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Original Research Paper

Respiratory Medicine

A CASE REPORT OF ISOLATION OF MYCOBACTERIUM ABSCESSUS IN A CHILD OF MENDELIAN SUSCEPTIBILITY TO MYCOBACTERIAL DISEASES.

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ABSTRACT Mendelian susceptibility to mycobacterial diseases (MSMD) is an inborn error categorized by defects in intrinsic and innate immunity with defects in the production and levels of Interferon (IFN). There is vulnerability to less virulent mycobacteria, such as Bacillus Calmette-Gu´erin (BCG) vaccine strains, as well as nontubercular mycobacteria (NTM). A definitive diagnosis is made by genetic analysis. The NTM group, though ubiquitous in nature, presents mostly in patients with immunodeficiency or underlying lung disease. A case of NTM in a patient with MSMD has been portrayed here accompanied by difficulties in diagnosis and management in a resource limited setting.

KEYWORDS :

INTRODUCTION

Mendelian susceptibility to mycobacterial diseases represents a group of diseases characterized by increased susceptibility to the less virulent strains of mycobacterium species.[1] The term coined for the disease is a misnomer, given the incidence of organisms such as salmonella, listeria, histoplasmosis, klebsiella etc. in these patients[1].

Physicians should take steps in evaluating recurrent lymphadenitis considering other possible infective causes of granulomatous lesion instead of rushing to initiate antitubercular treatment on clinical basis as per NTEP[2], one possible etiology being non tubercular mycobacteria among others. However, the NTM group of bacteria requires a prolonged course of a combination of antibiotics, to be administered orally and parenterally as well. The regimen advised as per BTS guidelines[3] differs in different groups of NTM. No guidelines that recommend the drug regime for NTM in paediatric cases has been published to the best of our knowledge.

We would like to report a case that presented at our department of NTM discovered in a child with underlying MSMD among the other limited cases reported so far in India.

CASE REPORT

A 5-year-old girl presented with complaints of pain, swelling and discharge from neck and behind ears on both sides over a period of 1 month. She developed episodes of fever, cough and gradually progressive shortness of breath over this period following which she was brought to our tertiary centre designed to treat both pulmonary and extrapulmonary tuberculosis and other chest diseases. A history of night sweats and weight loss was also elicited that raised the suspicions of tuberculosis being the culprit.

Parents gave history suggestive of Bacille calmette Guerin (BCG) adenitis at 1 month of age in left axilla followed by pus formation for which incision and drainage was done. She was started on ATT at 3 months of age which was given for 11 months duration. She was asymptomatic for 2 months after completion of ATT but developed fever and lymph node enlargement, this time in the inguinal area. Lymph node biopsy done showed evidence of tubercular granulomatous lymphadenitis. A course of ATT was prescribed at 2 years of age for a period of 15 months.

Patient was evaluated in our centre with routine investigations that were unremarkable. Chest X ray suggested consolidation, non contrast CT of chest was suggestive of multiple foci of subsegmental consolidation with diffuse lymphadenopathy. Lymph node fine needle aspiration cytology (FNAC) was suggestive of granulomatous inflammation which was however not supported by results from smear microscopy or catridge based nucleic acid amplification test (CBNAAT) from samples of lymph node aspirate or gastric lavage. USG guided right cervical lymph node biopsy was done and tissue culture revealed MYCOBACTERIUM ABSCESSUS. Meanwhile a search for possible underlying immunodeficiency yielded an abnormal Pstat1 with increased expression of IFNgR1 suggesting partial dominant IFNGR1 deficiency.

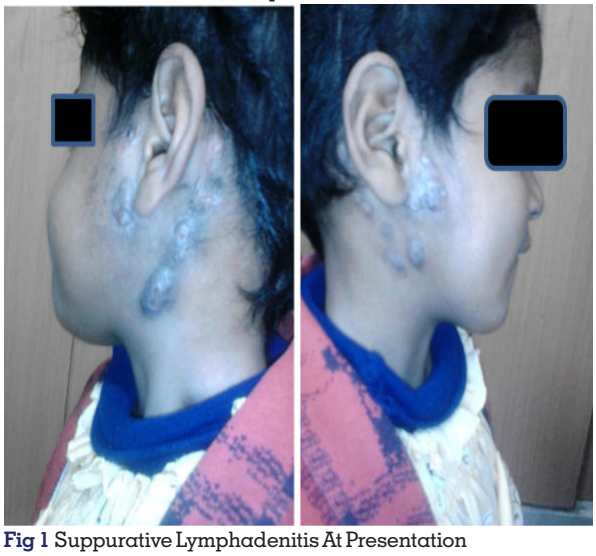

Fig 1 Suppurative Lymphadenitis At Presentation

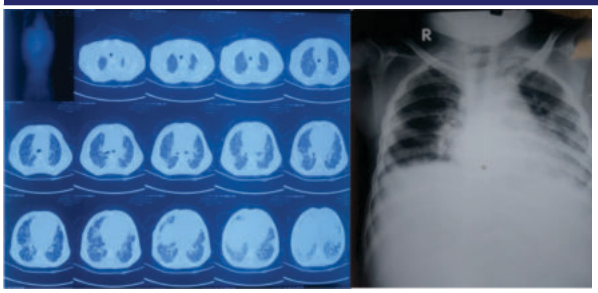

Fig 2 CT And Chest Xray Findings Suggestive Of Consolidation Of Middle And Lower Lobes Bilaterally

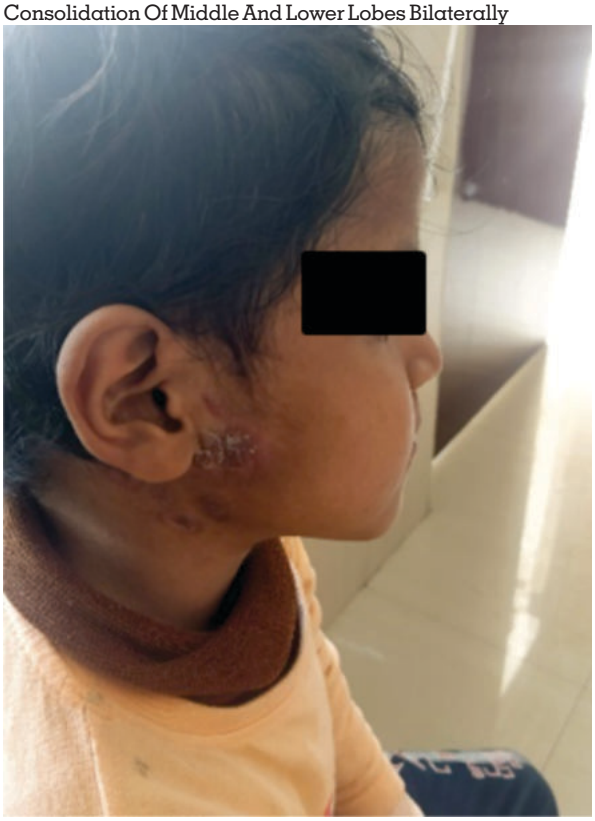

Fig 3 clinical resolution of symptoms at one year

Her treatment was initiated with parental antibiotics (Amikacin, Meropenem, Tigecycline) and oral Azithromycin. There was improvement in respiratory symptoms with a period of 1 month of treatment and lymphadenopathy subsided with scarring of lesion by 2 months. On follow up at 1 month, radiological resolution of consolidation was observed. The patient was kept on follow up at regular intervals with serial radiological monitoring for a period of 2 years. Follow up culture was found to be negative. She remained asymptomatic over the course of this period. An advice for hematopoietic stem cell transplant was suggested in view of underlying immunodeficiency.

REVIEW OF LITERATURE

Mendelian susceptibility to mycobacterial diseases cases have been published in limited numbers from the Indian subcontinent[1].

An inability to handle intracellular pathogens due to defects in IFN γ production (IL-12B, IL-12Rγ1, IL-12Rγ2) or response (IFN γR1, IFN γR2, STAT1) result in MSMD[4]. There are 16 major mutations involving 9 genes responsible for the condition which includes IFNγR1, IFNγR2, pSTAT1, RORγ T deficiency etc. the IFNγR1 deficiency was the first to be described[4].

AD partial IFNγR1 deficiency is characterized by increased expression of receptors on the cell surface due to a defect in the recycling of these receptors. Osteomyelitis caused by atypical mycobacteria is peculiar to this disease, and all patients presenting with mycobacterial osteomyelitis must be investigated for MSMD.[5,6]So far 7 cases have been reported in India to the best of our knowledge[1]. Our case was also found to have the same genetic deficiency. Moreover the presentation was not as osteomyelitis, but rather as pneumonia with lymphadenitis.

There is also an AR partial IFNγR1 deficiency which is a milder disease and cells of these patients show residual response to higher concentrations of IFN γ. They are susceptible to BCG and environmental mycobacteria but respond well to antitubercular drugs. Interferon γ injections are useful in this condition, and HSCT is not recommended[5,6.]

A study conducted in India showed BCG adenosis being the most common presentation followed by lymph node, bone and GI involvement.Lung involvement was seen in 6 % cases[1].

The organism reported in our case, M. Abscessus (Mycobacterium Abscessus), was first recognized as a human pathogen in the 1950s. A rapidly growing (NTM), this organism is mainly an environmental contaminant. Transmission of M. Abscessus occur via inhalation,ingestion or direct contact with an environmental source . It is regarded as the most pathogenic and chemotherapy- resistant mycobacterium.

The most common clinical presentation of M.Abscessus infection has been pulmonary disease (with cystic fibrosis as the most common clinical presentation) followed by skin and soft tissue infection[7].

Diagnosis of infection requires isolation of organism from atleast two sputum samples or one culture positive or histopathological evidence of the same[7]. Primary management should be combination of antimycobacterial therapy. Here in our case, we combined a combination of Amikacin, meropenem, tigecycline and azithromycin wherein the dose was adjusted according to weight and the choice of drugs were guided by drug sensitivity reports.

M. abscessus and *M. bolletii* exhibit extensive intrinsic and acquired resistance mechanisms due to a full-length functional *erm* (41) gene, while *M. massiliense* exhibits reduced resistance because of partial *erm* (41) gene expression[8]. Although consensus guidelines suggest preferential use of azithromycin over clarithromycin to limit inducible macrolide resistance, not all authors agree that the latter is a stronger inducer of the *erm* gene (41) than azithromycin[9,10].

Another study instead showed that M. a. abscessus may be less sensitive to clarithromycin than azithromycin, in contrast to *M.* a. massiliense, which appeared sensitive to both macrolides[8].

The resistance of M. a. abscessus to macrolides, streptogramins, and lincosamides may be mediated by mutations in the 23S rRNA[10].

The most active drugs for the treatment of MAbsC infection, in addition to azithromycin, are amikacin (IV, nebulized), cefoxitin (IV), and linezolid (IV, PO)[8,9]. Treatment should theoretically be continued 12 months beyond the last negative sputum culture in accordance with consensus guidelines, but it is burdensome, and in up to 50% of patients with MAC infection and in almost 100% of patients with MAbsC, it is interrupted because of its duration and adverse effects[10].

Surgical therapy should be considered as important adjunct when debridement of diseased tissue can be performed. We

were unable to perform whole genome sequencing and molecular techniques for subspecies typing due to the resource limited settings.

CONCLUSION

The authors aim to highlight the importance of non tubercular mycobacterial etiologies among the vast majority of tubercular cases that requires prolonged and combined treatment strategies. The identification of immunosuppressive states enables to identify less virulent and uncommon organisms and adopt prophylactic and curative measures as needed.

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AUTHOR CONTRIBUTIONS The authors contributed equally towards treatment, collection, analysis and interpretation of data, drafting, editing and revision of this manuscript.

CONSENT TO PARTICIPATE informed consent was obtained from the atient being reported in the manuscript.

CONSENT TO PUBLISH The authors affirm that human research participant provided informed consent for publication of images in figure 1 and 3.

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