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CASE REPORTS

Leukaemoid reactions associated with fulminating ulcerative colitis

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Summary

The association between fulminating ulcerative colitis and the presence of primitive white cells in the peripheral blood is reported in three patients. Some of the diagnostic problems encountered are discussed.

Introduction

Changes in the peripheral blood picture, including toxic granulation and a shift to the left in the white cell series, is frequently observed in patients with fulminating ulcerative colitis (Marshak *et al.*, 1960; Neschis, Siegelman and Parker, 1968). However, the presence of blast cells in the peripheral blood appears to be extremely uncommon. No mention of this phenomenon is made in two recent comprehensive texts and a search of the literature did not reveal any previous accounts (Avery-Jones, Gummer and Lennard-Jones, 1968; Goligher *et al.*, 1968). In reporting three cases in which these changes were observed we wish to emphasize some of the diagnostic problems encountered.

This association may be more common than is generally recognized as all three cases were observed in the same hospital over a period of 18 months.

Case 1

A 48-year-old housewife was admitted to hospital following the onset of severe watery diarrhoea, mouth ulceration and a pyrexia of 103°F. She had recently received a course of ampicillin for a sore throat. On admission, investigations showed a haemoglobin of 4·7 g%, an haematocrit of 15% and a mean corpuscular haemoglobin concentration of 31%. The white cells count was 15,600 per mm^3 with a differential of 32% neutrophils, 36% lymphocytes, 8% metamyelocytes, 12% myelocytes, 4% promyelocytes and 3% blasts. There were 4 nucleated red cells/100 white cells. The bone marrow showed increased granulopoiesis, much of the proliferation being in the myelocyte stage. A differential count of the white cell series showed 15% of the cells were neutrophils and metamyelocytes, 50% were myelocytes, 12% were promyelocytes and 7% were blasts. No Auer rods were seen but the granulocyte series showed marked toxic granulation and cytoplasmic vacuolation. Erythropoiesis was moderately megaloblastic and the megakaryocyte series was normal. No pathogens were isolated from the stools. A diagnosis of chronic myeloid leukaemia was made and she was treated with busulphan 2 mg daily to a total dosage of 14 mg. She was also given a blood transfusion but failed to improve and was transferred to the London Hospital.

On admission she was severely dehydrated and pyrexial. There was no lymphadenopathy and the spleen was not palpable. The abdomen was tender and distended and sigmoidoscopy showed a granular haemorrhagic mucosa with ulceration. The haemoglobin at this time was 11 g% and the white blood cell count was 4900/mm^3 with a differential of 20% neutrophils, 68% lymphocytes, 2% myelocytes and 10% blasts. The platelet count was 30,000/mm^3 and the neutrophil alkaline phosphatase score 120. A prothrombin ratio was 1·4, the calcium thrombin time was normal and the plasma fibrinogen was 130 mg/100 ml. Abdominal radiology demonstrated distended loops of bowel and dilatation and ulceration of the colon.

A diagnosis was made of ulcerative colitis with toxic dilatation accompanied by a leukaemoid reaction and she was treated vigorously with fluid replacement, antibiotics, hydrocortisone and finally with intermittent positive pressure ventilation. At no time was she fit enough for surgery, and she died 48 hr after admission. At post mortem the colon was found to be grossly dilated and studded with ulcers. The liver weighed 2 kg and the spleen, which was firm

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and congested, weighed 325 g. Histology showed typical changes of ulcerative colitis and there was no evidence of leukaemia on full histological examination. No evidence of any other type of marrow infiltration was demonstrated and in particular there were no granulomata or micro-abscesses.

Case 2

A 21-year-old woman with previous good health and without any history of gastro-intestinal symptoms, developed a pyrexial illness during delivery of her first child. *Escherichia coli* were grown from throat and vaginal swabs and ampicillin was prescribed. The following day an erythematous, macular rash appeared and this was attributed to penicillin hypersensitivity, as on further enquiry a past history of allergy to this drug was established. The pyrexia and rash were controlled by oxytetracycline and chlorpheniramine but 10 days after stopping therapy a relapse occurred. Over this period the haemoglobin had fallen from 12 g% to 9·2 g% and the white counts ranged from 3900 to 13,000. The neutrophil series showed many immature forms including numerous myelocytes, occasional promyelocytes and blast cells in the peripheral blood film. It was felt at this stage that the clinical and haematological picture was most likely to be due to a combination of drug hypersensitivity and continuing infection, although blood, stool and urine cultures and repeated throat and vaginal swabs failed to confirm this.

In view of these negative findings and the continuing abnormality of the peripheral white cells, the diagnosis of a primary blood disorder was considered. A bone marrow examination showed increased cellularity with mildly megaloblastic erythropoiesis; granulopoiesis showed marked toxic granulation and 21% of the cells were neutrophils and metamyelocytes, 52% myelocytes, 8% promyelocytes and 5% blasts. No Auer rods were seen. The neutrophil alkaline phosphatase score was 294.

At this point, 15 days after the start of her illness, she passed a loose stool for the first time. The diarrhoea increased in severity during the following 24 hr and sigmoidoscopy demonstrated ulceration of the rectal mucosa. A diagnosis of ulcerative colitis was made, and steroid therapy was commenced. She failed to respond to this treatment and over the next 36 hr a toxic dilatation of the colon developed. Total colectomy was performed but the patient died in septicaemic shock 24 hr later. Examination of the colectomy specimen confirmed extensive and severe ulcerative colitis.

Case 3

A 28-year-old woman was admitted with a 3-year history of intermittent diarrhoea and lower abdominal pains. For 6 weeks before admission the diarrhoea had been continuous and accompanied by mucus and blood. On examination she was dehydrated with a pyrexia of 101°F. She had an enlarged lymph node in the left axilla. The liver was enlarged 3 cm below the costal margin and peristalsis of the small bowel was observed. Radiology of the abdomen demonstrated fluid levels in both the small and large intestine and there was marked dilatation of the transverse colon. Sigmoidoscopy revealed ulceration of the rectal mucosa with copious mucus and pus. A diagnosis of fulminant ulcerative colitis was made and parenteral steroid therapy was given. At this stage her haemoglobin was 11·9 g% and the white cell count was 19,000/mm^3 with numerous large lymphocytes, myelocytes and occasional promyelocytes and blast cells. Although there seemed little doubt that ulcerative colitis was the underlying pathology, the abnormality in the peripheral blood and the presence of lymphadenopathy raised the possibility of an additional primary haematological or lymphoreticular disorder. Further investigations showed marked proliferation of the bone marrow but in this case there was little toxic granulation, and 37% of the granulocyte series were neutrophils and metamyelocytes, 13% were myelocytes, 4% promyelocytes and only 2% blasts. Again, there were no Auer rods demonstrated. The neutrophil alkaline phosphatase score was 99.

The colitis by now, however, was responding to treatment and her general improvement was paralleled by a return of the blood picture to normal over the following 3 weeks. The colitis has subsequently remained under control with intermittent courses of Salazopyrin.

Discussion

The stimuli governing the normal maturation and release of cells from the bone marrow are unknown. Animal experiments have demonstrated humoral factors following bacterial infection which affect granulocyte release (Marsh *et al.*, 1967) and human neutropenic plasma has been shown to induce a leucocyte response (Marsh and Levitt, 1971). The importance of these observations in the leukaemoid reaction accompanying fulminant ulcerative colitis is not clear, but it is likely that bacteria and bacterial toxins crossing the severely diseased colonic mucosa are involved.

It was the failure to realize that blast forms may be present in fulminating ulcerative colitis which led to diagnostic difficulty in all three of the above patients. In the first case, treatment for leukaemia had been started and in the second the possibility of a primary haematological condition was receiving serious consideration until the advent of diarrhoea made the diagnosis clear. In the third patient the diagnosis of ulcerative colitis was never in doubt but the markedly

abnormal blood picture and lymphadenopathy raised the possibility of additional pathology.

The presence of marked toxic granulation in two cases and cytoplasmic vacuolation in the first case pointed to an inflammatory process and the absence of Auer rods made a diagnosis of acute myeloblastic leukaemia less likely in the first two cases. Although the bone marrow blast count in these patients was above the accepted normal range (Dacie and Lewis, 1968) this in itself does not necessarily indicate a diagnosis of leukaemia at this level and in these circumstances. The third case was altogether milder and the patient survived. Here, there was little toxic granulation, the blast count in the marrow was normal and the neutrophil alkaline phosphatase score was only just above the normal range.

It is important to bear in mind the possibility of such pronounced haematological changes in association with ulcerative colitis. Apart from the clinical picture which would usually establish the correct diagnosis, the neutrophil alkaline phosphatase score, which was elevated in all three of these patients, should be helpful where doubt exists. In addition, the experience of the second patient would suggest that fulminating ulcerative colitis should be considered in the differential diagnosis of pyrexia associated with this type of peripheral blood picture in the rare instance when these features precede gastroenterological symptoms or signs.

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Hodgkin's disease of the duodenum presenting with haemorrhage and perforation

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Summary

A case of Hodgkin's lymphoma confined to the duodenum, draining lymph nodes and spleen, presenting with haematemesis and perforation, thus mimicking a peptic ulcer, is recorded. Such a case is not known to have been previously reported.

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Case report

A 61-year-old man was admitted to hospital after suddenly developing epigastric pain followed by haematemesis and melaena. For some weeks previously he had upper abdominal discomfort and night pain, and in the week before admission had taken phenylbutazone regularly for osteoarthritis of the knees. He was obese, pale, hypotensive (blood