AMINO-ACIDURIA IN THE MEGALOBLASTIC ANAEMIAS

BY

K. J. KEELEY AND W. M. POLITZER

From Baragwanath Hospital and the South African Institute for Medical Research, Johannesburg

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The report by Weaver and Neill (1954) of amino-aciduria in subjects with pernicious anaemia prompted us to examine the urine of patients suffering from other varieties of megaloblastic anaemia. The object of the investigation was to determine whether amino-aciduria was common to the megaloblastic anaemias.

Materials and Methods

One-dimensional chromatography (Dent, 1946) was carried out on morning specimens of urine. Had results from this screening test indicated an excess or abnormal pattern of amino-acids, two-dimensional chromatography would have been necessary for the identification of the amino-acids.

Seven African women suffering from proven megaloblastic anaemia who were admitted between October, 1954, and October, 1955, were studied before treatment was started.

Results

One-dimensional chromatography showed normal amounts of amino-acids in the urine specimens.

The control specimen of urine from a European patient suffering from untreated pernicious anaemia showed an excess of amino-acids.

Case Reports

The cases fell naturally into two groups, those associated with recent pregnancy and those without such a history.

Cases 2–6.—These comprised the first-mentioned group. The mean age of the mothers was 23 years (range 18–37 years); the infants' ages ranged from 10 days to 5 months (approximate average 2 months). The mean haemoglobin value on admission was 4.5 g./100 ml. (2.2–7.2 g./100 ml.) and the mean corpuscular haemoglobin concentration (M.C.H.C.) varied between 30 and 35%. In all cases the marrow contained megaloblasts, of the early and intermediate variety, as well as giant myeloid forms. Two patients had diarrhoea. Pathogenic organisms were not recovered, but ova of Strongyloides stercoralis and Schistosoma mansoni were found in one stool. Gastric analysis done in two cases revealed free hydrochloric acid. Fever was recorded in four cases; puerperal fever was responsible in one case, but there was no cause other than the anaemia detected in the remaining cases. It is noteworthy that one patient was in congestive heart failure. Thymol turbidity and other liver-function tests were normal in two cases.

Case 1.—This patient, aged 56, complained of weakness and dysphagia and gave a history of alcoholism. Glossitis and peripheral neuritis were present. The haemoglobin value was 11.8 g./100 ml.; the red cells were normochromic and normocytic and megaloblasts were seen in the marrow. Histamine-fast achlorhydria and absence of peptic activity was demonstrated on gastric analysis; the serum bilirubin level was 0.6 mg./100 ml. Gastroscopy was not performed. Oral administration of vitamin B₁₂ has been without effect. We do not know whether the condition has relapsed, as the patient left the district after a single injection of 1 mg. of vitamin B₁₂.

Case 7.—This woman was aged 37 years. Her last pregnancy occurred 13 years previously. She was febrile and had retinal haemorrhage, but glossitis and peripheral neuritis were absent. Malaria parasites were not detected; the haemoglobin was 4.5 g./100 ml. and the M.C.H.C. 37%; the serum bilirubin was 1.2 mg./100 ml. and intermediate megaloblasts were present in the marrow. Histamine-fast achlorhydria was demonstrated.

Discussion

Although the number of cases investigated was small, the uniform nature of the results is in direct contrast to the findings described in pernicious anaemia and confirmed by our control case. The negative results support the conclusions of Weaver and Neill (1954) that anaemia of itself is not the underlying cause of amino-aciduria. These authors emphasize this point by the detection of amino-aciduria in cases of subacute combined degeneration of the cord with achlorhydria but without megaloblastic anaemia. Their two groups had achlorhydria in common and a deficiency of vitamin B₁₂. Certainly the excess of amino-acids disappeared from the urine after therapeutic doses of
vitamin B₁₂. Histamine-fast achlorhydria in two of our cases can be absolved from responsibility for amino-aciduria. Amino-aciduria is therefore not an attribute of the group of megaloblastic anaemias; nor is it significantly related to megaloblastic metamorphosis of the bone marrow but is possibly induced by vitamin B₁₂ deficiency.

Case 1 exemplifies the clinical and haematological difficulty of differentiating pernicious from non-pernicious anaemia. Fully substantiated Addisonian anaemia in the African has, in fact, not been reported in South Africa. One-dimensional chromatography may prove a useful way of separating Addisonian anaemia from that of the megaloblastic group. Should our results be confirmed, it may be that amino-aciduria will be added to the already stringent criteria for the diagnosis of true pernicious anaemia. Urine testing will provide a method simpler, for both patient and doctor, than biopsy of gastric mucosa as practised by Doig, Motteram, Robertson, and Wood (1950).

Addendum

Since this article was written five additional cases have been studied. In two cases of post-partum megaloblastic anaemia there was no significant increase of amino-acids. By kind permission of Dr. E. Kahn two infants of a year old, suffering from malnutrition and megaloblastic anaemia, were investigated with similar results. It was only in an African male of 48 years, re-admitted with Addisonian anaemia in relapse, that the pattern described by Weaver and Neill (1954) was found. Two-dimensional chromatographic analysis showed an abnormal excretion of tyrosine, taurine, lysine, alanine, and glycine. After treatment with vitamin B₁₂ and intrinsic factor (as “bifacton”) amino-aciduria could not be detected.

Summary

Amino-acids in excess were absent from the urine in seven cases of non-Addisonian megaloblastic anaemia in Africans.

It is suggested that urinary chromatography be used to differentiate Addisonian from other megaloblastic anaemias.

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K. J. Keeley and W. M. Politzer

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