inhibitors in the collecting tubes, minor aggregation of platelets and consequent release of TxB_2 during sampling is largely unavoidable. The raised plasma TxB_2 concentrations might therefore in part reflect the increased capacity of the platelets to produce TxB_2 during aggregation. That there is an increased generation of TxB_2 in response to thrombin-induced platelet aggregation during pregnancy and puerperium is, however, indisputable. What causes this stimulation remains to be investigated.

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Acute folate deficiency during peritoneal dialysis

Acute megaloblastic arrest of haemopoiesis in patients receiving parenteral nutrition after extensive surgery or trauma is well recognised.¹ Rapidly developing life-threatening pancytopenia in pregnancy complicated by severe bacterial infection has also been described.² Both have been attributed to acute folate deficiency. Less well recognised is the occurrence of acute folate deficiency in other conditions needing critical care.³ We report a case of severe rapid-onset pancytopenia resulting from acute folate depletion during the course of peritoneal dialysis.

Case report

A 64-year-old man was referred with acute tubular necrosis that developed after intravenous antihypertensive treatment. The results of initial haematological investigations (figure) were: haemoglobin concentration 13.7 g/dl, mean corpuscular volume 84 fl, white cell count $10.2 \times 10^9/\text{l}$ ($10\,200/\text{mm}^3$) with a normal differential count. The reticulocyte count was <1%. His platelet count was $280 \times 10^9/\text{l}$ ($280\,000/\text{mm}^3$), prothrombin time 12 s (control 12 s), partial thromboplastin time 40 s, (control 38 s), fibrin degradation products, <10 mg/l. His urine to serum osmolality ratio was <1.0, and urinary sodium concentration was 40 mmol (mEq)/l. Sediment microscopy showed red and white cells but no casts. Blood and urine cultures were sterile. Renal tomography showed large swollen kidneys.

He required three courses of peritoneal dialysis, each consisting of 40 exchanges, during the oliguric phase of 16 days. During peritoneal dialysis he suddenly had generalised bleeding and blood staining of the dialysate. Repeat investigations showed that his white cell count had fallen to $1.2 \times 10^9/\text{l}$ ($1200/\text{mm}^3$) and the platelets to $12 \times 10^9/\text{l}$ ($12\,000/\text{mm}^3$). The haemoglobin was 8.4 g/dl, mean corpuscular volume 87 fl, mean corpuscular haemoglobin concentration 32.4 g/dl, and mean corpuscular haemoglobin 28.0 pg. The reticulocyte count was <1%. Occasional macrocytes and hypersegmentation of polymorphs were noted on the peripheral blood film. Bone marrow aspirate showed severe megaloblastic change particularly affecting the white cell series. Megakaryocytes were present and the myeloid-erythroid ratio was 11:1. Folate concentrations measured at the time of the pancytopenia later showed a much diminished serum folate concentration of 0.5 $\mu\text{g}/\text{l}$ (normal 2.7-20 $\mu\text{g}/\text{l}$) and a normal red cell folate concentration of 224 $\mu\text{g}/\text{l}$ (normal 150-1000 $\mu\text{g}/\text{l}$). His vitamin B_{12} concentration was 230 ng/l (normal 150-1000 ng/l).

Intravenous folate 10 mg/day was given and his platelet and white cell counts returned to normal levels within four to five days. Associated with this was a mild reticulocyte response of 3%. He was given a further two-week

course of folate 5 mg/day by mouth. He made a satisfactory recovery and when discharged his full blood count and peripheral film were normal and his renal function mildly impaired. His renal function has since improved further and there has been no recurrence of any haematological abnormalities.

Comment

Apart from ethanol, which may interfere with the intermediary metabolism of folate, other factors may contribute to the development of acute folate deficiency in severely ill patients.¹ In normal subjects taking a diet deficient in folate it may be 18 to 20 weeks before megaloblastic changes appear within the bone marrow although serum folate concentrations may become subnormal within two to three weeks. Therefore anorexia probably had only a minor role in our patient. Systemic infection appreciably interferes with jejunal absorption of folate and may also adversely affect folate metabolism.⁴ Our patient showed no evidence of local or systemic infection at any time. Folate is loosely bound to protein in serum and is thus lost from the body during haemodialysis⁵—about 50 μg in each exchange. Similarly, serum folate is lost during peritoneal dialysis, although how much is lost is uncertain. In the absence of any of the recognised precipitating factors we are tempted to speculate that the recurrent peritoneal dialysis, by rapidly removing folate, played a predominant part in causing our patient's pancytopenia.

The diagnosis depends on being aware of the condition and of the implication of a rapidly developing pancytopenia in a severely ill patient. It is confirmed by examination of a bone marrow aspirate. Because of the delay in recovery of white cell and platelet counts, even after early diagnosis and treatment, we suggest that prophylactic folic acid supplements should be given to patients having repeated peritoneal dialysis. At a minimum white cell and platelet counts should be closely monitored.

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