Case Report

FOLATE DEFICIENCY IN A SURGICAL PATIENT

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Abstract

Acute folate deficiency with Pancytopenia and megaloblastic haemopoiesis developed in a patient after abdominal operations. The patient had been given intravenous nutrition with Aminoacid ; the blood count returned to normal over 4-6 days after starting folic acid.

Introduction

The requirements of folic acid are increased by inflation or malignant diseases. The supply of folic acid can be reduced by diseases which cause poor intake or increased losses of folate ; absorption can be impaired by infection and bacterial overgrowth. This report describes a patient whose general nutritional status was impaired by chronic

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ill health and repeated abdominal operations. A negative folate balance developed rapidly after he was given nutrition with intravenous fluid containing Aminoacid.

Case Report

Mr. N.C. 30 years old, Shipping manager was first seen in the hospital in February, 1973. He complained of recurrent abdominal pain, diarrhoea and weightloss. After investigation and laprotomy a diagnosis of Crohn's disease was established and treatment with low dose steroid was started.

However the disease progressed and resection of 9" ileum, and right half of colon was done 3 months later. He had a stormy post-operative course but recovered subsequently. The next three years were relatively symptom free but in January 1979 he was re-admitted because of exacerbation of disease. Laprotomy was done and a further 5" of ileum and 2" of colon were resected. Post operative wound infection was controlled with exhaustive antibiotic regime. Intravenous nutrition was commenced on 6th February, 1979 with Synthamin 17 (Aminoacid 100g). Next day another laprotomy had to be done due to intestinal perforation; another few inches of terminal ileum and 2" colon were resected. One week later he developed haematuria and generalised bleeding tendency. Blood count done showed pancytopenia; bone marrow was aspirated for examination.

Results

The results are summarized in table I. The blood count done before commencing Synthamin 17 showed: haemoglobin 8.7g/dl, total white cell count 5.7 × 10^9/1 and a normal number of platelets (assessed on examining the peripheral blood smear).

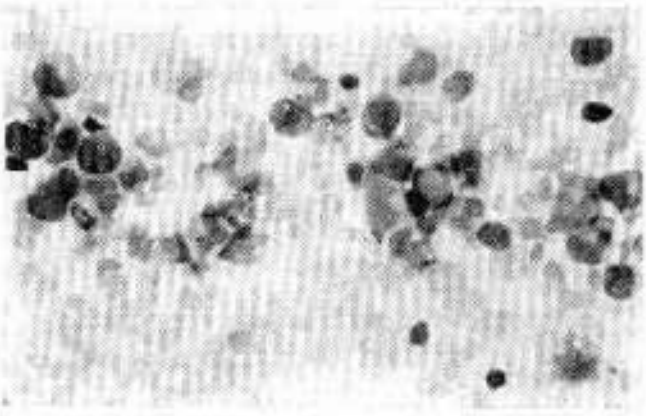

Fig. 1a. Bone Marrow × 54 showing giant metamyelocytes megaleblasts and one miteotic.

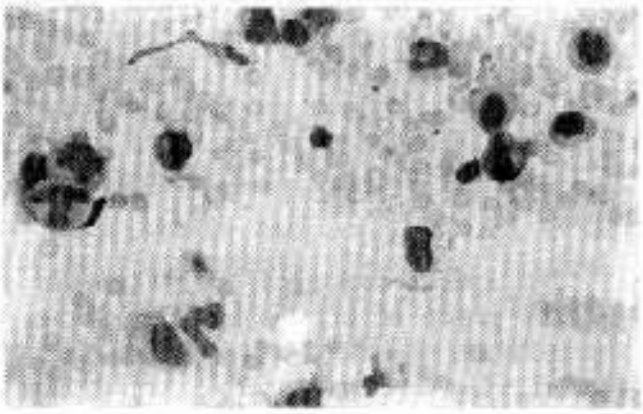

Fig. 1b. Bone Marrow × 54 showing Intermediate megaloblasts and Giant metamyelocytes.

Eight days later the total white cell count had dropped to 1.2 × 10^9/1 and the platelet count was less than 10 × 10^9/1. Changes in the blood film were modest, and only few hypersegmented neutrophils were seen. Coagulation screening was normal. Bone marrow showed frank megaloblastic haemopoiesis (Fig. 1a1b). Folate therapy was commenced on 14th February, 1979: four days later the white cell count had risen to 6.8 × 10^9/1 and the platelets to 70 × 10^9/1 (Fig. 2).

Table 1: Blood Count at the Time of Taking Bone Marrow

		(Normal values)
Haemoglobin	9.9 g/dl	(15.5 ± 2.5 g/dl)
W.B.C.	1.2 × 10^9/1	(7.5 ± 3.5 × 10^9/1)
Platelets less than	10 × 10^9/1	(150-400 × 10^9/1)
Prothrombin time	14 seconds	(10-14 seconds)
Partial thromboplastin time	39 seconds	(36-40 seconds)
Serum folate	0.2 ug/l	(3-20 ug/l)
Red cell folate	145 ug/l	(160-640 ug/l)
Serum B12	136 ug/l	(160-925 ug/l)

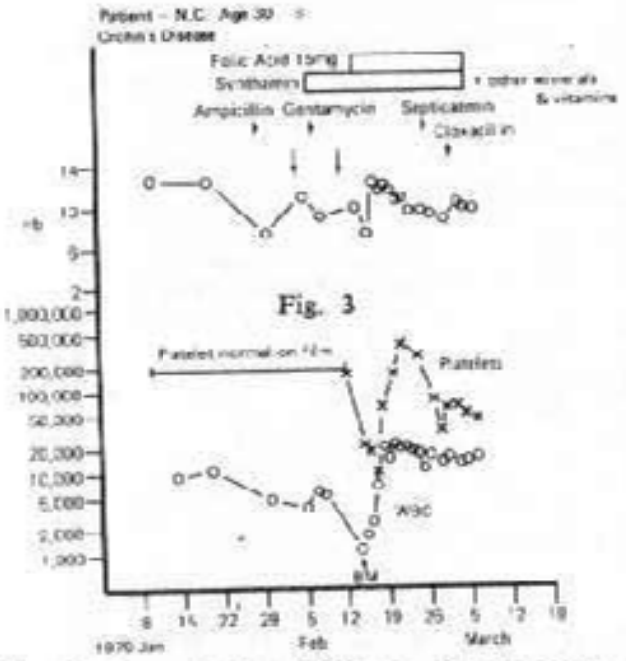

Fig. 2. Haemoglobin, WBC and Platelet count on log scale. Note the drop in WBC and Platelet count after starting synthamin infusion and the rapid recovery after folate therapy.

Discussion

Folic acid is required in the synthesis of deoxyribonuclei acid (DNA) (Fig. 3). It also serves as a coenzymes in other reactions requiring transfer of I-C units. A negative folate balance can develop when demands for folate exceed its supply, as in Crohn's disease of the intestines or gastric carcinoma. Acute post-operative pancytopenia is an example of a syndrome of rapidly developing folate deficiency associated with leucopenia and thrombocytopenia. The disorder could be fatal because of the risks of infection associated with leucopenia and of haemorrhage from thrombocytopenia.

The syndrome was first highlighted by a report from Wardrop et al. (1975); they described four patients who underwent abdominal operations and later developed megaloblastic haemopoiesis associated with panycytopenia. These authors subsequently carried out a controlled trial on 30 patients (Wardrop et al., 1977). The pre-operative folate level were normal in all patients, but fell within 48 hours by 60-95% in 20 patients who received intravenous nutrition with Aminoacid — Sorbitol — Ethanol (ASE). Folate levels in 10 normal patients not given ASE showed only minimal decline. Haematological changes were reduced to a minimum in 10 patients given 0.5 mg IV Folic Acid daily, while eight unsupplemented patients showed evidence of megaloblastic haemopoiesis. Ethanol may be the major factor in causing the precipitous fall in serum folate concentration but other regimes for parenteral nutrition may be contributed to a similar

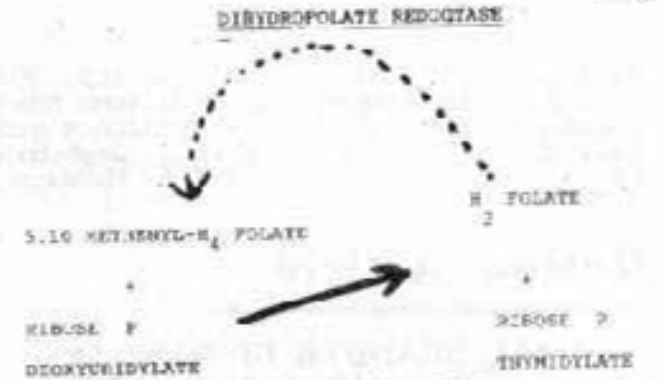

Fig. 3

syndrome (Ibbotson et al., 1975; Parry & Hoffbrand, 1976). Surgical trauma itself can cause a fall of serum folate and this can be exaggerated by Aminoacid infusion (Smith et al., 1978). Another theory has been put forward by Connor et al. (1978). They gave oral methionine supplements to normal volunteers on usual diet. This treatment resulted in significant fall in serum folate levels. They have suggested that by giving methionine which is a one carbon unit donor, the normal relationship between methionine and folate is disturbed. Methionine loading will probably increase the proportion of methyl tetra hydrofolic acid and other reduced folates in the serum. This could result in a redistribution of folate from serum to cells, because reduced folates are weakly bound to serum folate binding protein and are therefore more available for cellular uptake.

This causes a relative lack of folate in certain tissues. Methionine is one of several substrates used in parenteral nutrition which can serve as a source of one carbon unit, other Aminoacids which might contribute to folate depletion by this mean include histidine and serine. The significant benefits of parenteral feeding in anorexic malnourished patients will far outweigh the haematological complications which can be prevented by folate supplements. These patients, like the ante-natal cases would appear to be candidates for prophylactic vitamin therapy.

References

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