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Bacterial Arthritis Caused by *Mycobacterium terrae*

Summary. This paper deals with a case of arthritis of the knee with adjacent osteomyelitis caused by *Mycobacterium terrae* in a patient with rheumatoid arthritis; this confirms the pathogenicity of this organism.

Zusammenfassung. Bakterielle Arthritis durch *Mycobacterium terrae*. In diesem Artikel wird ein Fall von infektiöser Arthritis des Kniegelenks mit angrenzender Osteomyelitis bei einem Patienten mit rheumatoider Arthritis beschrieben. Diese Infektion wurde durch *Mycobacterium terrae* verursacht, womit die Pathogenität dieses Organismus bestätigt wird.

Introduction

Atypical mycobacteria have been shown to be the cause of septic arthritis (1), and there is evidence that *Mycobacterium kansasii*, *Mycobacterium avium*, *Mycobacterium intracellulare*, and *Mycobacterium marinum* can cause arthritis (2). After it was first described in 1950 (3), *Mycobacterium terrae* was considered non-pathogenic for quite some time, but a few reports suggest the contrary (4, 5, 6, 7).

This paper deals with a case of arthritis of the knee with adjacent osteomyelitis caused by *Mycobacterium terrae*, thus confirming the potential pathogenicity of this organism.

Case Report

A 57-year-old male who had a ten-year history of sero-positive rheumatoid arthritis and who had been receiving intra-articular glucocorticosteroid injections of an unknown preparation in both knees for six years complained of a swollen right knee in February, 1979. Because an exacerbation of the rheumatoid arthritis was suspected, therapy with D-penicillamine was initiated.

On April 7, 1979, he was admitted to another hospital because of a bleeding duodenal ulcer. The right knee was still swollen and painful, and was injected with triamcinolonhexacetonide. Five weeks later the pain and swelling increased. There was no history of trauma. He was admitted to our hospital on May 29 24 hours after the onset of a high fever (40° C) without chills. At the time of admission he was on D-penicillamine and indomethacin.

On examination, the patient was seen to be moderately ill. His temperature was 39° C, and his heart rate 92/min. The right knee and lower leg were red and swollen, but not warm. Physical

examination was otherwise unremarkable except for rheumatoid deformities.

Laboratory findings included an erythrocyte sedimentation rate of 80 mm/h (Westergren) and a hemoglobin value of 6.8 mmol/l with a hematocrit of 34%. The white cell count was $5.5 \times 10^9/l$ with a normal differential. Glucose, serum creatinine, alkaline phosphatase, SGOT, and lactic dehydrogenase were all normal; the total serum protein was 65 g/l, the serum albumin 31 g/l, α_1 globulin 4 g/l, α_2 globulin 9 g/l, β globulin 8 g/l, and γ globulin 14 g/l.

A chest radiograph revealed no abnormalities. An X-ray of the right knee showed a very narrow joint space, extensive erosion, and reactive sclerosis (Figure 1). Echography of the right lower leg revealed a large abscess (15 × 4 × 7 cm) extending medially from the knee to the lower calf (Figure 2).

Since a bacterial infection was suspected, aspiration of the right knee and the abscess was performed. Both sites yielded bloody fluid containing 5300 white blood cells per mm³ (90% polymorphonuclear cells). The Gram stain showed no microorganisms, but the Ziehl Neelsen stain showed acid-fast rods. Cultures for common bacteria and fungi were negative.

A skin test with purified protein derivative (1 TE in 0.1 ml, National Institute of Public Health [RIV], Bilthoven, The Netherlands) showed a 2 mm induration in 48 hours. Skin tests for six *Mycobacteria* species (*fortuitum*, *marinum*, *kansasii*, *scrofulaceum*, *avium*, and *batey* [RIV, Bilthoven]) were negative.

Based on the results of the Ziehl Neelsen preparation, the presumptive diagnosis on the day of admission was tuberculous arthritis in combination with a cold abscess in the calf. Therapy was started with 300 mg isoniazid, 600 mg rifampicin, and 800 mg ethambutol per day administered in one oral dose. After two weeks the patient started to vomit and developed jaundice. SGOT rose to 232 U/l and bilirubin to 72 μ mol/l. Rifampicin and isoniazid were discontinued, and SGOT, SGPT, and bilirubin returned to normal. Streptomycin (1 g/day) was administered intramuscularly, and ethambutol was continued.

After four weeks of this therapy the fever had not dropped and there was no improvement in either the knee or the cold abscess. On June 29 the abscess in the calf was drained, synovectomy and debridement of the knee were performed (Figure 3) and a drain was left *in situ*.

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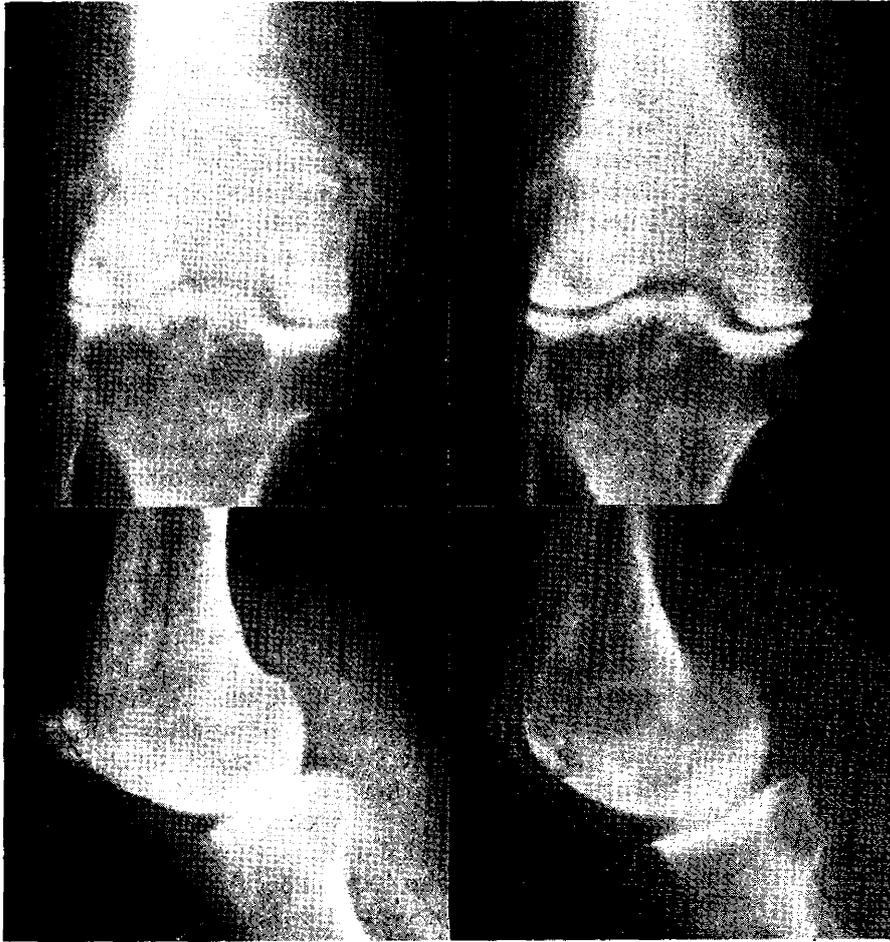


Figure 1: Planigrams of the right knee (upper right: posterior-anterior cut at 11.5 cm; upper left: 11 cm; lower right: transverse section at 11 cm; lower left: 7.5 cm) showing destruction of both femoral and tibial condyles.

Microbiological investigations of other specimens (e. g. stomach washings, sputum) were carried out to determine the presence of acid-fast bacteria. Acid-fast rods could not, however, be identified by Ziehl Neelsen staining, and all cultures were sterile.

Fourteen days after the inoculation of synovial fluid samples on Loewenstein Jensen media, large flat creamy white colonies measuring approximately 1 mm were observed. Tubes inoculat-

ed at 25° C, 30° C, and 37° C all showed growth. Transferring the colonies to fresh Loewenstein media resulted in growth after four days at all three temperatures. Further details are given in Table 1. In view of these findings, the presumptive diagnosis *Mycobacterium terrae* was reached four weeks after the synovial fluid had been inoculated. This diagnosis was later confirmed by the Department of Mycobacterioses, National Institute of Public Health [RIV], Bilthoven, The Netherlands.

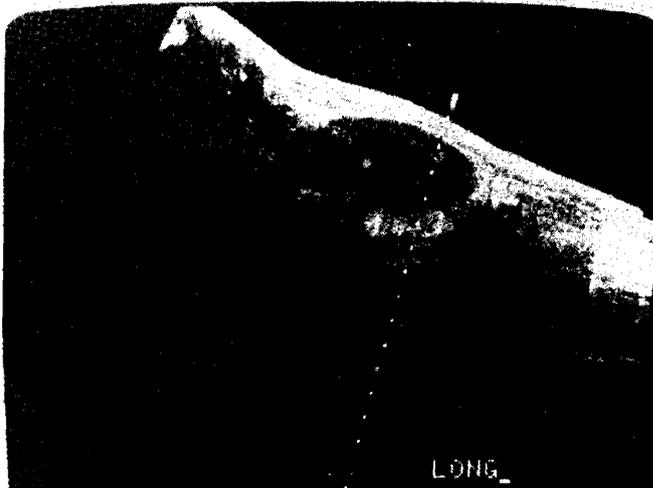


Figure 2: Echogram of the right calf.



Figure 3: Knee during operation, showing extensive area of necrotic tissue.

Table 1: Growth pattern and biochemical properties of the isolate identified as *Mycobacterium terrae*.

Growth pattern	Biochemical properties
Löwenstein at 25° C	++ Ureum -
30° C	++ Valeramide* -
37° C	++ Nicotinamide* ++
45° C	- Pyrazinamide* ++
Glycerol agar at 24° C	+ Capronamide* -
37° C	++ Allantoine* -
Löwenstein-pyruvate	++ Nitrate ±
Löwenstein-thiopen	++ Arylsulfatase -
Löwenstein-PAB	+ Katalase +++
McConkey agar	+ Tween hydrolysis ++
pigment	- Niacin -

* Tests for amidases performed only at RIV.

As soon as the microorganism was identified as *M. terrae*, the therapy was changed to 600 mg rifampicin and 1800 mg ethambutol; later, when the results of the *in vitro* sensitivity tests were known (Table 2), oral ethionamide was added at a dosage of 750 mg per day.

Table 2: Results of *in vitro* testing of the isolate identified as *Mycobacterium terrae* (MIC in mg/l).

Streptomycin	> 100	Thiacetazone	100
PAS	> 100	Kanamycin	> 50
Isoniazid	> 100	Amikacin	> 50
Cycloserine	> 100	Thiocarlide	> 5
Capreomycin	> 100	Rifampicin	5
Pyrazinamide	> 100	Ethionamide	2
Doxycycline	> 100	Ethambutol	0.5

Re-exposure to rifampicin did not lead to anomalous liver-function tests. On this combined therapy, repeated Ziehl Neelsen examination of fluid from the knee showed no acid-fast rods and the cultures became negative. The knee also showed improvement.

Discussion

Septic arthritis occurring in rheumatoid disease is rare but dangerous, not only to the limb but also to life (8). Since 1958, about 100 cases of rheumatoid disease complicated by septic arthritis have been reported in English language journals (8). Many microorganisms can infect the joints in rheumatoid arthritis, but *Staphylococcus aureus* is by far the most common. Mycobacteria are seldom the cause of

arthritis (9) and are not mentioned at all in some reports covering many patients (10, 11, 12).

Mycobacterial arthritis and osteomyelitis are usually caused by *Mycobacterium tuberculosis*. Of the atypical mycobacteria isolated from infected joints (1), two species - *Mycobacterium intracellulare* and *marinum* - have been considered the cause of arthritis and osteomyelitis (2).

Among the atypical species, *Mycobacterium terrae*, called the radish bacillus, has been considered non-pathogenic ever since it was first described in 1950 (3). Several investigators have reported the isolation of *Mycobacterium terrae* from soil (13, 14). The pathogenic potential of this species was first described by Kestle et al. (7). Of the 48 *Mycobacterium terrae* strains isolated, five were said to be associated with human disease; however, details concerning the patients were not given. Since then, only three reports indicating the pathogenicity of *Mycobacterium terrae* have been published (4, 5, 6).

Infections with *Mycobacterium terrae* resemble infections with any of the other atypical mycobacteria as far as the localization of the infection and the occurrence in immunocompromised patients are concerned.

The most common sites of synovial tissue infection caused by atypical mycobacteria are the tendon sheaths of the hand and wrist (15). There also seems to be a preference for damaged organs (16). Although usually encountered in immunocompromised patients, infections with atypical mycobacteria can also occur in healthy people (2).

Our patient with sero-positive rheumatoid arthritis had been treated for the last six years with frequent intra-articular injections (containing corticosteroids) in his damaged knees. Since both rheumatoid arthritis and intra-articular injections have been mentioned as factors which can lead to infectious arthritis (17), it seems likely that the right knee became contaminated with *Mycobacterium terrae* during the latter procedure, probably having been introduced by a non-sterile needle or with the injection fluid, as has been suggested for other atypical mycobacteria (17).

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