Findings in Six Patients with Amenorrhoea and Hirsutism

Case No.	Galactorrhoea	Serum Prolactin ($\mu\text{g/l}$)	Urinary 17-Ketosteroid ($\mu\text{mol/24 h}$)*	Urinary 17-Hydroxycorticoid ($\mu\text{mol/24 h}$)*	Urinary Pregnanetriol ($\mu\text{mol/24 h}$)*	Plasma Testosterone (nmol/l)*
1	—	20	20–45	26–60	0.6	2.57
2	—	35	50	40	N.D.	N.D.
3	—	45	35–48	19–30	0.45	1.98
4	—	210	15–37	25–35	1.2	4.58
5	+	55	23–30	23–32	1.5	1.49
6	+	240	42	55	1.6	2.22

*Normal ranges for healthy women under 40 years: 17-KS 15–58 $\mu\text{mol/24 h}$; 17-OHCS 21–63 $\mu\text{mol/24 h}$; pregnanetriol 0.3–5.4 $\mu\text{mol/24 h}$; plasma testosterone 0.85–2.85 nmol/l. N.D. = Not done.

Conversion: SI to Traditional Units—17-KS, 17-OHCS, and testosterone: 1 $\mu\text{mol/l} \approx 0.35 \text{ mg}$. Pregnanetriol: 1 $\mu\text{mol/24 h} \approx 0.3 \text{ mg}$.

We thank the National Pituitary Agency, NIAMDD, Bethesda, Md., for the human prolactin standard and the antiserum; Dr. V. Sternthal, Sandoz, Basle, for bromocriptine; and Miss Sirkka Soikkeli and Mrs. Virpi Tiilikainen for technical assistance. Our study was supported by grants from the Association of the Finnish Life Insurance Companies and the Sigrid Jusélius Foundation.

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Folic acid deficiency during intensive therapy

Folic acid is essential for normal haemopoiesis and in its absence megaloblastic maturation occurs. During intensive therapy, red cell changes are often obscured by transfusion and neutrophil hypersegmentation may be attributed to renal failure.¹ Severe thrombocytopenia may develop because of "megaloblastic" megakaryocyte maturation and this should respond to folic acid treatment. We report two cases which illustrate these points and draw attention to the rapidity of onset of the megaloblastic change.

Case reports

Case 1.—A fit 28-year-old man sustained an extensive crush injury to the lower limbs and developed acute renal failure requiring peritoneal dialysis. Haematology on admission was haemoglobin 14.6 g/dl, mean cell volume (M.C.V.) 86 fl, and platelet count $175 \times 10^9/\text{l}$. After 17 days the haemoglobin was 7.4 g/dl, M.C.V. 90 fl, and platelet count $60 \times 10^9/\text{l}$. The bone marrow was markedly megaloblastic. Microbiological estimation of serum vitamin B₁₂ and folic acid was attempted but was inhibited by antibiotics. Folic acid 15 mg intravenously daily was begun. Haematological follow-up showed no change in M.C.V. and no reticulocytosis. The response of the platelet count is shown in the figure. A repeat bone marrow at nine days was normoblastic.

Case 2.—A well-nourished 62-year-old man had an aortic aneurysm repaired with a Dacron prosthesis. Preoperatively his haemoglobin was 13.5 g/dl, M.C.V. 82 fl, platelet count $240 \times 10^9/\text{l}$ and postoperatively, respectively, 10.5 g/dl, 86 fl, $67 \times 10^9/\text{l}$ after an 18 pint (10.22 l) blood transfusion. The patient developed acute renal failure requiring haemodialysis. Seven days later the haemoglobin was 11.9 g/dl, M.C.V. 86 fl, platelet count $30 \times 10^9/\text{l}$, and the peripheral film showed hypersegmented neutrophils. The bone marrow was megaloblastic. Estimation of serum folic acid was inhibited by antibiotics but the vitamin B₁₂ concentration was 500 ng/l. Folic acid 15 mg intravenously daily was started. Follow up haematological data showed no change in M.C.V., an increase in reticulocytes of 5% at 10 days, and a recovery of the platelet count at eight days to $170 \times 10^9/\text{l}$ and at ten days to $300 \times 10^9/\text{l}$. Bone marrow examination after eight days showed normoblastic erythropoiesis.

Platelet and white cell counts in case 1 showing response to folic acid.

Discussion

The two cases show the occurrence of rapidly developing megaloblastosis and thrombocytopenia which respond to folic acid treatment. Vitamin B₁₂ radioimmunoassay was not available at that time and the possibility of vitamin B₁₂ deficiency in case 1 was considered extremely remote. The interval from admission to diagnosis was 17 days in case 1 and eight days in case 2, but Herbert² estimated that folic acid stores in the body can sustain normal erythropoiesis for 19 weeks. These patients developed megaloblastosis in less than three weeks suggesting that in the severely traumatized patient folic acid stores are either rapidly depleted or their metabolism is inhibited.

Infection affects folate metabolism, possibly by increasing folate requirements,³ and it has also been claimed that a factor develops during infection which antagonizes normal folic acid utilization.⁴ Haemodialysis in the management of renal failure depresses folic acid levels and folic acid is dialysable whereas vitamin B₁₂ is not.¹ Both our patients had infections and were being dialysed. In each case severe tissue trauma had occurred. Folic acid requirements increase in myelofibrosis,⁵ in which increased turnover of the expanded myeloid pool increases folate utilization. Massive tissue trauma may increase tissue demand in a similar way.

Our experience suggests that it is unwise to rely on the folic acid store of severely traumatized patients even for short periods. Normal vitamin B₁₂ stores should last for three years but a subclinical vitamin B₁₂ deficiency should be excluded when folic acid supplements are used in view of the risk of precipitating a neuropathy.

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