Reminder of important clinical lesson

Campylobacter jejuni cellulitis in a patient with pan-hypogammaglobulinaemiaS Hopkins,¹ M Abuzakouk,² E Brannigan,¹ C Bergin,¹ C Feighery^{2,3}¹Department of Infectious Disease, St James's Hospital, Dublin, Ireland;²Department of Immunology, St James's Hospital, Dublin, Ireland;³Department of Immunology, Trinity College Dublin, Dublin, IrelandCorrespondence to C Feighery, con.feighery@tcd.ie**Summary**

The case of a 17-year-old male with recurrent episodes of cellulitis affecting his left shin is presented. The cellulitis had been present on an intermittent basis over an 18-month period despite several courses of both intravenous and oral antibiotics. Each course of antibiotics resulted in a temporary remission, but on four occasions the cellulitis then relapsed. The patient was known to have pan-hypogammaglobulinaemia and was receiving intravenous IgG replacement therapy every 3 weeks. Other than cellulitis, he remained generally well. The organism responsible for the cellulitis was unknown until *Campylobacter jejuni* was grown in blood cultures during one of the relapse episodes. Based on microbial sensitivity, the patient was treated with ciprofloxacin. This resulted in full resolution of the cellulitis and he remains well. This case illustrates the value of blood cultures in helping microbial identification, particularly in immunocompromised patients with atypical infections.

BACKGROUND

This case report describes a patient with recurrent cellulitis which failed to respond adequately to antibiotic therapy. It was only when blood cultures were performed and these demonstrated *Campylobacter jejuni* infection, that satisfactory antimicrobial therapy was introduced. The patient was receiving immunoglobulin infusions for previously diagnosed hypogammaglobulinaemia and he appeared otherwise well. The case highlights the risk of infection with atypical organisms in patients with immunodeficiency despite adequate replacement therapy. Such organisms may only be identified via blood culture studies.

CASE PRESENTATION

A 17-year-old male was referred to an infectious disease outpatient service with an 18-month history of recurrent cellulitis in his left shin. He thought that the initial lesion had appeared after an injury during a football match. He had received multiple courses of intravenous and oral antibiotics including flucloxacillin, benzylpenicillin and co-amoxiclavulenic acid since this incident, with temporary resolution of the lesion. However, on each occasion, the cellulitis relapsed some weeks after discontinuing antibiotics.

The patient was diagnosed with agammaglobulinaemia at 15 months of age. He had initially presented with recurrent respiratory tract infections, sinusitis and otitis media. He subsequently had recurrent episodes of septic arthritis. In 1994, aged 9, a left lower lobectomy was performed for bronchiectasis. Laboratory findings demonstrated a total absence of IgG, IgA and IgM and very low numbers of circulating B cells ($2 \times 10^6/l$). There was no family history of immunodeficiency. The specific genetic defect causing agammaglobulinaemia has not yet been identified. The

patient was commenced on immunoglobulin replacement therapy aged 4 years and at 9 years of age started domiciliary intravenous immunoglobulin infusions at 3-weekly intervals. Prior to the onset of cellulitis, he remained clinically well at bi-annual review at the immunology clinic.

Apart from a possible football injury, there was no history of other factors which might have contributed to the cellulitis. The patient did not recall any bites or scratches from domestic animals. There was no history of contact with a known case of mycobacterial infection, no history of fresh water contact and no foreign travel. Systems review was non-contributory. In particular, there was no recollection of diarrhoeal illness.

On examination he had a left thoracotomy scar. The cardiovascular examination was normal. There was no evidence of septic arthritis. An erythematous, tender inflamed area of 10×15 cm was present on the anterior aspect of his left lower shin.

INVESTIGATIONS

A summary of the haematological and immunological parameters are shown (table 1). The patient's trough IgG level was within the normal range throughout this period and he had normal T cell subset numbers. No B cells were present. His renal and liver profiles were normal. A skin biopsy was performed and was consistent with cellulitis. Blood cultures were drawn and 3 days later, a curved gram-negative rod was isolated from both aerobic and anaerobic blood culture bottles. This was subsequently identified as *C jejuni*. No organism was identified on stool culture. An MRI scan of his lower limb confirmed an area of oedema with contrast enhancement in the anterior inferior tibial region, suggesting cellulitis, with no evidence of osteomyelitis. A transthoracic echo was normal.

Table 1 A summary of haematological and immunological investigations during infection

Parameter	Result (normal range)
White cell count ($\times 10^9/l$)	10.7 (4.0–11.0)
Neutrophils ($\times 10^9/l$)	8.0 (2.0–7.5)
Lymphocytes ($\times 10^9/l$)	1.7 (1.5–3.5)
Monocytes ($\times 10^9/l$)	1.0 (0.2–0.8)
Haemoglobin (g/dl)	12.2 (13.5–18.0)
Platelets ($\times 10^9/l$)	547 (140–450)
ESR (mm/h)	26 (1–15)
C reactive protein (mg/l)	104 (0–10)
IgG (g/l)	7.78 (6.4–15.0)
IgA (g/l)	<0.06 (0.48–3.44)
IgM (g/l)	<0.04 (0.29–1.86)
T lymphocytes ($\times 10^6/l$)	1136 (1400–2000)
B cells ($\times 10^6/l$)	2 (30–470)
NK cells ($\times 10^6/l$)	122 (200–400)

TREATMENT

Before the identification of *C jejuni* in blood cultures, given the prior failure of β -lactam therapy for the complicated recurring soft tissue infection, the patient was commenced on empiric broad-spectrum antibiotics. In light of microbial sensitivities, the antibiotic ciprofloxacin was administered for 6 weeks.

OUTCOME AND FOLLOW-UP

After completion of treatment, there was full resolution of the area of cellulitis and the C reactive protein level returned to its baseline value. Seven years later, the patient remains well and continues on 3-weekly infusions of IgG replacement therapy.

DISCUSSION

The 17-year-old male described here had suffered from relapsing cellulitis affecting the anterior aspect of his left lower leg over an 18-month period. Infection was presumed to be the cause and on four separate occasions treatment with different antibiotic regimens resulted in a temporary resolution of the cellulitis. However, on each occasion it relapsed again. Relapse episodes were usually accompanied by mild systemic inflammatory features and the presence of cellulitis was the dominant clinical finding. It was only when *C jejuni* was cultured from the patient's blood that a specific microbial infectious agent was identified as the cause of the relapsing cellulitis.

The patient had pan-hypogammaglobulinaemia diagnosed when aged 15 months. Although he had the laboratory features of X linked agammaglobulinaemia, this diagnosis was not established at the genetic or molecular level. He was being treated with IgG infusions every 3 weeks and since the introduction of this therapy had remained free of upper and lower respiratory tract bacterial infections. Importantly, despite treatment with immunoglobulin replacement, patients with agammaglobulinaemia remain susceptible to certain infectious agents.¹ These include infections caused by enteroviruses (such as echovirus and coxsackie virus), acellular bacteria (such as mycoplasma and ureaplasma) and opportunistic pathogens (such as *Pneumocystis carinii*).

Chronic infection with *C jejuni* has been described in individual patients with agammaglobulinaemia.^{2–6} In one case report, *C jejuni* associated cellulitis was described in a patient with agammaglobulinaemia, with relapse of the cellulitis 5 years later and again associated with the same species of *Campylobacter*.² A further report described relapsing *C jejuni* infection causing arthritis in a patient with X linked agammaglobulinaemia.³ Earlier studies also reported *C jejuni* associated cellulitis in patients with immunoglobulin deficiency.^{4–6}

The development of chronic *C jejuni* infection in patients with agammaglobulinaemia may help define the mode of immune defence against this organism. In untreated patients, the absence of antibody may predispose to the infection, suggesting that antibodies are critically involved in defence against this organism. Even in subjects receiving antibody replacement, as in the case reported here, the level of transfused specific antibody may be inadequate to protect the patient. However, it is possible that other elements of the immunological defect in patients with agammaglobulinaemia may be involved. For example, the absence of B cells might result in a defect in antigen presentation, with the effect that the T cell response to organisms such as *C jejuni* is impeded.⁷

Learning points

- ▶ Patients with hypogammaglobulinaemia, even when given adequate replacement therapy, are liable to develop atypical infections.
- ▶ Identification of the infectious agent may require culture of biological samples, including blood, synovial fluid and tissue biopsies.
- ▶ Knowledge of the infectious agent allows institution of appropriate antimicrobial therapy.
- ▶ An extended course of antimicrobials, for example, 6 weeks, is appropriate in this setting.

Competing interests None.

Patient consent Obtained.

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