Locoregional Multiple Nodular Panniculitis Induced by *Pseudomonas aeruginosa* Without Septicemia: Three Cases and Focus on Predisposing Factors

Mélanie Roriz, MD; Annabel Maruani, MD, PhD; Emmanuelle Le Bidre, MD; Marie-Christine Machet, MD; Laurent Machet, MD, PhD; Mahtab Samimi, MD

**IMPORTANCE** *Pseudomonas aeruginosa*-induced locoregional multiple nodular panniculitis without septicemia is an underreported condition, with only 3 cases reported to date. We report 3 new cases of *P aeruginosa*-induced multiple nodular panniculitis without septicemia and describe common features among all 6 cases, thus providing the first description, to our knowledge, of the natural history and potential predisposing factors for this entity.

**OBSERVATIONS** Median age of the 6 patients was 74 years (range, 54–84 years). Patients had inflammatory nodules on a lower limb (n = 6) that were unilateral (n = 6) and had no fever (n = 5). Blood cultures were negative (n = 5). Skin biopsy specimens revealed panniculitis (n = 5), with skin cultures positive for *P aeruginosa* (n = 6). Skin nodules resolved with systemic antibiotics (n = 5). The comorbidities recorded were type 1 or 2 diabetes mellitus (n = 5), overweight (n = 3), and combined locoregional anatomical changes in the lower limbs (n = 5). Local skin injury, which constituted the portal entry, was present in all cases, especially leg ulcers (n = 3).

**CONCLUSIONS AND RELEVANCE** We describe *P aeruginosa*-induced locoregional nodular panniculitis as a distinct entity. This should be investigated in elderly, diabetic, overweight patients with inflammatory nodules on a lower limb associated with locoregional anatomical changes and skin injury, with the optimal antibiotic regimen introduced as rapidly as possible.


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Skin manifestations caused by *Pseudomonas aeruginosa* are classified as primary or secondary cutaneous lesions. 

Primary cutaneous lesions (eg, pyoderma, intertrigo, and folliculitis) arise in previously healthy patients with predisposing factors such as maceration and skin damage, whereas secondary cutaneous lesions usually occur in immunosuppressed patients by blood dissemination of *P aeruginosa* in a context of bacteremia or septicemia. Such secondary cutaneous lesions include ecthyma gangrenosum, hemorrhagic vesicles and blisters, cellulitis, fasciitis, gangrene, and panniculitis. Indeed, multiple nodular panniculitis classically constitutes a secondary cutaneous manifestation of *P aeruginosa* in a context of septicemia in immunosuppressed patients. On the other hand, *P aeruginosa*-induced locoregional multiple nodular panniculitis without septicemia seems rare, and to our knowledge, only 3 cases have been reported. The natural history and predisposing factors of this condition, therefore, have not been assessed. We report 3 new cases of *P aeruginosa*-induced multiple nodular panniculitis without septicemia and describe common features in the 6 cases, thus constituting the first description, to our knowledge, of the natural history and potential predisposing factors of this probably underdiagnosed entity.

**Report of Cases**

**Patient 1**

A woman in her 80s was admitted for chronic leg ulcers related to venous insufficiency and chronic limb lymphedema. Her medical history included type 1 diabetes mellitus, chronic renal failure, and atrial fibrillation. She was treated with insulin, acetylsalicylic acid, fluindione, ramipril, atorvastatin, and bisoprolol. On admission, she had multiple ulcers on the right lateral malleolus and macerated interdigital intertrigo of both feet. She also had inflammatory nodules on the left thigh that had appeared 6 days before with no systemic symptoms (Figure 1A). Relevant clinical and paraclinical findings are reported in Table 1 and Table 2. In particular, there was no bacteremia or evidence of underlying immunosuppression. A skin biopsy specimen of a nodule showed neutrophilic panniculitis and no vasculitis (Figure 2A), and multisensitive *P aeruginosa* was isolated from a skin biopsy sample. *Pseudomonas aeruginosa* with the same antibiogram profile had been isolated from the ulcer on her contralateral limb 1 month earlier. No bacteriologic sampling of the interdigital intertrigo was performed. The nodules resolved rapidly after treatment with ciprofloxacin hydrochloride for 14 days.
Patient 2
A man in his 50s was referred for infiltrated and necrotic purpuric lesions of the legs that had appeared 10 days previously with progressive extension to the trunk. He had a medical history of obesity, type 1 diabetes mellitus, and dilated heart disease. His treatment consisted of insulin, furosemide, fluidione, bisoprolol, perindopril arginine, atorvastatin, and digoxin. Sildenafil citrate had been introduced 12 days before for pulmonary hypertension related to his heart condition. Clinical and histologic findings were consistent with leukocytoclastic cutaneous vasculitis (LCV). No systemic involvement was ruled out by clinical examination, laboratory tests (C-reactive protein, 10 mg/L [to convert to nanomoles per liter, multiply by 9.524]; complete blood count; and renal and liver function tests), and imaging (chest radiography and echocardiography). There was no evidence of an infectious process accounting for the LCV. Investigations (protein and immunoglobulin electrophoresis, autoimmune antibodies, cryoglobulinemia, and hepatitis B virus, hepatitis C virus, and human immunodeficiency virus serology) were unremarkable. Sildenafil was suspected and withdrawn. There was progressive resolution of the LCV with topical corticosteroids and colchicine. One month later, the patient developed inflammatory nodules on his left leg, where there remained some infracentimetric cutaneous ulcers secondary to the necrotic purpura. Relevant clinical and paraclinical findings are reported in Table 1 and Table 2. A skin biopsy specimen showed neutrophilic panniculitis (Figure 2B), and skin culture was positive for multisensitive P aeruginosa. The nodules rapidly resolved after treatment with ciprofloxacin for 15 days.

Table 1. Systemic and Local Conditions in the Reported Cases of Pseudomonas aeruginosa–Induced Locoregional Multiple Nodular Panniculitis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Present Case Series</th>
<th>Literature Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 or 2 diabetes mellitus (level of control)</td>
<td>Yes (ID) (well controlled)</td>
<td>Yes (ID) (NA)</td>
</tr>
<tr>
<td>Patient 2</td>
<td>Yes (ID) (well controlled)</td>
<td>Yes (ID) (well controlled)</td>
</tr>
<tr>
<td>Other medical history</td>
<td>Heart disease and chronic renal failure (glomerular filtration rate, 35 mL/min)</td>
<td>Heart disease and HBV cirrhosis</td>
</tr>
<tr>
<td>Antihypertensive treatment</td>
<td>Yes (ramipril and bisoprolol hemifumarate)</td>
<td>Yes (bisoprolol hemifumarate and perindopril arginine)</td>
</tr>
<tr>
<td>Immunosuppressive therapy</td>
<td>Clobetasol propionate (20 g/d)</td>
<td>No</td>
</tr>
<tr>
<td>Locoregional anatomical changes</td>
<td>Lymphedema and venous insufficiency</td>
<td>Venous insufficiency</td>
</tr>
<tr>
<td>BMI</td>
<td>23</td>
<td>NA</td>
</tr>
<tr>
<td>Serum albumin, g/dL (normal, &gt;3.50)</td>
<td>3.10</td>
<td>NA</td>
</tr>
<tr>
<td>γ-Globulin, g/dL (normal, &gt;0.50)</td>
<td>0.95</td>
<td>NA</td>
</tr>
<tr>
<td>IgM, mg/dL (normal, &gt;40)</td>
<td>55</td>
<td>NA</td>
</tr>
<tr>
<td>IgG, mg/dL (normal, &gt;700)</td>
<td>1046</td>
<td>NA</td>
</tr>
<tr>
<td>Total lymphocyte count, /μL (normal, &gt;1500)</td>
<td>1200</td>
<td>NA</td>
</tr>
<tr>
<td>HIV serology</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HBV, hepatitis B virus; HIV, human immunodeficiency virus; ID, insulin dependent; NA, not available.

Multiple erythematous subcutaneous nodules on the left thigh in patient 1 (A) and on the right thigh in patient 3 (B).
### Table 2. Clinical and Paraclinical Outcomes of *Pseudomonas aeruginosa* Infection in the Reported Cases*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Present Case Series</th>
<th>Literature Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Place of onset</strong></td>
<td>Out of hospital</td>
<td>In hospital</td>
</tr>
<tr>
<td><strong>Duration before admission, d</strong></td>
<td>6</td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Fever or sepsis</strong></td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>Left thigh</td>
<td>Left leg</td>
</tr>
<tr>
<td><strong>Skin injury</strong></td>
<td>Contralateral leg ulcer, interdigital intertrigo, and IJ</td>
<td>LCV with secondary ulcers and IJ</td>
</tr>
<tr>
<td><strong>CRP, mg/L</strong></td>
<td>301</td>
<td>21</td>
</tr>
<tr>
<td><strong>Leukocytes, /μL</strong></td>
<td>15 900</td>
<td>10 400</td>
</tr>
<tr>
<td><strong>Blood cultures</strong></td>
<td>Before antibiotics</td>
<td>Not performed</td>
</tr>
<tr>
<td><strong>Time of assessment</strong></td>
<td>Before antibiotics</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>Negative (×2)</td>
<td>Negative (×3)</td>
</tr>
<tr>
<td><strong>Endocarditis on USC (TTE or TOE)</strong></td>
<td>No (TTE)</td>
<td>No (TTE)</td>
</tr>
<tr>
<td><strong>Portal entry sampling</strong></td>
<td>PAE (ulcer) 1 mo before</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Skin nodule histology</strong></td>
<td>Lobular panniculitis</td>
<td>Septal and lobular panniculitis</td>
</tr>
<tr>
<td><strong>Results from culture (skin biopsy and pus)</strong></td>
<td>PAE ticarcillin, piperacillin, and ciprofloxacin sensitive</td>
<td>PAE ticarcillin, piperacillin, and ciprofloxacin sensitive</td>
</tr>
<tr>
<td><strong>Antibiotics</strong></td>
<td>Ciprofloxacin, 1 g/d orally (14 d)</td>
<td>Ciprofloxacin, 1 g/d orally (15 d)</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>Resolution</td>
<td>Resolution</td>
</tr>
</tbody>
</table>

*Abbreviations: CRP, C-reactive protein; IJ, insulin injections; IV, intravenous; LCV, leukocytoclastic cutaneous vasculitis; MRSA, methicillin-resistant *Staphylococcus aureus*; NA, not available; TOE, transesophageal echocardiogram; TTE, transthoracic echocardiogram; USC, ultrasound cardiology.

**SI conversion factors:** To convert CRP to nanomoles per liter, multiply by 9.524; leukocytes to ×10^9/L, multiply by 0.001.

*Piperacillin was given as piperacillin sodium; ciprofloxacin as ciprofloxacin hydrochloride; and ceftazidime as ceftazidime pentalhydrate.*
He had no other flare-up of vasculitis during the following 6 months with colchicine.

**Patient 3**
A woman in her 70s was referred for a venous ulcer on the right leg lasting for 2 months. Her medical history included hypertrophic cardiomyopathy and high blood pressure. Her long-term treatment included atenolol. Six days after admission, she developed inflammatory nodules on the right limb (Figure 1B) with no systemic symptoms. Relevant clinical and paraclinical findings are reported in Table 1 and Table 2. Amoxicillin trihydrate-potassium clavulanic, 3 g/d, was introduced for the panniculitis after systemic blood cultures. Her condition rapidly worsened with confusion and ascites. Laboratory investigations revealed deterioration of hepatic function (prothrombin index, 35%; factor V, 47%; aspartate aminotransferase, 94 U/L [normal, <45]; alanine aminotransferase, 211 U/L [normal, <35]; total bilirubin, 2.16 mg/dL [normal, <25]; serum ammonia, 79.82 μg/dL [normal, <50]; and serum albumin, 2.4 g/dL) that led to the diagnosis of a chronic active hepatitis B virus infection (hepatitis B core antibody IgG positive, hepatitis B core antibody IgM negative, hepatitis B surface antigen positive, and hepatitis B virus DNA, 7 log copies/mL) to convert aspartate aminotransferase and alanine aminotransferase to microkatal per liter, multiply by 0.01667; and 0.0167, respectively. Total bilirubin and serum ammonia to micromoles per liter, multiply by 17.104 and 0.714, respectively; and serum albumin to grams per liter, multiply by 10). Results of abdominal ultrasonography were consistent with liver cirrhosis. Further bacteriologic sampling (cerebrospinal fluid, ascites, and blood cultures), performed during amoxicillin–clavulanic treatment, was negative. A biopsy specimen of a cutaneous nodule showed neutrophilic panniculitis and no vasculitis (Figure 2C), and culture was positive for multiresistant *P aeruginosa*. Ceftazidime pentahydrate and amikacin sulfate were started and the nodules had resolved when she died of grade IV hepatic encephalopathy 15 days later.

**Discussion**

Nodular panniculitis due to *P aeruginosa* classically constitutes manifestation of blood dissemination of the bacteria during septicemia in immunosuppressed patients. 2-4 We report 3 cases of *P aeruginosa*-induced locoregional panniculitis with no septicemia and discovered only 3 such cases reported in the literature, 5-7 making it probably an underdiagnosed and/or underreported condition. Interestingly, we found striking similarities among the previously reported cases and our 3 cases, allowing for a description of the natural history and the predisposing factors for this entity.

The clinical and paraclinical outcomes of the *P aeruginosa* infection in these 6 cases are summarized in Table 2. Multiple inflammatory nodules had developed out of the hospital (n = 3) or during hospitalization (n = 3). There was no fever or systemic signs (n = 3) or only a transient fever with no systemic signs (n = 1). Nodules were located unilaterally on a lower limb (n = 6). There was a high level of inflammatory syndrome (median C-reactive protein, 168 mg/L; range, 21-301 mg/L). Blood cultures were negative (n = 5) or had not been performed because of the absence of fever with a minor inflammatory syndrome (n = 1). There was no evidence of endocarditis on echocardiography (n = 5). Skin or pus cultures were positive for *P aeruginosa* (n = 6), most with a multisensitive profile (n = 4). Biopsy specimens revealed neutrophilic lobular (n = 3) or septal and lobular (n = 2) panniculitis, with extension to the deep dermis. In one patient, clinical features were consistent with panniculitis, whereas histopathologic findings and magnetic resonance imaging revealed abscesses. 6 It remains unclear whether this patient had pseudomonal abscesses rather than panniculitis.

The anatomoclinical features of our cases distinguished them from ecthyma gangrenosum, another secondary cutaneous manifestation of *P aeruginosa* that has also been described with no septicemia, 6 including in immunocompetent patients. 9 There has been some controversy whether ecthyma gangrenosum without bacteremia represents a manifestation of initially undetectable bacteremia or a primary cutaneous infection. 6 Our case series showed no evidence that panniculitis indicated initially undetectable bacteremia, based on the absence of systemic signs and the negativity of blood cultures drawn before administration of antibiotics.

Regarding the diagnosis of the infectious process, skin nodules resolved under systemic antibiotics (n = 5) or with an additional surgical incision (n = 1), and no patients developed septicemia. All patients had been treated within 7 days after the onset of panniculitis, and it is unclear whether they would have developed septicemia without prompt therapy. We did not find any reports in the literature in which *P aeruginosa*-induced locoregional panniculitis turned into septicemia.

The overall prognosis of such panniculitis is more debatable. *Pseudomonas aeruginosa* bacteremia, irrespective of the cutaneous findings, is associated with mortality rates up to 39%. 10 Patients developing ecthyma gangrenosum with no septicemia had a better prognosis than those with septicemia. 6 Similarly, 1 death from septicemia was reported in the 17 previous cases of *P aeruginosa* panniculitis with septicaemia, 7 whereas none occurred in our case series. However, the patients in our series were older and had more comorbidities, and the outcome was fatal for 2, despite the absence of septicemia. These 2 patients developed the nodules in the hospital, with the intermediate-sensitive *P aeruginosa* possibly being acquired there. It is possible that the infectious process worsened organ failure; therefore, early diagnosis and treatment of such panniculitis should be recommended, especially in debilitated patients.

The predisposing factors for all reported cases of *P aeruginosa*-induced locoregional panniculitis are reported in Table 1. Median age was 74 years (range, 54-84 years). Frequent comorbidities were type 1 or 2 diabetes mellitus (n = 5), for which 4 patients received insulin therapy, and chronic heart disease (n = 5). Type 1 and 2 diabetes mellitus may represent a predisposing factor due to immunity impairment, although it was well controlled in 3 patients. Heart disease is usually not associated with a heightened risk of skin infections, although one study reported an increase in wound infections in patients receiving antihypertensives. 11 The high prevalence of chronic heart disease in this series may also be related to the high median age. Body mass index, when available (n = 4), indicated that most patients were overweight (n = 3), which is also related to an increased risk of infection. 12 Inter-
Dermatolateralskininjuryastheprimarysiteof
bacteriologicresultswereavailablefortheother3casestoconfirmho-
woundcolonizationmayhavefavoredskininfection.Nobacte-
isolatedfromcutaneousulcers(n = 3),suggestingthatlong-term
infection.Pseudomonas aeruginosa

Conclusions

Pseudomonas aeruginosainducednodularpanniculitisisprob-
ablyanunderrecognizedcondition.Itshouldbesuspectedin
anelderly,diabetic,overweightpatientwithunilateralinfla-
mmatorynoduleson ablowlowerlimb,evenintheabsenceoffever,
systemicmanifestations,orimmunosuppressivecondition,andes-
speciallywhencombinedwithlocoregionalanatomicalchanges
andconcomitantskininjury,soonthataneffectiverereg-
imenecanbeintroducedasarapidlyaspossible.

REFERENCES

1. Silvestre JF, Betloch Mi. Cutaneous manifestations due to Pseudomonas infection. Int J

2. Schlossberg D. Multiple erythematous nodules as a manifestation of Pseudomonas aeruginosa

3. Fleming MG, Milburn PB, Prose NS. Pseudomonas septicaemia with nodules and bullae. Pediatr

4. Tarig S, Hameed S, Tyer M, Johnson M, Lipman M. Pseudomonal septis with subcutaneous nodules

5. Alemán CT, Wallace ML, Blaylock WK, Garrett AB. Subcutaneous nodules caused by Pseudomonas


and influence of delayed receipt of effective antimicrobial therapy on clinical outcome. Clin

11. Pennington A. Ulceration and antihypertensive use are risk factors for infection after skin lesion


ulcers of the lower limb: a prospective observational cohort study. ANZ J Surg. 2006;76
(8):688-692.

immunocompromised patients with extensive skin lesions caused by Pseudomonas aeruginosa