

***Citrobacter koseri* Cellulitis During Anti-CD20 Monoclonal Antibody (Ofatumumab) Treatment for B-cell Chronic Lymphocytic Leukaemia**

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Sir,

Patients with leukaemia are at high risk of developing cutaneous or invasive opportunistic infections caused by unusual bacteria of low virulence or by fungi. Immunosuppression is related to the malignancy itself and/or the therapies. We report here an atypical presentation of bilateral cellulitis of the lower limbs secondary to *Citrobacter koseri* in a patient with B-cell chronic lymphocytic leukaemia (B-CLL) who was receiving a new anti-CD20 monoclonal antibody (ofatumumab).

CASE REPORT

A 60-year-old woman was referred for bilateral, migrating, painful, disabling, inflammatory plaques of the lower limbs with fever (38.5°C) evolving for 3 weeks (Fig. 1). She had been followed for B-CLL stage B since 2003 and treated successively with chlorambucil, fludarabine, fludarabine+cyclophosphamide+rituximab and alemtuzumab. In August 2007, ofatumumab, a



Fig. 1. Bilateral inflammatory erysipelas predominating on the right leg.

humanized IgG1κ antibody directed against the CD20 antigen, was initiated (one dose at 300 mg followed by seven weekly infusions at 2000 mg and then four monthly infusions at 2000 mg). Meanwhile, she was diagnosed with rectal- and anal-specific infiltration by B-neoplastic cells. After the fifth cycle, she developed inflammatory plaques of the lower limbs. The rest of the physical examination showed known palpable peripheral lymph nodes, spleen enlargement and tonsil hypertrophy. Laboratory tests disclosed anaemia (haemoglobin 9.8 g/dl), elevated C reactive protein (74 mg/l) without elevated polymorphonuclear cells and chronic hypogammaglobulinaemia (3.2 g/l). Blood cultures remained negative. Magnetic resonance imaging of the lower limbs showed diffuse infiltration of the skin and the underlying soft tissue without any collection or joint suffusion. Microscopic analysis of a full-thickness skin biopsy was uninformative. The direct tissue microbiological examination of a skin biopsy was negative, but the culture was positive for *C. koseri*. Anaerobic bacteria, mycobacteria, and fungi cultures were negative. Amoxicillin-clavulanic acid (oral, 1 g × 3/day) and ofloxacin (oral, 200 mg × 2/day) were prescribed for one month, with full regression of the lesions. Ofatumumab was maintained for two additional cycles before being withdrawn. At the 18-month follow-up, no relapse had occurred.

DISCUSSION

The genus *Citrobacter* belongs to the *Enterobacter* family of aerobic, non-spore-forming, Gram-negative bacilli that inhabit the human intestine and are commonly found in the environment. The most frequent species are *C. amalonaticus*, *C. koseri* (formerly known as *C. diversus*) and *C. freundii*, often nosocomially acquired and responsible for septicaemia or severe visceral opportunistic infections in newborns, the elderly and immunocompromised hosts (1). *Citrobacter* is rarely involved in skin and soft tissue infections (2). Scalp folliculitis (3–5), ecthyma gangrenosum (6), papulopustules, Janeway lesions (7) and cellulitis (8) have been described, including in patients with underlying hematologic malignancies (6–8).

The source of bacteraemia is tissue trauma or inflammation at the site of colonization (gastrointestinal tract, wounds, and decubitus ulcers). Our patient was diagnosed with specific rectal and anal localization of

the malignancy, and a biopsy was performed to confirm the diagnosis before ofatumumab therapy was initiated. This specific location and the rectal biopsy may have played a role in the initiation of infection.

Patients with chronic lymphocytic leukaemia (CLL) display multiple humoral and cellular defects that predispose them to infection. The role of ofatumumab, a fully human anti-CD20 monoclonal antibody, remains speculative, but should not be neglected. Cutaneous infection under rituximab, a chimeric anti-CD20 monoclonal antibody, is uncommon, as no case of cellulitis has been reported. Nevertheless, ofatumumab is more effective than rituximab on leukaemic cells. It may have a more powerful immunodepressive action. However, few infectious adverse events were noted during a phase one study with ofatumumab in a series of patients with refractory or relapsing CLL (9).

The authors declare no conflict of interest.

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