CASE REPORT

A 72-year-old man presented with a 3-week history of painful erythematous lesions of the right foot. His medical history was marked by a rectal adenocarcinoma with lung metastasis managed by chemotherapy and radiotherapy and complicated by radiation-induced pulmonary disease. Three weeks before his admission, he was hospitalized for pneumonitis, which was treated empirically with a combination of piperacillin and tazobactam (Pip/Taz; 4/0.5 g given intravenously for 30 min every 8 h) for 15 days. His fever and respiratory signs resolved but were followed by the occurrence of the skin lesions that led to his hospitalization. On admission, clinical examination revealed no fever and stable hemodynamic parameters. Skin examination revealed two newly appearing erythematous plaques over the internal malleolus and the second and third metatarsophalangeal joints of the right foot, measuring approximately 30 mm in diameter each, in the absence of previous local trauma. Palpation of the lesions revealed fluctuation signs with tenderness. The rest of the clinical examination was normal, with neither pulmonary abnormalities nor cardiac murmur. His white blood cell count was 10,900 leukocytes/mm³ with 80% neutrophils. His serum C-reactive protein level was increased to 60.3 mg/liter. Other routine laboratory blood tests were normal. A computed tomography (CT) scan of the right lower limb revealed two subcutaneous collections below the erythematous plaques (Fig. 1). As fine-needle aspiration of the subcutaneous collections revealed frank pus, surgical drainage of the abscesses was performed before antibiotic therapy based on amoxicillin-clavulanate was started. The pus samples were processed according to standard operating procedures. Gram staining of tissue samples did not show any bacteria, and samples were inoculated into Columbia sheep blood agar (Oxoid), supplemented chocolate agar (bioMérieux), and thioglycolate broth (Oxoid) and incubated for 15 days at 37°C with 5% CO₂. Additionally, brucella blood agar (BD) was inoculated and incubated for 15 days at 37°C under anaerobic conditions. The Columbia sheep blood agar, thioglycolate broth, and anaerobic cultures did not show growth after 3 weeks of incubation. On day 9, small, catalase-positive, oxidase-positive pinpoint colonies were noted only on the supplemented chocolate agar medium (Fig. 1). No identification was obtained by conventional phenotypic methods. Analysis of the 16S rRNA gene sequence by a previously described method (1) revealed 100% identity with Legionella pneumophila. A Legionella-specific PCR assay (with primers designed to amplify a 106-bp DNA fragment of the 16S rRNA gene specific to Legionella species) secondarily performed was positive, explaining the absence of growth on the other media. In consequence, the colonies were plated on buffered charcoal yeast extract (BCYE) with L-cysteine, the medium routinely used for Legionella culture. A latex agglutination test (Oxoid Ltd.) of a colony then identified L. pneumophila serogroup 1. The BinaxNOW Legionella Urinary Antigen Test (Alere) was positive, while blood cultures and serology tests remained negative. Transesophageal echocardiography was negative for an endocarditic process. We performed a thoracic CT scan that revealed improvement of the previous pulmonary infection. On the basis of these elements, a diagnosis of L. pneumophila subcutaneous abscesses was made and levofloxacin (250 mg twice a day for 3 weeks) was started. The patient’s symptoms gradually disappeared in parallel with the healing of the skin lesions, and he was discharged. During a long follow-up period, the skin lesions did not recur.

Only 19 cases of cutaneous involvement of Legionella sp. infections have been reported. Among these, only nine cases were re-
lated to L. pneumophila (2), most of which occurred in immunocompromised patients and generally after a mild pulmonary episode identified as Pontiac fever. The overrepresentation of Legionella spp. other than L. pneumophila (50% of isolates) could be explained by a diagnostic bias. Indeed, if an antigenuria test for L. pneumophila (first-line test) is positive in the face of severe or moderate respiratory symptoms, appropriate treatment (fluoroquinolones or macrolides) might prevent any remote dissemination and therefore any extrapulmonary infection. In the case of a negative antigenuria test result, the introduction of inappropriate antibiotics such as penicillin, which will act only on extracellular bacteria, could promote the spread of Legionella bacteria through the intracellular reservoir. Our patient was admitted for newly appearing skin lesions without evidence of previous local trauma, but owing to the scarcity of extrapulmonary legionellosis reports, neither a Legionnaire’s disease nor a Pontiac fever diagnosis hypothesis was initially raised, explaining why we did not perform the antigenuria test earlier. On the basis of the absence of previous trauma and the absence of a waterborne source of Legionella bacteria after a thorough investigation, we concluded that the most likely hypothesis was pulmonary spread of L. pneumophila (3). In this case, the pneumonitis that preceded skin lesions was cured with Pip/Taz, since it works efficiently against this strain. Indeed, Legionella sensitivity to Pip/Taz was determined with a PTC Etest (bioMérieux) strip on a BCYE–L-cysteine agar plate (Oxoid) after 3 days of incubation at 35 ± 2°C. The quantitative MIC was 0.016 µg/ml. Our results showed a lower MIC than previous reports by Edelstein et al. and Collins et al., which showed MICs between 0.12 and 1 µg/ml and between 0.03 and 2 µg/ml, respectively, reinforcing the effectiveness of these antibiotics against extracellular forms (4, 5).

However, because Pip/Taz is not active on intracellular bacteria (5), one could speculate that the Legionella bacteria were cleared spontaneously from the lungs, as described in Pontiac fever. We hypothesize that in our immunocompromised patient, even if Pip/Taz might have participated in the killing of extracellular bacteria, a remaining fraction of the inoculum was disseminated hematogenously, allowing the development of abscesses on the right lower limb. The paradoxical combination of a negative serology test result and a positive urinary Legionella antigen test result, as found in our patient, was reported in other cases of extrathoracic Legionella infections (2). This could be explained by the inability of an immunocompromised patient to develop proper humoral immunity to L. pneumophila. This emphasizes the utility of urinary antigen testing as a preferred tool for the diagnosis of L. pneumophila infections in the context of immunosuppression.

The small number of cases of cutaneous Legionella infection may be explained by the use of inappropriate culture media. Indeed, Legionella bacteria need L-cysteine to grow (6). In the case presented here, biopsy specimens could have induced the growth of L. pneumophila on chocolate agar by releasing suitable nutrients. That is why subcultures were performed in triplicate on Columbia agar, BCYE without L-cysteine, and BCYE with L-cysteine to test its ability to grow in the absence of L-cysteine. Cultures were positive on BCYE with L-cysteine, slightly positive on BCYE without L-cysteine (Fig. 2), and negative on Columbia agar. Numerous reports in the literature have described Legionella isolation on selective supplemented media such as glycopeptide-polymyxin B-cycloheximide agar or BCYE supplemented with glycine, vancomycin, polymyxin B, and anisomycin, but only a few have described Legionella isolation on routinely used enriched media such as chocolate agar (6, 7). Two cases of infection with L. pneumophila serogroup 4 recovered from chocolate agar plates after 7 days of incubation were identified in Los Angeles in 1978 and 2003 (6). Recovery of L. pneumophila from a pleural fluid specimen and a lung tissue specimen on commercially available chocolate agar at 4 and 9 days was also reported (8). As a result, the frequency at which this organism has been recovered from chocolate agar supplementation is not known.

In conclusion, Legionella spp. may cause extrapulmonary manifestations, especially in immunocompromised patients. This case highlights the reliability of Legionella antigenuria testing in the
screening of immunocompromised patients for L. pneumophila infections and illustrates the importance of the broad-spectrum PCR as a valuable tool for microbiological investigations especially to detect extrapulmonary Legionella bacteria, organisms that remain undetected most of the time unless special media are used (2, 9).

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REFERENCES