A 45-year-old man with sarcoidosis, fever and skin lesions

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A 45-year-old man was referred to the rheumatology outpatient clinic in 2008 because of subcutaneous sarcoidosis and arthralgias. Both the tuberculin skin test (TST) and acid-fast bacilli (AFB)-stain on the skin biopsy specimen were negative. In 2009, the patient developed arthritis of the left knee. Treatment with methotrexate 20 mg/week, folic acid 10 mg/week and hydroxychloroquine 400 mg/day for 2 years did not result in resolution of the arthritis. A conventional radiograph of the left knee showed minimal joint space narrowing. Synovial biopsies of the left knee (sampling in 2009 and 2011) showed histological evidence of non-caseating granulomas, consistent with sarcoid arthritis. Both the Interferon Gamma Release Assay (IGRA) test and AFB-stains on all biopsy specimens were negative. Because of persistent arthritis of the left knee, adalimumab 40 mg every other week was initiated, resulting in complete remission of disease. One year later (2012), the patient developed erythematous cutaneous and subcutaneous nodules (Figure 1), metacarpophalangeal joint arthritis and general malaise. A chest radiograph was normal. A complete blood cell count was within normal limits; the erythrocyte sedimentation rate was 31 mm/1st hr. The TST was negative and a new skin biopsy specimen only revealed evidence of sarcoidosis (negative AFB-stain). Intensification of antirheumatic therapy including addition of glucocorticoids only provided short-term symptom relief. The condition of the patient gradually deteriorated. A new biopsy of a skin lesion was performed (sampling 2013).

The AFB-stain on this last biopsy specimen revealed several acid-fast bacilli, and the Polymerase Chain Reaction (PCR) for Mycobacterium species identified *Mycobacterium haemophilum*. The mycobacterial culture using heme-supplemented media incubated at 30° Celsius also showed growth of mycobacteria. The National Institute for Public Health and Environment (RIVM) confirmed our identification of *M haemophilum*. All slides of biopsy specimens obtained earlier (2008, 2009, 2011, 2012) were revised. In retrospect, also the AFB-stain on the first biopsy specimen obtained in

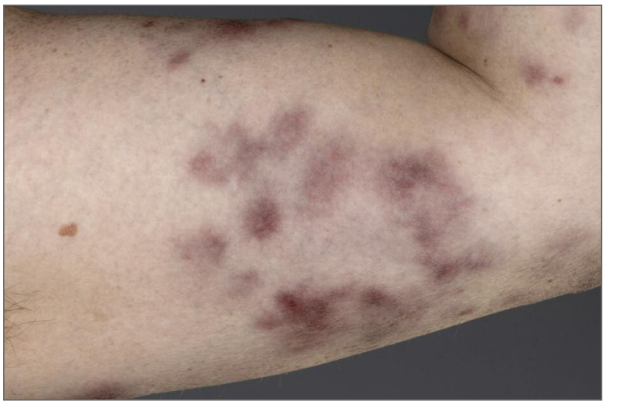

FIGURE 1. Erythematous nodules

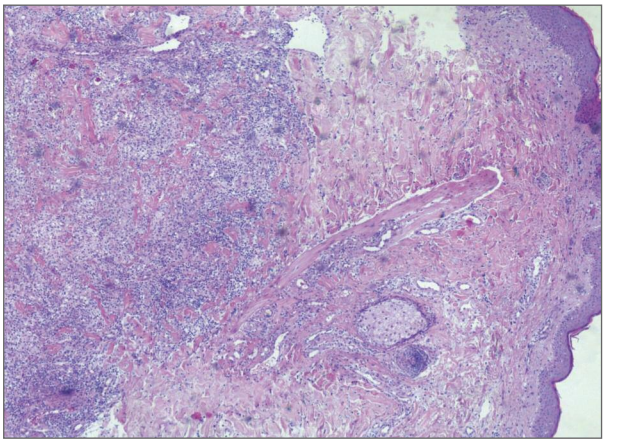

FIGURE 2. Irregular foci of interstitial granulomatous inflammation

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2012 revealed AFB. The other specimens were still consistent with a diagnosis of sarcoidosis and were histologically characterized by typical "naked" non-caseating granulomas with well-defined borders. This was in contrast to the specimen obtained in 2012 that showed irregular foci of interstitial granulomatous inflammation (Figure 2).

M haemophilum mainly causes skin and soft-tissue infections in immunocompromised patients, although arthritis, osteomyelitis and cervical lymfadenitis have also been described[1,2]. Several studies suggest that engineered water systems or open water are a source of *M haemophilum*[3,4]. Our patient had been swimming in a lake shortly before he developed symptoms, which might be the source of infection.

No guidelines exist for treatment of *M haemophilum*. The patient in our case was successfully treated for 1 year with rifampicin 600 mg/day, ciprofloxacin 500 mg twice a day and clarithromycin 500 mg twice a day. All disease-modifying antirheumatic drugs were discontinued; prednisone was tapered off. However, the arthritis of the left knee returned after discontinuation of anti-rheumatic therapy. In conclusion, our patient had two diagnoses: sarcoidosis and, after initiation of a Tumor Necrosis Factor (TNF)-inhibitor, generalized infection with *M haemophilum*.

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