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## Tuberculous osteomyelitis of OS Calcis

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### Abstract

There is little data regarding Vitamin D deficiency in Greece. Also conflicting are the data regarding the bone turnover during the acute hip fracture interval and the situation is even more complex considering the recently developed bone turnover markers (BTMs). The aim of this study was to evaluate the parameters of bone mineral homeostasis of women with fragility hip fracture using the recently developed BTMs of carboxy-terminal collagen crosslinks (CTX) and the procollagen type 1 amino-terminal propeptide (PINP) and to determinate vitamin D (25-OHD) levels of elderly Greek women with acute hip fracture. 38 self-sufficient, community-living Greek women with acute hip fracture were included. A similar number of age- and sex-matched controls with no clinically evident fractures were included in the study meeting the same inclusion and exclusion criteria. To exclude the effect of trauma blood samples were drawn within 24 hours from the fracture. Hip fracture group had significantly lower serum 25-OHD levels and significantly higher intact parathormone (PTH) levels compared to the control group but no correlation between PTH and 25-OHD was found in both groups. CTx was significantly correlated with PINP in the total group and in both groups separately but there was no statistical difference of their levels between the two groups. There was high prevalence of severe Vitamin D deficiency within the postmenopausal Greek women with acute hip fracture and the fracture did not influence the above mentioned BTMs. The processes of bone resorption and bone production are in balance during the first 24 hours after the fracture.

**Keywords:** Tuberculosis, calcaneum, osteomyelitis, foot

### 1. Introduction

#### 1.1 Tuberculosis of calcaneum

Tuberculosis (TB) is a disease caused by Mycobacterium Tuberculosis which usually involves the lungs, but however can involve many other locations in the human body. Osteoarticular tuberculosis occurs in 1–3% of instances of which around 10% influences the foot and lower leg <sup>[1]</sup>. Extra-pulmonary tuberculosis favours those with suboptimal immune resistance displaying a bimodal distribution thereby affecting the young and the elderly and those in an immuno-compromised state such as patients with Human Immunodeficiency Virus infection (HIV) and renal failure <sup>[2]</sup>. In TB of the foot, calcaneum is predominantly involved. TB affecting the foot and ankle is relatively hard to diagnose on the account of absence of awareness among the treating surgeons, being one among the many reasons. Joint involvement occurs because of spread from a periarticular bony focus, and especially in the midfoot, the disease may spread to involve all the interconnected small joints, leading to a stiff foot with residual deformities <sup>[2]</sup>. Literature suggests foot involvement in only 8-10% of the patients with osteoarticular tuberculosis (approximately 0.1% to 0.3% of all patients with extra-pulmonary disease) <sup>[3]</sup>. Tuberculous infection of the calcaneum can have varied presentation and can be mirrored by other pathologies like chronic osteomyelitis, maduramycosis, actinomycosis, multiple myeloma or secondary malignant deposits. This combined with an absence of awareness can delay the diagnosis and can consequently result in an unacceptable clinical outcome, morbidity and functional disability. The paucibacillary nature of this extra-pulmonary tuberculous infection even with a discharging sinus makes the bacteriological affirmation more troublesome and warrants invasive procedure to confirm the bacilli.

## 1.2 Clinical signs and symptoms

Calcaneal tuberculous infection can present with pain, stiffness, swelling of the heel, sinuses and muscle wasting. Symptomatology is generally chronic and insidious, coupled with features like fever, night sweats and weight loss. Patients may likewise present with inability to heel weight-bear and hence have a 'tip-toe' gait, which is known as the 'heel-up' sign prompting a misdiagnosis of pyogenic calcaneal osteomyelitis. Tubercular osteomyelitis can occur in any part of the calcaneum or the whole bone. There are three patterns of involvement of the bone. A focal granuloma type, which is the most widely recognized pattern and has the best prognosis. The other two types are, a diffuse seeding type with multiple lytic lesions and a periarticular granuloma type with soft tissue component. The latter two types can have poorer prognosis since they can advance to the adjacent articulations, especially the subtalar joint and hence the deformities. Early diagnosis and management is significant for better clinical result<sup>[3,4]</sup>.

## 1.3 Purpose of study

Albeit a few published studies, there is an overall paucity in the literature on early diagnosis and management of osteoarticular TB in the foot and lower leg<sup>[5]</sup>. Here we discuss a series of cases of isolated tuberculous osteomyelitis of the calcaneum who were diagnosed early and treated effectively with anti-tubercular drugs with protected weight-bearing prompting a good functional outcome thereby avoiding any extensive surgical treatment. This article gives an account of six cases of tuberculosis infection of the calcaneum featuring the indicative pitfalls prompting delay in the commencement of treatment. This case series has been accounted for in line with the PROCESS 2018 criteria.

## 2. Materials and Methods

### 2.1 Study design

It is a retrospective study carried out in a single tertiary level university hospital and the cases were consecutive. The period of study was from November 2017 to July 2018. After obtaining ethical clearance from the local ethics committee, a total of six patients who presented with isolated calcaneal tuberculous osteomyelitis were included. Three patients underwent surgical curettage while the remaining three were started on anti-tuberculous medications on an empirical basis based on their clinical presentation. In those three patients who had surgical curettage of the osseous lesion, the diagnosis was confirmed either by microbial cytology (Ziehl-Neelsen staining) or histopathological examination of the material from the lesion. GeneXpert testing was also performed in them. Anteroposterior and lateral radiographs of the affected site were done on day one and repeated every three months. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) scans were performed, as appropriate to look for extent of destruction, collection of abscess or joint involvement. The clinical and radiological evaluations till the final follow-up visit were recorded. Out of six patients reviewed four had a lesion in the calcaneal body and two in the posterior tuberosity of which one is more of enthesitis type of lytic lesion near the tendoachilles attachment to the calcaneum along with the presence of a prominent posterior tuberosity.

### 2.2 Surgical procedure

Out of six patients, three patients were biopsied by surgical curettage as they had presented with no systemic symptoms.

Their presentation was pain in the undersurface and back of the heel, difficulty in weight-bearing and impaired normal mobility. Of these three biopsied patients, posterior midline approach was used in two and an extensile lateral approach in one. In the enthesitis type, about 70% of the tendinous attachment to the calcaneum was tenuous. While curetting the lesion to take the biopsy sample, most of the tendinous attachment came off from the calcaneum. Calcaneoplasty was also performed to address the other calcaneal pathology. The tendon was reattached using 2 suture anchors. The other patient with the posterior tuberosity lesion had an equinus deformity of 15 degrees due to tendoachilles tightness. Hence the posterior approach for 'Z' lengthening of the tendoachilles and curettage/biopsy of the lesion. The third patient had a lesion in the calcaneal body and so, the extensile lateral approach.

### 2.3 Medical management

Remaining three patients had systemic symptoms with mild intermittent fever, fatigue, malaise, loss of appetite and weight. Of these three, one had a previous history of TB. Ideal is to have specimen sample for diagnosis but because the clinical and radiological signs were convincing and the patients were reluctant for any surgical procedure for confirmation of diagnosis, they were started empirically on anti-tuberculous medications for which they responded well. There was no discharging sinus and no residual deformity.

All six patients were treated with anti-tuberculous medications in two phases; intensive phase and continuation phase. The intensive or primary phase was with 4 drugs [Isoniazid, Rifampicin, Pyrazinamide and Ethambutol] for 2 months. Then the continuation phase was with Isoniazid and Rifampicin for 10-16 months depending on their response and recovery. The surgical samples were subjected to Zeihl-Neelsen staining, histopathology and GeneXpert. All were found to be 'Rifampicin sensitive'. Increased Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and Lymphocytes were seen in four cases but in one case there was only increase in ESR. Among all these patients, the ESR ranged about 44-70 mm per hour. Thereafter all the patients were followed up with the minimum period being until they finished their anti-tuberculous treatment. Calcaneum remineralised and osteosclerosis happened in 3-4 months. Evidence of disappearance of cavities and trabecular restoration occurred in 6-12 months.

### 2.4 Statistical analysis

Descriptive statistics were reported as mean (Standard Deviation-SD) for continuous variables and frequencies (percentage) for categorical variables. Data were statistically evaluated with IBM SPSS Statistics for Windows, Version 20.0., IBM Corp., Chicago, IL.

## 3. Results

### 3.1 Demographics

There were six cases of tuberculous osteomyelitis of calcaneum included in the current study. Gender distribution was equal with 50% being males and 50% were females (Table 1). The common presenting symptoms were pain and swelling. The lesions were located in the calcaneal body in four patients and posterior tuberosity in two. The ideal method of diagnosing extra-pulmonary and especially musculoskeletal tuberculosis is by biopsy. Although 100% diagnosed among those biopsied in our study, the biopsy was done in 50% (3 out of 6) of our patients.

**Table 1:** Baseline description of cases of tuberculous osteomyelitis of calcaneum (n=6)

Age/Sex	Area of bone	Symptoms and signs	Biopsy	Treatment	Complications	ATT Period
43/F (Fig 1-6)	Body	Pain	Yes	Curettage for biopsy + ATT	Superficial wound infection	14 months
56/F	Body	Pain & swelling	No	ATT	Nil	12 months
37/F	Body	Pain	No	ATT	Nil	18 months
61/M	Body	Pain & swelling	No	ATT	Nil	12 months
48/M (Fig 7)	Posterior tuberosity	Pain & equinus deformity	Yes	Curettage + 'Z' lengthening of TA + ATT	Delayed wound healing	13 months
50/M (Fig 8-9)	Apophysis - Posterior tuberosity	Pain, swelling and prominent posterior tuberosity	Yes	Curettage + Calcaneoplasty + TA reattachment with suture anchors + ATT	Nil	12 months

ATT - Anti-tuberculous treatment. TA -Tendoachilles.

### 3.2 Complications

Superficial wound infection was noted in the diabetic patient who had an extensile lateral approach and was treated with antibiotics. Delayed wound healing was found in a smoker with a posterior midline approach who had a 'Z' lengthening of the tendoachilles as well. Normally, the sutures were removed in 2 weeks but not for this patient. Both these complications were managed conservatively and they never required any surgical input.

### 3.3 Weight-bearing

Five patients had below knee posterior back slab for 6 weeks and were advised to be non weight-bearing but can remove the slab and perform ankle range of motion exercises except for the one with delayed wound healing. Remaining one patient who had tendoachilles reattachment with the suture anchor had his foot immobilised in equinus, semiequinus and plantigrade for 3 weeks each and was non weight-bearing followed by 3 weeks of partial weight-bearing in a boot.

## 4. Discussion

Osteoarticular tuberculosis is less than 3% of the cases of extra-pulmonary tuberculosis, of which around 10% involve the foot and lower leg [1, 6]. The most widely affected foot bone is calcaneum [7]. Calcaneal tuberculous infection is debilitating if the treatment is delayed which may lead to functional disability [8]. Chest x-ray should be included in suspected cases given that the disease's primary focus is in the lungs. Plain radiographs of the foot and ankle may not be informative in the early cases of musculoskeletal TB. When the foot radiographs exhibit destructive bony changes, then the TB had already established and advanced showing potential spread to other sites [9]. CT scan shows bone destruction sooner than the plain radiographs and is useful in addition to biopsy. MRI shows bone marrow edema and is helpful to recognize the pre-destructive phase and spread of infection into soft tissue. ESR and CRP are not explicit to the conclusion of TB. Biopsy and culture had the advantage of exhibiting the mycobacterium, although it may be difficult at times in this paucibacillary infection. Culture additionally permits testing for resistance and drug sensitivity. Histological assessment uncovers a trademark granuloma, caseous necrosis and Langhans giant cells.

The radiographic highlights of osteoarticular tuberculosis are vague [2, 3, 10]. Radiographic findings are normally noted 2-5 months after the start of illness and just a joint effusion might be evident in the beginning phase [11, 12]. The typical radiographic presentation of tuberculous arthritis is portrayed by juxta-articular osteoporosis, peripheral osseous erosions and steady decrease of joint space, known as the Pheemister triad [11, 12], is not a common entity in calcaneum. Lytic territories of destruction and minor erosions are regularly

observed along the articular edges in weight-bearing articulations such as the hip, knee and ankle [12]. In any case, as opposed to the pyogenic arthritis, there is relative protection of joint space in early stages of the disease attributable to the absence of proteolytic enzymes in the exudate. Extreme osteopenia is distinctively noted, and particularly in adults, there is an absence of sclerosis or periostitis in the beginning phase when the infection is dynamic. Serious joint destruction and, in the long run, sclerosis and fibrous ankylosis are noted in the late stages when dynamic infection has settled [1, 11, 12].

Advanced imaging is more dependable on detecting the disease early and helps in surgical planning. As CT scan is helpful to outline the bony anatomy, the MRI provides in-depth information about the soft tissue involvement. As the bony lesions appeared late in the start of the disease, the radiologic findings fall behind the genuine healing process as well. Dhillon and Nagi [1] suggested at any rate 6-7 months of multimodal treatment before rehashing cross-sectional imaging to diminish the rate of false positives for illness progression.

Hematological and biochemical tests give strong proof of progressive infection (White Cell Count, CRP and ESR) and bone activity (Alkaline Phosphatase), however don't give a clear determination specific to TB. Interferon gamma release assays such as T-SPOT and QuantiFERON-TB Gold used for testing for the presence of TB, in any case, are restricted as they don't recognize active and latent case of TB as they only evaluate the immune response against mycobacterium TB antigens [13]. The National Institute of Clinical Excellence (NICE) suggests that all patients with non-respiratory TB ought to have a chest x-ray to reject or affirm co-existing pulmonary TB [14]. Molecular diagnostics such as line probe assays Nucleic Acid Amplification Tests (NAAT) has been demonstrated to be a dependable option contrasted with segregation of tubercular bacilli [15]. At times, image guided fine needle aspiration may be helpful [16].

Almost 50% of our patients presented with no symptoms related or suggestive of tuberculous infection. Six patients in this short study period of 9 months suggest that this infective pathology should always be considered in the differential diagnosis of calcaneal lytic lesions. Anti-tuberculous treatment should begin as soon as possible under the circumstances and should proceed for at least 12 months [1]. Generally, surgical treatment is not required for foot and ankle TB. The primary indication for surgical intervention is to obtain tissue for diagnosis and in patients who are resistant to anti-tuberculous chemotherapy. In the healed phase of the disease, surgery is considered for pain relief, deformity correction or joint reconstruction [17, 18].

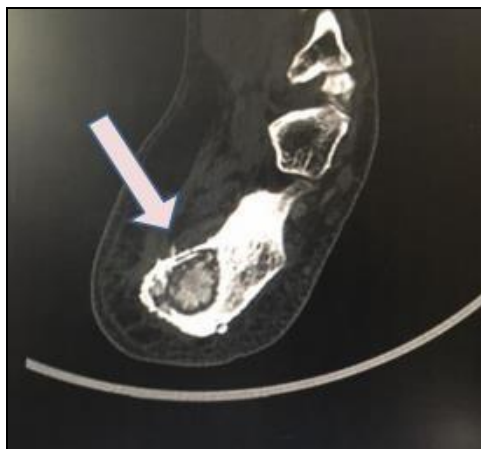




**Fig 1:** Lateral view of Os Calcis (Pre-operative)



**Fig 2:** Sagittal CT image of calcaneal lesion (Pre-operative)



**Fig 3:** Axial CT image of calcaneal lesion (Pre-operative)



**Fig 4:** Coronal CT image of calcaneal lesion (Pre-operative)



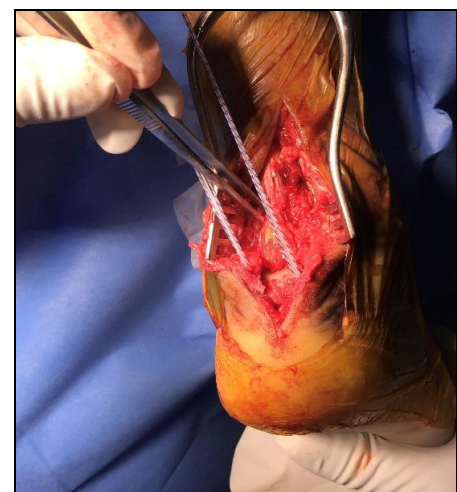
**Fig 5:** Intra-operative fluoroscopy image of curettage



**Fig 6:** Intra-operative clinical photograph after curettage through the extensile lateral approach



**Fig 7:** Intra-operative clinical photograph after 'Z' lengthening and curettage



**Fig 8:** Intra-operative clinical photograph with suture anchors in the calcaneum after curettage



**Fig 9:** Post-operative radiograph showing the suture anchors after curettage of the lesion

## 5. Conclusion

Tuberculous osteomyelitis of the Os Calcis is not that uncommon, especially in some parts of the world. A high index of clinical suspicion with advances in the diagnostic modalities help the cause. Early diagnosis is essential to prevent the disease spread and long term morbidity. Conservative management with anti-tuberculous chemotherapy is the mainstay and this alongside restrictions in weight-bearing help in complete resolution of infection with good outcomes. Definitive surgical treatment is reserved for specific musculoskeletal pathologies emanating as post-tuberculous sequelae.

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