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Blairon, Laurent; Everaert, Johnatan; Baillon, Bruno; Collignon, Sophie; Coenen, François; Cupaiolo, Roberto; Beukinga, Ingrid; Tré-Hardy, Marie

*Published in:*

New Microbes and New Infections

*DOI:*

[10.1016/j.nmni.2024.101524](https://doi.org/10.1016/j.nmni.2024.101524)

*Publication date:*

2024

*Document Version*

Publisher's PDF, also known as Version of record

#### [Link to publication](#)

*Citation for published version (HARVARD):*

Blairon, L, Everaert, J, Baillon, B, Collignon, S, Coenen, F, Cupaiolo, R, Beukinga, I & Tré-Hardy, M 2024, 'Mixta calida, not only an environmental bacterium, but a potential opportunistic threat: Case report of an osteitis with skin necrosis and mini review of the literature', *New Microbes and New Infections*, vol. 62, 101524.  
<https://doi.org/10.1016/j.nmni.2024.101524>

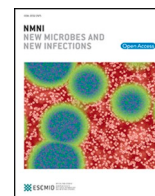
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## Mini-Narrative Review

## *Mixta calida*, not only an environmental bacterium, but a potential opportunistic threat: Case report of an osteitis with skin necrosis and mini review of the literature

Laurent Blairon<sup>a,\*</sup>, Johnatan Everaert<sup>b</sup>, Bruno Baillon<sup>b</sup>, Sophie Collignon<sup>c</sup>, François Coenen<sup>c</sup>, Roberto Cupaiolo<sup>a</sup>, Ingrid Beukinga<sup>a</sup>, Marie Tré-Hardy<sup>a,d,e</sup>

<sup>a</sup> Department of Laboratory Medicine, Iris Hospitals South, Brussels, Belgium

<sup>b</sup> Department of Orthopedics, Iris Hospitals South, Brussels, Belgium

<sup>c</sup> Department of Emergency Medicine, Iris Hospitals South, Brussels, Belgium

<sup>d</sup> Faculty of Medicine, Université libre de Bruxelles, Brussels, Belgium

<sup>e</sup> Department of Pharmacy, Namur Research Institute for Life Sciences, University of Namur, Namur, Belgium

## ARTICLE INFO

Handling Editor: Patricia Schlagenhau

## Keywords:

*Pantoea calida*

*Mixta calida*

Osteitis

Skin necrosis

Immunocompromised host

Orthopedics

Amputation

## ABSTRACT

**Background:** *Mixta calida*, previously known as *Pantoea calida*, is an environmental bacterium rarely associated with human pathologies. Rare case reports mention sepsis, meningitis and implantable defibrillator infection.

**Case presentation:** A 67-year-old female with multiple comorbidities was referred to the emergency room for a comminuted fracture of both right tibial plateaus secondary to a fall and for which she benefited from an external fixator. After removal of the fixator, failure of osteosynthesis and placement of a new fixator, a skin necrosis appeared and a propeller distal anteromedial thigh perforator flap was performed. After 6 weeks, she presented a necrosis of the flap and an osteitis. The bone biopsy was positive with pure *M. calida*. The patient underwent an above-knee amputation, but 6 weeks later the wound was dehiscent and again positive with pure *M. calida*.

**Conclusions:** Serious infections due to *M. calida* are uncommon but can occur in immunocompromised patients. This case illustrates the first reported osteitis and skin necrosis due to *M. calida*.

## 1. Introduction

The genus *Mixta*, first described in 2018, groups Gram-negative bacilli of the order *Enterobacterales* belonging to the *Erwinaceae* family. It is distinguished from *Pantoea* by the absence of yellow pigment and its ability to grow at 44 °C. *Mixta calida*, (formerly *Pantoea calida*, discovered in 2010), gets its name from this particular property [1]. We report, here, a case of osteitis with skin necrosis due to *M. calida* infection in a 67-year-old female with numerous comorbidities: osteoporosis, smoking, chronic alcoholism, Gold III stage COPD, hypertension, history of melanoma and squamous cell carcinoma of the left anterior tonsil pillar with local invasion. A thorough literature review was conducted using PubMed database. The search strategy for the clinical part incorporated keywords such as "*Mixta calida*" and "*Pantoea calida*" for publications up to and including 2024. Only articles in English language were included. Exclusion criteria were articles primarily focused on other *Erwinaceae*, other species of *Mixta* or *Pantoea*, or articles focused on

taxonomy and mechanisms of antibiotic resistance. Non-clinical papers were also excluded.

## 2. Case report

Four months before the diagnosis of *M. calida* infection, the patient had been brought to our emergency room following an alcohol-induced fall resulting in a comminuted fracture of both right tibial plateaus, after which she received an external fixator to bridge the fracture (Figure-1A). Two weeks later, a second operation was performed to remove the fixator and for a double screw plate osteosynthesis. Multiple attempts to osteosynthesise the medial and the lateral plateau were unsuccessful due to comminution. The osteosynthesis material was therefore removed and a new fixator was placed. During her hospital stay, she developed hypoxemic SARS-CoV-2 pneumonia. One week after discharge, the patient returned with skin necrosis for which she underwent debridement and propeller distal anteromedial thigh perforator flap. One and a half

\* Corresponding author. Department of Laboratory Medicine, Iris Hospitals South rue Jean Paquot 63, 1050, Brussels, Belgium.

E-mail address: [lblairon@his-izz.be](mailto:lblairon@his-izz.be) (L. Blairon).

<https://doi.org/10.1016/j.nmni.2024.101524>

Received 17 August 2023; Received in revised form 31 October 2024; Accepted 1 November 2024

Available online 2 November 2024

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months later, she was readmitted to hospital with necrosis of the flap (Figure-1B) with a loss of substance of 15 cm by 8 cm opposite the knee joint. An above-knee amputation was performed, as coverage with viable soft tissue was very difficult, given the poor vascularity and undernutritional status of the patient. A bone biopsy taken at the time of amputation showed a pure grow of *M. calida*, identified by MALDI-TOF mass spectrometry (score 2.5). The isolate was susceptible to amoxicillin, alone and in association clavulanic acid, and to cefotaxime, ceftazidime, cefepime, meropenem, ciprofloxacin, aminoglycosides and co-trimoxazole. To avoid septic dissemination, the patient was treated preventively with piperacillin with tazobactam and vancomycin preoperatively to the amputation for a period of 14 days. Six weeks after amputation, the wound showed partial dehiscence due to delayed healing requiring revision surgery (Figure-1C). A skin necrosis biopsy was again positive for *M. calida* in pure culture (score 2.5). At discharge, the wound was healing with standard wound care, without a directed wound healing device (Vacuum-Assisted Closure). The patient was then referred to the revalidation service.

### 3. Discussion

The *Pantoea* genus, from which *Mixta* is derived, is essentially a group of environmental bacteria. Very few authors report cases of infections linked to *M. calida*. To our knowledge, only four cases of serious infections related directly to *M. calida*, or in association with another opportunistic agent, have been described to date and summarized in Table 1. Yamada et al. reported the case of a 77-year-old patient with end-stage gastric neoplasia and *P. calida* bacteremia [2]. Fritz et al. described a case of *P. calida* meningitis secondary to pituitary adenoma resection surgery in a 52-year-old patient [3]. The third case involved an implantable electronic defibrillator infection in a 61-year-old patient. This was a coinfection also involving *Stenotrophomonas maltophilia* [4]. All these cases involved adults over 50 years of age. A case of isolation of *P. calida* with resistance factors from a screening rectal swab in a pre-term infant has been described [5]. However, the patient had no clinical signs and was only a carrier. More recently, Van Hees et al. reported a

meningitis due to *M. calida* in a 5-week infant, putatively due to contaminated powdered formula [6]. However the bacteria had not been found in the powder, this hypothesis was strongly suggested by a previous report mentioning a contamination of milk formula with *P. calida* [7]. With the exception of this most recent pediatric case, all previously mentioned case reports involve adult women with comorbidities or predisposing risk factors, such as alcoholism, smoking, hypertension, an implantable device, recent chemotherapy treatment, or active neoplasia.

Although *M. calida* is usually considered as environmental, it can be involved in severe infections in patients with immunosuppression related to an underlying co-morbidity or following a surgical act. Our patient, aged more than 50 years, also presented risk factors of immunosuppression and recent surgery. In addition to her extensive history of neoplastic pathologies and her COPD, she had a chronically altered general condition due to her undernutrition and heavy alcohol consumption. Her knee surgery was highly complicated, with failed osteosynthesis and poor wound healing due to poor vascularity, severe malnutrition, and the corticosteroid therapy received for the treatment of her respiratory deterioration caused by a SARS-CoV-2 infection.

Through this clinical case, we extend the spectrum of opportunistic infections with *M. calida* to osteitis and necrotizing skin infections. The fact that the same pathogen was isolated twice in pure culture a few weeks apart strengthens the probable involvement of *M. calida* in this type of infections.

### CRedit authorship contribution statement

**Laurent Blairon:** Conceptualization, Data curation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. **Johnatan Everaert:** Investigation, Visualization, Writing – original draft. **Bruno Baillon:** Investigation, Visualization. **Sophie Collignon:** Investigation, Visualization. **Francois Coenen:** Investigation, Visualization. **Roberto Cupaiolo:** Investigation, Visualization. **Ingrid Beukinga:** Supervision, Visualization. **Marie Tré-Hardy:** Data curation, Formal analysis, Investigation, Writing – review & editing.



**Fig. 1.** A. (Day 0) Three-dimensional CT scan. The reconstruction reveals a complex high-energy mechanism involving valgus forces with significant axial loading. B. (Day 108) Necrosis of the « propeller » distal anteromedial thigh perforator flap. Failure of the graft, inflammatory collection with osteitic infiltration of the anterior part of the right lateral tibial plateau, clinical necrosis of the flap and oozing led to the decision to amputate. A bone biopsy positive for *M. calida* in pure grow suggested an infection by this bacterium. C. (Day 151) Amputation wound with necrosis of the edges and dehiscence of the wound. Intraoperative tissue samples from the necrotic area were again positive with pure *M. calida*.

**Table 1**  
Summary of the four cases of severe infection due to *Mixta calida* reported to date.

Authors	Year of publication	Age	Gender	Clinical focus	Specimen	Associated microorganism	Comorbidities and causes
Fritz et al.	2014	52	F	Meningitis	Cerebro-spinal fluid	None	Hypertension, smoking, alcoholism;
Yamada et al.	2017	77	F	Bacteremia	Blood	None	Post-surgical Gastric neoplasia, anti-cancer chemotherapy
Ajam et al.	2019	61	F	Defibrillator pocket infection	Wound debridement	<i>S. maltophilia</i>	Foreign body (Implantable defibrillator)
Van Hees et al.	2024	5-week infant	M	Meningitis	Blood; Cerebro-spinal fluid	none	Contaminated powdered infant formula

#### 4. Ethical approval

All the procedures were in accordance with the 1964 Helsinki Declaration and its later amendments.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Acknowledgements

The authors thank all the members of the clinical laboratory staff for technical assistance.

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