Haematological Complications of Proguanil in a Patient with Chronic Renal Failure

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Dear Sir,

Proguanil hydrochloride, a dihydrofolate reductase inhibitor which is used as an anti-malarial agent, is generally regarded as a safe drug with few side effects. There has been a report of serious haematological complications arising from its antifolate activity in 2 patients with chronic renal failure [1].

While on a visit to India, a 38-year-old Dutch lady, known to have chronic renal failure, was taking a proguanil tablet (200 mg/day) for malaria prophylaxis. Fifteen days after commencing treatment with proguanil she developed generalized weakness, malaise, anorexia, nausea, dizziness and epistaxis. Five days later she noted ecchymotic and purpuric lesions all over the body. At that time her haemoglobin was 8 g/dl, total leucocyte count $6.7 \times 10^9/l$, platelet count $5 \times 10^9/l$, blood urea nitrogen 77 mg/dl and serum creatinine 7.3 mg/dl. Peripheral smear showed anisocytosis, macro-ovalocytes, elliptocytes, a few target cells, a few fragmented red blood cells and hyperseg-

mented neutrophils. Reticulocyte count was 0.5%, mean corpuscular volume 93.4 fl, mean corpuscular haemoglobin 29.9 pg, mean corpuscular haemoglobin concentration 32 g/dl.

Coagulation profile was normal. A bone marrow examination revealed megaloblastic erythropoiesis with dyserythropoietic changes and 'giant' metamyelocytes and myelocytes. Serum proguanil estimation was not possible. Proguanil was discontinued and the patient was treated with citrovorum factor and oral folic acid. Her general condition improved and by the 8th day her platelet count was $160 \times 10^9/l$. The haematological abnormalities mentioned above also reversed gradually.

Since 40-60% of a dose of proguanil is excreted by the kidney [2], in patients with impaired renal function there is an accumulation of the drug resulting in toxicity. It should therefore be avoided by patients with renal failure.

References

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