Clinical Section

President Harold Ellis MCh

Meeting October 8 1971

Cases

Acquired von Willebrand's Syndrome and Systemic Lupus Erythematosus

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(for N F Jones MD FRCP)
(*St Thomas's Hospital, London SE1*)

Mr H G, aged 55. Machiner of nylon

History: Three months of severe epistaxes, intraorbital ecchymoses and prolonged bleeding from dental extractions and shaving cuts; unproductive cough, exertional dyspnœa, fatigue, weight loss of 12 kg; acute arthritis of left wrist.

Past and family history: 1951, dental extraction. 1953, excision of exostosis on foot. 1968, pharyngeal diverticulum excised. 1968, right wrist arthrodesis. No abnormal bleeding during these procedures. Kept racing pigeons for ten years twenty years ago. Cigarettes 30 per day for 30 years. One brother, four children: no family history of bleeding.

On examination: No clubbing or skin abnormality. Moist eyes and mouth. Bilateral basal crepitations. Acute arthritis of left wrist.

Investigations: Hæmatology: Hb 14·8 g/100 ml, WBC 9,600, platelets 390,000/mm³. Blood film normal. ESR 36, 62, 49 mm in 1 hour (Westergren). Bleeding time 14 min. Prothrombin time ratio 1·1:1. Partial thromboplastin time +21·6 seconds (normal <6). Factor VIII 0·02–0·22 iu/ml (normal 0·5–2·0). No von-Willebrand-like response to infusion of cryoprecipitate. Hess test negative. Incubation test for factor VIII inhibitors negative.

Immunology: Protein strip showed diffuse increase of Y-globulin. No paraproteins. Antinuclear factor (immunofluorescence) 1:50. Gastric parietal cell antibodies weakly positive. LE cells present on three occasions. Serum complement C_3 255 mg/100 ml (normal 120–170). IgG 2,400 (normal 500–1,600), IgA 450, IgM 83 mg/100 ml. Coombs, Rose-Waaler and latex tests negative. Wassermann reaction negative. Mantoux 1:1,000 positive. No cryoglobulins or cold agglutinins. Thyroid, smooth muscle and mitochondrial antibodies absent.

Chemistry: Electrolytes, urea, calcium, phosphate, bilirubin, uric acid, alkaline and acid phosphatase, SGOT, albumin – all normal. Urine analysis, pitressin and ammonium chloride tests normal.

ECG normal. Barium meal, swallow, enema and small bowel meal normal. Fluid from left wrist-joint clear. Chest X-ray, bilateral fine basal mottling.

Lungs: Vital capacity 3,050 ml (predicted 3,740). Total lung capacity 6,130 ml (predicted 5,910). Functional residual capacity 4,030 ml (predicted 3,480). FEV_1/FVC ratio 75%. Diffusing capacity 10·9 mlCO/min per mmHg (predicted 21·6). Blood gases at rest Po_2 72, Pco_2 43, pH 7·42; on exercise Po_2 82, Pco_2 33; on MC mask Po_2 230, Pco_2 44. Precipitin tests against pigeon, budgerigar and hen negative. No acid-fast bacilli.

Progress: Following treatment with prednisone 30 mg/day, ESR was 3, 6, 9, 10 mm in 1 hour, factor VIII 1·13–2·88 iu/ml, bleeding time 4 min, IgG 960 mg/100 ml. There was no improvement in breathlessness and no change on the chest X-ray. After four months therapy was stopped, and ESR then rose to 62, 37, 53 mm in 1 hour, factor VIII 1·20–2·30 iu/ml, bleeding time 5 min, IgG 1,680, serum complement C_3 190 mg/100 ml. Chest X-ray, FEV_1 and FVC showed no change.

Comment

This patient had systemic lupus erythematosus (SLE), a condition in which bleeding abnormalities may be due to thrombocytopenia, circulating anticoagulant, hyperglobulinæmia or corticosteroid therapy. Acquired von Willebrand's

syndrome, which was the cause of bleeding in H G, is characterized by a low level of factor VIII, prolonged bleeding time and lack of family or past history. The abnormality has been reported in only 6 patients. Ingram *et al.* (1971) described the hæmatology of 4 patients, including H G. Veltkamp *et al.* (1970) demonstrated the defect transiently following ingestion of pesticide. Simone *et al.* (1968) observed the disorder in a child with SLE in whom, as in H G, factor VIII levels rose to normal on steroid therapy and were maintained when therapy ended. Acquired von Willebrand's syndrome has not previously been described in an adult with SLE.

Bilateral basal lung fibrosis, causing a restrictive lesion with a reduced diffusing capacity, was also present. Breathlessness did not respond to steroid therapy.

REFERENCES
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Simone J V, Cornet J A & Abilgaard C G
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Macrocytic Anæmia Complicated by Polycythæmia

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(Shrodell's Wing,
Watford General Hospital, Watford)

Mrs F C, aged 69

History: The patient had been in a home for the mentally deficient since 1935. About 15 months ago she looked unwell, but complained of no symptoms. Her complexion was pale but no other clinical abnormality was detected. Blood count (June 1970) showed macrocytes in the peripheral film. Hb 4·5 g/100 ml, PCV 13%, ESR 40 mm in 1 hour (Westergren), platelets 240,000. Serum B_{12} 50 and 80 pg/ml. Serum folate 5·5 ng/ml. No red cell folate tests were done.

Although no further investigations were performed, she was thought to have pernicious anæmia and injudiciously started on vitamin B_{12} therapy, at first weekly, then fortnightly, and finally monthly (23 injections) until late February 1971, when she became polycythæmic and was referred for further investigations; Hb rose to 20 g/100 ml on one occasion.

No history could be obtained from the patient, whose mental age was about 5 years.

Past history: No epilepsy, no anti-epileptic or other drugs. Known to have mild hypochromic anæmia related to bleeding hæmorrhoids; it responded well to oral iron.

On examination (June 1971): Dusky colour. Normotensive. No other abnormality, except an easily palpable spleen 2–4 cm below left costal margin.

Investigations: Hb 18·9 g/100 ml, PCV 70%, RBC 6,600,000, WBC 10,000/mm³ with a normal differential, ESR 1 mm in 1 hour. A marrow section showed findings consistent with polycythæmia. Total blood volume 5·22 litres, blood volume 118 ml/kg, red cell volume 83 ml/kg, plasma volume 35 ml/kg. Serum uric acid, calcium, phosphorus, alkaline phosphatase and leukocyte alkaline phosphatase and lactic dehydrogenase normal.

The patient showed initial reticulocyte response to vitamin B_{12} and her hæmoglobin rose quickly to normal levels; so despite no marrow evidence of pernicious anæmia, the possibility of co-existing pernicious anæmia crossed our minds. Serum B_{12} now 170 pg/ml, although she had been off vitamin B_{12} injections for 4 months. Red cell folates 300 ng/ml.

However, relevant tests showed free hydrochloric acid in the stomach. No autoantibodies for intrinsic factor or parietal cells. Methylmalonic acid excretion normal (0·9 mg/24 h).

Xylose excretion test after a 25 g xylose intake was impaired to 1·3 g/100 ml. Glucose tolerance normal; fæcal fats within normal limits. Schilling's test, jejunal biopsy and follow-through pattern of small intestine normal. No evidence of fish tapeworm in fæces.

Discussion

This woman has definite primary polycythæmia and a macrocytic anæmia, but not pernicious anæmia. There is no evidence of failure to absorb vitamin B_{12}, or of a blind loop.

It is possible that the condition is of nutritional origin, as she lives in a mental deficiency home and may not be eating all that she is served.

Dr J S Stewart (*Department of Medicine, West Middlesex Hospital, Isleworth*) said that despite what appeared to have been a good diet, dietary vitamin B_{12} deficiency must still be considered in the absence of evidence of malabsorption. It was recognized that strict lacto-vegetarians included not only increasing numbers of Indian immigrants who kept to their diet for religious reasons but also mentally subnormal or disturbed people with gross dietary fads (Stewart J S, Roberts P D & Hoffbrand A V, 1970, *Lancet* ii, 542).

Dr J P Miller (*Royal Postgraduate Medical School, London W12 0HS*) wondered if the patient had some form of bacterial overgrowth in the small bowel despite the normal barium follow-through. The subsequent normal Schilling test would be explicable if the patient had recently received broad-spectrum antibiotics.