CASE REPORT

Corticosteroid treatment of severe, non-responsive Clostridium difficile induced colitis

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Corticosteroids have been shown to be effective against the inflammatory diarrhoea associated with inflammatory bowel disease. Their effectiveness against the inflammatory diarrhoea of C difficile, however, has not been reported. In this case report we describe the outcome of using corticosteroids in a young boy suffering from severe C difficile diarrhoea and colitis that was refractory to standard treatments.

CASE REPORT

 Prior to hospitalisation, the patient, a 5 year old African American boy, had been treated for a presumptive sinusitis with amoxicillin for 10 days. He had not shown any improvement after 10 days and was subsequently started on amoxicillin-clavulanate. After five days of treatment with amoxicillin-clavulanate, the patient developed a profuse diarrhoea (more than 10 loose stools per day) with tenesmus and the appearance of frank blood in his stools. He was hospitalised at a community hospital for fluids and electrolyte replacement. A stool sample taken at that time was positive for C difficile toxin. After 48 hours without improvement he was transferred to the Pediatric Gastroenterology Service at Westchester Medical Center for evaluation and treatment of bloody diarrhoea.

On admission he had a temperature of 102.3° F. His weight and height were 31 pounds (~5th percentile) and 42 inches (25th percentile), respectively. On examination, he had diffuse abdominal tenderness, rebound tenderness, mild distension, and active bowel sounds. He had 1+ pitting oedema of his ankles, and periorbital and sacral regions. Rectal examination showed haem positive stool and no perianal disease. An abdominal flat plate x ray showed an ileus pattern.

Laboratory values on admission included a white blood cell count of 19 x 10^9/L (80% polymorphonuclear neutrophils, 5% bands, 2% eosinophils), an erythrocyte sedimentation rate of 32 mm/h, a haemoglobin of 72 g/L, a haematocrit of 21% a total protein of 43 g/L, and an albumin of 21 g/L. Liver enzymes, reticuloocytes, prothrombin time, platelet count, blood urea nitrogen, creatinine, urinalysis, and urine culture were all within normal limits. His stool was still positive for C difficile toxin. Stools sent for culture, cryptosporidium, and ova and parasites were all negative.

The patient was immediately started on intravenous metronidazole (20 mg/kg/day divided into eight-hourly doses) and oral vancomycin (40 mg/kg/day divided into six-hourly doses) because of the severity of the diarrhoea and colitis. He was continued on this regimen for two weeks. During this time he was also transfused twice with 1 g/kg albumin on days 1 and 10, and with 10 ml/kg packed red blood cells on day 4. Despite this aggressive antibiotic treatment, his diarrhoea persisted over the course of these two weeks with approximately 10-15 loose bloody stools per day.

On hospital day 14 a flexible sigmoidoscopy was performed up to 30 cm. The mucosa was noted to be friable and oedematous, and studded with raised nodules that exhibited a green-yellow exudate, consistent with a pseudomembrane. During

Clostridium difficile can cause inflammatory diarrhoea and colitis by disrupting normal colonic flora. Corticosteroids are effective against diarrhoea associated with inflammatory bowel disease, but their effectiveness in treating inflammatory diarrhoea of C difficile has not been reported. In this preliminary report, we describe the use of corticosteroids in a child with severe C difficile diarrhoea and colitis refractory to standard treatments.
the procedure the patient was noted to have marked abdominal distension. A biopsy was therefore not taken to avoid the possibility of bowel perforation.

After sigmoidoscopy, the patient was started on intravenous methylprednisolone (2 mg/kg/day in two divided doses). His diarrhoea resolved within 24 hours of initiating the methylprednisolone. Stool samples for C difficile toxin were positive three days after starting steroid therapy, but were negative after seven days. On day 17 he was switched to oral prednisone (2 mg/kg/day in two divided doses). Steroid therapy was gradually discontinued over the course of one month. A repeat colonoscopy to the level of the caecum was performed two weeks later, which showed a completely normal appearing colonic mucosa. The patient was followed for one year, and a colonoscopy was performed to the level of the terminal ileum. The colon was normal, both visually and histologically. He continued to be asymptomatic for one additional year. His weight and height were at the 25th percentile at this time. He was subsequently lost to follow up.

DISCUSSION

The patient presented with a classic history associated with C difficile infection, specifically, a regimen of antibiotic therapy shortly before the development of profuse diarrhoea. The diagnosis of C difficile infection was supported by the detection of C difficile toxin in the patient’s stool as well as by visualising pseudomembrane structures during endoscopy. The patient’s diarrhoea and abdominal discomfort continued for two weeks despite aggressive treatment for C difficile colitis with metronidazole and vancomycin. Although refractory to these first treatments, this patient’s infection did appear to have a favourable response to methylprednisolone.

While metronidazole and vancomycin are successful in rapidly treating C difficile induced diarrhoea and colitis in a majority of patients, a small percentage will have a delayed or incomplete response. The reason for this difference in responses has not been explained, but it has been shown that a low serum albumin and prolonged duration of antibiotic therapy are both strong predictors of a prolonged course of C difficile colitis despite treatment.13 The hypoalbuminaemia seen in these patients is likely the result of protein loss through the stool from inflammatory exudates.14

In patients with C difficile colitis, a serum albumin of less than 25 g/l and a fall of serum albumin of more than 11 g/l have been associated with increased mortality.15 According to a prospective study by Nair et al, the mean serum albumin in patients who responded promptly (≤14 days) was 26.7 g/l versus 20.7 g/l in those who failed to respond promptly (>14 days, if at all).16 The more severe hypoalbuminaemia, rather than being a cause of the poor prognosis, may simply be an indicator of a more severe colitis with an accompanying higher protein loss.17 In our patient a serum albumin of 21 g/l on admission was likely anti-inflammatory, as the clinical response has not been explained, but it has been shown that corticosteroids may also have a therapeutic effect on C difficile colitis. The reduction of inflammation within the colon by steroids may facilitate clearance of the C difficile toxins and recovery from the disease. In our patient, the initial effect of the steroids was likely anti-inflammatory, as the clinical symptoms improved while the stools remained positive for the C difficile toxin.

It is also possible that corticosteroids may have a direct inhibitory effect on the C difficile toxins. In a study by Chang et al, inhibition of binding of the C difficile toxin to human erythrocyte lysate was found with a number of steroids.18 Further studies are necessary to see whether this inhibition of C difficile binding also occurs with human colonic epithelial cells.

Although corticosteroids are generally not utilised as therapy for C difficile colitis, a one month course of therapy is unlikely to result in significant side effects. The most common steroid induced side effects are acne, moon facies, hirsutism, and cutaneous striae, which are reversible following discontinuation of therapy. More serious side effects such as muscle weakness, osteoporosis, aseptic necrosis, diabetes mellitus, glaucoma, and psychosis would rarely occur as a result of one month steroid administration. High doses of corticosteroids can cause immunosuppression and compromise the ability to resist infections; however, this was not an issue for this patient. Careful monitoring of this potential problem is strongly recommended.19,20

It is possible that our patient’s symptoms may have resolved despite corticosteroid treatment. However, he had failed to show improvement after 14 days of antibiotic therapy, while most patients usually exhibit some resolution of symptoms within 2–3 days.5 While we cannot be certain that corticosteroids were a direct cause of our patient’s improvement, he did appear to have a dramatic response once methylprednisolone was started. The only steroid induced side effect exhibited by our patient was weight gain, which resolved rapidly following discontinuation of steroids. Our observations suggest that corticosteroids may be an effective therapy for cases of severe, non-responsive C difficile induced colitis. As this is a preliminary report, further controlled studies are necessary to confirm this observation.

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Accepted 20 August 2002

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*Arch Dis Child* 2003 88: 342-344
doi: 10.1136/adc.88.4.342