fixed to surrounding tissue owing to periadenitis. Stage 3: central softening due to abscess formation. Stage 4: collar-stud abscess formation. Stage 5: sinus tract formation. The patient in our case presented in stage 2, where there was signs of inflammation and periadenitis. Majority of the patients with cervical tuberculous lymphadenitis do not present with systemic symptoms, as was seen in our case. Our patient was treated with various courses of antibiotics misdiagnosing the neck mass to be of bacterial origin and a bacterial lymphadenopathy. The absence of constitutional symptoms like malaise, fever were against the bacterial etiology.

Lymphoma patients usually present with symptoms like fever and other constitutional features, while the malignant cases of head and neck present with lesions in ear, nose and throat. A differential diagnosis which should also be kept in mind is Kikuchi disease. It is also known as histiocytic necrotising lymphadenitis and typically presents with cervical lymphadenopathy which is painless in nature with or without systemic signs and symptoms.

The disease is usually self-limiting and has an autoimmune nature. The treatment modality usually remains as supportive only. The diagnosis in cases of cervical nodules usually relies on Fine-needle aspiration cytology (FNAC). The test has sensitivity as well as specificity.

Ziehl-Neelsen (ZN) staining for Acid fast bacilli (AFB) with culture either on solid or liquid media forms the mainstay of diagnosis of Tuberculosis in any case. However, a negative ZN stain does not rule out the possibility of tuberculosis. [5,6] In the cases where AFB load is thought to be scanty or less in the sample or in extrapulmonary tuberculosis, Real Time Polymerase chain reaction (RT-PCR) has proven to be a boon. RT-PCR by TrueNat not only detects the presence of *M.tb* but also tests the sensitivity to Rifampicin. ATT in cases of extrapulmonary TB is started with intensive phase of 6 months combination chemotherapy of rifampicin, isoniazid, pyrazinamide and ethambutol. Renal and liver function tests are a priority before the initiation of therapy.

M. abscessus belongs to the group of rapid growers of Non-Tuberculous Mycobacteria. The Colonies of rapid growers appear within 7 days of incubation as was seen in the above case. 6 major groups of rapid growers have been studied in literature: *M. fortuitum* group, *M. chelonae*/ *M. abscessus*, *M. smegmatis* group, Early pigmented RGM, *M. mageritense*/ *M. wolinskyi* group, *M. mucogenicum*. Speaking of the disease spectrum, the rapid growers are implicated in pulmonary or disseminated disease in the form of nodules, post-injection abscesses, wound infections. Outbreaks of abscesses following injection of vaccines contaminated by these have also been reported.

Here, we present an analysis and review of the cases of NTM in population in the recent years cited in literature with their management.

Diagnosis and management of NTM cervical tuberculous lymphadenitis is a challenge for the treating doctors as there are no clear guidelines for the same. A well established diagnostic laboratory for the diagnosis of these cases is also a limitation. Approximately, 15%–30% of the cases of cervical lymphadenopathy present with residual lymph nodes after the completion of therapy. But, their presence usually does not always imply failure of the treatment

,it can also be a case of reactive lymphadenitis. Follow up and close monitoring of these cases is hence very vital. Chemotherapy provides a favourable prognosis in the patients of cervical TB lymphadenitis and neck swellings;provided the compliance is good. [23]This was also seen with our patient on follow up after one month as the symptoms started subsiding and no new nodules were seen during the course of treatment.The patient was advised and counselled for regular follow-ups and strict compliance to the chemotherapy regimen.

Conclusion :

Diagnosis of Non tuberculous mycobacteria cervical lymphadenitis is quite challenging but the prognosis is usually good with chemotherapy regimen ,compliance and follow ups. The developing countries of the Asian subcontinent are beaming with the loads of undiagnosed pulmonary as well as extrapulmonary cases of tuberculosis.The untreated or improperly treated cases further lead to the development of resistance for the currently used anti-TB drugs .Hence, timely diagnosis and management of such extrapulmonary cases of tuberculosis is the only weapon to fight this demon.

Ethics approval: Informed consent was obtained from the patient regarding the publication of images and clinical information in the journal.He was informed of the confidentiality of the data ,however ,the anonymity cannot be guaranteed.

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Author	Year of publication	Patient demographics	Pathogens isolated	Management
Goutzamanis and Gilbert (7)	1995	Review of 8 children	<i>M. ulcerans</i>	Surgical excision for all patients with one patient requiring limb saving heat treatment after both anti-mycobacterial drug and surgery failed to stop progression of necrotizing ulceration
Wright (8)	1996	Review of 89 children ages 1 to 10 years old	Unspecified NTM isolates	55 surgical excisions with one recurrence and eight excision and curettage with two recurrences
Wark <i>et al.</i> (9)	1998	Review of 10 children ages 1 to 5 years old	<i>M. avium, intracellulare, gordanae</i>	Nine surgical excisions as initial management with one developing a discharging sinus requiring 2 weeks of Trimethoprim/Sulfamethoxazole and Rifampicin
				1 incision and drainage with recurrence of disease requiring complete excision
Fergusson and Simpson (10)	1999	Review of 10 children	Unspecified NTM isolates	Ten successful curettages with two experiencing delayed wound healing and one requiring a repeat curettage 7 months post-primary excision due to recurrence
O'Brien <i>et al.</i> (11)	2000	Review of 4 children ages 0 to 9 years old	<i>M. avium</i> complex, <i>fortuitum, gordanae</i>	All 4 underwent surgical excision for lymphadenitis with no adjunctive chemotherapy and no relapse of disease detected

Flint <i>et al.</i> (12)	2000	Review of 57 children	<i>M. avium intracellulare, kansasii</i>	Eleven received surgical excisions, 30 patients received incision and drainage, 13 received incision and curettage and three had aspirations
Daley (13)	2001	3-year-old patient	<i>M. avium</i> complex	Spontaneous resolution of lymphadenopathy, no medical or surgical intervention
Blyth <i>et al.</i> (14)	2009	Review of 102 children ages 1 to 14 years old	<i>M. avium</i> complex, <i>intracellulare</i>	78 surgical procedures and 42 received anti- mycobacterial therapy, 25 received both therapies
Sparks and Khatami (15)	2014	14-year-old patient	<i>M. fortuitum</i>	10-week course of oral Trimethoprim/ Sulfamethoxazole and Moxifloxacin
Chong <i>et al.</i> (16)	2015	12-year-old patient	<i>M. avium</i> complex, <i>intracellulare</i>	12-month course of Ethambutol and Clarithromycin
Tebruegge M <i>et al.</i> (17)	2016	Review of 140 children with NTM disease	<i>M. avium</i> complex, <i>ulcerans, marinum</i>	97.2% of lymphadenitis cases underwent surgical excision with reduced disease recurrence in groups treated with Clarithromycin and Rifampicin compared with groups with Clarithromycin alone or no anti-mycobacterial drugs
Mahadevan (18)	2016	Review of 97 children ages 8 to 15 years old	<i>Unspecified NTM isolates</i>	Higher cure rates with excision compared to incision and drainage
Freyne and Curtis (19)	2017	3-year-old patient	<i>M. gordonae</i>	Excision biopsy followed by treatment of Clarithromycin, Rifampicin and Ethambutol for 3 months. Clarithromycin changed to Azithromycin for improved compliance and oral regimen continued for 6 months total
Berkhout A <i>et al.</i> (20)	2020	13-year-old patient	<i>M. abscessus</i>	Initial treatment with two surgical debridements and insertion of Vancomycin beads followed by 8-week oral course of Azithromycin and Linezolid followed by 6-month course of same while awaiting definitive procedure
Aliano and Thomson (21)	2020	Review of 99 children ages 0 and 12 years old	<i>M. avium</i> complex, <i>intracellulare, haemophilum</i>	Not discussed in article

Foley et al. (22)	2021	12-year-old patient	<i>M. fortuitum</i>	Initial treatment with surgical debridement, oral Rifampicin and Doxycycline. Changed to intravenous Meropenem and oral Azithromycin, Doxycycline, Ciprofloxacin and Fluconazole on day 6. Antimicrobials rationalised to Doxycycline, Ciprofloxacin and Fluconazole on day 30
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Fig 1 : Neck region revealing two swellings in the left supraclavicular region



Fig 2 : Pus AFB staining revealed the presence of multiple acid fast bacilli , suggesting the presence of Mycobacterium.

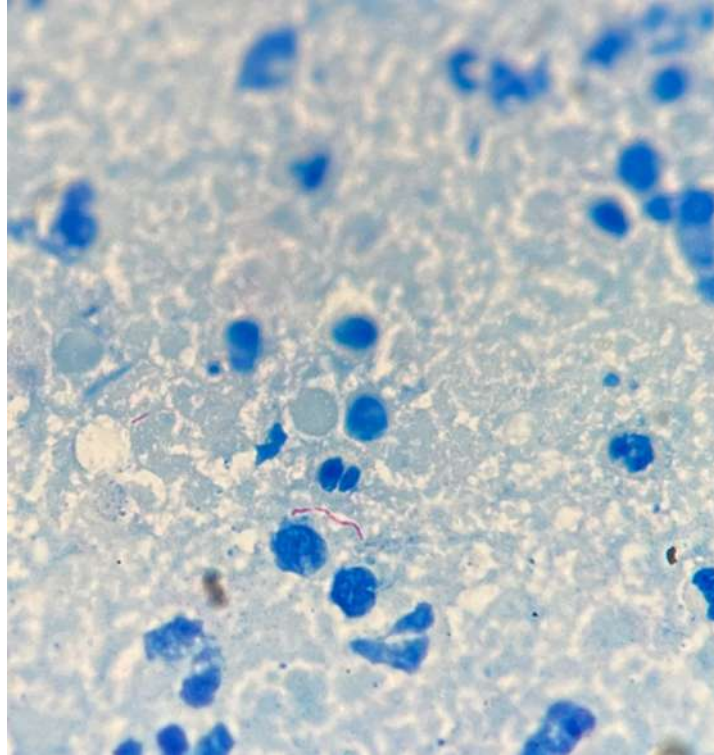


Fig 3 : Lowenstein-Jensen (L-J) media showing the characteristic growth of *M.abscessus* colonies.

