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Case report

Clostridium difficile induced colitis occurring during cefotaxime therapy

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INTRODUCTION

While not unique to anti-microbial therapy, *Clostridium difficile* induced colitis is most frequently encountered as a complication of treatment with one or more of several antibiotics.[1-4] The condition has been described in association with some members of the cephalosporin group of drugs.[5] Only on a few occasions has cefotaxime been implicated in the past[6-11] and, to date, no cases have been reported in the United Kingdom. We describe a case in which a patient receiving intramuscular cefotaxime developed a severe persistent diarrhoea which proved to be the result of a *C. difficile* infection.

CASE REPORT

A 75-year-old man was admitted in March 1984 (day 1) with urinary retention and increasing immobility. Four years previously he had been diagnosed as having Parkinson's disease and there was a long history of prostatism complicated by recurrent bladder outlet obstruction and urinary tract infections. Apart from a degree of constipation during the months preceding admission, he had had no other symptoms referrable to the gastrointestinal tract. He had no known allergies and he had received amoxycillin and co-trimoxazole 6 months earlier without ill effect. His medication consisted of bromocriptine 2.5mg bd, levodopa 200mg tid and carbidopa 50mg tid. Examination revealed a frail man with signs of Parkinsonism and an abdomen unremarkable except for a tender distended bladder. The rectum was empty and the urine, obtained by catheterisation, was cloudy. Culture of the urine yielded *Proteus mirabilis* and *Pseudomonas aeruginosa,* both sensitive to cefotaxime. This antibiotic was commenced at a dose of 1g bd, given intramuscularly, and no other antibiotics were administered (day 6). On day 11, some faecal staining was noted on the patient's clothing. The patient's urine became sterile and cefotaxime was discontinued on day 14. In the following days the patient developed worsening faecal incontinence and the stools became foul-smelling. Faecal cultures were

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negative for shigella, salmonella and camphylobacter species while no pathogens were seen on microscopy. Codeine phosphate was commenced. On day 22, *Ps. aeruginosa,* sensitive to cefotaxime, was again cultured from the patient's urine so cefotaxime was recommenced using the same dose and route as previously. By day 29 the urinary problems had cleared and the drug was again withdrawn. The patient's diarrhoea continued to worsen, and microbiological stool analysis still yielded no definite pathogens. On day 33, the patient became toxic with a temperature of 39.2°C and he sustained several rigors. Intramuscular cefotaxime was again started after blood had been drawn for culture. These cultures grew *Ps. aeruginosa* sensitive to cefotaxime. The patient responded well to therapy, and cefotaxime was discontinued on day 46. The problem with diarrhoea had worsened but, by day 46, results obtained by applying gas-liquid chromatography to enrichment cultures of the patient's faeces suggested that the infecting agent was *C. difficile.* Oral vancomycin was commenced at a dose of 500mg tid and, after initial improvement, the dose was reduced to 125mg qid, finally being discontinued on day 57. By this time, the presence of *C. difficile* had been confirmed and *C. difficile* toxin had been detected in the stool at a titre of more than 1/800. The diarrhoea again worsened and by day 75 it became necessary to re-start oral vancomycin 500mg tid for 5 days. By day 102, the diarrhoea had recurred and was once again a serious problem. On this occasion oral metronidazole was prescribed at a dose of 200mg qid. Following this, the problem settled and by day 108 no toxin was detectable in faecal samples. On day 114, metronidazole was discontinued and the patient has since remained free from diarrhoea. Owing to the patient's physical frailty, sigmoidoscopy was not performed during his illness. He was discharged on day 121, his urinary problems having also settled.

DISCUSSION

C. difficile is an anaerobic spore-forming gram-positive organism with the ability to manufacture a potent exotoxin.[1-4] This bacterium is responsible for an acute purulent infection of the colon, and the condition can manifest itself as a pseudomembranous colitis or as diarrhoea and colitis without pseudomembrane formation.[3,4] The resulting clinical picture can be mild and self-limiting or severely debilitating and prolonged, and on occasions the condition can present as a life-threatening toxic megacolon, necessitating emergency colectomy.[3] Both organisms and free toxin are encountered in the stools of affected patients but not in the faeces of patients with other established causes for diarrhoea and, in addition, *C. difficile* is rarely carried by healthy adults.[3] Consequently, if the toxin is demonstrated in the stool, the diagnosis is considered established,[3] and it has been shown that clinical improvement is associated with the disappearance of the toxin from faecal samples.[4] Vancomycin is the established therapy of choice, and metronidazole and bacitracin are also recognised as effective drugs in this clinical setting.[3,4]

Cases of colitis (and, rarely, of pseudomembranous colitis) have been encountered in patients receiving certain cephalosporin antibiotics.[5] Cefotaxime, a third generation cephalosporin, was first isolated in 1978.[12] There have been few reports of *C. difficile* induced colitis occurring with this drug, and these cases have been encountered in West Germany,[6] France[7] and the U.S.A.[8-11] This is the first instance of the complication occurring with cefotaxime in the United Kingdom.

This case emphasises and reinforces the importance of maintaining a high index of clinical suspicion during and following cefotaxime therapy in order to avoid the patient reaching the fulminating stages of a potentially lethal but nevertheless treatable complication.

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REFERENCES

1. Larson HE, Parry JV, Price AB, Davies DR, Dolby J, Tyrrell DAJ. Undescribed toxin in pseudomembranous colitis. *Br Med J* 1977; **1**: 1246-1248.
2. Larson HE, Price AB. Pseudomembranous colitis: presence of clostridial toxin. *Lancet* 1977; **2**: 1312-1314.
3. Larson HE. Botulism, gas gangrene and clostridial gastrointestinal infections. In: Weatherall DJ, Ledingham JGG, Warrell DA, eds. Oxford textbook of medicine. Oxford: Oxford University Press, 1983; **5**: 230-237.
4. Smith JWG, Smith G. Gas gangrene and other clostridial infections of man and animals. In: Wilson G, Miles A, Parker MT, Smith GR, eds. Topley and Wilson's Principles of bacteriology, virology and immunity, 7th ed, vol. 3. London: Arnold, 1984: 327-344.
5. ABPI data sheet compendium 1984-5. London: Datapharm Publications, 1984: 385-386, 393-394, 739-740, 743-745, 885-888, 1226-1227.
6. Freitag V, Friedrich O, Kopf P-O, Wittman DH. Bacteriological testing of cefotaxime, a new semi-synthetic cephalosporin. *Infection* 1980; **8** (suppl. 4): S397-S400.
7. Gineston J-L, Henry X. Recto-colite pseudomembraneuse après traitement par le céfotaxime. *Nouv Presse Med* 1982; **11**: 1951-1952.
8. Cone LA, Woodard D, Helm NA. Clinical experience in the diagnosis and treatment of infections in the compromised host. *Clin Ther* 1981; **4** (suppl. A): 45-84.
9. Yakabow AL, Wood PD. Clinical experience with cefotaxime: a review. In: Neu HC, ed. New beta-lactam antibiotics: a review from chemistry to clinical efficacy of the new cephalosporins. Philadelphia: College of Physicians of Philadelphia, 1982: 287-328.
10. Karakuis PH, Feczko JM, Goodman LJ, Hanlon DM, Harris AA, Levin S, Trenholme GM. Clinical efficacy of cefotaxime in serious infections. *Antimicrob Agents Chemother* 1982; **21**: 119-124.
11. Mader JT, LeFrock JL, Hyams KC, Molavi A, Reinherz JA. Cefotaxime therapy for patients with osteomyelitis and septic arthritis. *Rev Infect Dis* 1982; **4** (suppl. September): S472-S480.
12. Chabbert YA, Lutz AJ. HR 756, the syn-isomer of a new methoxyiminocephalosporin with unusual antibacterial activity. *Antimicrob Agents Chemother* 1978; **14**: 749-754.