Results of haematological investigations

	Patient	Father	Mother
Haemoglobin (g/dl)	4.6	14.0	13.0
Packed cell volume	0.17	0.42	0.38
Reticulocytes (%)	6.0	1.2	1.5
Plasma haemoglobin (%) ..	40.0	15.0	17.0
Fetal haemoglobin (%) ..	8.0	<1.0	<1.0
Sickling test	Positive	Positive	Positive
Solubility test	Positive	Not done	Not done
Haemoglobin electrophoresis ..	SA ₂	ASA ₂	ASA ₂
Haemoglobin-S quantification (%) ..	89	26	29
GPD (mmol TPNH/h/g Hb) ..	231	601	527
PGD (mmol TPNH/h/g Hb) ..	724	362	329

GDP = Glucose-6-phosphate dehydrogenase.

PGD = Phosphogluconate dehydrogenase.

TPNH = Dihyronicotinamide adenine dinucleotide phosphate.

Conversion: SI to traditional units—GPD and PGD: 1 mmol TPNH/h/g Hb ≈ 0.75 g TPNH/h/g Hb.

Comment

Between February 1974 and May 1976, 780 cases of haemolytic anaemia were investigated in our haematology laboratory.³ Of these, 57 were β -thalassaemia and only one was sickle-cell anaemia (the present case). Several groups of workers² had previously failed to find sickle-cell trait among natives of the Punjab. In 1973 three cases of sickle-cell trait were reported among 140 Hindu and Sikh adults in the Punjab⁴ (Chandigarh) but none of homozygous sickle-cell disease. This rarity of sickle-cell abnormality in Punjabis in comparison with thalassaemia is consistent with the racial origin of Punjabis, which has been traced to classic Mediterranean and Indo-Nordic subtypes of the composite Indo-Dravidian race.⁵ Except for the present case, all six cases recorded in Indian Moslems have been of sickle-cell thalassaemia.

¹ Lehmann, H, and Cutbush, M, *British Medical Journal*, 1952, **1**, 404.² Sukamran, P K, *Trends in Haematology*, J B Chatterjea memorial volume. Calcutta.³ Dash, S, and Das, K C. Unpublished data.⁴ Papiha, S S, *Human Heredity*, 1973, **23**, 147.⁵ Hooton, E A, *Up from the Ape*, rev edn. London, Macmillan, 1960.

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Factor VII deficiency associated with nephrotic syndrome

Subclinical disturbances of the blood clotting mechanism in association with the nephrotic syndrome (NS) have been reported on several occasions.¹⁻³ We describe a patient with NS who developed subcutaneous and muscle haemorrhages associated with gross depression of factor VII activity, diminished factor V activity, and raised factor X levels.

Case report

A previously healthy 68-year-old Asian woman presented with a two-week history of swollen legs. She had no other symptoms, there was no history of renal disease, malaria, tuberculosis, diabetes, or bone infection, and she had not recently taken any drugs. She was pale, blood pressure was 150/90 mm Hg, and a third heart sound was heard. Pitting oedema of the legs extended to the inguinal regions. Liver, spleen, and kidneys were not palpable, and there was no ascites.

Haemoglobin 11 g/dl (normochromic and normocytic anaemia); white cell count $5.6 \times 10^9/l$ ($5600/mm^3$); erythrocyte sedimentation rate (Westergren)

66 mm in the first hour; blood urea 8.8 mmol/l (53 mg/100 ml); serum cholesterol 7.1 mmol/l (275 mg/100 ml); total serum protein 41 g/l (albumin 17 g/l); plasma electrolytes normal; liver function values normal; Wassermann reaction negative; hepatitis B surface antigen and antinuclear factor not detected; urine analysis: protein + + +; white cells $20 \times 10^6/l$ ($20/mm^3$); no bacterial growth; protein 8.3 g/24 hours; potassium 17 mmol (mEq)/24 hours; sodium 11 mmol (mEq)/24 hours. Chest x-ray examination showed mild cardiomegaly, and electrocardiography left axis deviation. Rectal biopsy showed no amyloid.

NS was diagnosed and treatment instituted with spironolactone 75 mg eight-hourly and a high-protein vegetarian diet. Three weeks later spontaneous haemorrhages developed in the skin and muscles of both arms. Investigation showed a haemoglobin of 8 g/dl, a prolonged prothrombin time, a normal partial thromboplastin time with kaolin, and a normal thrombin time (see table). Platelet count was $450 \times 10^9/l$ ($450\,000/mm^3$). Russell's viper venom corrected the prothrombin time, indicating factor VII deficiency.

Blood clotting activity and serum and 24-hour urinary protein concentrations before and after steroid treatment. Normal and control values are given for comparison

	Before steroid treatment	At 10 days	At 30 days
Prothrombin time (s) { Patient's value 50 } ratio 3.8	13	34 } ratio 2.6	15.5 } ratio 1.3
Factor VII activity (%) (control value 100)	9	28	100
Factor V activity (%) (control value 100)	40	60	100
Factor X activity (%) (control value 100)	580	550	120
24-hour urinary protein (g) (normal <0.1)	8.3		0.2
Serum proteins (g/l) { Total (normal 66-75) 41 } { Albumin (normal 36-47) 17 }			53
			26

Circulating inhibitors were not detected. In clotting factor assays activity of factor V was 40%, factor VII 9%, and factor X 580%. The patient was transfused with fresh blood, vitamin K₁ was administered parenterally, and prednisolone 40 mg daily was given by mouth. The prothrombin time slowly returned to normal, accompanied by a rise in factors V and VII, and a fall in factor X (see table). Urinary protein fell from 8.3 to 0.2 g/24 hours, and total serum protein rose to 53 g/l (albumin 26 g/l). The haematomas and oedema resolved completely.

Comment

This is the first reported example of haemostatic failure due to acquired factor VII deficiency associated with NS. Previous cases have shown deficiency of either factors IX, XI, or XII, and in none has there been haemorrhage. The cause of the factor VII depletion in our patient was probably excess loss in the urine. Urinary loss of factor IX² and of factors II and VII⁴ has been reported in NS. The absence of liver disease and the increased blood levels of factor X suggest that the factor VII deficiency was not caused by decreased hepatic synthesis of clotting factors. Furthermore, other evidence indicates that protein synthesis is enhanced in NS,³ which might also explain the raised blood levels of factor X in this patient. We found no evidence of circulating factor VII inhibitors.

Clotting factor assays were kindly undertaken by Dr R Mibashan, of Hammersmith Hospital.

¹ Handley, D A, and Lawrence, J R, *Lancet*, 1967, **1**, 1079.² Natelson, E A, et al, *Annals of Internal Medicine*, 1970, **73**, 373.³ Rahman, F, et al, *Journal of Urology*, 1975, **113**, 853.⁴ Yatzidis, H, and Richet, G, *Revue Française d'Etudes Cliniques et Biologiques*, 1957, **2**, 717.⁵ Takeda, Y, and Chen, A Y, *Journal of Laboratory and Clinical Medicine*, 1967, **70**, 678.

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