Case report

Pseudotumoral enterocolitis and massive eosinophilia

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SUMMARY We report a seven year history of a 23 year old woman born in the Antilles, with pseudotumoral enterocolitis and massive eosinophilia. In 1973 she developed a haemorrhagic colitis with massive peripheral eosinophilia of up to 60 000/mm³. Medical treatment, mainly corticosteroids, failed to control the disease. The patient temporarily improved after colectomy and remained in remission for two years. In 1978 the disease recurred in the rectum and small intestine with formation of tumour-like granulomata and massive infiltration by eosinophils, unresponsive to corticosteroids. Intestinal blood and protein loss continued until death seven years after onset. In spite of exhaustive investigation, no parasites, allergens, or other aetiological agents could be found. As only the gut was infiltrated, the hypereosinophilic syndrome could be excluded. The enterocolitis here described does not correspond to an eosinophilic gastroenteritis, nor to other known inflammatory bowel diseases and to our knowledge has not been reported previously.

We wish to report an unusual case presenting with bloody diarrhoea and massive eosinophilia. Schistosomiasis diagnosed at the start of the illness was cured, however, intestinal symptoms and peripheral eosinophilia were to continue and no aetiological agent could be found. The disease was unlike ulcerative colitis and Crohn's disease¹⁻³ and did not correspond to eosinophilic gastroenteritis⁴ nor the hypereosinophilic syndrome.^{5,6} It therefore seemed of interest to report the case.

Case report

In March 1973, a 23 year old woman, born in Guadeloupe (the Antilles), in Europe for one year, developed abdominal pain and bloody diarrhoea. The leucocyte count was 76 000/mm³, with 87% eosinophils. *Schistosomiasis mansoni*, discovered in rectal and liver biopsies, was treated repeatedly with niridazole and hycanthone. Immunofluorescence serology, initially positive at a serum dilution of 1/320, became negative. Search for parasites in the stools and in repeated hepatic and colonic biopsies remained negative. Serology for filariasis, strongy-

loidiasis, distomatosis and amoebiasis were negative, in spite of persistence of the abdominal symptoms and eosinophilia of 40 to 50 000/mm³ (Fig. 1). Bone marrow aspiration showed myeloid hyperplasia, mainly of the eosinophil stem; all the maturation stages were represented, and no atypical cells were seen. A barium enema showed loss of haustrations in the left colon. Radiology of the stomach and small bowel was normal, as were gastric and jejunal biopsies. Sigmoidoscopy revealed a mucosa coated with a muco-purulent membrane; histology showed acute proctitis with eosinophilic infiltration. By April 1974, she had 15 to 20 bowel movements per day and had a weight loss of 6 kg. Repeated colonoscopies showed a congested mucosa, and ulcerations more compatible with Crohn's disease than with ulcerative colitis. Histology revealed chronic inflammatory changes, erosions and massive eosinophilic infiltration, but no granulomata or parasites. A barium enema showed mucosal ulceration and shortening of the colon; the rectum and ileocaecal region were spared. Eosinophilia was still present at 40 000/mm³; IgE values were normal. Bone marrow aspiration, chromosomal study, parasitological and immunological investigations were negative. Antibodies to milk, egg, and cereal proteins prompted us, despite

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Fig. 1 Course of white cell and eosinophil counts in relation to medical and surgical treatment. $\circ$ represent white cells count, $\bullet$ eosinophils count, $\blacktriangle$ IgE values.

normal histologic examination of the stomach and small bowel, to try an elimination diet and treatment with sodium cromoglycate. These measures, however, did not result in any improvement. Prednisone 30 mg daily relieved the symptoms temporarily, then alone or in combination with azathioprine, prednisone failed to control the disease and a sub-total colectomy was done in January 1976. The colectomy specimen showed chronic and acute severe colitis, unclassified, with heavy eosinophilic infiltration. The postoperative course was stormy, with peritoneal abscesses, multiple fistulae, septic shock with metabolic acidosis and acute renal failure requiring four months of intensive care. The patient eventually recovered and was almost symptom free. The eosinophilia disappeared and the white cell count returned to normal. In October 1977, sigmoidoscopy appeared normal but histology showed chronic proctitis. An ileorectal anastomosis was performed and she was free of symptoms for one year.

In the autumn of 1978, after a holiday in the French Antilles, diarrhoea and eosinophilia ($20\text{--}40\,000$ eosinophils/ mm^3) recurred. At rectoscopy, there was striking proctitis with loss of mucosa and inflammatory pseudopolyps. Steroids failed to control the disease and the rectum was resected at the end of July 1979. The specimen contained an ulcerated submucosal tumour and many mucosal ulcers (Fig. 2). The ileum was infiltrated with eosinophils and macrophages with

Sternberg-like nuclei (Figs. 3, 4). After discharge, weight loss and abdominal pain persisted and ulcerated tumours measuring 2×1.5 cm (Fig. 5) appeared on the ileostomy, which later ulcerated and necrosed. Leucocyte count was 70 to $100\,000/\text{mm}^3$ with 70% of normal looking eosinophils, unaffected by adrenaline or large doses of corticosteroids. Bone marrow aspiration displayed reactive hyperplasia only. Electrolytes were within normal limits; proteins were decreased at 57 g/l (albumin: 25 g/l, γ -globulins: 10 g/l). Radiographic examination of the small bowel showed ulcerations and nodules involving the distal 30 cm of the ileum (Fig. 6). Pyrexia and pain localised to the right iliac fossa and the ischio-rectal region appeared, with purulent discharge from the anus: an abdominal abscess was confirmed by CT-scan. Despite total parenteral nutrition (4000 Kcal/day), antibiotic therapy (chloramphenicol, oxacillin, gentamicin, and metronidazole) and corticosteroids, ileal inflammation worsened, the number and the size of the tumours increased and weight loss, anaemia and hypoproteinaemia occurred. Mebendazole therapy was also tried without any effect and the patient died from septic shock with metabolic acidosis and electrolytic disorders. At necropsy, the small bowel contained intramural polypoid tumours, one of them having intussuscepted (Fig. 7). Pseudotumours were present on the mesentery. All the tumours were heavily infiltrated by mature eosinophils; no abnormal macrophages were seen. Bone marrow was characterised by eosinophilic hyperplasia,

Fig. 2 Proctectomy specimen: mucosa is infiltrated by large tumour-like masses, some of which are confluent and ulcerated. Rectal orifice is shown at bottom.

without evidence of leukaemia. The other organs, particularly the heart and lungs, were not infiltrated by eosinophils; the right kidney showed acute pyelonephritis with infiltration by neutrophils.

Discussion

The history of this case falls into two periods, divided by the colectomy and the two-year remission, and by two characteristics: the eosinophilia and the intestinal disorder. During the first three-year period, the inflammatory colonic disease temporarily responded to corticosteroids, but remission was only achieved by colectomy.⁷ The presumed diagnosis was atypical ulcerative colitis, which could account for the clinical manifestations, evolution and topography of the lesions, but did not explain the eosinophilia. An eosinophilic gastroenteritis without any infiltration of the stomach and small bowel unresponsive to corticosteroids was excluded. After a peak of 60 000/mm³, at the time of the postoperative complications, eosinophilia disappeared. The second period started early after returning from the Antilles, when mild peripheral eosinophilia, and then digestive symptoms reappeared. The inflammatory lesions and the infiltration by eosinophils affected not only the rectum, leading to proctectomy, but also the small bowel. The inflammation became transmural and polypoid tumours consisting mainly of eosinophils occurred.

The association of a bowel disease and eosinophilia in a patient from the Antilles suggested a parasitic aetiology, especially as schistosomiasis had been diagnosed at the start of the illness. After several courses of therapy, the serology for schistosomiasis became negative and all the histological examinations (colectomy specimen, autopsy)

Fig. 3 Ileoproctectomy specimen showing marked infiltration by granulation tissue and disappearance of mucosal pattern. Mucosal surface on top of figure. m = Muscularis propria. * Detail shown in Fig. 4 (haematoxylin-eosin, $\times 3.5$ original magnification.)

Fig. 4. Detail of Fig. 3 showing marked eosinophilic infiltration; in centre note a Sternberg-like macrophage (arrow) (haematoxylin-eosin, $\times 480$ original magnification).

Fig. 5 Ulcerated tumours on ileostomy.

Fig. 6 Small bowel radiographic examination showing ulcerations and nodules on last 30 cm of ileum.

Fig. 7 Small intestine at necropsy: groups of tumour-like masses are apparent.

failed to show any parasites. Other possible parasitic diseases, such as angiostrongyloidiasis⁸ or anisakiasis⁹ were also ruled out by negative serology. The recurrence of disease immediately after a stay in the Antilles, however, may have been because of repeated exposure of a previously sensitised organism to the causal agent. Some nematodes occur as tumour-like granuloma formations, but the size of the tumour is parallel to the size of the larvae, and usually the diagnosis is made by surgical resection of the granuloma in which the worm is found. Moreover, the IgE levels, raised in parasitic eosinophilia, were persistently normal.

Eosinophilic bowel disease because of a non-parasitic allergen has been considered. Idiopathic eosinophilic infiltration of the gut¹⁰ may be circumscribed, often a single lesion corresponding to the inflammatory fibroid polyp¹¹ or diffuse as in eosinophilic gastroenteritis.¹² The assumed allergen of this disorder leads to an inflammatory reaction of the stomach and small bowel and to a malabsorption syndrome. Systemic allergy is often associated.^{4, 13} Unusual cases of eosinophilic gastroenteritis have been reported: one started in the colon and the ileum and secondarily spread to the stomach;¹⁴ another involved the jejunum only and was unresponsive to corticosteroids.¹⁵ An eosinophil count more than 1500/mm³ for longer than six months without evidence of parasitic, allergic or other known causes of eosinophilia and organ

involvement could suggest the hypereosinophilic syndrome.⁵ A case has been reported where a large mass (8 cm) attached the distal jejunum to the sigmoid colon. In addition there were several enlarged lymph nodes at the root of the jejunal mesentery. Histologically, there was an extensive infiltration of the widened submucosa with mature eosinophils, which eroded the overlying mucosa producing acute superficial ulcerations; some scattered histiocytes had large atypical hyperchromatic nuclei.¹⁶ The histology bears some resemblance with our case, necropsy examination, however, revealed myocardial involvement consisting of granulomatous lesions and dense infiltration by mature eosinophils. The only infiltrated organs in our case were the gut and some draining lymph nodes; heart and lungs were not involved and the kidney showed infiltration by neutrophils. A syndrome of generalised vasculitis with eosinophilia would have been found at necropsy.¹⁷ Multifocal eosinophilic granulomata (histiocytosis X) have been described in the liver and the biliary tree.¹⁸ In such cases there is also involvement of the CNS and skin. Histopathology showed lymphohistiocytic tumours. Hodgkin's disease of the gut is very rare and recent series do not report isolated gut involvement.^{19, 20} Primary intestinal lymphoma can be polypoid and sometimes heavily infiltrated by eosinophils.^{21, 22} Some cells with Sternberg-like nuclei had been seen in our case on biopsy material;

these were not found at autopsy and a careful search failed to show any blastic cells. Thus a lymphoma seems to be unlikely. The clinical manifestations and the evolution of our case do not correspond to those of the known inflammatory bowel diseases even if the diagnosis during the first phase was ulcerative colitis. The histopathologic examination showed a pseudotumoral enterocolitis accompanied by a massive infiltration by eosinophils. Clinical manifestations are those of severe enterocolitis, with loss of blood and protein, infectious complications and eventually intussusception on a polypoid tumour and death. This case does not correspond to anything reported in the past and gives rise to several problems and unanswered questions. What is the allergen? Is the massive eosinophilia responsible for the inflammatory damage? If it is, why was the gut the only organ involved?

The only person concerned to whom it was all perfectly clear was the patient herself: a Voodoo sorcerer had quite obviously cast a spell on her.

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