Pure red-cell aplasia associated with carbamazepine

A case report

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Summary

A 3-year-old girl developed pure red-cell aplasia while being treated with carbamazepine for a seizure disorder. Spontaneous recovery took place after discontinuation of the drug. The association between pure red-cell aplasia and carbamazepine intake is briefly discussed.

S Afr Med J 1990; **78**: 214-215.

Carbamazepine is a drug frequently prescribed for patients suffering from both partial and generalised seizure disorders.[1] It is an iminostilbene derivative, chemically related to the tricyclic antidepressants.[2] Undesired side-effects may occur and involve the haematopoietic, hepatic, genito-urinary, nervous, digestive, cardiovascular, ophthalmological, musculoskeletal and metabolic systems.[2]

Case report

A 3-year-old girl was admitted to H. F. Verwoerd Hospital on 1 August 1988 with anaemia. Her mother had noted that she had developed progressive pallor during the preceding 2 weeks and that she had a poor appetite.

The child had suffered from a seizure disorder from the age of 7 months and was initially treated with a combination of phenobarbitone and clonazepam without success. On 1 February 1988 medication was changed to carbamazepine (50 mg in the morning and 100 mg at night), which controlled the seizures satisfactorily. She received no other drugs. A full blood count done on 23 March 1988 was within normal limits with a haemoglobin value of 13 g/dl, a red cell count of $4{,}04 \times 10^{12}$/l and 0,7% reticulocytes.

On examination after admission to hospital the child appeared ill and very pale. No signs of jaundice, hepatosplenomegaly, lymphadenopathy, petechiae or any other abnormalities were apparent. The full blood count was as follows: haemoglobin value 3,3 g/dl; red cell count $1{,}18 \times 10^{12}$/l; haematocrit 0,097 l/l; mean cell volume 81,8 fl; mean cell haemoglobin 28,0 pg; mean cell haemoglobin concentration 34,2 g/dl; reticulocytes 0,0%; white cell count $5{,}3 \times 10^{9}$/l and platelets 201×10^{9}/l. The erythrocyte sedimentation rate (Winthrobe method) was 83 mm/1st h. A bone marrow aspirate revealed decreased bone marrow cellularity, very little erythropoietic activity with ± 1% pro-erythroblasts present, normal leucopoiesis, and megakaryocytes as well as free platelets visible. The myeloid:erythroid ratio was 45:1.

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Accepted 28 Feb 1990.

Other special investigations included: carbamazepine blood level — 3,7 mg/l (therapeutic range 4,3 - 12,0 mg/l); blood electron microscopy for parvovirus[3] — negative; skeletal radiography[4] — within normal limits; chromosomal analysis[3] — normal 46,XX female karyotype and no structural abnormalities. An electro-encephalogram was within normal limits. Computed tomography (CT) of the brain showed an enlarged cysterna magna and enlarged frontal horns of the lateral ventricles (similar to results of CT on 4 February 1986).

On 2 August 1988 the patient was given a blood transfusion of washed, packed red cells low in white cell and platelet antigens.[4] The haemoglobin level increased to 10,2 g/dl and the red cell count to $3{,}43 \times 10^{12}$/l. Carbamazepine therapy was discontinued on 3 August 1988. On 10 August, without any further blood transfusions having been administered, the haemoglobin level was 11,2 g/dl, the red cell count $3{,}7 \times 10^{12}$/l and there were 7,1% reticulocytes on the smear. During hospitalisation the patient did not suffer any further seizures and was discharged without any anticonvulsive therapy. The red cell count and haemoglobin value spontaneously became normal over the next few months (Fig. 1).

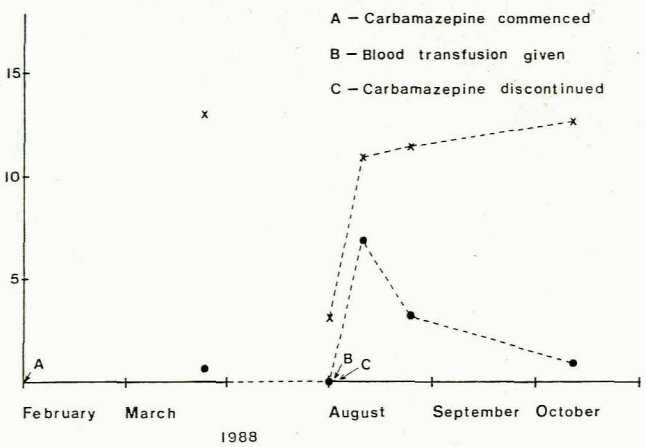

Fig. 1. Serial haemoglobin and reticulocyte determinations (● ---- ● = reticulocytes (%); x ---- x = haemoglobin (g/dl)).

Discussion

Acquired pure red-cell aplasia is usually transient in nature in contrast to the congenital variety (Blackfan-Diamond syndrome).[4] The former has been associated with malnutrition[4] and a variety of drugs,[4,5] toxins[4] and infectious agents[3,4] or it may result from unknown causes.[4]

Carbamazepine is one of the drugs known to cause pure red-cell aplasia.[5] The patient described developed isolated failure of red cell production. This most probably resulted from carbamazepine intake, since she improved rapidly after discontinuation of the drug, responding with an increase in the reticulocyte and erythrocyte counts. Isolated bone marrow fail-

ure of the red cell line after anticonvulsive therapy may be delayed.[6] This could have happened in this case, where clinical anaemia developed 6 months after initiation of carbamazepine therapy.

According to Pisciotta,[2] it is not morally or ethically justifiable to rechallenge a patient with the drug suspected of causing the haematological abnormality in order to confirm the diagnosis. For this reason, the patient was not re-exposed to carbamazepine after recovery.

In a study conducted in the USA it was reported that only 5,1/million patients taking carbamazepine developed aplastic anaemia.[1] This side-effect of carbamazepine, although not common, should nevertheless be borne in mind due to the serious, prolonged and sometimes even fatal consequences.[1,2] The manufacturers recommend that a full blood count should be done before starting therapy, weekly thereafter for the first 4 weeks and then monthly. This should be continued for the duration of the therapy.

I would like to acknowledge the help of Professor C. van Heerden and Professor J. G. Prinsloo in the preparation of the manuscript.

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