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Case Report

Pathology Section

Extra-Pulmonary Tuberculosis Presenting as Established Non-Union Tibia Shaft Fracture

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ABSTRACT

Extra-pulmonary tuberculosis (EPTB) is a great mimicker as it can present extraordinarily as a non-resoluting inflammatory pathology or can even mimic as malignancy especially sarcomatous or metastatic deposits. It sometimes can be diagnostically challenging for both the treating clinician and pathologist. The present case report documents a 47-year-old male agricultural worker who was immunocompetent and showed no signs and symptoms of pulmonary tuberculosis. His intradermal tuberculin sensitivity test was also negative. He presented with non-union of right tibia shaft fracture. A modified technique was employed i.e. of doing Fine needle aspiration cytology (FNAC) with Sahli's bone marrow aspiration needle from the non-united ends of the tibia shaft. This led to the documentation of caseating granulomas and later on positive Ziehl-Neelsen (ZN) staining confirmed the diagnosis of EPTB.

The case is worth reporting because of the unusual presentation of EPTB as non union with involvement of marrow and how a systemic approach with cytology and microbiology can lead to a quick and confirmative diagnosis, thus avoiding open biopsies which are not only expensive for the patient but are also associated with a share of morbidity.

Keywords: Bone marrow, Cytology, Granulomas, Skeletal tuberculosis

CASE REPORT

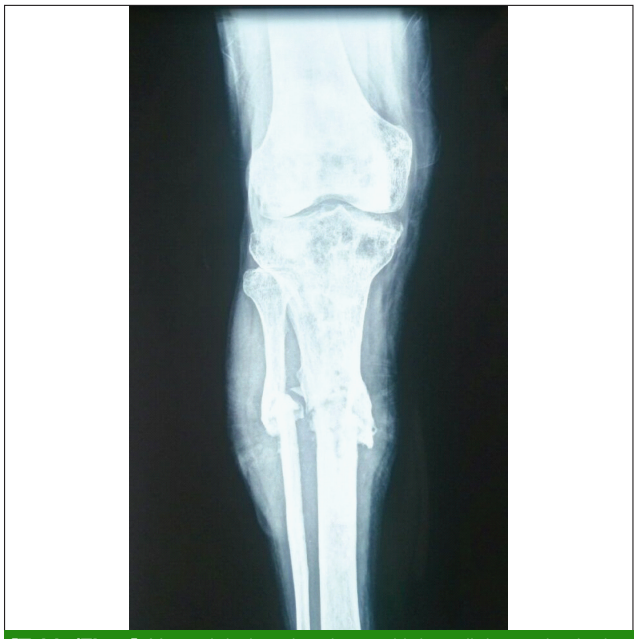
A 47-year-old male, agriculturist by occupation presented to an Outpatient Department of a Multispeciality Hospital with 16 months history of pain and swelling at the junction of middle and upper one third of the right tibia shaft. It was also associated with limitation of knee movements because of a reported fracture which was not uniting despite of previous four surgical attempts to unite it internally at an outside centre.

On physical examination he was relatively healthy and afebrile. Complete blood counts showed a mild leucocytosis. Biochemical tests were mostly unremarkable apart from raised aminotransferases levels. Ultrasound abdomen showed abdominal lymphadenopathy. However, no organomegaly or superficial lymphadenopathy was noted. Local examination of the tibia shaft revealed a firm tender swelling approximately 3cm in diameter with associated redness and pain at the junction of upper and middle one third. Superficially 2-3 multiple openings were noted which patient claimed appeared after he was put on external fixator. These openings were dry and showed no active oozing of any purulent material. On enquiring it was revealed that he suffered fracture after a trivial trauma by missing a step while coming down stairs for which he was treated with bone plating at an outside centre. However, after few months there was failure of the procedure in the form of bending of the plate subsequent to which internal fixation was done by the means of nailing twice, both of which also failed. According to the patient he was investigated vigorously at that centre for the cause of failure of procedures and all haematological, serological (including the markers), microbiological cultures and biochemical reports were normal. As the skin condition was not good because of repeated surgeries, the non united fracture was fixed with external fixator along with a course of intra-venous antibiotics but it also did not result in any resolution of patients complaints and fracture healing.

A repeat X-ray was done at the centre and it revealed multiple small radiolucencies in the proximal and mid shaft tibia along with an evidence of non-union of two ends of shaft of tibia and fibula with partial callus formation. Mild periosteal elevation was also noted along with soft tissue changes [Table/Fig-1]. The radiological opinion thus pointed towards an inflammatory pathology but no cause could be visualised for the established non-union.

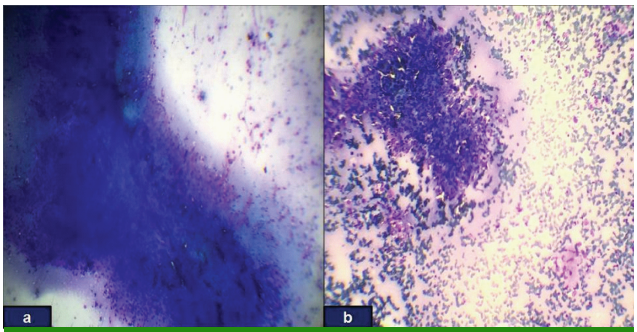
A clinico-pathological meet was initiated and all the available past and current medical treatment and investigation records were retrieved and discussed. It was decided that a cytological approach with the aid of ultrasonography be first attempted to look into the possibility of any underlying lesion causing a detrimental effect on union of both the ends.

Fine needle aspiration cytology (FNAC) was attempted under radiological guidance with 21G needle and 20cc syringe. 2-3 passes and attempts were given but the smears were non-diagnostic. A modification of FNAC technique was

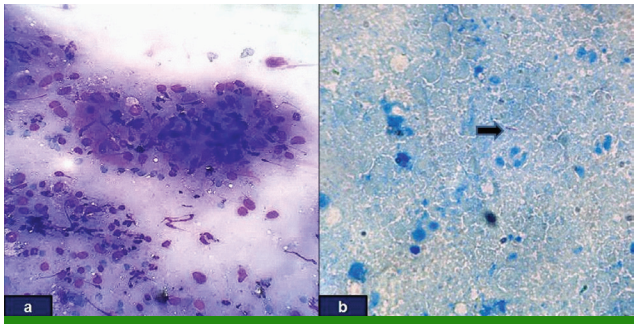


[Table/Fig-1]: X-ray right leg showing multiple radiolucencies in the tibia along with non union of two ends of tibial and fibular shafts with partial callus formation.

attempted with FNAC being done with Sahli's bone marrow aspiration needle from the same site under radiological guidance. Smears were air dried and stained with May-Grünwald-Giemsa (MGG) stain. Smear revealed presence of normal hematopoietic elements along with scattered caseating granulomas and necrosis [Table/Fig-2a,2b]. Based on these findings a diagnosis of caseating granulomatous pathology was made. On one of the smears Ziehl-Neelsen (ZN) staining for acid fast bacilli (AFB) was done which revealed pink coloured rod shaped acid fast bacilli [Table/Fig-3a,3b]. Correlating the clinical and cytological findings a final diagnosis of Extra-pulmonary tuberculosis (EPTB) was rendered. The patient was started on anti-tubercular treatment (ATT). Patient showed good response in form of decrease in the pain and signs of healing at the fracture site within initial 2 weeks of the treatment with ATT and is now on regular follow-up.



[Table/Fig-2a, 2b]: a: Bone marrow fragment on cytology. (MGG, 200X).
b: FNAC smears showing epithelioid cell granulomas with necrosis. (MGG, 200X).



[Table/Fig-3a, 3b]: a: Caseating epithelioid cell granulomas against the background of normal haematopoietic cells. (MGG, 400X).
b: ZN stain showing presence of AFB (Marked by an arrow).

DISCUSSION

EPTB can pose considerable problem if it presents at an unusual location and with atypical symptoms [1]. In spite of availability of better diagnostic modalities in radiology, the diagnosis of EPTB remains difficult and elusive leading to much morbidity and diagnostic dilemma for both pathologist and treating clinician. In this context early recognition of this lesion can be helpful in timely initiation of ATT there by alleviating the patient's symptoms. A close interaction between diagnostic and clinical teams in such circumstances based on algorithmic approach is ultimately beneficial for the patient.

The purpose of the present case report was to highlight one such unusual clinical presentation of EPTB presenting as established non-union tibia shaft fracture and the role of cytology in clinching the diagnosis.

Over the time because of better and early usage of diagnostic modalities and good therapeutics, the incidence of classical pulmonary tuberculosis has declined but there has been resurgence in EPTB due to isolation of multidrug resistant strains of tuberculosis [2-4] and also because of the delay in recognition of this entity as it presents usually or in many cases masquerades as malignancy because of non specific extra-pulmonary signs and symptoms [5]. The baseline workup of tuberculosis is mostly non invasive with radiological studies, spectrum studies, and tuberculin tests constituting the three essential pillars [6].

All of these were inconclusive in our case as chest X- ray was unremarkable and did not show the miliary pattern often encountered in EPTB. The recording of negative tuberculin was ultimately on expected lines as in EPTB, Mantoux-test is most often negative [7]. The involvement of bone marrow by tuberculosis in our patient was not associated with any haematological or biochemical abnormality (except mildly elevated transaminase levels). This is in contrast with other reported cases of EPTB, involving marrow where pancytopenia is very common recorded finding because of hypersplenism, maturation arrest, histiocytic hyperplasia or even myelofibrosis arising out of direct granulomatous infiltration by tuberculosis. In literature, the reported incidence of finding bone marrow granulomas range from 0.38% to 2.2% and presence of granulomas in bone marrow

has been reported to be associated with increased mortality in which immunosuppression is the major contributory factor [5]. The patient in our case was immunocompetent. Many other factors are associated with its occurrence such as low socioeconomic status, malnutrition, delay in starting of the treatment, concomitant immunosuppressive treatment and macrophage activation syndrome (comprising of pancytopenia, hyperferritinemia, hypertriglyceridemia) [8,9].

Musculoskeletal involvement occurs in 1- 3 % of patients with tuberculosis due to haematogenous seeding and in more than half of these patients there is no active synchronous evidence of ongoing intra-thoracic pulmonary tuberculosis [10,11]. Although the commonest reported skeletal site is spine, femur, tibia, and small bones of hands and feet have also been often documented [12]. The clinical situation is confounded by the fact that often tubercular osteomyelitis is associated with pain, swelling and can also lead to alarming radiological appearances and even pathological fractures as noted in our case. Hence, in all such confounding and confusing cases where diagnostic and clinical discordance is present, a possibility of EPTB has to be kept in mind not only in developing countries but also in developed ones. In these cases cytology or a core biopsy followed by light microscopy can be useful to identify granulomas and subsequent ZN staining can confirm the diagnosis. Hence, the past dependence of open surgical biopsy can be obviated and tissue samples can be obtained with minimal invasion under image guidance. This is beneficial for the patient as in a rapid, inexpensive and outpatient setting a quick diagnosis can be rendered in diagnostically challenging cases as above. Much morbidity and expenses can thus be avoided.

CONCLUSION

The clinical and radiological features of EPTB can be confusing and can mimic an alarming underlying pathological lesion particularly a malignancy. Hence, one must be vigilant to a possibility of tuberculosis infection especially in resource challenged countries or till proven otherwise. A definite diagnosis will require a proper cytological and microbiological analysis. This case is worth reporting because of its unusual clinical presentation and modification of a conventional cytological process to reach a diagnosis thus helping the patient to start the therapy.

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