A Rare Case of Rifampicin Resistant Primary Sternal Tuberculosis Along with Miliary Tuberculosis of Lung

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Abstract
Skeletal Tuberculosis accounts for 1 to 4% of the patients with Mycobacterium infection. It occurs due to hematogenous spread and affects almost all the bones. Commonly, Tuberculosis affects the spine, hip, knee, foot bones, elbow and hand bones. Rarely, it affects the shoulder joint. Primary sternal tuberculosis is rare; its incidence has been reported to be less than 1% of TB osteomyelitis cases seen even in endemic countries. As a part of hematogenous spread, it can cause Miliary tuberculosis.

Keywords - Miliary TB, Disseminated TB, Sternal tubercular osteomyelitis, Extrapulmonary TB.

Introduction
Skeletal Tuberculosis accounts for 1 to 4% of the patients with Mycobacterium infection. It occurs due to hematogenous spread and affects almost all the bones. Commonly, Tuberculosis affects the spine, hip, knee, foot bones, elbow and hand bones. Rarely, it affects the shoulder joint. Primary sternal tuberculosis is rare; its incidence has been reported to be less than 1% of TB osteomyelitis cases seen even in endemic countries.¹,² A thorough literature search of Pub Med database for keywords “primary tuberculosis of sternum” and “primary tubercular osteomyelitis of sternum” yielded 30 and 22 articles, respectively.³

Disseminated tuberculosis refers to concurrent involvement of at-least two non-contiguoussites of the body. Or, involvement of blood or bone marrow by tuberculosis process.⁴,⁵,⁶ One form of disseminated TB, which is Miliary TB, results from massive hematogenous dissemination of tubercle bacilli which results in tiny discrete foci usually the size of millet seeds(1to2 mm)more or less uniformly distributed in the lungs and other viscera.⁷,⁸,⁹

Miliary tuberculosis accounts for less than 2% of all the cases of TB and up to 20% of all extrapulmonary disease.

Rifampicin resistance is a relatively rare event and leads to the selection of mutants that are already resistant to other components of short-course treatment. Therefore Rifampicin resistance is often regarded as a surrogate marker for MDR-TB.¹⁰ RNA polymerase Sub-unit ‘B’ is the gene involved in Rifampicin resistance.¹¹,¹²,¹³

We present our experience of an older man with swelling arising from sternum. This type of presentation needs a high amount of suspicion for diagnosis and management.

Case Report
A 65-year-old male admitted with chief complaints of fever, weight loss, loss of appetite, easy fatigability, edema of both feet for 2 months. He gives the history of swelling over sternum which was small at the onset and gradually reached a size of 7 cm×4 cm over a period of 2 months.
He gives no history of Diabetes, Chronic renal failure/hemodialysis, organ transplantation, HIV-AIDS, connective tissue disorders, past history of tuberculosis, household TB contact. He denies usage of corticosteroids, immunosuppressive, immune-modulator drugs. He took over the counter drugs for minor illness from the pharmacy. On physical examination, he is thin, with BMI 17 kg/m². He looked pale, and he had pedal edema. He was worried about having malignancy. He had 7cm×4cm swelling over the sternum and there were no discharging sinus tracts. His lungs were clear to auscultation. He had no enlarged lymph nodes and the rest of the physical examination was unremarkable.

His laboratory parameters were as follows:
Haemoglobin=9.1g/dl, TWBC=4100(N-50, L-44, M-03,E-03) RBC=3.06Lac/mm³, Haematocrit=34%, MCV=111.2 fl, MCH= 29.8pg, MCHC=26.8g/dl, RDW=20.2, Platelets=58000cells/mm³. Peripheral smear examination: RBC—mild Anisopoikilocytosis, microcytic hypochromic RBC, macrocytic cells are also seen, WBC—appear normal in number and morphology, Platelets—appear reduced in number, Hemo-parasites—not seen. Impression—dimorphic anaemia with thrombocytopenia, Reticulocyte count-0.5%. QBC- negative for Malaria parasite, Widal—negative for Enteric fever,RBS=125mg/dl.
Serum total proteins=5.1mg/dl, ESR= 49mm/1st hour.RFT: Serum Creatinine=0.7mg/dl, Blood urea= 21mg/dl. LFT: Total serum bilirubin=1.0mg/dl, SGOT=26 IU/L, SGPT=61 IU/L, ALP=19 IU/L.

Blood Culture—sterile after 72 hours of aerobic incubation for enteric and pyogenic organisms. Urine Microscopy—few pus cells and gram-negative bacilli seen, Urine Culture—Escherichia coli isolated. FNAC of the swelling- smears studied show the features suggestive of “CHRONIC GRANULOMATOUS INFLAMMATION” with Caseous necrosis.

CXR—nodular opacities seen bilaterally. HR-CT chest—small multiple miliary nodules noted in both lung fields diffusely—likely tuberculosis,
mediastinal lymphadenopathy noted, focal destruction of sternum is seen. USG Abdomen—Spleenomegaly with altered echotexture.
2D Echocardiography—no regional wall motion abnormality no pericardial effusion, good LV and RV function. Sputum examination—Acid Fast bacilli detected, CB-NAAT—MTB detected and Rifampicin resistance is detected.

Figure 4—CXR (P/A view) of the patient showing bilateral nodular pattern.

Figure 5—CT chest (saggital view) showing swelling over the sternum. A bulge on the anterior side can be noted.

Figure 6—CT chest (saggital section) showing features of miliary tuberculosis.

Figures 7 and 8—CT chest(axial sections) showing features of Miliary TB.

Discussion
Tuberculosis can disseminate to almost every organ after a primary infection or reactivation of latent foci. As per the global TB report 2019, 10 million people fell ill with TB 2018. Adult men were mostly
affected, which was 57% of total TB cases in 2018. Eight countries accounted for 2/3rd of global disease burden, India-27%, China-9%, Indonesia-8%, Philippines-6%, Pakistan-6%, Nigeria-4%, Bangladesh-4%, South Africa-3%.14
In India total of 21.5lac TB cases were notified, of which 25% was from the private sector, 89% of the TB cases were from age group 15 to 69 years. About 2/3rd were males. Uttar Pradesh with 17% of the population of the country, is the most significant contributor to TB cases. 20% of the disease notifications were from this state.15
The rate of extra pulmonary TB world-wide has become 10 to 15%. Out of all the extra pulmonary cases, 10 to 25% have Musculo-skeletal TB with the most commonly affected site being the spine.14
Approximately 60 to 80% of the cases of skeletal TB involve the spine or weight-bearing joints while the sternum is involved in about 1% of cases. It is a rare form of TB, may occur in isolation or association with pleuro-pulmonary or lymph node involvement.
Sternal Mycobacterial infections can be categorized into three varieties—Primary, Secondary, Post-operatively.16
Tuli and Sinha studied 14 cases of Sternal tuberculosis in a series of 980 cases of Osteo-articular TB.17
Eyer et al. reviewed 27 articles reporting 32 cases from 1966 to 2013 and found that Primary Sternal tuberculosis was more common in men and occurred at a young age.18
The reactivation of latent foci formed during hematogenous or lymphatic dissemination of primary TB is the primary cause of tubercular sternal osteomyelitis. Direct extension from contiguous mediastinal lymph nodes or infection of retro-sternal lymph nodes that erode into the sternum over time are other mechanisms.16,19,20,21
Thoracic TB disease most commonly involves shafts of ribs or the costovertebral or costochondral junctions, where-as lesions of sternum are more common in the manubrium than the body.
Swelling and pain localized to sternum are the most common presenting symptoms. Constitutional symptoms include malaise, fever, night sweats, and weight loss. In this patient, constitutional symptoms were present and he had swelling over the sternum. Blood investigations are essentially normal in most cases reported apart from raised ESR. Chest radiographs are normal in approximately 70% of these cases and approximately 40% have evidence of TB in sites other than sternum. More than 81% cases of sternal TB have abnormal Tuberculin skin test results.
Plain radiographs are often normal but radiographic techniques like HR-CT and MRI are more valuable. A needle aspiration or excisional biopsy is mandatory for histopathological diagnosis of sternal TB osteomyelitis. The diagnosis is usually confirmed by caseous necrosis and granulomas on histopathological examination.
The frequency of positive cultures is up to 75%. The newer tests like PCR, Gene Xpert, Nucleic acid amplification can also aid in diagnosis.
A high index of suspicion is required for early diagnosis and prompt treatment that can prevent complications. ATT is the mainstay of treatment with standard four-drug regimen for 6 to 9 months. Surgical drainage of the abscess should be considered only if it does not resolve by aspiration and anti-tubercular therapy.

Conclusion
Isolated Primary sternal tuberculosis along with miliary tuberculosis, is still rare despite the high prevalence of TB in endemic countries like India. Tubercular involvement of sternum along with other foci can occur with various presentations and can involve any age group. It needs a high index of suspicion. An HR-CT can provide essential clue but confirmation is by culture or histopathological examination remains the mainstay of treatment. Surgical drainage of the abscess should be considered only if it does not resolve by aspiration and anti-tubercular therapy.

References