Pseudomembranous colitis in four patients with cystic fibrosis following lung transplantation

B Yates, D M Murphy, A J Fisher, F K Gould, J L Lordan, J H Dark, P A Corris

Pseudomembranous colitis is an uncommon complication in patients with cystic fibrosis, despite the use of multiple high-dose antibiotic regimens and the frequency of hospital admissions. Four patients from a total of 137 patients with cystic fibrosis undergoing lung transplantation are described who developed fulminant pseudomembranous colitis. Initial presentation was variable and the mortality rate was 50% despite urgent colectomy. In one case the presenting abdominal distension was thought to be due to meconium ileus equivalent. It is concluded that *Clostridium difficile* colitis may be a difficult diagnosis in patients with cystic fibrosis and follows a fulminant course after lung transplantation.

*Clostridium difficile* colitis is rare in patients with cystic fibrosis (CF), although asymptomatic carriage has been reported to occur in up to 50%. We describe four patients who developed severe pseudomembranous colitis with variable presentation following lung transplantation with significant morbidity and mortality. The role of CT scanning in diagnosis is discussed.

CASE REPORTS

Case 1

Two months after lung transplantation, a 22-year-old man with CF was treated for acute allograft rejection and pulmonary infection with steroids and antibiotics. He initially received piperacillin-tazobactam which was subsequently changed to flucloxacillin after 48 hours following culture of *Staphylococcus aureus* from bronchoalveolar lavage fluid. His respiratory status improved over the following days but he developed abdominal pain, constipation and a palpable mass in the right iliac fossa. A clinical diagnosis of meconium ileus equivalent was made, a condition he had experienced previously. He was treated with gastrografin and had a good bowel movement later that day. Although his symptoms initially settled, he developed further pain 3 days later with associated diarrhoea and a neutrophil leukocytosis. An abdominal radiograph showed thickened large bowel with very little luminal gas. A CT scan of the abdomen showed thickening of the colon. Flexible sigmoidoscopy with biopsies failed to show any evidence of infection or colitis. She improved over the next 3 days but then developed profuse diarrhoea and a neutrophil leukocytosis. A presumptive diagnosis of pseudomembranous colitis was made and metronidazole commenced. Stool analysis subsequently confirmed *C difficile* and she gradually improved.

Case 3

A 28-year-old man with CF underwent lung transplantation and received aztreonam and clindamycin. His initial post-operative course was complicated by reperfusion injury requiring reintubation and renal failure. He developed abdominal distension and initially a clinical diagnosis of meconium ileus equivalent was made. Abdominal radiography showed a grossly dilated large bowel and a manual evacuation was performed. The following day he became septic and hypotensive and antimicrobial treatment was changed to piperacillin-tazobactam and fluconazole in the light of bronchoalveolar lavage culture. A laparotomy was performed on the suspicion of perforation. No perforation was found but a caecostomy was fashioned to decompress his bowel. At 37 days after transplantation he remained dependent on a ventilator and dialysis but without further bowel problems and off antibiotics. He developed right upper abdominal pain; ultrasonography revealed gallbladder sludge but also a thickened colon suggestive of colitis. A CT scan confirmed a grossly thickened large bowel at risk of perforation despite minimal diarrhoea rectally and only soft stool from his stoma. Piperacillin-tazobactam, metronidazole and caspofungin were commenced. Colectomy was delayed as he initially refused consent but by this time he was deteriorating rapidly with sepsis. He died 1 week following colectomy from multiple organ failure. Histological examination of the resected colon showed severe pseudomembranous colitis.

Case 4

A 38-year-old woman with CF underwent lung transplantation, complicated by early haemodynamic instability followed by renal failure and failed extubation. She then developed abdominal distension and diarrhoea, negative for *C difficile* toxin. Despite continuing episodes of diarrhoea and distension, stool toxin remained persistently negative. Bronchoalveolar lavage isolated *Pseudomonas* spp and she was commenced on ciprofloxacin and aztreonam. Diarrhoea, abdominal pain and distension remained problematic, and a CT scan showed thickened large bowel consistent with pseudomembranous colitis. A further stool specimen tested positive for *C difficile*. Metronidazole was commenced with resolution of diarrhoea and negative stool toxin after 5 days. However, her clinical condition remained critical and she died 42 days after transplantation from multiorgan failure.
DISCUSSION

Clostridium difficile is a spore-forming Gram positive bacillus. It is a well recognised cause of antibiotic-associated diarrhoea. Asymptomatic carriage is rare in healthy adults but it is more frequent during hospitalisation, occurring in up to 25% of inpatients. A genotype link (N1303K mutation) has been described between CF and C difficile carriage of C difficile in patients with CF following lung transplantation. The persistent carriage of C difficile in the bowel of prospective transplant recipients with CF may represent a relative contraindication, and we recommend all lung transplant centres to be vigilant for this problem.

In conclusion, we present a series of four patients with CF who developed severe C difficile colitis following lung transplantation. Two patients died, two required a colectomy, and the disease was certainly a significant event in the decline of a further patient. In one case the presentation of the disease was mistaken for meconium ileus equivalent and in a further case a diagnosis took several days to secure, highlighting the need for a high level of clinical suspicion. CT scanning revealed colitis in all patients; it not only suggested the diagnosis but gave an important indicator to the severity of the disease. Clostridium difficile colitis is an uncommon but important diagnosis in patients with CF following lung transplantation. The persistent carriage of C difficile in the bowel of prospective transplant recipients with CF may represent a relative contraindication, particularly patients with a prior history of pseudomembranous colitis, and we recommend all lung transplant centres to be vigilant for this problem.

Authors’ affiliations

B Yates, D M Murphy, A J Fisher, F K Gould, J L Lordan, J H Dark, P A Corris, Institute of Cellular Medicine, University of Newcastle and The Freeman Hospital, High Heaton, Newcastle upon Tyne, NE7 7DN, UK

Conflicts of interest: None.

Correspondence to: Professor Paul A Corris, The William Leech Centre for Lung Research, The Freeman Hospital, High Heaton, Newcastle upon Tyne, NE7 7DN, UK; paul.corris@ncl.ac.uk

Received 15 September 2005
Accepted 11 February 2006
Published Online First 6 April 2006

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LUNG ALERT

Bronchial thermoplasty may improve asthma control up to 12 months after treatment

This randomised controlled study was designed to assess the efficacy of bronchial thermoplasty up to 12 months after treatment. Participants had moderate to severe persistent asthma and were receiving treatment with inhaled corticosteroid and long acting β agonist (LABA) inhalers. Only patients with worsening asthma control after temporary withdrawal of the LABA inhaler were eligible for entry. One hundred and twelve subjects were enrolled; 56 subjects received three treatments of bronchoscopic thermoplasty over 6 weeks in addition to their usual treatment. No sham bronchoscopies were administered to the control group. All subjects were assessed at 3, 6 and 12 months. Assessments at 6 and 12 months were performed after the withdrawal of LABA inhaler treatment. The primary outcome measure was the frequency of mild exacerbations.

At 12 months, only the bronchial thermoplasty group showed a significant reduction in mild exacerbations (0.18 (SD 0.31) per patient per week compared with 0.35 (0.32) at baseline). Compared with the control group, secondary endpoints including morning peak expiratory flow rate, asthma quality of life questionnaire score, symptom free days and symptom scores showed significantly greater improvements. Adverse events were significantly higher in the thermoplasty group during their 6 weeks of treatment.

The authors conclude bronchial thermoplasty in patients with moderate to severe persistent asthma results in an improvement in asthma control with benefits persisting at 1 year. This result was observed after a reduction in asthma maintenance treatment. However, the benefit of any reduction in the number of mild exacerbations seemed to be outweighed by the side effects of treatment and duration of hospital stay required for the procedures. It would be interesting to study the efficacy of bronchial thermoplasty in comparison with stable treatment with inhaled corticosteroid and LABA inhalers, which may be associated with fewer adverse effects.

Neil Ward
Specialist Registrar, Royal Devon and Exeter Hospital, Exeter; neil.ward@nhs.net