Osteoarticular tuberculosis – a ten years case review

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Abstract

Extrapulmonary sites of tuberculosis must not be neglected as they are not so rarely fortuitous discovering. The morphological diagnosis of tuberculosis is generally easy to do. However, there are the atypical lesions rising diagnostic difficulties. The authors reviewed the histopathological diagnostic in 19 cases of osteoarticular tuberculosis lesions selected from 390 cases of surgical extrapulmonary granulomatous lesions, using for difficult cases, with atypical lesions, new diagnostic tools as immunohistochemistry and DNA amplification technique by the polymerase chain reaction.

Keywords: tuberculosis, bone and joints, diagnosis.

Introduction

Osteoarticular tuberculosis remains a significant worldwide problem, being a source of functional disability, which could lead to severe infirmities. Therefore, it should be recognized and treated early, particularly in children, given that appropriate management can lead to a full recovery [1, 2].

This secondary tuberculosis is the result of tuberculous process development in bone, joints or both. Osteoarticular lesions usually occur following a paucibacillary haematological dissemination by the fixation of a colony inside the active bone marrow.

The retrograde lymphatic dissemination (*i.e.*, from the mediastinal lymph nodes to the dorsal spine or from the mesenteric lymph nodes to the lumbar spine) or the contiguity disseminations (such as rib tuberculosis following pleurisy or humeral head tuberculosis secondary to a shoulder bursitis) should be mentioned among other less significant mechanisms involved in the pathogenesis of osteoarticular tuberculosis [3].

This process may involve any bone or cartilage, *i.e.*, both vertebrae and weight-bearing bones and cartilages [4–6]. Thus, Farer *et al.* (1979) found the following distribution of the sites of development in a retrospective study performed on 676 cases of osseous and cartilage tuberculosis: 40.7% in the spine, 13.3% in the hips, 10.3% in the knees and 35.7% in other sites – ankle, long bones, hand joints, elbow, shoulder, ribs, pelvis, foot and hand bones [5].

The younger the age when the dissemination occurs, the more frequent are the spondylary and small bones sites of development. Belated dissemination, a consequence of primary infection at older ages, leads to a lesion prevalence in great pelvic joints [3]. In the past, bones and cartilages were affected in children with pulmonary tuberculosis [7]. Today, osteoarticular tuberculosis is a condition mostly associated with the elderly in Europe and America, but which still affects children in developing countries, the highest frequency being around 30 years of age [8].

A lot of studies have been carried out upon epidemiology, clinical aspects and therapeutic strategies for tuberculosis. But studies on extrapulmonary tuberculosis in general and osteoarticular location particularly are scarce because the diagnostic criteria are limited, thus, the positive diagnostic being established only by histologic examination [9].

Therefore, we retrospectively reviewed all cases with extrapulmonary mycobacterial lesions in the university hospital, and focused our study on some epidemiological and morphological features and on the diagnostic of osteoarticular locations.

Material and methods

Our study was carried out on 390 patients hospitalized in the surgical departments of Emergency County Hospital Craiova, between 1990 and 2001, whose pathologic diagnostic established in the Pathology Department of the same hospital was granulomatous inflammatory lesion.

We selected 20 of these 390 cases, which showed bone and / or joint granulomatous inflammatory lesions.

The materials were obtained from two different data sources:

– first one was represented by the clinical, surgical and histopathological records.

– second one was represented by the histopathological samples from each case and the paraffin blocks from the Pathology Department's archives.

The surgically removed or biopsy samples were processed using the classical histopathologic technique (fixation and paraffin embedding) and then stained with Haematoxylin-Eosin. In two cases we identified the different lymphocyte and macrophage populations using immunohisto-chemical staining methods. The used antibodies are listed in Table 1.

Table 1 – ***Antibodies used to identify the lymphocyte and macrophage populations***

Antibody	Specificity	Source	Dilution
Rb a Hu CD3	T cells	*DAKO*	1:100
Mo a Hu CD20 cy, clone L26	B cells	*DAKO*	1:75
Mo a Hu CD68, clone KP1	Macrophages	*DAKO*	1:75

In two other cases, we used the PCR technique on paraffin embedded blocks to establish the etiological diagnosis.

The study was of retrospective type and had two components, depending on the assessed parameters:

– a *clinical study* including: department where the patient was hospitalized, gender, age, the lesion's location and suspicion of the etiological diagnosis.

– a *histopathologic study* that focused on diagnosis assessment on routine stained samples and clearing up of borderline cases using the immunohistochemical and PCR techniques.

Results and discussions

Combining the different pathologic investigation techniques allowed us to establish tuberculosis etiology in 373 cases out of the 390 extrapulmonary granulomatous inflammatory lesions. There were 19 cases of osteoarticular tuberculosis, which accounted for 5% of the cases (Figure 1).

Our data were in concordance with other studies that stated an osteoarticular presence in up to 10–13.5% of extrapulmonary tuberculosis and 0.8–4.5% of all cases with tuberculosis [9–12].

The biopsy material came from almost all surgical departments that could use surgical therapy on bone lesions, but most of it came from the Department of Orthopaedic Surgery (Figure 2).

Sex distribution revealed a clear prevalence of this type of lesion in males (15 cases – 79%) as compared to females (4 cases – 21%), our data being in a certain concordance with some studies (Teklali *et al.*, 2003) but different from other studies where osteoarticular lesions were prevailing in women [2, 9, 10].

Age distribution revealed that almost two thirds of al the cases were over 40 years of age and one quarter were teenagers and young adults (Figure 3).

We should mention the 2 cases of tuberculosis in children that were encountered, and the fact that usually, at this age, the primary tuberculosis is a more common finding. It also should be noticed that the aged people accounted for one third of the cases, data in concordance with those from other studies probably because this period of life is characterized by a decrease in the immune system efficiency [9, 10].

The tuberculous process was encountered both in the long bones of the limbs and ribs. There were no cases of tuberculosis in the spine (Figure 4).

In a more recent study the spine was involved in 50% of the patients (50% – thoracic spine, 25% – cervical spine and 25% – lumbar spine), the pelvis in 12% of the cases, the hip and femoral bone in 10%, the ribs in 7%, the ankle, shoulder, elbow and wrist in 2%.

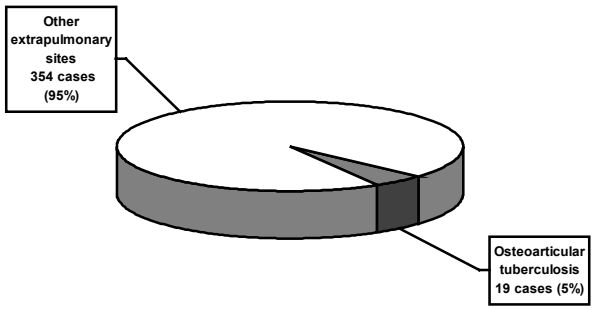

Figure 1 – ***Osteoarticular presence in studied group***

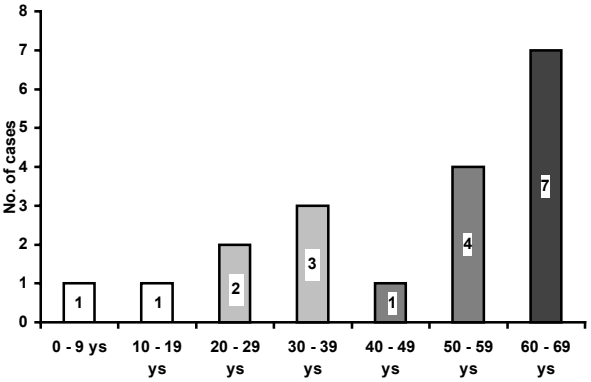

Figure 3 – ***Age distribution***

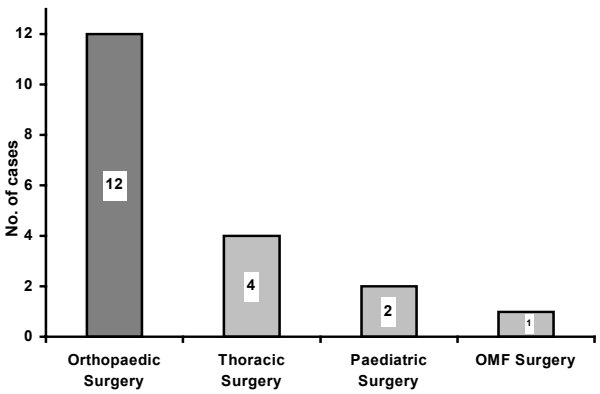

Figure 2 – ***Departments that sent the specimens***

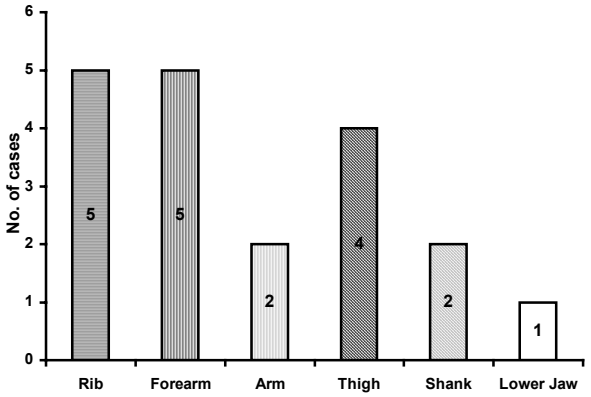

Figure 4 – ***Site of lesions***

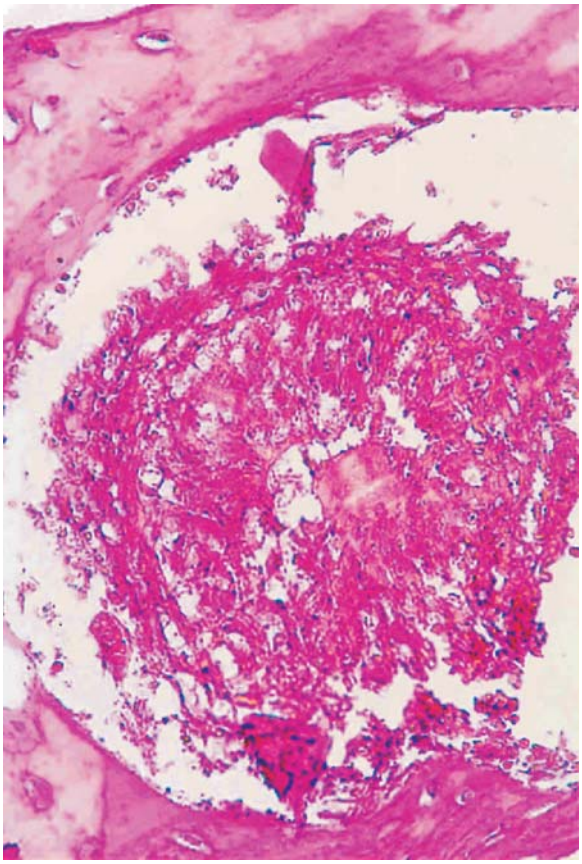

Figure 5 – ***Multinucleated granuloma. Extended osteolysis around granulomatous reaction***

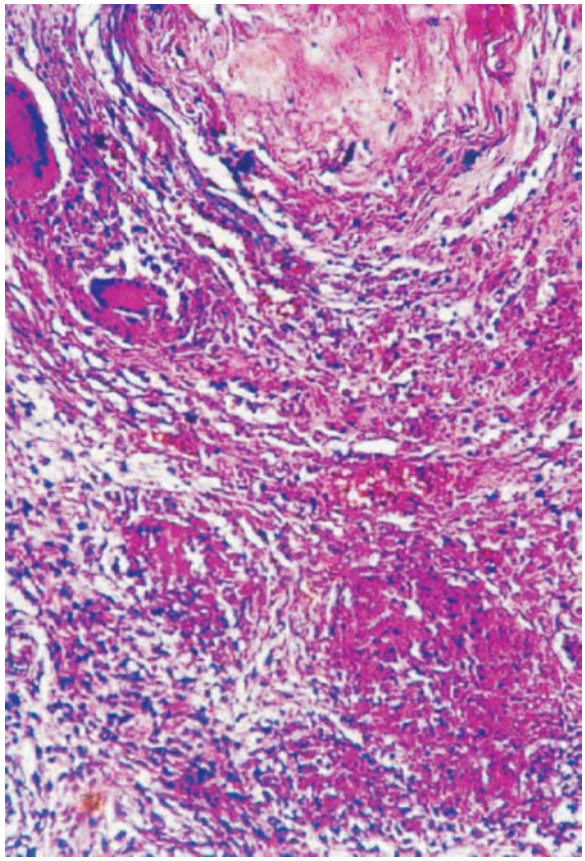

Figure 6 – ***Epithelioid and multinucleated granulomas around devitalized bone fragments***

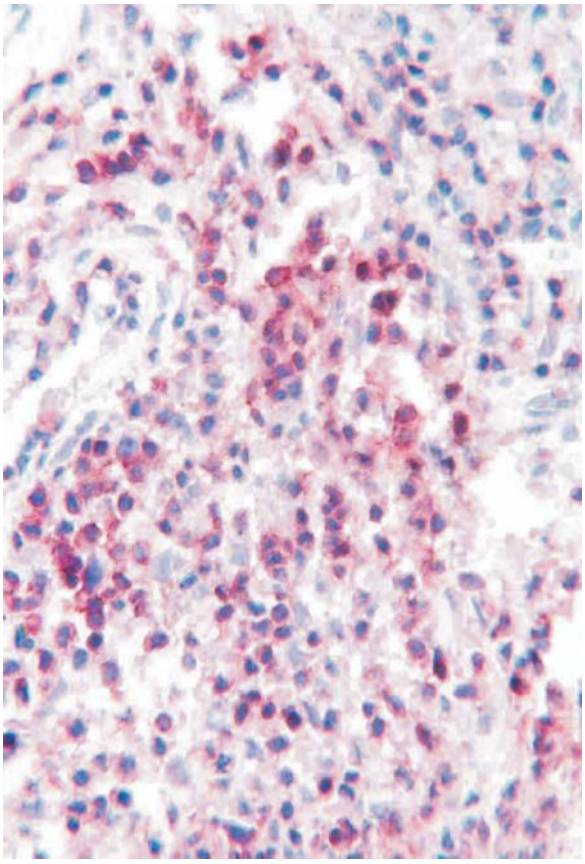

Figure 7 – ***T-Lymphocytes Cd3+ in the granulomatous cellular complex***

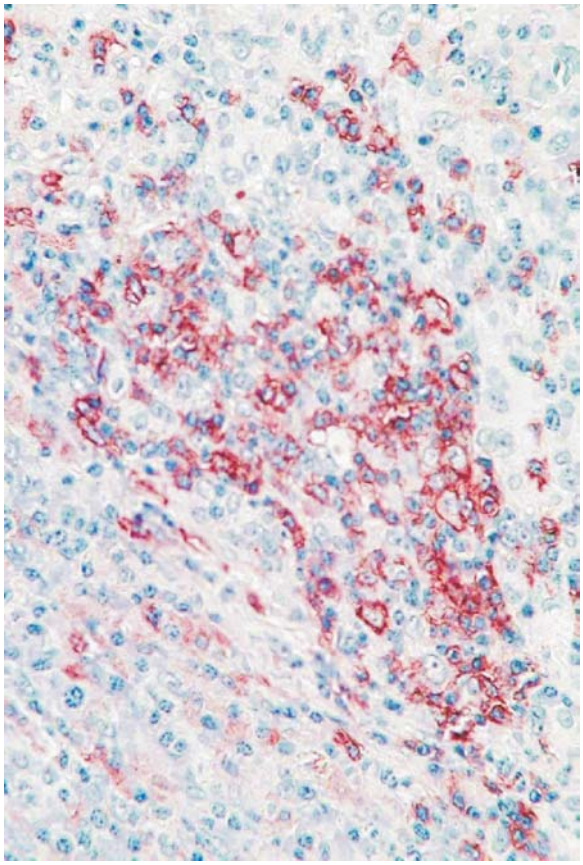

Figure 8 – ***B-Lymphocytes Cd20+ in the granulomatous cellular complex***

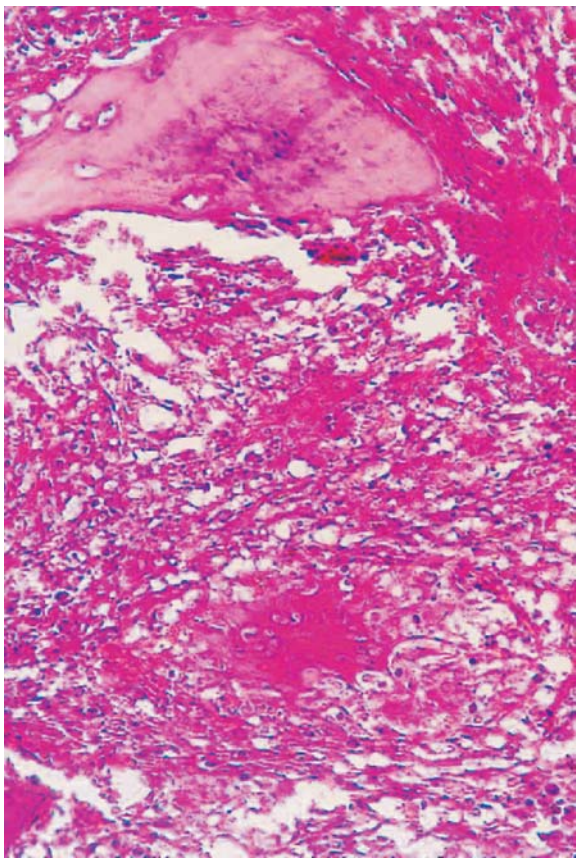

Figure 9 – ***Multinucleated granuloma. Fragment of devitalized bone surrounded by caseous necrosis***

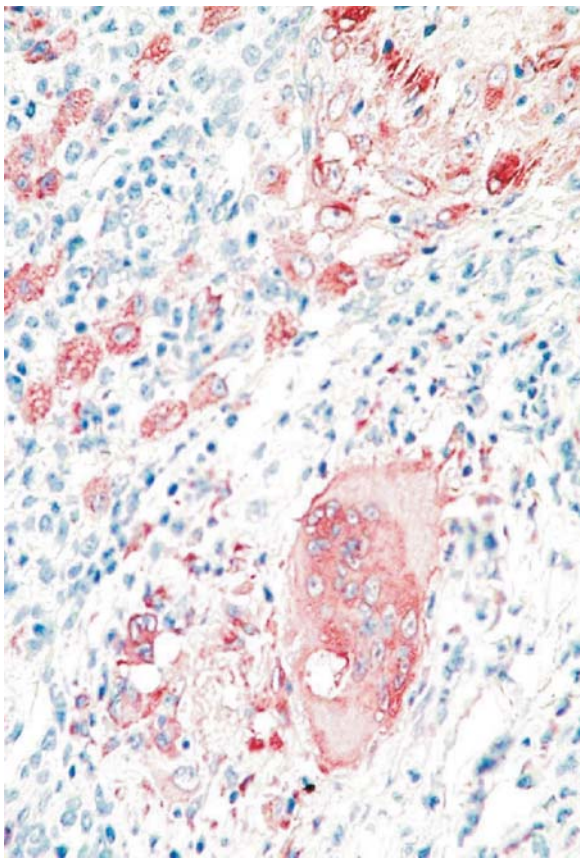

Figure 10 – ***Multinucleated granuloma. Mononuclear and multinucleated macrophages Cd68+***

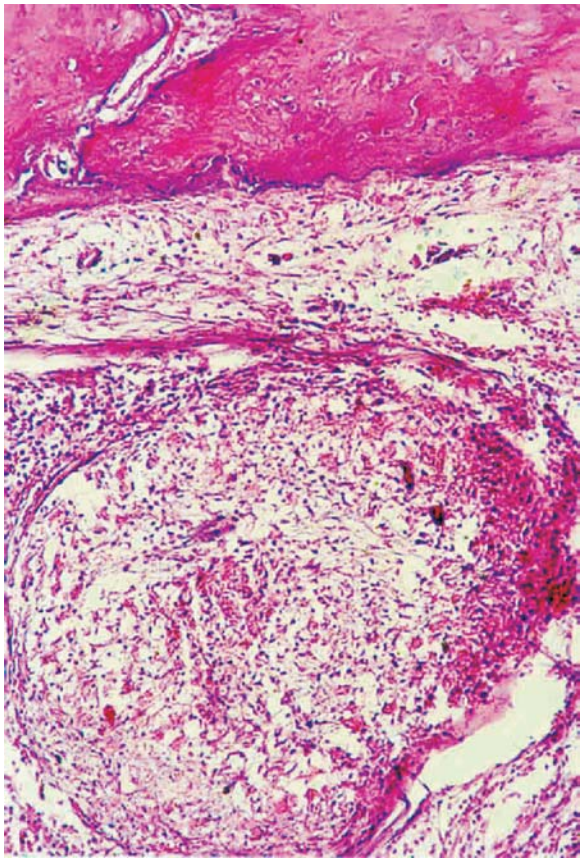

Figure 11 – ***Osteolysis. Atypical granulomatous reaction***

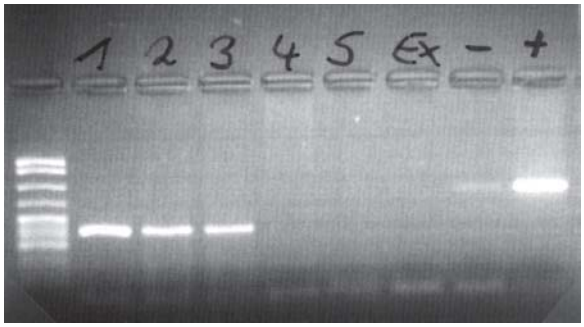

Figure 12 – ***PCR. Probe 3: presence of mycobacterial DNA in the studied material. Probe 5: absence of mycobacterial DNA in the studied material***

There were multiple determinations of the tuberculous process in 3% of the cases [13].

Our data differ from other studies probably because of the small number of cases and because the vertebral tuberculosis is usually treated in clinics specialized in the orthopaedic surgery of tuberculosis.

The analysis of the clinical diagnostic revealed that the surgeons suspected the etiological diagnosis only in a relatively small number of cases (5 of the 19 cases, *i.e.*, 26%).

The suspicion diagnosis percentage ranged widely in different studies, up to around 69% [9].

The diagnostic was established in 18 cases only using the classical staining technique with haematoxylin-eosin (Figures 5, 6 and 9). In all these cases typical epithelioid or Langhans granulomas, which determined large areas of bone, osteolysis and caseous necrosis could be observed.

However, immunohistochemical stains with specific antibodies for different populations of lymphocytes and macrophages (*i.e.*, antibodies anti CD3, CD20 and CD68) were necessary to clear up the diagnostic in 2 cases (Figures 7, 8 and 10).

In 27 cases representing 7% of all 390 granulomatous lesions investigated, the inflammatory granulomas revealed atypical features. In two of these 27 cases, the lesions were found in osteoarticular sites.

Caseous necrosis and osteolysis dominating the lesion but with a nonspecific granulomatous reaction around were seen in both cases (Figure 11). Even phenotyping of lymphocytic and macrophagic cells brought no further evidence of the tuberculous origin. We used, therefore, the PCR method to establish if the two lesions are tuberculous or not.

PCR technique is a rapid and accurate method for determining the presence of mycobacteria in biological samples, thus avoiding a MT culture [14–18]; this technology provides the unique possibility of accurately determining the mycobacterial DNA, even in cases where cultures are impossible [19–22].

The results showed that one of the cases had indeed osseous tuberculosis but with an atypical granulomatous pattern (Figure 12, probe 3) whereas the other was only an atypical nonspecific granulomatous reaction (Figure 12, probe 5).

We could find out, asking for further clinical data, that the patient has had local periosteal administration of an anti-inflammatory depot steroid in the upper third of the femoral bone.

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Conclusions

Tuberculosis continues to be a health problem in some countries. Tuberculosis in extrapulmonary sites discovered in surgery departments is more and more frequent.

Extrapumonary locations and particularly the osteoarticular one must not be left out from the differential diagnosis of patients with obscure illnesses. A high degree of suspicion is still needed to avoid a delayed diagnosis that might complicate the outcome.

The histopathologic investigations together with a DNA amplification technique such as the polymerase chain reaction can establish the certain, etiologic diagnostic.

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