Case Series

Osteoarticular tuberculosis: A series of six cases diagnosed on fine-needle aspiration cytology

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ABSTRACT

A few studies are dealing with the role of fine-needle aspiration cytology in diagnosing osteoarticular tuberculosis (TB). The present study was undertaken to study the cytomorphological features of six cases of osteoarticular TB throughout 1 year, diagnosed by fine-needle aspiration cytology. The Papanicolaou, Giemsa, Ziehl–Neelsen, and periodic acid–Schiff stains were used in each case. The sampled material was also cultured in Lowenstein–Jensen media for Mycobacterium species and polymerase chain reaction assay for Mycobacterium tuberculosis. Histopathological findings were correlated whenever available. There were four male and two female patients. The age of the patients ranged from 15 to 53 years, with a mean age of 37 years. Most cases involved small bones (4/6) and long bones of upper and lower limbs (2/6). Radiologically, the suspected lesions presented as osteolytic lesions, fractures, and joint destruction. The smears showed epithelioid cell granulomas in 5 out of 6 cases (83.3%), multinucleate and Langhans’ giant cells in 3 out of 6 cases (50%), and only necrosis in 1 case (16.7%). Inflammatory cells were seen in the background in 5 out of 6 cases (83.3%). AFB was positive in 3 cases (50%). Culture in Löwenstein–Jensen media, done in three cases, showed growth of M. tuberculosis. PCR showed positivity for M. tuberculosis in all six cases. Fine-needle aspiration cytology is an easy procedure that can be used for the diagnosis of osteoarticular tuberculosis. Cytomorphologically, smears show epithelioid cell granulomas, multinucleated and Langhan’s giant cells, and necrosis.

Keywords: Granuloma, Mycobacterium, Osteomyelitis

INTRODUCTION

India has the highest burden of tuberculosis (TB) globally.[1] Skeletal TB accounts for 1%–3% of all TB cases and usually involves joints and bones.[2] The most commonly affected skeletal sites by TB are the spine, hip, knee, and foot bones.[2] In the cases without joint involvement, the tuberculous osteomyelitis may involve the ribs, metatarsals, metacarpals, sternum, pelvic bones, skull, and rarely the large tubular bones.[2] The solitary osteomyelitis is generally observed only at the beginning of the disease process, with the clinical presentation of localized pain, swelling, and eventually painful walking.[2] The fine-needle aspiration cytology (FNAC) acquired importance for diagnosing and managing bone tumors.[3,4] However, few studies addressed the role of FNAC in the diagnosis of osteoarticular TB.[1,4] Therefore, the present study was undertaken to study the cytomorphological features of osteoarticular TB.
MATERIAL AND METHODS

Cases of osseous TB, diagnosed on FNAC, were collected from the archives in 1 year. A total of six cases of osseous TB were retrieved. The age, gender, presenting complaints, radiological, and FNAC findings were noted. FNAC was performed using a 22-gauge needle with a 20 ml syringe over the visible swelling or guided by ultrasonography if the definite swelling was not precise. The prepared FNAC smears were fixed in 95% alcohol and stained with Papanicolaou and hematoxylin and eosin. The remaining air-dried smears were stained with Giemsa and Ziehl–Neelsen (ZN). Periodic acid–Schiff (PAS) stain for fungi was done wherever applicable. The remaining sufficient material was submitted for culture in Löwenstein–Jensen media for Mycobacterium species and real-time polymerase chain reaction (RT-PCR) assay for Mycobacterium tuberculosis. Chest X-ray and sputum examination for AFB were done in all the cases. Histopathological findings were correlated whenever available.

RESULTS

There were four female and two male patients with a male: female ratio of 1:2. The age of the patients ranged from 15 to 53 years, with a mean age of 37 years. Four out of six cases had involvement of the small bones. Long bones of upper and lower limbs were involved in 2 out of 6 cases (33.3%). All the patients had an insidious onset and presented with pain and swelling. One case was presented with a pathological fracture of the femur’s neck and another case with a non-healing ulcer with discharging sinus on the right upper arm. Radiologically, 3 out of 6 (50%) cases had osteolytic lesions. Two cases (33.3%) revealed the fusiform expansion of the middle phalanx with underlying bone destruction and overlying periosteal new bone formation [Figure 1]. One patient had osteoporosis with a pathological fracture of the neck of the femur [Table 1]. A chest X-ray was done in all the cases. One patient showed cavity changes in the upper lobes bilaterally and patchy consolidation with positive AFB in the sputum. The remaining 5 cases did not show any concomitant pulmonary disease with sputum negative for AFB. The FNAC aspirate provided a bloody sample in three cases, caseous material in two cases, and only pus in one case. The cytological smears showed epithelioid cell granulomas in 5 out of 6 cases (83.3%), multinucleate and Langhans’ giant cells in 3 out of 6 cases (50%), and only necrosis in 1 out of 6 cases (16.7%) [Figure 2]. Inflammatory cells were found in the background in 5 out of 6 cases (83.3%). ZN stain was positive in 3 cases (50%). PAS stain for fungal elements was negative in all six cases. The cytologic findings were subdivided into the following categories: (i) Only necrosis, (ii) epithelioid cell granulomas with necrosis, and (iii) epithelioid cell granulomas without necrosis [Table 2]. Culture in Lowenstein–Jensen media was done in three cases, and all the three cases showed growth of M. tuberculosis. PCR assay was done in all six cases, which showed positivity for M. tuberculosis. Three cases had a biopsy, which showed necrotic bone, Langhans’ giant cells with focal areas of caseous necrosis. All patients were prescribed the World Health Organization directly observed treatment, short-course Category I anti-tubercular therapy (ATT) for a minimum period of 9 months. All the patients were regularly followed up, with all the patients responding to ATT and doing well.

DISCUSSION

The incidence of osteoarticular TB in Western countries represents 2.2–4.7% of all cases of TB and around 10–15% of extra-pulmonary TB.[9] The later rises to 15–20% in Asian countries.[9] The hematogenous spread of the mycobacterial infection is considered the common cause of musculoskeletal TB.[1,3,4] Usually, it affects the young patients in the second and third decade of life with female predilection.[3,4] About one-third to one-half of the cases show pulmonary disease, but active pulmonary TB is infrequent.[5] Therefore, attempts should be made to ruling out concomitant pulmonary TB.[7] However, in the present study, only one case showed concomitance with pulmonary involvement.

The typical clinical presentation of tuberculous osteomyelitis is the insidious painful swelling of the involved joint or bone, non-healing ulcer, and discharging sinus.[8] The stiffness of the joints leads to disuse atrophy and periarticular osteoporosis.[6] In the present study, all the patients had an insidious onset of swelling and pain. Non-healing ulcers with discharging sinus and osteoporosis with pathological fracture were seen in one patient each. Clinically, osteoarticular TB may mimic other inflammatory and neoplastic bone lesions such as pyogenic osteomyelitis, fungal infection, multiple myeloma, and metastatic disease.[2,4] Osteoarticular TB usually involves the spine, hip, knee, ankle, tarsus joint, sacroiliac, shoulder, and elbow region, and less commonly the finger, toe, sternum, clavicle, ischium, pubis, calvarium, and ribs.[2,4] The radiological features of skeletal TB are nonspecific.[2,4] Radiological features may vary from the lytic lesion, periarticular osteoporosis to bone marrow edema, joint effusion, tenosynovitis, and soft-tissue collections.[2] Joint TB shows a triad of radiological findings, namely, (i) periarticular osteoporosis, (ii) marginal erosion, and (iii) joint space narrowing, known as the Phemister triad.[6] Peripheral marginal erosion of joint is the earliest change detected in the plain radiography.[8] TB of the foot occurs in five typical types: (i) Cystic or osteolytic, (ii) rheumatoid, (iii) subperiosteal, (iv) kissing, and (v) spina ventosa.[8,9] The osteolytic has the best outcome and is characterized by a radiolucent area in the intraossseous
Table 1: The clinical and radiological findings.

| S. No. | Age | Sex | Site of involvement       | Radiological findings                                                                 | Clinical diagnosis          |
|--------|-----|-----|---------------------------|---------------------------------------------------------------------------------------|-----------------------------|
| 1.     | 27  | F   | Neck of femur             | Osteoporosis with fracture of neck of femur                                            | Chronic osteomyelitis       |
| 2.     | 45  | F   | Ankle joint and tarsal bones | Multiple irregular lytic foci involving the talar, navicular, part of calcaneum, and lateral cuneiform | TB osteomyelitis            |
| 3.     | 15  | F   | Humerus                   | Lytic lesion with discharging sinus                                                    | TB osteomyelitis            |
| 4.     | 37  | M   | Ankle joint and tarsal bone | Multiple irregular lytic foci involving ankle joint and tarsal bones                  | Chronic osteomyelitis       |
| 5.     | 45  | F   | Middle phalanx            | Fusiform expansion of middle phalanx, underlying bone destruction, and overlying periosteal new bone formation with destruction of interphalangeal joint | TB osteomyelitis            |
| 6.     | 53  | M   | Middle phalanx            | Fusiform expansion with underlying bone destruction of middle phalanx of middle finger | Giant cell tumor            |

Figure 1: (a) X-ray of the ankle and foot showing multiple irregular lytic foci involving the ankle joint and tarsal bones. (b) View of the left hand showing fusiform expansion of the middle phalanx. (c) X-ray of the left hand showing spina ventosa with underlying bone destruction and overlying periosteal new bone formation.

Figure 2: (a) Epithelioid cell granuloma with dead bone fragments (MGG, ×400). (b) Langhan's giant cell (Papanicolaou, ×400). (c) Necrosis (MGG, ×200).
location with loss of trabeculae. Spina ventosa is the tuberculous osteomyelitis of the phalanges, metacarpal, and metatarsal bones characterized by fusiform expansion of the bone, underlying bone destruction, and overlying periosteal new bone formation. The osteolytic type was the most frequent radiological finding in the present study followed by spina ventosa. The paucibacillary cases of osteoarticular TB challenge the diagnosis as the cultured samples lack a reasonable positivity. Another drawback of conventional culture is that it has a long incubation period of 6–8 weeks. Thus, the definite diagnosis depends on pathological investigations such as FNAC and biopsy. FNAC has an advantage over biopsy as it is a minimally invasive procedure and does not require anesthesia. FNAC is a simple procedure that can be easily performed in the pathologically altered bone to diagnose osteoarticular TB. The FNAC aspirated material is usually of three types: Blood mixed particles, caseous material, and pus. In the present study, the nature of the FNAC aspirates was represented by all types. The cytological smears may show the presence of epithelioid cell granulomas with or without necrosis and with or without Langhans’ type of giant cell. Few cases may show only granular necrotic material, degenerated inflammatory cells, histiocytes without epithelioid cell granuloma, or giant cells.

Handa et al. and Masood observed epithelioid cell granulomas with or without necrosis in 85.2% and 73% of cases, respectively, scattered multinucleated giant cells in 55.6% and 45.4% of cases, respectively, and only necrosis in 14.81% and 27.27%, respectively. The present study’s cytology showed the epithelioid cell granulomas with or without necrosis in 83.3% of cases, multinucleate giant cells in 50% of cases, and only necrosis in 16.7% of cases. Smeared background usually had inflammatory cells, osteoblasts, and proliferating fibroblasts. The main cytomorphological differential diagnoses of osteoarticular TB are fungal infections, sarcoidosis, and eosinophilic granuloma. The absence of fungal elements rules out fungal infections. In the present study, the PAS stain for fungal elements was negative in all the cases. The absence of characteristic lymphocyte poor granuloma and the presence of necrotic or inflammatory background rule out sarcoidosis. The absence of Langerhans’ cells with coffee-bean nuclei and nuclear grooves, the paucity of eosinophils, and the presence of necrosis in the smears are clues to rule out eosinophilic granuloma. The ZN staining method is commonly used to identify M. tuberculosis bacilli.

Handa et al. and Agarwal observed positive ZN staining for AFB in 22.2% and 86% of cases, respectively. AFB was positive in 50% of cases in the present study. The paucibacillary nature of osteoarticular TB can explain the variability of AFB positivity. In this setting, the role of RT-PCR becomes crucial in demonstrating M. tuberculosis with specificity as high as 99.8%. The sensitivity ranges from 61% to 91.9%. Thereby, FNAC has the added advantage of getting material for advanced molecular methods. However, if the results of RT-PCR are negative, further decisions are based on the biopsy findings. ATT is started if biopsy findings are positive regardless of the RT-PCR results. In the present study, three cases had a biopsy confirmation. Many a time, a tissue biopsy may not be possible due to the deep inaccessible nature of osteoarticular TB. In such a scenario, FNAC comes as a rescue procedure.

CONCLUSION

Osteoarticular TB is an uncommon form of TB. In clinically suspected cases of osteoarticular TB, FNAC serves as a rapid diagnostic procedure. FNAC is a simple outdoor procedure, which can be easily performed in deep inaccessible lesions of osteoarticular TB. It also serves as an inexpensive diagnostic tool in resource-poor settings without facilities of advanced molecular methods such as PCR.

COMPETING INTEREST STATEMENT BY ALL AUTHORS

No competing interests.

AUTHORSHIP STATEMENT BY ALL AUTHORS

Drafting of manuscript: Biswajit Dey, Jitendra Singh Nigam, Jyotsna Naresh Bharti, Ashok. Literature search: Vivek Nair, Jitendra Singh Nigam, Ashok Singh, Jyotsna Naresh Bharti. Case acquisition: Biswajit Dey, Ashok Sing, Vivek Nair. Case analysis & interpretation: Biswajit Dey, Ashok Sing.
Vivek Nair, Jitendra Singh Nigam, Jyotsna Naresh Bharti. Manuscript preparation: Jitendra Singh Nigam, Biswajit Dey, Jyotsna Naresh Bharti, Vivek Nair. Manuscript editing: Ashok Singh, Jitendra Singh Nigam, Jyotsna Naresh Bharti, Biswajit Dey. Manuscript review and approval: Biswajit Dey, Ashok Singh, Vivek Nair, Jitendra Singh Nigam, Jyotsna Naresh Bharti.

ETHICS STATEMENT BY ALL AUTHORS
The informed and written consent was obtained from all the patients. The cases were submitted without identifiers.

LIST OF ABBREVIATIONS (IN ALPHABETIC ORDER)

AFB – Acid fast bacilli
ATT – Anti-tubercular treatment
FNAC – Fine-needle aspiration cytology
PAS – Periodic acid-Schiff
PCR – Polymerase chain reaction
RT-PCR – Real time polymerase chain reaction
TB – Tuberculosis
ZN – Zeihl-Neelsen.

EDITORIAL/PEER-REVIEW STATEMENT
To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a double-blind model (authors are blinded for reviewers and vice versa) through automatic online system.

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