Sepsis due to *Erysipelothrix rhusiopathiae* in a patient with chronic lymphocytic leukemia associated with bronchopneumonia due to P*seudomonas aeruginosa* and *Escherichia coli*: A case report

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INTRODUCTION: The present report describes a case of sepsis due to *Erysipelothrix rhusiopathiae* in a patient with B-cell chronic lymphocytic leukemia with no animal exposure, associated with concomitant bronchopneumonia due to *Pseudomonas aeruginosa* and *Escherichia coli*.
CASE PRESENTATION: A 54-year-old Caucasian man presented to an emergency room with a three-day history of chest pain, fever, cough with purulent sputum, chills and dyspnea. The patient had associated erythematous papules on the chest and enlarged axillary, submandibular, pectoral and supraclavicular lymph nodes, which regressed under treatment with penicillin. The patient was found to have sepsis without endocarditis caused by *E rhusiopathiae*, associated with bronchopneumonia that was induced by a double Gram-negative infection.
CONCLUSIONS: The underlying-B cell chronic lymphocytic leukemia may have favoured the development of bacteremia due to *E rhusiopathiae*, which occurred subsequent to glossitis in an immunocompromised host being treated with methylprednisolone and cladribine.

Key Words: Erysipelothrix rhusiopathiae; *Immunocompromised host; Sepsis*

Un sepsis causé par un *Erysipelothrix rhusiopathiae* chez un patient atteint d'une leucémie lymphoïde chronique associée à une bronchopneumonie attribuable à un *Pseudomonas aeruginosa* et un *Escherichia coli* : un rapport de cas

INTRODUCTION : Le présent rapport décrit un cas de sepsis causé par un *Erysipelothrix rhusiopathiae* chez un patient atteint d'une leucémie lymphoïde chronique à cellules B sans exposition à des animaux, associée à une bronchopneumonie concomitante attribuable à un *Pseudomonas aeruginosa* et un *Escherichia coli*.
PRÉSENTATION DE CAS : Un homme blanc de 54 ans s'est présenté à l'urgence parce que, depuis trois jours, il avait des douleurs à la poitrine, de la fièvre, une toux accompagnée d'expectorations purulentes, des frissons et une dyspnée. Il avait des papules érythémateuses sur la poitrine et une hypertrophie des ganglions lymphatiques axillaires, submandibulaires, pectoraux et supraclaviculaires, qui ont régressé sous traitement à la pénicilline. Il était atteint d'un sepsis sans endocardite causé par un *E rhusiopathiae*, associé à une bronchopneumonie induite par une double infection Gram négatif.
CONCLUSIONS : La leucémie lymphoïde chronique à cellules B sous-jacente peut avoir favorisé l'apparition d'une bactériémie attribuable à un *E rhusiopathiae*, qui s'est déclarée après une glossite chez un hôte immunodéprimé traité à la méthylprednisolone et à la cladribine.

Erysipelothrix rhusiopathiae has been recognized as an etiological agent of infection in animals and humans since 1880 (1), affecting mammals, birds and fish. In humans, infections caused by this agent occur occupationally, especially due to exposures in butchers, farmers and veterinarians, but also builders and fishermen.

The infection occurs after direct manipulation of animals or their products. The manifestations of the infection varies in humans from localized skin infections (erysipeloid) (2) to diffuse skin forms and systemic infections and to sepsis or endocarditis (which may appear after oropharyngeal or gastrointestinal colonization in one-third of patients with skin infection) (3,4).

We report a case of sepsis caused by *E rhusiopathiae* resulting from oropharyngeal colonization and associated with bronchopneumonia induced by a double Gram-negative infection (*Escherichia coli* and *Pseudomonas aeruginosa*) in a patient with chronic leukemia, after a recent course of chemotherapy with methylprednisolone and cladribine.

CASE PRESENTATION

A 54-year-old Caucasian man presented to an emergency department with a three-day history of chest pain, fever, cough with purulent sputum, chills and dyspnea.

The patient had been diagnosed five years previously with B cell chronic lymphocytic leukemia, Binet stage B, and had responded neither to treatment with fludarabine, cyclophosphamide and rituximab regimen, nor a cyclophosphamide, doxorubicin, vincristine and prednisolone regimen.

His current treatment regimen consisted of methylprednisolone 1 g/day, five days/month and cladribine 10 mg/day, three days/month. During these chemotherapy regimens, he had experienced several episodes of soft tissue infections, bacterial pneumonia, disseminated herpes simplex infection and hepatitis B virus infection, and was also undergoing treatment with entecavir.

On physical examination, the patient was observed to have a temperature of 39.6°C, erythematous papules on the chest, a heart rate of

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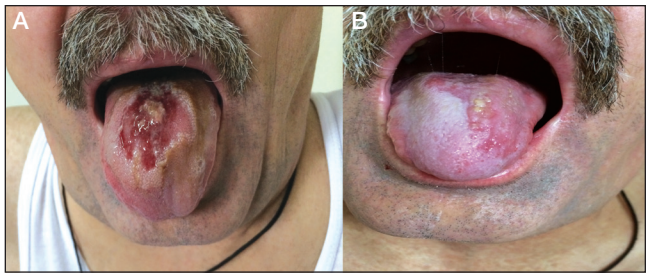

Figure 1) *Ulcerative-necrotic glossitis*. **A** *On admission;* **B** *At discharge*

118 beats/min, blood pressure of 84/50 mmHg, oxygen arterial saturation of 94%, labial herpes, ulcerative-necrotic glossitis (Figure 1) and enlarged axillary, submandibular, pectoral and supraclavicular lymph nodes (Figure 2), with bilateral crackles on chest examination and hepatosplenomegaly. The neurological examination was normal.

Laboratory investigations revealed the following: white blood cell count 3.8×10^9/L (21.6% segmented neutrophils, 54.6% lymphocytes and 19.4% monocytes), hematocrit 35.9%, hemoglobin level 115 g/L, erythrocyte sedimentation rate 82 mm/h, C-reactive protein level 192 mg/L and fibrinogen level 5.44 g/L (15.99 µmol/L). Liver and renal function tests as well as coagulation tests were within normal ranges. Examination of the urine revealed significant pyuria.

An electrocardiogram showed a normal sinus rhythm without conduction abnormalities, and a transesophageal echocardiogram was normal.

Pulmonary radiography showed left perihilar and right infrahilar congestion, and a left pleural effusion. The sputum culture was positive for *P aeruginosa* and *E coli*. The *P aeruginosa* was susceptible to imipenem, meropenem, cefotaxime, ceftazidime, piperacillin, amikacin, netilmicin and fluoroquinolones. The *E coli* was susceptible to amikacin, ceftazidime, gentamicin, imipenem and meropenem. Because the patient had previously developed infections with *P aeruginosa* and *E coli*, empirical treatment with imipenem and gentamicin was initiated. Three days after admission, blood cultures detected the presence of *E rhusiopathiae* (two blood cultures were positive for this bacterium). The laboratory could not test the antibiotic sensitivity of *E rhusiopathiae* in a standardized manner. Therefore, penicillin G 12 million units/day in divided doses was added. During four weeks of treatment with this therapeutic regimen, the patient's symptoms and signs resolved and the patient was discharged in good health. Regression of the enlarged lymph nodes during antibiotic treatment was noted.

DISCUSSION

E rhusiopathiae is a pleomorphic, nonsporulating, nonencapsulated Gram-positive rod-shaped aerobic or facultatively anaerobic organism. *E rhusiopathiae* is recognized as being highly resistant to environmental factors. In the skin, it is capable of producing enzymes, such as hyaluronidase and neuraminidase (5), that facilitate tissue invasion. *E rhusiopathiae* expresses two adhesive surface proteins (6) that bind to collagen types I and IV. In the pathogenesis of infections caused by *E rhusiopathiae*, the following are considered to be important: the neuraminidase, capsule (7) (78.7% of the strains are encapsulated), surface proteins and SpaA antigens (8,9), resistance to phagocytosis and intracellular survival in macrophages.

The role of hyaluronidase in the pathogenesis is controversial because avirulent strains are associated with the loss of the capsule rather than of the hyaluronidase (10). The immunosuppressive conditions in CLL clearly favour the occurrence of *E rhusiopathiae* infections in a suitable host.

The virulence factors cleave the alpha-glycosidic bonds of sialic acid, the mucopolysaccharides present on the surface of mammalian cells, and also play a role in the pathogenesis of arthritis and thrombocytopenia in systemic infection.

CLL is associated with a greater susceptibility to infections due to multiple mechanisms: immunosuppression due to the primary disease,

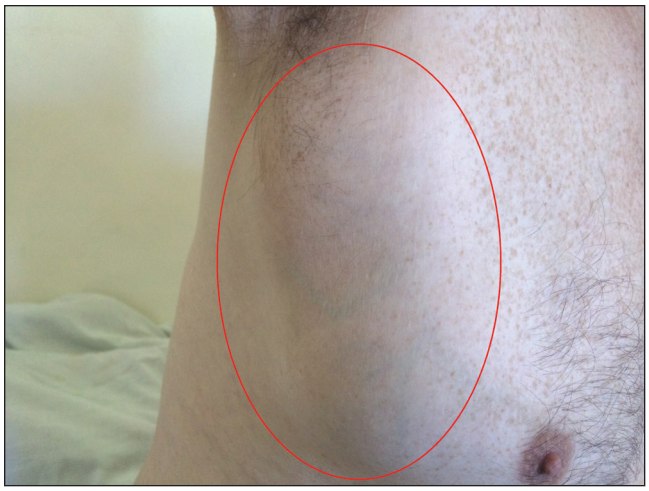

Figure 2) *Axillary lymph nodes*

association with a deficit of cellular-mediated immunity through intrinsic deficiencies or consequent to immunosuppressive therapy (11) (eg, the functional deficit of the T helper cells [12]), an increased activity of T suppressor cells or an inverted CD4/CD8 ratio (13) combined with hypogammaglobulinemia. Deficiency in the complement system also plays an important role in the development of infections due to encapsulated organisms in patients with advanced-stage CLL, along with the decrease in expression of the complement receptors at the level of the B-cell CLL cells (the CR1 and CR2 receptors) and the reduction of the alternative pathway of the complement system (14). The risk for infection in patients with CLL is associated with neutropenia following a progressive bone marrow invasion and immunosuppressive chemotherapy, and also with the decrease in chemotaxis induced by the complement fragment C5a.

In the present case, the patient exhibited relative neutropenia (3.8×10^9/L leukocytes and 21.6% segmented neutrophils), which may have increased the risk for developing a bacterial infection. Facilitating factors associated with the cladribine treatment (15) may have included a decrease in the CD4 level since the beginning of the therapy, which is associated with a greater risk for pneumonia infections and bacterial sepsis (16).

In our case, the patient was undergoing treatment with entecavir due to the reactivation of hepatitis B virus infection, and the last regimen of CLL he was treated with included cladribine and methylprednisolone – all risk factors that favoured the infection. The sputum examination revealed the presence of *P aeruginosa* and *E coli*, sensitive to ciprofloxacin, medication under which the present respiratory manifestations appeared.

E rhusiopathiae infection is described in human pathology as erysipeloid (appearing two to seven days after the skin injury), preceded by local pain or rash, or a purplish plaque at the inoculation site, which is typically very well delimited. Occasionally, there are vesicles with satellite lymphangitis and, rarely, fever, arthralgia or a purpuric rash, appearing as follicular, erythematous papules or a diffuse cutaneous rash with systemic infection – bacteremia and endocarditis (usually aortic valve lesion, sometimes with perivalvular and myocardial abscesses) (17). In immunocompromised hosts, the *E rhusiopathiae* infection may present with bacteremia (18) or endocarditis after oropharyngeal or gastrointestinal tract colonization. *E rhusiopathiae* has been associated with acute leukemia in a child (19) and in neonatal sepsis (20) but has not, to our knowledge, been associated with double Gram-negative infection in B-cell CLL in an adult patient. Some authors have described an association with lupus (21), oropharyngeal cancer (17), perforation of the sigmoid colon (22) and HIV infection. A variety of infections have been reported including acute meningitis (23), chronic meningitis, cerebral abscesses, peritonitis associated with peritoneal dialysis, pleural effusion, septic arthritis (24) and septic

shock (25). Recently, a case of pneumonia caused by *E rhusiopathiae* was described in an immunocompetent patient (26). To date, >90 cases of bacteremia have been described, most with endocarditis affecting native valves, especially the aortic valve, with an associated 38% mortality, as compared with 20% for other etiologies. The treatment of choice is penicillin; however, *E rhusiopathiae* is also sensitive to cephalosporins, quinolones, clindamycin, erythromycin and imipenem, but resistant to vancomycin, chloramphenicol, daptomycin and tetracycline. We postulate that our patient acquired *E rhusiopathiae* by ingestion of undercooked fish and became bacteremic, consequent to glossitis occuring in an immunocompromised setting induced by treatment with methylprednisolone and cladribine.

Bacteremia was suspected in the present case because the patient was found to have *P aeruginosa* and *E coli* in the sputum; three days after admission, *E rhusiopathiae* was isolated in blood cultures. The patient had associated erythematous papules on his chest and axillary, supraclavicular and pectoral lymphadenopathy was present, which regressed under treatment with penicillin. The clinical improvement was not observed after starting the imipenem treatment, but the patient became afebrile with the addition of the penicillin to the treatment regimen. The present case highlights the importance of complete bacteriological identification of isolates in the immunocompromised patient who is at risk for developing multietiological infections.

CONSENT: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The study was accepted by the Ethics Committee of the hospital, which encouraged publication of the article.

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