CLOSTRIDIUM SEPTICUM SEPTICAEMIA IN A PATIENT WITH LEUKAEMIA

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ABSTRACT

Clostridium septicum infection has been shown to have a strikingly high association with either bowel or blood malignancies. The infection may be fatal if unrecognised. We report a case of C. septicum bacteremia in a man diagnosed with acute myeloid leukaemia.

Keywords: Clostridium septicum, leukaemia, septicaemia

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INTRODUCTION

Invasion of the blood stream by clostridia may occur late in anaerobic myonecrosis. Bacteremia of this nature is largely due to *Clostridium perfringens* which is usually associated with postabortal or puerpural infection of the uterus. *C. septicum* however is increasingly being recognised as a cause of bacteremia in patients with malignancies of the blood or the bowel. Alpern and Dowell in their review of 27 *C. septicum* infected patients showed that 23 of them had some form of malignancy and *C. septicum* was isolated from the blood of 18 of these patients[1]. The present report describes a bacteremia caused by *C. septicum* in a patient with acute myeloid leukaemia presenting with abdominal symptoms and fever.

CASE REPORT

The patient is a 39-year-old lorry driver who presented with gum bleeding and easy bruising of 4 weeks duration. There was no history of fever or diarrhoea prior to admission. On examination he was found to have hepatosplenomegaly, bruises on all 4 limbs and also fundal haemorrhages.

Laboratory investigations revealed Hb level of 86 gm/l, platelet counts of $43x10^9$/l and total white cell count of $41.8x10^9$/l of which 80% were blast forms. A bone marrow examination confirmed the diagnosis of acute myeloid leukaemia (FAB classification M2). He was treated with I/V Daunorubicin 50 mg/m^2 for 3 days and I/V cytosinearabinoside 100 mg/m^2 for 7 days. He subsequently developed fever and in view of his neutropenic state, I/V ceftazidime and gentamicin were commenced. Blood cultures were all negative for pathogens and fever settled after several days. The antibiotic treatment was discontinued after 7 days. On the 21st day of chemotherapy, he again developed fever, pain in the right iliac fossa associated with several bouts of diarrhoea. The stools were watery yellow but did not contain mucus or blood. He was still neutropenic at that time with a total white cell count of only $0.8x10^9$/l. The abdomen was tender in the right iliac fossa and there was rebound tenderness. A provisional diagnosis of acute appendicitis was made and he underwent surgery. At the time of operation, about half a litre of straw coloured peritoneal fluids was noted. The caecum showed a yellowish discolouration and was hard in consistency. The appendix was normal. A right hemicolectomy was performed. Histopathological examination of the caecum showed a transmural necrosis and features consistent with a severe enterocolitis. Blood cultures and stool culture subsequently grew *C. septicum*. The post-operative course was stormy but eventually the fever and diarrhoea subsided after about 2 weeks of I/V ceftazidime and metronidazole. The patient went on to achieve remission and is currently well and receiving consolidation chemotherapy. There were no further episodes of Clostridia enterocolitis or septicaemia.

Bacteriolgy studies

The organism *C. septicum* was isolated from the blood and stool cultures. On anaerobic blood agar, the colonies spread, producing a fine lawn on the agar surface with filamentous edges. The isolate was identified by fermentation of various carbohydrates using the criteria of Holderman by the method of Phillips[2,3]. The gas liquid chromatography study of the volatile fatty acids further confirmed the identity of the organism. Final confirmation was made by the Anaerobic Reference Laboratory, Luton, England.

DISCUSSION

The organism *Clostridium septicum* is a Gram positive, motile, sporing anaerobic bacillus. *C. septicum* besides producing a lethal alpha toxin also produces two haemolysins, a deoxyribonuclease, a hyaluronidase and a fibrinolysin enzyme which aids its invasiveness. It has been isolated from soil, clothing and animal faeces. The presence of this organism as part of the normal flora of the human gut has been refuted by several authors who had shown in their studies that among the many organisms isolated from a normal stool, *C. septicum* is not one of them[4,5]. Thus its infection appears to be exogenous in nature.

Infections by *C. septicum* are not commonly diagnosed. The organism is infrequently isolated, occurring in only 1-2% of all clostridial infection[6,7]. This maybe due to the difficulty in its identification and the fact that some laboratories may find it unnecessary to speciate clostridium beyond that of *C. perfringes*. *C. septicum* shares many similar cultural and biochemical characteristics with *C. chauveoi*. Therefore, suspected isolates of *C. septicum* must be differentiated by animal toxin neutralisation test.

Many authors, besides Alpern and Dowell, have shown the association between *C. septicum* infections and malignancies[1,6,8]. These studies showed that almost half of the patients had haematological malignancies while the other half had solid tumours of which bowel malignancy is the main carcinoma found. Kornbluth et al in their review found that almost 30% of these cases had occult malignancies, mainly carcinoma of the colon, at the time of presentation with the infection. Patients with occult malignancies are mainly in the older age group associated with diabetes mellitus[6]. It appears that infection by this pathogen is extremely rare in healthy individuals but occurs usually in those with underlying debilitating illness which predispose them

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to some form of injury which then allows the pathogen to invade and multiply.

The most common portal of entry of *C. septicum* is the gastrointestinal tract. Enterocolitis seems to play a major part in the pathogenesis of the infection. *C. septicum* infection has not been reported in those having single defects of the humoural or cell mediated immune system or in patients with iatrogenic immunosuppression following steroid therapy. The infection has not been reported in patients with AIDS, renal transplant or collagen vascular disease.

Leukaemic patients may become susceptible to the invasion of this organism in the presence of enterocolitis which developed following treatment with particularly cytosine arabinoside which had been reported to cause gastrointestinal necrosis[9]. Most of the leukaemic patients with *C. septicum* infections were under chemotherapy at the time of presentation of the infection. Leukaemic filtrate may also damage the gastrointestinal mucosa providing a portal of entry for *C. septicum*. The neutropenic state also allows the organism to grow unchecked. The necrotic tissues in neutropenic enterocolitis or colonic cancer provides a conducive environment for the spores of *C. septicum* to germinate. However, the question here is why a rare pathogen like *C. septicum* is more commonly isolated in these patients than the other common Clostridia species which are normally found in the gut? One possible explanation is that *C. septicum* is relatively aerotolerant and therefore, is more capable of initiating infection in tissues which are not obviously damaged.

It is important to emphasise that the mortality of this infection in unrecognised and therefore untreated cases is virtually 100%. It is imperative therefore, to diagnose this condition early and that aggressive treatment should be initiated immediately after blood and other appropriate specimens are taken for culture, both aerobically and anaerobically. It has been suggested that neutropenic patients presenting with fever, acute abdominal symptoms mimicking those of acute appendicitis while under chemotherapy should be suspected of Clostridium septicaemia[6,10] and thus should be treated accordingly. Most patients with *C. septicum* septicaemia who died were either undiagnosed, thus untreated, or if treated promptly and correctly, died before an adequate blood level of the antibiotics could be achieved[8]. The treatment of choice is intravenous penicillin and in those patients who cannot tolerate penicillin, alternative antibiotics include cephalothin, metronidazole and clindamycin[8]. Surgical treatment of the necrotic site is necessary to eradicate the infection. Our patient had the incriminating site of infection removed and then treated early with I/V ceftazidime and metronidazole.

Clinicians and microbiologists alike must therefore be aware that clostridal septicaemia, especially that of *C. septicum* may complicate conditions like leukaemia and colonic cancers and that mortality of such condition, if unrecognised, is very high.

Abdominal symptoms along with fever in these patients should be treated for possible clostridia infection. Treatment with both antibiotics and surgery when necessary must be instituted early to ensure survival.

As has been shown in several studies[6,8] occult malignancy should also be suspected in those presenting only with *C. septicum* septicaemia and efforts must be made to exclude the presence of malignancy, especially that of the colon.

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