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SCISCORE® REPORTS: MDAR CHECKLIST FOR AUTHORS AND SCISCORE CORE REPORT

SciScore® (https://sciscore.com) scans the methodology section of an article for important scientific rigour criteria and key biological resources and highlights if these are accessible or have problems associated. The Materials, Design, Analysis, and Reporting (MDAR) report and Core report generated from this are included here for transparency and can be cited independently using the DOI below.

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Table 1: Rigor Adherence Table

Ethics
Consent: Arthrodesis procedures are primarily recommended for the foot and ankle. (8)Ethical approvalWritten informed consent was obtained from the patient to publish this report in accordance withthe journal's patient consent policy
Inclusion and Exclusion Criteria
not detected.
Attrition
not detected.
Sex as a biological variable
not detected.
Subject Demographics
Age: ObservationIt’s about a 71-year-old patient with a medical history of type 2 diabetes, hypertension, and right hemiparesis due to a prior ischemic stroke, without any surgical or allergic history, and no known exposure to tuberculosis.
Randomization
not detected.
Blinding
not detected.
Power Analysis
not detected.
Replication
not required.

Table 2: Key Resources Table

Your Sentences	REAGENT or RESOURCE	SOURCE	IDENTIFIER

Other Entities Detected

Your Sentences	Recognized Entity
Statistical Tests	
Laboratory tests revealed the presence of an inflammatory syndrome.	Laboratory tests

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Materials Design Analysis Reporting (MDAR) Checklist for Authors

The MDAR framework establishes a minimum set of requirements in transparent reporting applicable to studies in the life sciences (see Statement of Task: doi:10.31222/osf.oio/9sm4x.). The MDAR checklist is a tool for authors, editors and others seeking to adopt the MDAR framework for transparent reporting in manuscripts and other outputs. Please refer to the MDAR Elaboration Document for additional context for the MDAR framework.

Materials

Antibodies	Yes (indicate where provided: page no/section/legend)	n/a
For commercial reagents, provide supplier name, catalogue number and RRID, if available	No antibodes detected. Please add identifiers for all resources where possible	

Cell Materials	Yes (indicate where provided: page no/section/legend)	n/a
Cell lines: Provide species information, strain. Provide accession number in repository OR supplier name, catalog number, clone number, OR RRID	No cell lines detected Please add identifiers for all resources where possible	
Primary cultures: Provide species, strain, sex of origin, genetic modification status.	Not currently checked by SciScore	

Experimental Animals	Yes (indicate where provided: page no/section/legend)	n/a
Laboratory animals: Provide species, strain, sex, age, genetic modification status. Provide accession number in repository OR supplier name, catalog number, clone number, OR RRID	No organisms detected Please add identifiers for all resources where possible	
Animal observed in or captured from the field: Provide species, sex and age where possible	Not currently checked by SciScore	
Model organisms: Provide Accession number in repository (where relevant) OR RRID	See laboratory animals section for information.	

Plants and microbes	Yes (indicate where provided: page no/section/legend)	n/a
Plants: provide species and strain, unique accession number if available, and source (including location for collected wild specimens)	Not currently checked by SciScore	
Microbes: provide species and strain, unique accession number if available, and source	Not currently checked by SciScore	

Human research participants	Yes (indicate where provided: page no/section/legend)	n/a
Identify authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval.	Not detected.	
Provide statement confirming informed consent obtained from study participants.	Arthrodesis procedures are primarily recommended for the foot and ankle. (8)Ethical approvalWritten informed consent was obtained from the patient to publish this report in accordance withthe journal's patient consent policy	
Report on age and sex for all study participants.	**Age:**ObservationIt’s about a 71-year-old patient with a medical history of type 2 diabetes, hypertension, and right hemiparesis due to a prior ischemic stroke, without any surgical or allergic history, and no known exposure to tuberculosis. **Sex:**not detected.	

Design

Study protocol	Yes (indicate where provided: page no/section/legend)	n/a
For clinical trials, provide the trial registration number OR cite DOI in manuscript.	Not detected.	

Laboratory protocol	Yes (indicate where provided: page no/section/legend)	n/a
Provide DOI or other citation details if detailed step-by-step protocols are available.	Not detected.	

Experimental study design (statistics details)	Yes (indicate where provided: page no/section/legend)	n/a
State whether and how the following have been done, or if they were not carried out		
Sample size determination	not detected.	
Randomization	not detected.	
Blinding	not detected.	
inclusion/exclusion criteria	not detected.	

Sample definition and in-laboratory replication	Yes (indicate where provided: page no/section/legend)	n/a
State number of times the experiment was replicated in laboratory	Not detected.	
Define whether data describe technical or biological replicates	Not detected.	

Ethics	Yes (indicate where provided: page no/section/legend)	n/a
Studies involving human participants: State details of authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval.	Not detected.	
Studies involving experimental animals: State details of authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval.	Not detected.	
Studies involving specimen and field samples: State if relevant permits obtained, provide details of authority approving study; if none were required, explain why.	Not detected.	

Dual Use Research of Concern (DURC)	Yes (indicate where provided: page no/section/legend)	n/a
If study is subject to dual use research of concern, state the authority granting approval and reference number for the regulatory approval	Not currently checked by SciScore	

Analysis

Attrition	Yes (indicate where provided: page no/section/legend)	n/a
State if sample or data point from the analysis is excluded, and whether the criteria for exclusion were determined and specified in advance.	not detected.	

Statistics	Yes (indicate where provided: page no/section/legend)	n/a
Describe statistical tests used and justify choice of tests.	Laboratory tests revealed the presence of an inflammatory syndrome.	

Data availability	Yes (indicate where provided: page no/section/legend)	n/a
State whether newly created datasets are available, including protocols for access or restriction on access.	Not detected.	
If data are publicly available, provide accession number in repository or DOI or URL.	Not detected.	
If publicly available data are reused, provide accession number in repository or DOI or URL, where possible.	Not detected.	

Code availability	Yes (indicate where provided: page no/section/legend)	n/a
For all newly generated code and software essential for replicating the main findings of the study:		
State whether the code or software is available.	Not detected.	
If code is publicly available, provide accession number in repository, or DOI or URL.	Not detected.	

Analysis

Adherence to community standards	Yes (indicate where provided: page no/section/legend)	n/a
MDAR framework recommends adoption of discipline-specific guidelines, established and endorsed through community initiatives. Journals have their own policy about requiring specific guidelines and recommendations to complement MDAR.		
State if relevant guidelines (eg., ICMJE, MIBBI, ARRIVE) have been followed, and whether a checklist (eg., CONSORT, PRISMA, ARRIVE) is provided with the manuscript.	Not currently checked by SciScore	

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By Zakaria Malihy

WORD COUNT	3593	TIME SUBMITTED	02-OCT-2023 11:13AM
		PAPER ID	103166686

Access Microbiology

Osteoarticular tuberculosis of the ankle, a rare localization: a case report

--Manuscript Draft--

Osteoarticular tuberculosis of the ankle, a rare localization: a case report

Author's response to editor

We would like to thank all the reviewers for their valuable comments and suggestions. Please find below our point-by-point responses to the comments.

These are the answers to the Editor comments and suggestions:

- Please provide more detailed description for the images, with arrows pointing to areas of interest. In your revision, please include more up-to-date literature for your references (see point 4 reviewer 1). Consider re-organising the narrative and include more details in parts as specified by the reviewer comments.
  - Answer: thank you for this comment. It has been modified.

Author's response to reviewer 1

We would like to thank all the reviewers for their valuable comments and suggestions. Please find below our point-by-point responses to the comments.

These are the answers to the reviewer 1 comments and suggestions:

1. *Description of the case:*

   Answer: Thank you for your comment. It has been taken into consideration. I have incorporated additional details related to the clinical examination (Lines 39 to 56), as per your suggestion. Furthermore, I have restructured the narrative within the Observation section and provided further elaboration on the laboratory findings (Lines 57 to 90).

2. *Presentation of results :*

   Answer: Thank you for this comment. I have added the corresponding arrows to indicate the lesions observed on the radiological images. (Figure 2 and 3)

How the style and organization of the paper communicates and represents key findings

Answer: Thank you for this comment. I have revised the terminology and reduced redundancy in the manuscript

4. *Literature analysis or discussion:*

Answer: Thank you for this comment. I have updated the references to include more recent sources. I have also included articles mentioning the rare nature of ankle tuberculosis (lines 34 and 117)

Author's response to reviewer 2

We would like to thank all the reviewers for their valuable comments and suggestions. Please find below our point by point responses to the comments.

These are the answers to the reviewer 2 comments and suggestions:

A. 1) *line 50- "The patient did not present any signs of tuberculosis infection". Please broaden the signs of tuberculous infection such and such or does it mean any systemic constitutional symptoms? Please clarify and broaden.*

Answer: thank you for this comment. I have described the signs of tuberculosis infection. Signs of tuberculosis infection refer to the symptoms commonly found in this disease (line 43)

2) *Examination should have included systemic examination -especially chest examination even if it was normal as this will be the first thing to ask how the chest sounds like. And, can I know what the indication of doing CT chest scan was? Was it because the chest auscultation was abnormal or was something else suspected such as cancer? Is it a normal practise there?*

Answer: Thank you for this comment. It has been taken into consideration. I have added details of the clinical examination within the observation. (Lines 39 to 56) The chest examination did not report any anomalies. As mentioned in the paper, the CT chest scan was performed at the request of the pulmonologist as part of an extended investigation to identify the initial site of tuberculosis (line 98)

3) Was there any radiologist comment on CT chest scan finding on "diffuse bronchial micro nodules"? Did you discuss with respiratory physician regarding bilateral pleural effusion for the possibility of pleural tap and sampling? Even if there was no discussion such, please mention.

Answer: Thank you for your comment. Actually, "the diffuse bronchial micronodules" was the commentary of the radiologist. The discussion with the respiratory physician led to the decision not to perform a sampling due to the low quantity of pleural fluid

4*) Last but not least, please mention if the case has been discussed and managed among multidisciplinary team as I gathered the patient presented to trauma centre in the first place so I presumed that later it would have been managed under physician or joint collaboration with physicians/Infectious diseases team etc. The practice/system might be a bit different from place to place, but if possible, please mention if there was collaboration or joint management.*

1

Answer: Thank you for your comment, it has been taken into consideration. Yes, a collaboration between microbiologists, pulmonologists, and traumatologists took place, during which the treatment was discussed. (line 99)

B. in line 108, "The atypical location, the insidious clinical presentation, the lack of an initial diagnosis of pulmonary 109 tuberculosis, as well as the hemiparesis, explains the delayed diagnosis" -- the case did not give enough evidence of delayed diagnosis. I gathered from case description that the patient had ONLY a month history of ankle pain and swelling, then admitted, and the team performed examination, scans, surgery and sampling, then got diagnosis with ZN stain and Gene Expert straight away, which all means quite straight forward and fast. Can you clarify this?

Answer: Thank you for your comment. I have added more details in the observation section to explain the diagnostic delay (lines 66 and 79). The patient was admitted on October 4, 2022 (Day 1), and the diagnosis was made on October 29, 2022 (Day 25). The patient underwent surgery twice for joint lavage on October 4, 2023, and October 25, 2023. During the first procedure, the physician requested a classic cytobacteriological examination only. However, due to persistent symptoms and after the second surgical procedure, in collaboration with the clinician, we performed a Mycobacteriological analysis.

Osteoarticular tuberculosis of the ankle, a rare localization: a case report

Malihy Zakaria*, Benaissa Elmostafa*, Ben Lahlou Yassine*, Maleb Adil**, Elouennass Mostafa*

* Department of Bacteriology, Mohammed V Military Teaching Hospital/Faculty of Medicine and Pharmacy (University Mohammed V), Rabat, Morocco.

** Laboratory of Microbiology, Mohammed VI University Hospital/Faculty of Medicine and Pharmacy (University Mohammed the first), Oujda, Morocco.

Corresponding author:

Malihy Z

Email addresses

Zakaria-malihy@um5.ac.ma; benaissaelmostafa2@gmail.com; benlahlouyassine@gmail.com; maleb.adil@gmail.com; elouennassm@yahoo.fr

DATA SUMMARY

No data was reused or generated.

Summary

Tuberculosis is a real scourge, posing a real public health problem in countries where the disease is endemic. Osteoarticular tuberculosis represents 3% to 5% of all tuberculosis cases and 10% to 15% of extra-pulmonary tuberculosis cases. Involvement of the foot and ankle is rarer. We report the case of osteoarticular tuberculosis of the ankle in a 71-year-old patient with type 2 diabetes and hypertension who presented to the trauma department of the Mohammed V Military Hospital with a painful swelling of the ankle. Standard X-rays and CT scan of the ankle showed inflammatory involvement of the bone and joints. Antitubercular therapy was instituted. Given the context of endemicity, any atypical presentation of lingering bone lesions should raise the suspicion of an osteoarticular tuberculosis in order to ensure early therapeutic management.

Keywords: tuberculosis, ankle, PCR

Introduction

Tuberculosis represents a significant public health problem and ranks among the top 10 causes of death worldwide. According to the World Health Organization (WHO), Morocco reported nearly 35,000 cases of tuberculosis in 2021.

Osteoarticular tuberculosis accounts for a relatively small percentage of all tuberculosis cases, approximately 3% to 5%, and a larger proportion, around 10% to 15%, of extrapulmonary tuberculosis cases (1,2). Among the osteoarticular manifestations, tuberculous spondylodiscitis is the most common, accounting for approximately 50% of cases, followed by tuberculous arthritis and extra vertebral tuberculous osteomyelitis (3). In contrast, involvement of the foot and ankle is rarer. (4,5)

In this report, we present a rare case of osteoarticular tuberculosis affecting the ankle of a 71-year-old patient with diabetes and hypertension. We also underscore the importance of molecular biology techniques in the early diagnosis and management of such uncommon pathologies.

Observation

It's about a 71-year-old patient with a medical history of type 2 diabetes, hypertension, and right hemiparesis due to a prior ischemic stroke, without any surgical or allergic history, and no known exposure to tuberculosis. The patient was admitted with a complaint of swelling in the right ankle that had been present for over a month, with no history of trauma. The patient did not report any signs of infection, such as cough, burning during urination, or diarrhea nor signs of tuberculosis infection such as fatigue, fever, or night sweats.

The clinical examination revealed an afebrile patient with normal conjunctivae. At the ankle level, there was warm, red, fluctuant, and painful swelling. Joint mobilization was painful.

Neurologically, the patient was conscious (Glasgow Coma Scale score of 15/15), well-oriented in time and space, and did not exhibit any sensory or motor deficits. Pupils were equal and reactive.

In terms of respiratory examination, the respiratory rate was 18 cycles per minute, with no cyanosis, digital clubbing, or thoracic deformities observed. There were no signs of respiratory distress or paradoxical breathing. Breath sounds on lung and chest examination were clear, and oxygen saturation was at 94%.

The patient was hemodynamically stable with a blood pressure of 12/5 cmHg, showing no signs of hypoperfusion, and had a regular and strong pulse with a heart rate of 74 beats per minute. Regarding

cardiac auscultation, both the first heart sound (S1) and the second heart sound (S2) were clearly audible.

On a biological level, the complete blood count (CBC) showed lymphopenia at 0.5 G/L and normochromic microcytic anemia at 9.5 g/dL, while the rest of the CBC showed no abnormalities. The peripheral blood smear was normal with no atypical cells. Fibrinogen level was at 9.1 g/L. The activated partial thromboplastin time (APTT) ratio and prothrombin time (PT) were 1.6 and 61%, respectively.

On the renal front, urea and creatinine levels were normal at 0.25 g/L and 6 mg/L, respectively. C-reactive protein (CRP) was at 138.7 mg/L, and total proteins were at 58 mg/L. No hydro electrolytic abnormalities were found in the blood electrolyte panel. Liver function was normal, with aspartate aminotransferase (ASAT) at 8 IU/L and alanine aminotransferase (ALAT) at 12 IU/L. Serology for hepatitis B (HBV), hepatitis C (HCV), and HIV were all negative.

On day 1 of admission, the patient underwent joint drainage with lavage procedure for abscess evacuation, during which pus and joint lavage fluid were collected for cytobacteriological analysis. Direct examination of the deep pus and lavage fluid, stained by Gram's method, revealed an inflammatory cellular response primarily consisting of polynuclear leukocytes with a more significant presence in the pus. No bacterial flora was detected.

The samples were cultured on Columbia agar with 5% sheep blood, Polyvitex® chocolate agar, and in Brain-Heart Infusion (BHI) broth for enrichment, which was then subcultured onto blood agar. Incubation was performed aerobically at 37°C for 18-24 hours. Schaedler agar and Columbia blood agar supplemented with nalidixic acid and colistin were inoculated and incubated anaerobically at 37°C for 48 hours. Anaerobic conditions were achieved using an anaerobic jar (Oxoid©) and an anaerobic gas-generating system (Anaerogen© by Oxoid©). Observation of the culture plate was done every 24 hours for cultures incubated aerobically and every 48 hours for cultures incubated anaerobically. After 15 days of incubation, all cultures and subcultures returned as sterile.

On day 21, due to the lack of clinical improvement, the patient underwent a second procedure for joint drainage and lavage. Due to the persistent sterility of the cultures and the chronic nature of the lesion, the pus and joint washing fluid were sent to the microbiology lab where a search for mycobacteria was conducted in addition to the standard cytobacteriological examination to search for common pathogens. Concerning the latter, the culture media used were the same as previously mentioned and were incubated and examined in the same manner. All of the media returned sterile results.

Mycobacterial testing was conducted on the lavage fluid and revealed acid-fast bacilli (AFB) on direct examination (Fig. 1) using the Ziehl-Neelsen staining method (1 to 10 AFB per 100 fields). Culture on solid Löwenstein-Jensen medium and in liquid MGIT (Mycobacteria Growth Indicator Tube) medium turned positive at day 21 and day 10, respectively. Real-time PCR (GeneXpert MTB/RIF®, Cepheid) detected the *Mycobacterium tuberculosis* complex at very low levels with no detection of rifampicin resistance.

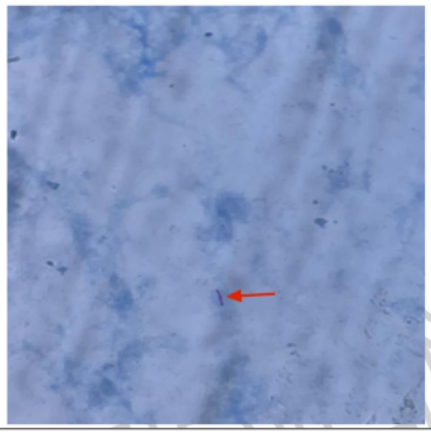

Figure 1: The red arrow indicates an acide-fast bacillus (AFB) found on direct examination using the Ziehl-Neelsen staining

Soft tissue ultrasound revealed a poorly defined hypoechoic, heterogeneous swelling that extended into the joint, with infiltration of the muscular and tendinous structures. This finding suggested a complicated abscessed tenosynovitis and myositis.

The ankle CT scan showed diffuse infiltration of the soft tissues with significant gas extending from subcutaneous soft tissues and penetrating between bone structures. (Fig.2).

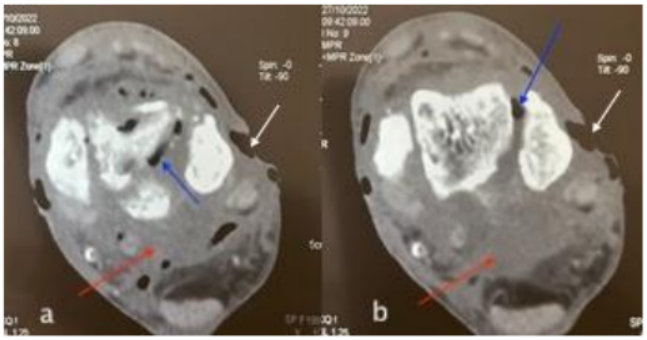

Figure 2 : Axial ankle CT scan showing diffuse infiltration of the soft tissues (red arrows) with significant gas extending from subcutaneous soft tissues and penetrating between bone structures (blue arrows). Note loss of cutaneous substance (white arrows).

The thoracic CT scan, conducted by the request of the pulmonologist to investigate the extent of the disease, revealed bilateral pleural effusion which was notably more pronounced on the right side (Fig. 3). The limited amount of pleural fluid made it impossible to perform a puncture.

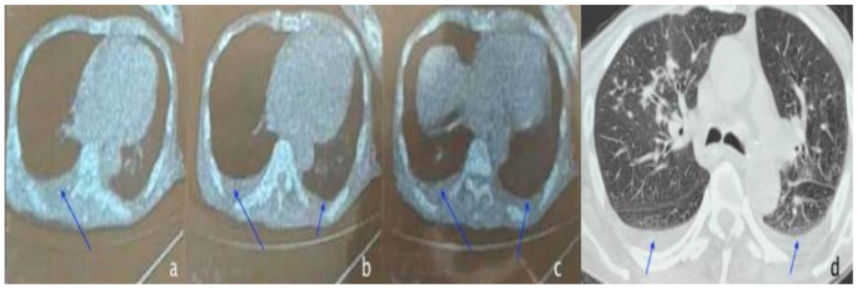

Figure 3: Axial CT scan mediastinal (a, b and c) and lung (d) windows showing bilateral pleural effusion (blue arrows) which is more pronounced on the right side.

Following the detection of the *Mycobacterium tuberculosis* complex, a multidisciplinary collaboration involving a pulmonologist, traumatologist, and microbiologist took place to discuss the treatment. The therapeutic decision was to initiate anti-tuberculosis treatment in accordance with Morocco's national tuberculosis control program. The treatment was successfully undertaken, resulting in significant clinical, biological, and radiological improvement.

Discussion

Tuberculous osteoarthritis typically arises from hematogenous dissemination originating from an initial infection, often in the lungs, lymph nodes, or another organ. This primary infection can be either symptomatic or asymptomatic (5). Osteoarticular tuberculosis predominantly manifests in immunocompromised individuals, such as those with HIV infection, undergoing corticosteroid therapy, receiving immunosuppressive treatments, having diabetes, or suffering from chronic renal failure. This condition exhibits a bimodal age distribution, with a peak occurrence at around 55 years in native populations and another peak between 20 and 35 years among immigrants. (6) The least common location is the ankle, accounting for less than 1 to 6% of cases. (7)

The atypical location, subtle clinical presentation, initial absence of a diagnosis of pulmonary tuberculosis, and the presence of hemiparesis collectively contributed to the delayed diagnosis in this case. Typical tuberculosis impregnation signs such as night sweats and general deterioration are infrequent. Instead, the primary clinical manifestations are pain, swelling, and functional impairment (8). The chronic nature suggests a probable tuberculous etiology.

The chest X-ray and CT scan lacks specificity. In fact more than 80% of patients do not have concomitant active tuberculosis. (9,10) The standard ankle radiography and ankle CT scan are also nonspecific.

(9,10) However, these examinations are valuable in detecting lesions and assisting in determining their nature. MRI stands as the preferred imaging examination as It offers the advantage of early detection, starting from the initial stages of infection, allowing for the visualization of affected bone structures and their extension into surrounding soft tissues and adjacent joints. (8)

In our case, the appearance of the thoracic CT scan was suggestive of pleurisy, raising the suspicion of a tuberculous origin.

An anatomopathological study, while specific, was not conducted due to the purulent nature of the sample.

Laboratory tests revealed the presence of an inflammatory syndrome. Elevated CRP and fibrinogen levels and a significant cellular reaction in the pus and joint washing fluid, coupled with sterile cultures, prompted the investigation for Koch's Bacillus using molecular methods and as well as conventional classical methods. In cases of extrapulmonary tuberculosis, samples often contain few bacteria (paucibacillary), highlighting the importance of molecular methods. These methods offer high sensitivity and specificity (92-98%) for diagnosing the *Mycobacterium tuberculosis* complex, provide rapid results (within 2 hours), and exhibit a strong positive predictive value for rifampin resistance detection (98%). (11) Direct examination and culture remain essential components of the diagnostic process. Culture on solid media provides strains for in-depth studies, particularly in cases of therapeutic failure where exploring drug resistance is crucial. Additionally, culture in liquid media compensates for the slow growth observed on solid media. A positive direct examination confirms the presence of Mycobacterium spp. by visualizing acid-fast bacilli.

The treatment primarily depends on anti-bacillary drugs, which serve to inhibit the progression toward potential sequelae, such as chronic pain and deformity. (8) In most cases, lesions tend to heal within 6-12 weeks with appropriate medical treatment. (12)

Surgical treatment is recommended when medical treatment fails, and when there are persistent issues such as synovitis, fistulas, or abscesses (8). With the introduction of four-drug anti-tuberculosis chemotherapy, surgical indications have become highly limited and selective. They are primarily focused on preventing or correcting deformities and enhancing the function of the affected joint (12). Arthrodesis procedures are primarily recommended for the foot and ankle. (8)

Conclusion

In an endemic context, any unusual presentation of persistent bone lesions should prompt suspicion of osteoarticular tuberculosis to ensure timely therapeutic intervention. The management of osteoarticular tuberculosis is multidisciplinary and necessitates coordination among physicians, bacteriologists, and surgeons.

Ethical approval

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Author contributions

ZM contributed to the initial drafting of the manuscript, while BE, BY, and MA revised it. ELM provided the final approval for the version that will be published.

Funding information

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Competing interests

The authors declare no competing interest.

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ORIGINALITY REPORT

15%
SIMILARITY INDEX

PRIMARY SOURCES

1	ELMOSTAFA BENAISSA, Elmehdi Belouad, Adil Maleb, Mostafa Elouennass. "<xhtml:span xmlns:xhtml="http://www.w3.org/1999/xhtml" xml:lang="en">Risk factors for acquiring Acinetobacter baumannii infection in the intensive care unit: experience from a Moroccan hospital </xhtml:span>", Microbiology Society, 2023 Crossref Posted Content	182 words — 6%
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