Letters to the Editor

Role of clostridial organisms in neutropenic enterocolitis

Neutropenic enterocolitis affects the ileocecal region of the bowel and is characterised by intense thickening and oedema with mucosal necrosis. It is associated with agranulocytosis, often with Clostridium septicum infection, and commonly occurs in patients with acute leukaemia, many of whom have been treated with cytosine arabinoside. The strong association with C septicum has led to reports that this organism may have a primary causative role in the condition. We report two cases with other clostridial organisms which, we propose, may act as opportunistic invaders.

Case reports

CASE 1
A 57 year old woman presented with acute myeloid leukaemia. Remission was achieved, followed by relapse and a second remission 10 months later. She again relapsed and received chemotherapy comprising rubidomycin, cytosine arabinoside, and 6-thioguanine. After this she developed intestinal obstruction, with a temperature of 37.5°C and a white cell count of 10.4 × 10⁹/L, comprising 98% blasts and 2% lymphocytes, with complete agranulocytosis. She died shortly afterwards.

Postmortem examination, performed four hours after death, showed multiple gaseous spaces within the liver and spleen, with haemolytic staining of the inferior vena cava. There was obstructive thickening of the ileum 50 cm proximal to the ileocecal valve, occupying a 20 cm segment of bowel. Blood cultures before and after death produced pure growths of C welchii, as did swabs from the affected area. Histologically there was intense transmural oedema and congestion, with patchy mucosal necrosis, but no evidence of leukaemic infiltration. Gram positive bacilli were numerous and immunofluorescence staining was negative for C septicum but positive for C welchii.

Postmortem examination showed evidence of clostridial infection, together with pronounced thickening along a 10 cm segment of ascending colon, which was adherent to the inferior surface of the liver. Multiple mucosal ulcers were noted. Culture of swabs from colon, liver, and spleen produced a heavy growth of C sordellii. Histological examination showed mucosal ulceration with gross transmural oedema and congestion of the affected colon. Gram positive bacilli were clustered around the ulcerated areas and on the serosal surface. There was no leukaemic infiltrate.

Clostridial septicaemia in patients with malignancy, particularly leukaemia, is well recognised. Wynne and Armstrong reported 15 episodes, 11 of which were due to C welchii. In all instances the portal of entry was the gastrointestinal tract, due to varying causes including recent anti-neoplastic chemotherapy or radiation, an invasive diagnostic procedure, or malignant disease of the bowel.

C sordellii is rarely regarded as a pathogen, and neither it or C welchii have been reported as the sole organism in association with neutropenic enterocolitis. We feel these cases strongly imply that this condition may be complicated by clostridial species other than C septicum and that they are behaving opportunistically in a patient with immune deficiency and a mucosal defect of the gastrointestinal tract, rather than that they have a primary causative role. The cause of the initial insult remains unclear, although neutropenic ulceration and damage by cytosine arabinoside are contenders, there is no malignant infiltration of the bowel. Other possibilities are intramural haemorrhage due to thrombocytopenia and localised ischaemic damage.

Clinically, it is important to consider neutropenic enterocolitis in the appropriate clinical setting, and if suspected, antibiotic treatment to cover clostridial sepsis would seem advisable in view of the poor prognosis associated with the condition.

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References

Serum alkaline phosphatase isoenzymes

The novel technique for quantitation of serum alkaline phosphatase (ALP) isoenzymes is interesting and clearly permits identification of the source of the serum enzyme. Although we agree that knowledge of the alkaline phosphatase isoenzyme type provides clinically useful information, the clinical evaluation does not really provide sufficient evidence to justify this claim. It is likely that several other tests would be performed prior to the request for quantitative ALP isoenzyme determination; therefore it is essential to evaluate the additional contribution that this test would make to diagnosis, not its contribution in isolation. The authors state that several other biochemical variables were available for each patient but apparently fail to take these into account in their analysis.

We examined serum total ALP activity prospectively in 2884 acute medical admissions and found it to be increased (>1.5 times upper reference limit) in 204 patients (7.1%). Diagnoses were established by means of predetermined clinical, radiological, and histopathological criteria and patients were allocated to one of six diagnostic categories (table 1). Qualitative assessment of ALP isoenzyme type by polyacrylamide gel electrophoresis (PAGE) was available for 178 patients and was consistent with the clinical diagnosis in 70% (80% of those for whom the diagnosis was definitely established).

One hundred and fifty seven had a definite diagnosis and a PAGE result, and of these, 140 had a full complement of the following tests: haemoglobin, white cell count, bilirubin, total protein, albumin, globulin, aspartate transaminase (AST), alanine transaminase (ALT), gamma glutamyl transferase (GGT), as well as the initial ALP.

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