

CNS Tuberculosis and Peripheral Medium Vessel Vasculitis: A Rare Presentation of Mycobacterium Tuberculosis Infection

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Abstract

Background: Tuberculosis is a very common disease in India with varied presentations. CNS Tuberculosis (TB) is the most severe form of TB in children and leads to mortality, if not treated timely and effectively (1).

Case report: A 7-year-old boy born out of a non-consanguineous marriage was admitted with a history of acute onset of extreme irritability, agitation and inability to recognize parents. Our patient presented with CNS TB and peripheral gangrene for which no cause could be ascertained clinically. We considered that the gangrene resulted from vasculitis secondary to tuberculosis infection based on the pathological presentation, radiographic changes and therapeutic response to ATT. The patient was treated with Antitubercular therapy (Isoniazid, Rifampicin, Pyrazinamide and Ethambutol) for 6 months, oral Prednisolone @ 2 mg/kg/day for 4 weeks with subsequent tapering to 1mg/kg/day for another 4 weeks and oral Aspirin @ 3 mg/kg/day for 6 months. He showed significant improvements with the above said management, with pain significantly decreased and range of motion improved after 2 weeks of starting treatment. He was discharged after 2 weeks. The child was followed up over a period of 2 years and there had been no reappearance of the above mentioned symptoms.

Conclusion: Overall, in this case, it was presumed that Mycobacterium tuberculosis infection was responsible for the neurological manifestations (CNS Tuberculosis) and it also induced the vasculitis process, ultimately causing gangrene and diminished pulsations of extremities.

Key Words: Case study, CNS Tuberculosis, Mycobacterium Tuberculosis Infection, Peripheral Medium Vessel Vasculitis.

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1- INTRODUCTION

Tuberculosis is a very common disease in India with varied presentations. CNS Tuberculosis (TB) is the most severe form of TB in children and leads to mortality, if not treated timely and effectively (1). Mycobacterium tuberculosis induced peripheral vasculitis involving medium sized vessels is very uncommon. I present a child with this rare presentation of a common disease.

2- CASE REPORT

A 7-year-old boy born out of a non-consanguineous marriage was admitted with a history of acute onset of extreme irritability, agitation and inability to recognize parents. There was no history of fever, cough, hemoptysis, headache, vomiting, convulsion, blurring of vision, weakness of limbs associated with this episode. 15 days later, he developed pain in left elbow and left knee and was not able to extend them. He started having a burning sensation in left foot while walking. The pain was so severe that he was not able to walk. He then developed painful digital tip blackish discolouration of left hand and foot (Fig. 1). His birth history, dietary and developmental history were unremarkable. His immunization was up to date. He had no family history of similar illness. There was no history of contact with tuberculosis. He belonged to a lower middle class family and studied in primary school.

On admission he was sick looking, conscious but irritable. Vitals were stable with a respiratory rate of 32/minute, pulse rate of 84/minute, and SpO₂ of 98% in room air. He had diminished left sided radial and brachial artery pulses in upper limbs and diminished left sided popliteal and posterior tibial arterial pulsation in lower limbs. Bilateral femoral pulses were equally palpable. There were intact pulsations in bilateral carotids having regular rhythm and average volume. Blood pressure in right sided upper and lower limbs were within normal limits, but it was 70/30 (diminished) in left upper limb and unrecordable in left lower limb. His weight for height was below -3SD and height for age was between -2 to -3 SD. Head to toe examination revealed early dry gangrenous changes in tips of thumb and ring finger of left hand and left great toe. Musculoskeletal examination revealed that the left upper limb was cold to touch, and the left elbow joint was in a flexed position with painful restriction of range of motion of the left elbow. There was visible wasting of the left thigh and left knee joint was flexed with restricted movements. Neurological examination was normal. Examination of other systems revealed no abnormality.

The blood investigations revealed: Mentioned elaborately in Tables 1, 2 and 3.

Table-1: Complete Hemogram

Variable	Value
Hemoglobin	8.6 g/dl
Total leucocyte count(TLC)	16500/cu.mm
Neutrophil(N)	85 %
Lymphocyte(L)	12 %
Platelet Count	5.9 lacs/cu.mm
ESR	120 mm in 1 st hour
CRP	72 mg/dl

Table-2: Cerebrospinal Fluid (CSF) Analysis

Variable	Value
Cell count	20 /cu.mm
Neutrophil	10 %
Lymphocyte	90 %
Protein	170 mg/dl
Sugar	65 mg/dl (CBG - 134 mg/dl)
CSF CBNAAT	Positive
Mantoux test	Negative

Table-3: Rheumatologic Workup to find Etiology

Variable	Value
Anticardiolipin Antibody Profile, Antineutrophil cytoplasmic antibody(ANCA), Antinuclear Antibody(ANA) profile, Antiphospholipid antibody(APLA)	Negative
Serum Homocysteine	5.2 μ mol/L(WNL)
Serum C3, C4	Negative
Direct Coombs Test	Negative
Serological Tests:	
HIV I & II, HbsAg, Anti HCV	Non-reactive
Immunoglobulin Profile:	
Ig G, M, A	WNL

Brain MRI showed that ring enhancing altered signal intensity lesions of variable sizes with surrounding edema in bilateral cerebral, cerebellar hemispheres, and thalamus suggestive of multiple

tuberculoma with mildly dilated supratentorial ventricles (Fig. 1). MR Spectroscopy showed increased lipid peak with increased choline: creatinine ratio.



Fig. 1: Dry gangrenous changes of the left thumb and left ring finger

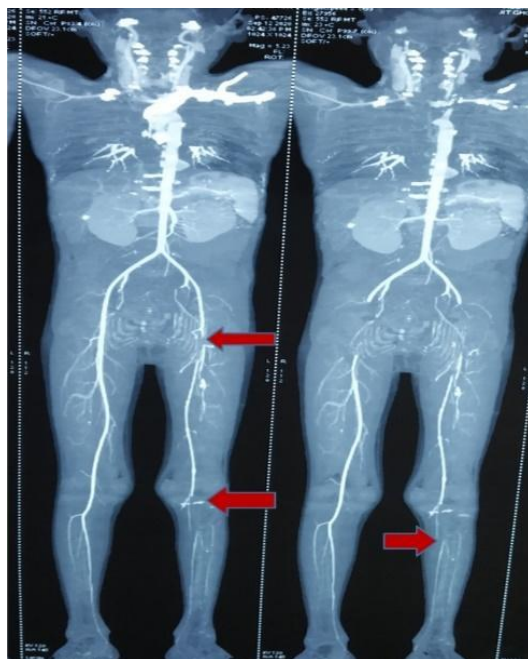


Fig. 2: Short segment narrowing in the left CFA, obliteration of the left PA.

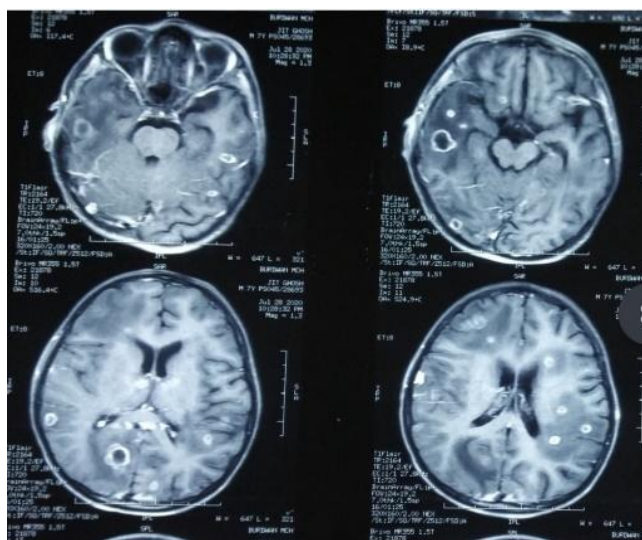


Fig. 3: MRI Brain showing multiple ring enhancing lesions and mildly dilated supratentorial ventricles

USG Doppler study (arterial and venous) of all four limbs showed partial thrombosis of left brachial artery above cubital fossa with no flow in left ulnar artery and narrowed lumen of left radial artery with completely thrombosed pseudoaneurysm with narrowed lumen of left superficial femoral artery. CT Angiography of thorax, abdomen, and lower limbs showed short

segment narrowing in left Common Femoral Artery (CFA), obliteration of left Popliteal Artery (PA) and focal narrowing in left Anterior Tibial Artery (ATA) and Posterior Tibial Artery (PTA). MR angiography of Brain was found to be normal. And echocardiography revealed no abnormality.

The patient was treated with Antitubercular therapy (Isoniazid, Rifampicin, Pyrazinamide and Ethambutol) for 6 months, oral Prednisolone @ 2mg/kg/day for 4 weeks with subsequent tapering to 1mg/kg/day for another 4 weeks and oral Aspirin @ 3mg/kg/day for 6 months. He showed significant improvements with the above said management, with pain significantly decreased and range of motion improved after 2 weeks of starting treatment. He was discharged after 2 weeks.

Initially he was followed up monthly for the first 6 months during which clinical examination revealed disappearance of gangrenous changes and improved arterial pulsations at the end of 10 weeks. ESR and CRP were checked at monthly intervals which were normalized after 10 weeks of starting treatment. MRI brain was done at the end of 3 months, 6 months and 12 months which showed resolution of ventricular dilatation. USG Doppler study of the left upper limb done at the end of 6 months showed improved flow in the left brachial and radial artery. The child was then followed up yearly with ESR, CRP, MRI Brain and USG Doppler study over a period of 2 years and there had been no reappearance of the above mentioned symptoms.

3- DISCUSSION

The co-existence of tuberculoma with tubercular meningitis and medium vessel vasculitis represents an uncommon manifestation of Mycobacterium tuberculosis infection. CNS TB is categorized through imaging, based on the location of the disease into leptomeningeal, parenchymal or other involvements. Leptomeningeal involvement presents as meningitis, cranial nerve (CN), palsies (CN 2, 3, 4 and 7), and communicating hydrocephalus. Leptomeningeal involvement results from either hematogenous spread or rupture of subpial or subependymal foci (Rich foci)

into the subarachnoid space. Even though TB Meningitis constitutes a small proportion of the total reported TB cases (around 1%), it causes a disproportionate amount of suffering with very high rates of mortality and morbidity, having a poor prognosis and survivors often have severe disabilities (2). Parenchymal disease is categorized into tuberculomas with or without meningitis and rarely brain abscess.

Tuberculomas are organized as clusters of inflammatory cells which are meant to limit the spread of Mycobacterium bacilli. Multiple lesions are more common than solitary tuberculomas. Classically they are supratentorial in adults and infratentorial in children. Its radiological appearance is neither constant nor specific, suggesting numerous other inflammatory pathologies (cysticercosis, neoplasms like metastases, glioma or lymphomas).

Peripheral gangrene refers to situations that induce diminishing of blood supply or oxygen to the tissues or organs for a prolonged period of time. Peripheral gangrene resulting from TB is uncommon (3). Our patient presented with CNS TB and peripheral gangrene for which no cause could be ascertained clinically. We considered that the gangrene resulted from vasculitis secondary to tuberculosis infection based on the pathological presentation, radiographic changes and therapeutic response to ATT.

Vasculitis secondary to TB was first described by Parish and Rhodes in 1967 (4). TB could result in granulomatous arteritis and affect Aorta and its branches, mimicking large vessel vasculitis. Involvement of the descending aorta or renal artery might resemble Takayasu's Arteritis (5). TB is also a cause of small vessel vasculitis e.g leukocytoclastic vasculitis (6). However, association of TB with medium vessel vasculitis is uncommon. The symptoms and angiography in the case reported here

show that vasculitis secondary to MTB infection has involved medium sized arteries such as the left brachial, radial, anterior and posterior tibial artery. The exact pathogenic mechanisms remain uncertain. Stratta et al. proposed that *M.tuberculosis* could result in granulomatous arteritis leading to vessel wall thickening, aneurysm formation, and stenosis that could affect the large vessel and its branches (7). They suggested that MTB was a stimulus for an immunogenic reaction which could induce vasculitis by activation of cell mediated immunity. Moreover, some studies showed that hyperaggregation of platelets participated in the process⁷; presence of gangrene was associated with abnormal platelet aggregation and anti-platelet therapy with Aspirin was of therapeutic value in this situation.

4- CONCLUSION

This case report highlighted an uncommon manifestation of *Mycobacterium Tuberculosis* infection, which is a common condition in India.

Overall, according to the character of the case, it was presumed that *Mycobacterium tuberculosis* infection was responsible for the neurological manifestations (CNS Tuberculosis) and it also induced the vasculitis process, ultimately causing gangrene and diminished pulsations of extremities.

5- FUNDING

None.

6- CONFLICTS OF INTERESTS

None.

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