**Case Reports**

**Di Guglielmo's Syndrome with Low Serum Vitamin B₁₂**


**Andrew Pollock, M.B., Ch.B., Dip.Path.**

Victoria Infirmary Clinical Laboratories

Leslie Stankler, M.B., Ch.B.

Victoria Infirmary, Glasgow

Di Guglielmo's syndrome is a rare myeloproliferative disorder characterized by malignant erythroid hyperplasia with megaloblastoid features. Di Guglielmo, who first described it, regarded it as a pure disorder of the erythropoietic tissue. Further work, notably by Dameshek and his colleagues, has shown this concept to be too narrow (Baldini and Dameshek, 1958; Baldini, Fudenberg, Dameshek and Fukutake, 1959; Dameshek, 1958; Dameshek and Gunz, 1958). The syndrome is now regarded as one that passes through three phases. In the first phase there is excessive erythroid proliferation of the marrow, the erythremic myelosis of Di Guglielmo. The second phase is one of erythroleukemia involving both red and white cell series, which finally passes into the third phase, an acute myeloblastic leukemia. The disease may present at any stage, the second being the most frequent, and may run a total course of a few weeks to several years, being fatal at any stage. Anerythremic forms may occur in which few or no nucleated red cells are found in the peripheral blood, and in these cases diagnosis depends on the appearances of the marrow, which also differentiate leukemia presenting with some nucleated red cells in the blood. In this paper another case of Di Guglielmo's syndrome is presented, with features of unusual interest.

**Case Report**

**History.** A man of 66 was admitted to the Victoria Infirmary on November 1, 1960, with a history of progressive loss of energy, dyspnoea, angina of effort and ankle oedema of one month's duration. He had been diabetic for seven years, well controlled on diet alone. Three months before admission he was passed as fully fit at medical examination before going to Canada, where he was in excellent health for two months until the onset of the above symptoms. One week after these started there was recurrence of glycosuria and a general practitioner prescribed tolbutamide and vitamin B complex tablets, with apparent improvement of his diabetic control. However, his general condition deteriorated so rapidly that within another week he was too weak to dress and undress himself. There was no history of exposure to ionizing radiation or to chemicals, and no family history of blood dyscrasias. There had been no obvious blood loss or purpura.

**Examination.** On admission the patient was extremely pale. There was ankle and sacral oedema and crepitations were detected at both lung bases. The liver, spleen and lymph glands were not enlarged. Purpura was not present but the capillary fragility test was positive. Retinal examination showed bilateral hemorrhages and exudates. The other systems were normal.

**Investigations.** Hb. 4.5 g./100 ml., r.b.c. 1.83 mill./cu. mm., PCV 18%, MCV 100 cu.μ, MCHC 25%. The initial 'white cell count' was 103,400/cu.mm., but examination of a stained film showed no mature white cells. The nucleated cells were in fact almost all red cell precursors. Differential count: Undifferentiated cells 8% (including a few myeloblasts and others which could not be identified), nucleated red cells 92% (basophilic 9%, polychromatophilic 41%, orthochromatophilic 42%). Many of these were megaloblastic. The red cells were hypochromic with moderate anisocytosis, slight poikilocytosis, and marked polychromasia. Reticulocyte count 3.2%, platelet count 59,000/cu. mm.

Sternal puncture revealed an intensely cellular marrow, containing many very primitive stem cells. There was extreme erythroid hyperplasia, with many pro-erythroblasts and early basophilic forms. At the later stages both normoblasts and megaloblasts were present. Many cells in mitosis could be seen, including some large polyploid forms. In the granular series there were a few myeloblasts and promyelocytes but no more mature forms, and no Aier rods were present. No megakaryocytes and no myeloma or other tumour cells could be seen. The periodic acid Schiff (PAS) reaction (Hayhoe, Quaglin and Flemans, 1960) was strongly positive in the erythroid precursors. Paraffin sections of the marrow confirmed the hypercellularity and the absence of megakaryocytes and tumour cells. Perls' reaction showed free iron to be reduced.

Direct and indirect Coomb's tests, Donath-Landsteiner, and Ham's acid serum tests were negative. Paper electrophoresis and alkali denaturation of haemoglobin gave normal results. The blood group was A, Rh. positive. Bleeding time by Duke's method was 7 min., and clotting time by Lee and White's method 7 min. Hess's capillary fragility test was strongly positive. Prothrombin time by Quick's one-stage method was 16 sec., control being 1 sec. Serum vitamin B₁₂ level was 20 μg./ml. on two occasions. An augmented histamine test meal (Kay, 1953) showed hyperchlorhydria. The direct serum bilirubin reaction was negative, but the indirect serum bilirubin was 2.4 mg./100 ml. Other liver function tests and plasma protein levels were normal. Urobilinogen, urobilin,
Discussion

Dameshek and his colleagues have proposed certain criteria in the diagnosis of this disease. The marrow should show erythroid hyperplasia with maturation arrest at a primitive level, megaloblastoid features, increased mitoses with frequent abnormal figures, degenerative features, and a varying degree of myeloblastic proliferation. The blood picture is that of a macrocytic anæmia, with aniso-
megaloblastic anaemia, with low serum B12, unresponsive to parenteral cyanocobalamin therapy. Although the patient's serum vitamin B12 level was raised from 20 to 1,000 μg./ml. by therapy, there was no clinical or haematological response. Further study of vitamin B12 metabolism in this disease is clearly required.

Summary

A case of Di Guglielmo's syndrome has been described, in which megaloblastic anaemia was associated with low serum vitamin B12 level. The case is compared with others previously described. The need for further study of vitamin B12 metabolism is emphasized.

We thank Dr. Ian Murray, Dr. M. J. Riddell, Dr. J. E. Craik and Dr. Ian Wang for encouragement and helpful criticism in the preparation of this paper, Dr. L. G. Bruce for assessment of serum B12 levels, and for access to his unpublished work, and Mr. H. C. Gray for preparing the photograph.

Addendum

Since this paper was prepared work has been published (Boczarow, 1961) suggesting that penicillin will invalidate B12 assay by the L. leichmannii method. Previous work by Dr. L. G. Bruce, in the clinical laboratories of the Victoria Infirmary, did not suggest this and estimations of serum vitamin B12 levels in our patient were done by his methods, which differ slightly from those of Boczarow. The validity of the results was confirmed by further studies, which will shortly be published.

REFERENCES


LIFE FROM A COUVELAIRE UTERUS


Consultant Obstetrician, City of London Maternity Hospital; Locum Consultant Obstetrician, St. Paul's Hospital, Hemel Hempstead

A. H. BISMILLAH, B.Sc., M.B., B.Ch., M.R.C.O.G.

Obstetric and Gynaecological Registrar, St. Mary Abbots Hospital; formerly Obstetric and Gynaecological Registrar, St. Paul's Hospital and West Herts. Hospital, Hemel Hempstead

As a result of the use of human fibrinogen in the treatment of the blood coagulation defect associated with abruptio placenta, for which work the authors were mainly responsible, it is now widely appreciated that, until the correction of this coagulation defect, active interference of any sort is fraught with danger. On the subject of the method of delivery, however, there appears to be a great divergence of opinion.

The fetal mortality rate in the more severe degrees of abruptio placenta is reported by almost all authors to be 100%. In the presence of a Couvelaire uterus a living infant is even more rare.

Case 1

A gravida three, aged 29, was admitted to St. Paul's Hospital, Hemel Hempstead, as an emergency case of ante-partum hemorrhage, on July 3, 1961. On admission a history of a sudden painless blood loss of approximately 10 oz. was obtained. The pregnancy had been uneventful. The estimated date of delivery was June 9, 1961.

The previous pregnancies had been 43 weeks and
Di Guglielmo's Syndrome with Low Serum Vitamin B₁₂

Iris I. J. M. Gibson, Andrew Pollock and Leslie Stankler

doi: 10.1136/pgmj.39.452.354

Updated information and services can be found at:
http://pmj.bmj.com/content/39/452/354.citation

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/