CASE REPORTS

Protracted enteric cryptosporidial infection in selective immunoglobulin A and saccharomyces opsonin deficiencies

M R Jacyna, J Parkin, R Goldin, J H Baron

Abstract

Chronic cryptosporidial infection in man usually occurs in those who are immunocompromised. We report a patient with a one year history of bowel symptoms resulting from persistent cryptosporidial infection of the colon. Investigations showed underlying selective IgA and saccharomyces opsonin deficiencies but no evidence of cell mediated immune dysfunction. Both selective immunoglobulin A and opsonin deficiencies are relatively common in the general population and may be a cause of susceptibility to persistent cryptosporidal infection.

Infection with cryptosporidium species is now recognised as a major cause of human diarrhoeal disease worldwide.1 In addition to diarrhoea, however, patients may have abdominal pain, cramps, anorexia, malaise, and weight loss.1 Most have a short, self-limiting illness that usually resolves spontaneously within one to two weeks.2,4 Rarely, symptoms may persist for more than one to two months,3 and this is more often the case if the person is immunocompromised.7,4 We report a case of chronic cryptosporidial infection of the colon that caused symptoms for more than 12 months in a patient with selective deficiency in both immunoglobulin A (IgA) and saccharomyces opsonins.

Case report

A 56 year old retired home help supervisor was referred with a 12 month history of intermittent colicky lower abdominal pain and diarrhoea which had begun suddenly while she was on holiday in Tunisia the previous year. Her husband and friends had developed similar symptoms while on holiday but in all cases the illness had resolved completely by two weeks. For the next year, however, the patient complained of recurring bouts of pain and diarrhoea lasting several days. These attacks occurred every one to two weeks and were characterised by watery inoffensive stools, without blood or mucus. Between attacks the patient was well and suffered no loss of appetite or weight and no rectal bleeding or pain when opening the bowels. Her only past illnesses had been recurrent sinusitis since childhood, and there was no previous gastrointestinal disease. The patient was married with three children, denied intravenous drug abuse, and had never had a blood transfusion.

She looked well and there were no abnormal signs. Sigmoidoscopy and double contrast barium enema x-ray findings were normal. Stool cultures were negative for ova, cysts, and parasites, and grew no shigellae, salmonella, or campylobacter species. Her haemoglobin concentration was 13·7 g/dl, her white blood cell count was 7·3×10^9/l with a normal differential count, the erythrocyte sedimentation rate was 6 mm/h, and the serum urea, creatinine, and hepatic biochemistry were all normal. A rectal biopsy specimen showed a mild mononuclear cell infiltrate in the lamina propria and there were numerous cysts typical of cryptosporidia in the crypts (Fig 1). Electron microscopic examination of the rectal mucosa confirmed numerous cryptosporidia in trophozoite and macrogamete forms (Figs 2 and 3).

Because of the unusual length of her symptoms (12 months) and the rarity of protracted cryptosporidial infection in immunocompetent people, we looked for immunological abnormalities. Peripheral blood lymphocyte subsets were estimated by indirect immunofluorescence analysed by a flow cytometer (EPICS V,
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Coulter). Total T lymphocyte numbers (CD3) were normal at 1·50×106/l, as were the CD4 (helper/inducer) count at 0·97×106/l, the CD8 (suppressor/cytotoxic) count at 0·44×106/l, and the CD4:CD8 ratio at 2·2. The B lymphocyte count was also normal at 0·25×106/l. Antibodies to the HIV-1 virus were not detected. Serum IgG was 12·1 g/l (normal 6·0–17·0 g/l), IgM was 0·9 g/l (normal 0·7–3·5 g/l), but the IgA value was abnormal at 0·1 g/l (normal 0·7–3·5 g/l).

Immunoperoxidase staining of the rectal biopsy specimen showed numerous IgG and especially IgM containing cells but no IgA containing cells (Figs 4 and 5). A complement profile showed normal C3, C4, and total haemolytic complement values but the complement-dependent saccharomyces opsonins were reduced at 1·7 (normally greater than 2·8), while the IgG antibody dependent opsonins were normal.

The patient’s symptoms persisted for a further four months and then resolved spontaneously. A repeat rectal biopsy specimen showed clearance of the previous chronic inflammatory infiltrate and disappearance of the cryptosporidia.

Discussion
Cryptosporidia, enteric protozoal parasites that are pathogenic in man, are now commonly identified in cases of acute self-limiting diarrhoeal illness in immunocompetent hosts.

In immunocompromised people (usually patients infected with the human immunodeficiency virus), the illness may last longer, however, and be far more severe, with profuse watery diarrhoea, abdominal pain, and cryptosporidia persisting for many months.

Although cell mediated immunity is the primary mechanism of host defense, humoral immunity is also required to eliminate the infection successfully and severe and protracted cryptosporidial infections have been described in some patients with hypogammaglobulinaemia.

To our knowledge there have been very few case reports of chronic cryptosporidial infection in patients with selective IgA deficiency. Protracted enteric cryptosporidiosis, however, has been described in a renal transplant recipient who was selectively deficient in IgA and was also receiving large doses of immunosuppressive drugs.

Infection with *Giardia lamblia* has also been reported to be more common and protracted in people who are selectively deficient in IgA. Selective IgA deficiency is one of the most common immunodeficiency disorders and it has been estimated that the incidence in the population varies between 1:800 and 1:600.

There is an increased association with allergies, recurrent sinopulmonary and gastrointestinal infections, and autoimmune disease (including coeliac disease and ulcerative colitis).

Cell mediated immunity is normal and the prognosis is excellent, although recurrent pulmonary infections may cause respiratory problems.

A further finding in this patient was of reduced...
Jazyna, Parkin, Goldin, Baron

Saccharomyces opsonin values. This is a common finding (occurring in 5–10% of the general population) and is caused by deficiency of a protein that regulates the rate of deposition of C3b/C3bi on particulate activators of the complement pathway. In infants absolute opsonin deficiency may be associated with failure to thrive and diarrhea, and in adults deficiency has been associated with chronic viral infection and disseminated gonococcal disease. Most people with selective IgA deficiency are asymptomatic and infections occur predominantly in those who also have an associated IgG2 subclass deficiency. This suggests that a combination of biological defects may be necessary for clinical expression of an immune defect. Although the patient described had normal IgG2 values, the additional deficiency in saccharomyces opsonins, leading to a functional complement defect, is likely to have increased the effect of the IgA deficiency.

Apart from recurrent sinusitis, the patient was well and had no previous history of gastrointestinal disease. The bowel symptoms were intermittent and not severe and they resolved spontaneously after more than 16 months. No specific treatment was required, which is usual in immunocompetent persons. Treatment of persistent cryptosporidiosis is, in any case, unsatisfactory and various antibiotics have been tried with only limited success. In patients with prolonged diarrhoea after visits abroad, stool microscopy and culture and examination of jejunal aspirate and biopsy specimens are the most useful tests. But this patient also emphasises the importance of taking a routine rectal biopsy specimen in cases of chronic diarrhoea, and also of immunological investigation of patients with unusually protracted gastrointestinal infections. Cryptosporidium species are now commonly identified in outbreaks of diarrhoeal disease, and protracted infections in otherwise immunocompetent people may indicate underlying defects in IgA and complement function.

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