



CASE REPORT

## Fulminant *Aeromonas hydrophila* infection during acute lymphoblastic leukemia treatment

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### KEYWORDS

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*Aeromonas hydrophila* septicemia has a fulminant course and it has been usually reported in immunocompromised hosts and rarely among children with leukemia. High morbidity and mortality is associated with *A hydrophila* infections. We describe the case of a child with acute lymphoblastic leukemia who presented with septicemia due to *A hydrophila*. The patient presented with fever and skin discoloration during a febrile neutropenia episode, which rapidly evolved into bacteremia and extensive thigh suppuration, fasciitis, and myonecrosis. Apart from antibiotic treatment, surgical debridement to relieve compartment pressure and prevent further lower extremity compromise was promptly performed. Despite long delays in chemotherapy and an extensive tissue gap, primary closure of the involved area was possible with full cosmetic and functional limb recovery, and the patient has remained in clinical remission for more than 7 years.

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### Introduction

*Aeromonas* species are gram-negative, nonsporulating facultative anaerobic rods that produce b-lactamase. The most common species responsible for human infection is *Aeromonas hydrophila*.<sup>1</sup> These pathogens are widely distributed in the aquatic environment (fresh and salt

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water) and in chlorinated tap water, including hospital water supplies.

*A. hydrophila* causes soft tissue infections in non-immunocompromised hosts, usually after local trauma, leech therapy, or surgery.<sup>2</sup> Similar complications have been described in patients with neutropenic cancer, mainly after chemotherapy for acute leukemia.<sup>3</sup> *A. hydrophila* aerolysin is a pore-forming toxin that can contribute to cell death and clinical onset of suppuration and myonecrosis, with or without gas formation.<sup>4</sup>

In the present study, we report the case of a child with acute lymphoblastic leukemia (ALL) who developed fulminant septicemia due to *A. hydrophila* infection as the presentation of a febrile episode during neutropenia. The patient presented with gangrenous lesions with necrosis of the skin of the thigh and eventually developed extensive thigh suppuration, fasciitis, and myonecrosis. Immediate antimicrobial administration and prompt surgical intervention resulted in the patient's excellent cosmetic and functional outcome, even in this case of extensive tissue damage.

## Case presentation

A girl 2.5 year of age was diagnosed with ALL. On admission to our unit, she was afebrile and pale, with a good level of consciousness. Initial complete blood count (CBC) revealed white blood cells (WBC),  $20.18 \times 10^9/L$  with 50% L<sub>1</sub> morphology blasts, Hb 4.8 g/dL, Ht 10.0%, and PLT  $101 \times 10^9/L$ . Serum biochemical profile was normal. The patient was found to have CD10 + B-cell ALL, TEL/AML+, so she was assigned to the median risk ALL group and treated according to the ALL-BFM-95 protocol. She responded favorably to 8 days of prednisolone and on day + 15 blasts were not detected by microscopy or flow cytometry.

On the 18th day of treatment, the patient presented with a high fever of 39°C and rigors. Physical examination was normal, apart from a nonspecific hip pain that progressed to the inner left thigh. She had no diarrhea. The CBC revealed very severe neutropenia (absolute neutrophil count,  $<0.1 \times 10^9/L$ , Hb 11.1 g/dL, Ht 33.7% and PLT  $45 \times 10^9/L$ ). A deep violet rash and skin infiltration with a purplish discoloration over the inner thigh was evident, which progressed to a gangrenous lesion with apparent skin necrosis. Hip and thigh plain x-rays did not reveal any bony lesions, but soft tissue gas formation into the inner aspect of the mid and proximal thigh was evident by plain x-rays and computerized tomography (Fig. 1E,1F). Ultrasound and computed tomography of the area showed the similar findings.<sup>11</sup> Technicium bone scan displayed no bone involvement. Piperacillin with tazobactam and amikacin intravenously together with fluconazole PO were commenced immediately. The ALL induction treatment was withheld, with the exception of prednisolone.

The patient's clinical condition deteriorated within the following 2 days; her body temperature was 38.5°C, but she had no signs of septic shock. The blood cultures revealed a gram-negative organism, but *in vitro* sensitivities were not available at this point. The treatment was modified to cefepime, tobramycin, and liposomal amphotericin, since the gangrene was extending apart from the skin and the underlying soft tissues to the vulva (Fig. 1A). In addition, edema and skin discoloration were evident.

The main concern was whether surgical dissection of the extensive necrotic tissue would be the optimal intervention at that point or whether it would create a major tissue deficit and, consequently, difficulty in healing. In the meantime, blood cultures revealed *A. hydrophila*, identified with the API-20E (BioMérieux, France) identification system. Following the Kirby-Bauer methodology and the Clinical Laboratory Standards Institute interpretation criteria, the antibiogram showed sensitivity to ceftazidime, cefotaxime, aztreonam, imipenem, meropenem, cefepime, gentamicin, tobramycin, amikacin, netilmicin, resistance to cephalothin and cotrimoxazole, and intermediate sensitivity to amoxicillin/clavulanic acid and ticarcillin/clavulanic acid. Stool cultures did not reveal any pathogen.

In the meantime, the patient's clinical condition was not improving, and she presented signs of septicemia, tachypnea, hypotension, impaired level of communication, and apparent blood gas abnormalities. Considering her clinical presentation and the major extension of the necrosis to the inner thigh and the muscles, a surgical intervention was decided. The skin, underlying muscles, and the surrounding necrotic soft tissues were removed and careful debridement of the inner aspect of the left thigh was undertaken. Compartment pressure was relieved. This created a skin gap of 21 × 11 cm. The underlying muscles were visible and the area of the vulva on the ipsilateral side was practically detached from the pelvic structures (Fig. 1B).

Additionally, granulocyte colony-stimulating factor was administered for 5 days since the patient was neutropenic. Daily tissue debridement and a local application of Alkanna tinctoria extract ointment were initiated to promote healing. Supportive care included passive and active physical activity in the context of a rehabilitation program.

The patient underwent deeper and more extensive local tissue care under anesthesia three more times. All necrotic muscles, fat, and skin tissues were removed, and an open granulating wound from the underlying structures was evident. The treatment plan was to repair and cover the gap with a homologous skin graft. However, 15 days from the initial surgery it was apparent that suturing the edges posed an acceptable tension to the skin. Thus, we proceeded with suturing of the area, without any graft implantation (Fig. 1C). The patient received cefepime and tobramycin for 22 and 20 days, respectively.

Twenty days following the presentation of *A. hydrophila* infection, the patient was still in clinical and morphological remission. At present, she has completed chemotherapy treatment and she remains in clinical and morphological remission, 75 months after ALL diagnosis. The lower limb has full functionality, without any disfiguration, apart from a well-healed extensive surgical scar (Fig. 1D).

## Discussion

The cure rate for childhood ALL has significantly improved over time, reaching approximately 85%. However, infection-related morbidity and mortality continues to be of great importance in immunocompromised patients, with bacterial pathogens being the most common cause.<sup>5</sup> Bacterial infections were the common cause of morbidity during the induction phase. In a previous study of our

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