CASE REPORTS

Intravenous immunoglobulin for resistant Clostridium difficile infection

C. Murphy, M. Vernon, M. Cullen

Department of Geriatric Medicine, Wythenshawe Hospital, Manchester, UK

Address correspondence to: C. Murphy. Email: drclmurphy@aol.com

Abstract

Clostridium difficile (CD)-associated diarrhoea and colitis may relapse in up to 20% of treated patients. We present a patient who failed to respond over a 6-month period to treatment either singly or in combination with metronidazole, vancomycin, rifampicin, cholestyramine and probiotics. Her diarrhoea rapidly resolved after a 3-day course of intravenous immunoglobulin. This treatment may compensate for a failed immune response to CD toxin and should be considered for relapsing CD-associated diarrhoea where there is no response to conventional treatment strategies.

Keywords: Clostridium difficile, diarrhoea, immunoglobulin, elderly

Introduction

Clostridium difficile (CD) is recognised as a major causative agent of antibiotic-associated diarrhoea and colitis [1, 2]. It is found in the normal flora of approximately 2% of healthy adults. Prevalence rises with age and older people have colonisation rates of up to 14% [2, 3]. CD infection is primarily acquired in hospitals and long-stay facilities, most commonly presenting as either mild colitis or watery, mucus-containing diarrhoea with no blood.

Patient management requires withdrawal of any precipitating antibiotics followed by oral metronidazole or vancomycin for 7–10 days [2, 3]. Up to 20% of patients will have a symptomatic relapse on completion of treatment, which can then prove difficult to treat.

Case report

A 57-year-old woman was transferred to an NHS Continu- ing Care unit in April 2003. She had been diagnosed with New York Heart Association stage III/IV heart failure and Barrett’s oesophagus requiring supplemental long-term nasogastric tube feeding. Following a protracted hospital stay she had become immobile with multiple joint contractures.

In December 2003, following a short course of ciprofloxacin for a urinary tract infection, she developed watery diarrhoea. Stool samples were positive for CD toxin detected by its cytopathic effect on Vero cell cultures and 7 days of oral metronidazole 400 mg tds was prescribed. The diarrhoea settled, but spontaneously recurred 1 month later. Further stool samples were positive for CD toxin and oral vancomycin 125 mg qds was commenced. Two weeks later she remained symptomatic and oral metronidazole was added.

After 2 weeks the diarrhoea failed to settle and single-agent probiotic therapy with Saccharomyces boulardii was commenced. This continued for 4 weeks. Throughout this period the patient remained symptomatic. After 1 month the diarrhoea resolved.

One month later the patient again developed spontaneous diarrhoea, testing positive for CD toxin. Vancomycin 125 mg qds, rifampicin 300 mg bd, and the anion exchange resin cholestyramine 3 g qds were commenced for 2 weeks. Over the next 6 weeks the patient experienced sporadic loose stools.

In May 2004, 5 months after the initial episode, she again developed spontaneous diarrhoea which tested positive for CD toxin. A further 1-month course of oral metronidazole failed to control symptoms. In June 2004 intravenous immunoglobulin (400 mg/kg) was administered on 3 successive days. The patient tolerated the infusion without adverse effects. The diarrhoea ceased within 1 week, but the patient developed constipation requiring low-dose sodium docusate. Four months later, despite her stools remaining CD toxin positive, there were no recurrences of diarrhoea.

Discussion

Relapsing CD infection occurs in up to 20% of patients [4]. Usual treatment for a relapse comprises a 7–10 day course of either metronidazole or vancomycin. Subsequent relapse may respond to probiotic therapy [5]. Some patients, however, continue to relapse whenever treatment is discontinued, creating a significant therapeutic challenge.
Cholestyramine binds CD toxin, but is not routinely used as it can also bind vancomycin [2]. There is increasing evidence that the immune response to CD toxin plays a major role in determining susceptibility to recurrent diarrhoea. Several investigators have found that patients with recurrent disease exhibit low antibody levels to CD toxin [4]. In one study of hospital-acquired CD-related diarrhoea, an increase in serum IgG anti-toxin antibody levels was strongly associated with asymptomatic carriage. Lack of antibody response was associated with a 48-fold increase in risk for CD diarrhoea [1]. An immune response to CD toxin may therefore protect against CD diarrhoea.

Intravenous immunoglobulin may effectively treat relapsing CD infection [6–8]. Our patient responded quickly to this intervention when all other treatment strategies had failed over the preceding 6 months. Further study may establish whether intravenous immunoglobulin has a role in routine treatment of recurrent CD infection. Presently it should be considered in cases of repeated relapse where conventional treatment has failed.

Key points
- **Clostridium difficile** is a major causative agent of antibiotic-associated diarrhoea.
- Prevalence of *Clostridium difficile* diarrhoea rises with age.
- Standard treatment is usually with oral metronidazole or vancomycin.
- Intravenous immunoglobulin may effectively treat relapsing *Clostridium difficile* infection.

References

Received 16 February 2005; accepted 24 August 2005