Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Capnocytophaga bacteraemia following rituximab treatment

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Summary

A case is presented of *Capnocytophaga* bacteraemia, in a juvenile chronic arthritis (JCA) patient receiving steroids, methotrexate and rituximab. This Gram-negative bacillus commonly found in dog saliva has been described to cause illness in immune compromised hosts such as oncology patients, those receiving cytotoxic or biological drugs, alcoholics or postsplenectomy. To the best of our knowledge, this is the first report of *Capnocytophaga* bacteraemia following rituximab treatment.

BACKGROUND

Capnocytophaga is a group of Gram-negative, rod-shaped organisms that are part of the Flavobacteriaceae family. These organisms are found in the oral cavity of both humans and dogs, and are part of the normal oral flora.

The common history is of an immunocompromised patient, presenting with fever, rigours and malaise 1–8 days after sustaining a dog or cat bite. Once sepsis is established, the course is often severe and even fatal. Immunocompromisation is a common risk factor for many sepsis cases, although 40% of life-threatening Capnocytophaga infections occur in immune competent subjects.¹ In such cases, anatomical abnormalities should be sought,² as well as oral ulcerations, periodontal disease and dental plaque. Although dog bite is the most common source of transmission to humans (54%), it has been reported also following a scratch (8.5%) or even mere exposure to animals (27%), for example, a dog licking a superficial skin wound.¹

We now describe for the first time a patient with *Capnocytophaga* bacteraemia following rituximab treatment.

CASE PRESENTATION

We present a 20-year-old female patient, who had been diagnosed with polyarticular juvenile chronic arthritis (JCA) at the age of 11 years, involving wrists, elbows, knees and feet. Rheumatoid factor was negative, antinuclear antibody (ANA) was positive with a titre of 1:320.

The patient's previous antirheumatic treatment included steroids, methotrexate, salazopyrine, hydroxychloroquine and two different tumour necrosis factor α inhibitors (infliximab, etanercept). Owing to active synovitis despite the above treatment, she was treated with intravenous rituximab 1000 mg, given twice in July–August 2008, in combination with methotrexate (22.5 mg/week) with significant improvement of the arthritis. In March 2009, (7 months following rituximab therapy) she experienced a disease flare-up and therefore received a second course of rituximab (1 g twice), resulting in arthritis remission.

In January 2010, 9 months after the last rituximab infusion, she was admitted to hospital due to temperature of 39°C and dysuria. She denied any additional symptoms, reported having a dog at home but denied any scratch or bite.

On examination, she appeared well, with no signs of distress. Blood pressure was 90/46. No rash was noted. Examination of the lungs and heart revealed no pathological findings. Abdomen was soft, tenderness of the lower abdomen and right flank were noted. Laboratory tests on admission included normal complete blood count, creatinine and electrolytes. Urine stick showed pyuria without any other abnormality. The blood CD19 count was low 2% (range 5–15%).

She was treated empirically with intravenous ceftriaxone, until receiving results of sterile urine culture.

Blood culture was positive for *Capnocytophaga* sp., for which she was treated with oral amoxycillin 1000 mg three times a day for 10 days. On follow-up, she was afebrile and symptom-free.

INVESTIGATIONS

Repeated blood cultures were negative. Oral examination by an otolaryngologist revealed good oral hygiene, with no obvious source of infection.

A transthoracic echocardiogram (TTE) was negative for valve vegetation, bone scintigraphy did not reveal any bone abnormality and an abdominal ultrasound study was unremarkable.

DISCUSSION

Capnocytophaga is a Gram-negative organism, found in dog saliva. It is an important cause of illness following dog bite, often resulting in septicaemia,^{1–3} meningitis, endocarditis,^{4–5} osteomyelitis,⁶ abscesses, rare ocular infections⁷ and even death (30%), especially in the immunocompromised host.

Persons at an increased risk of developing *Capnocytophaga canimorsus* infections include patients who have undergone splenectomy and those who abuse alcohol.^{8–9} Others at risk are children with neutropenia or leukaemia¹⁰ or adults

with malignancy, chemotherapy and/or granulocytopenia.¹¹ However, there are numerous reports in the literature of *Capnocytophaga* infection in immunocompetent patients without any known risk factors,^{6 12} some of them severe and even fatal.¹³

Our case is unique in several respects: First, to date, there have been no reports of *Capnocytophaga* infection following biological treatment for autoimmune diseases except for a single case of cellulitis caused by *Capnocytophaga* in an RA patient treated with etanercept,¹⁴ and specifically there have been no reports following rituximab therapy for RA.

Despite the fact that our patient was diagnosed with *Capnocytophaga* infection 9 months following the last rituximab treatment and was concurrently treated with oral methotrexate, the low CD19 count indicates she was B-cell depleted; therefore, it is most likely that this unusual opportunistic infection is due to B-cell depletion induced by rituximab.

Second, we could not find any evidence of a pet bite or scratch in our patients prior to this infection, although our patient did have a pet dog.

Learning points

Physicians who take care of patients with rheumatic diseases receiving Rituximab or other biological treatments should be:

- ▶ Aware of the possibility of this unusual infection.
- ▶ Advise patients who are treated with biological drugs to avoid close contact with domestic animals.
- ▶ The immunosuppression after treating with rituximab can be very prolonged, as in our patients. Her CD19 level was still low 9 months after the last infusion.

Competing interest None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Pokroy-Shapira E, Shiber S, Molad Y. *Capnocytophaga* bacteraemia following rituximab treatment. *BMJ Case Reports* 2012;10.1136/bcr-2012-006224, Published XXX

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