MEDICAL MEMORANDA

Absence of Glucose-6-phosphate Dehydrogenase in Red Cells of an African

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It has been widely accepted that the Caucasian gene of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency is accompanied by severe depression of dehydrogenase activity. Activity exceeding 5% of normal has never been found in the red cells of deficient male Caucasians (Larizza *et al.*, 1958; Childs and Zinkham, 1959; Choremis *et al.*, 1963; Motulsky, 1963). In Negro hemizygotes the enzyme deficiency is less severe (usually activities are around 15% of normal), and this difference in enzyme activities is regarded as one of the two main distinguishing features between the non-Negro and Negro types of G-6-PD deficiency (Marks and Gross, 1959; Marks, 1962; Motulsky, 1963). The second and more satisfactory criterion is provided by starch-gel electrophoresis of the enzyme. All data collected so far suggest that while the Negro G-6-PD deficiency is usually associated with the A- type of dehydrogenase, the non-Negro deficiency is associated with an enzyme having electrophoretic mobility B (Boyer *et al.*, 1962; Kirkman, 1962).

The present case shows that absence of G-6-PD activity in the red cells may occur in the African Negro.

Case Report

A 21-year-old Negro was admitted to hospital with a history of fever, headaches, increased salivation, and yellow discoloration of the eyes for five days.

On examination he looked ill, pyrexial (102° F; 38.9° C), and jaundiced. His pulse was 108/min, regular, and collapsing; blood pressure 100/50 mm Hg. Both heart sounds were normal, but there was a precordial systolic ejection murmur. His chest was clear. He had massive hepatosplenomegaly. There were no abnormal signs in the central nervous system. A provisional diagnosis of pyrexia of uncertain origin was made and investigations were started.

Routine blood tests were normal; E.S.R. 50 mm in one hour (Westergren); sickling negative; haemoglobin electrophoresis AA; red cell fragility 0.325% saline. Serum direct bilirubin 13.8 mg/100 ml; indirect bilirubin 9.6 mg/100 ml; total bilirubin 23.4 mg/100 ml; serum aspartate transaminase 390 IU/l; serum alanine transaminase 90 IU/l. Blood urea, chest radiograph, blood culture, urine culture and microscopy, and sputum all normal. Bone marrow hypoplastic. L.E. cells absent on two occasions. Liver biopsy showed subacute hepatitis consistent with early cirrhosis.

G-6-PD screening by Brewer's method showed no activity. Electrophoresis showed total absence of the enzyme on two occasions (see Fig.) with the fluorescent screening method fluorescence was absent under an ultraviolet hand lamp in both new and old red cells. The patient's mother also showed absent fluorescence in both new and old red cells. Enzyme electrophoresis of the mother showed a total defect (A-), and quantitative assay showed a very low red cell enzyme content (0.009 IU/g haemoglobin at 30°C; normal range with the G-6-PD Stat-Pack system

5-10 IU/g at 30°C). The patient was an only child so no sibling studies could be done.

He continued to have a swinging temperature and his haemoglobin fell progressively from 11.48 to 10.0 and then to 7.0 g/100ml, with corresponding reticulocyte counts of 0.4%, 0.3%, and 2.6%. Various antibiotics were given without much effect,

G-6-PD electrophoretic strip. The origins lie off the top of the figure. T = Patient. A- = Mother. A and B = Controls.

and as tuberculosis involving the liver could not be excluded antituberculosis treatment was started, again without much improvement in the patient's condition. He died six weeks after admission.

Necropsy findings were: hepatic failure secondary to hepatitis with fibrosis and extensive focal necrosis; aspiration pneumonia; and massive congestive splenomegaly. The liver was grossly firm and fairly nodular.

Comment

Absence of G-6-PD activity in the red cells is very rare. It has been described in children (Shahidi and Diamond, 1959; Zinkham and Lenhard 1959; Kirkman and Riley, 1961), and Escobar *et al.*, (1964) reported the case of a 59-year-old Caucasian man with haemolytic anaemia of more than 20 years' duration whose erythrocytes were found to have no recognizable G-6-PD activity.

Absence of G-6-PD in the red cells has not been described in Africans. G. R. E. Swaniker (personal communication, 1972) found three such cases, but no electrophoretic studies were done. In the so-called African type of total deficiency of G-6-PD new red cells have a full or almost full complement of the enzyme, but it gradually diminishes as the cells get older. The absence of the enzyme in new cells makes the present case similar to the Mediterranean type of total deficiency.

In this case the association with subacute hepatitis and early cirrhosis of the liver is interesting. A high incidence of viral hepatitis in G-6-PD deficient patients was noted by Morrow *et al.* (1968) in Accra. Such patients have significantly raised total bilirubin levels (Owusu and Foli, 1972). It has been suggested that this is due to the inability of the damaged liver to clear bilirubin. It is therefore not inconceivable that in the absence of the enzyme in the red cells in Africans the liver becomes even more susceptible to viral hepatitis and becomes severely damaged during the illness, resulting in fulminant or subacute hepatitis. Those who recover may then develop cirrhosis in a matter of weeks or months rather than years. Further work is required to confirm this, but in the meantime it is suggested that G-6-PD electrophoresis be carried out on all African patients with cirrhosis of the liver of unknown aetiology.

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Scrotal Gangrene in Asymptomatic Myeloma

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Idiopathic scrotal gangrene, or Fournier's gangrene (Fournier, 1884), is an uncommon condition of obscure aetiology. The present case arose apparently as a complication of myeloma—a disease in which there is increased susceptibility to infection.

Case Report

A 71-year-old bakery worker developed an influenza-like illness with pyrexia, anorexia, diarrhoea, and general malaise for two days. On the second day he had a fall, and over the next three hours his scrotum became swollen, discoloured, and increasingly painful. He vomited several times throughout the evening and was admitted to hospital next morning.

He had a long history of chronic bronchitis with productive cough, and smoked 20 cigarettes a day. Prostatectomy had been performed in 1968.

On examination he was severely dehydrated, pale, and toxic. His temperature was 37.5°C. The scrotum was grossly swollen and tender in the lower two-thirds and the skin was purple and gangrenous. The testes could not be palpated. Heart rate was 120/min, with moderate pulse volume, and he was tachypnoeic. Breath sounds were vesicular, with high-pitched inspiratory and expiratory rhonchi over all lung areas. The liver was just palpable below the right costal margin.

Haemoglobin was 11.5 g/100 ml, packed cell volume 35%, mean corpuscular haemoglobin concentration 33%, white cell count 3,200/mm³ (85% neutrophils). No glycosuria or proteinuria was present, and a midstream specimen of urine was sterile on culture. Serum electrolytes were normal but blood urea was 66 mg/100 ml. Chest x-ray examination showed only the changes of chronic bronchitis.

The patient was catheterized and rehydrated with intravenous fluids, and treatment was started with kanamycin 500 mg twice daily and benzylpenicillin 1 megaunit four times daily.

At operation the scrotum was opened above the gangrenous skin, which was excised completely. Both testes were viable and bilateral sympathetic hydroceles were present. The left testis was removed to allow the remaining scrotal skin to be brought over the right testis and closed in the midline.

Histological examination of the scrotal wall showed heavy bacterial infiltration of the necrotic skin consistent with the diagnosis of Fournier's gangrene. Coliform organisms, β -haemolytic streptococci, and *Staphylococcus pyogenes* were cultured from scrotal swabs.

There were no postoperative complications except that the wound was slow to heal, two areas of slough persisting for over three weeks.

A white cell count repeated the day after admission was noted to have fallen to 1,400/mm³ (72% neutrophils); E.S.R. was 144 mm/in one hour. Haemoglobin was 9.4 g/100 ml and the anaemia was normochromic and normocytic. Total serum proteins were 7.3 g/100 ml, with a definite band in the β -globulin range, which was markedly raised at 37.3 (normal 7-13) mg/100 ml. Serum albumin was reduced.

Sternal marrow examination showed infiltration by atypical plasma cells consistent with a diagnosis of myeloma. Cold agglutinins were present in the blood but no cryoglobulins were detected. Bence Jones protein was present in urine. The myeloma proteins were of the IgA type. Coagulation studies, serum folate and vitamin B₁₂, liver function tests, serum uric acid, calcium and phosphate, creatinine clearance, and skeletal survey were all normal.

A course of melphalan in combination with prednisone was begun once the scrotal wall had healed.

Comment

It is the exception rather than the rule for an underlying cause to be found in a case of Fournier's gangrene. Thomas (1956) reported that the condition was secondary to minor abrasions, balanitis, or chancroid in about one-third of cases, and it has been noted to occur after minor surgical procedures in this area, such as herniorrhaphy, incision of perirectal abscess, and injection of a hydrocele. It has been described after vasectomy (Pryor, Yates-Bell, and Packham, 1971). The possibility of trauma to the scrotum in this case as an aetiological factor may be considered, but it is debatable whether this precipitated the condition or merely drew the patient's attention to it.

The finding of myeloma suggests that the underlying disease may have contributed to the onset of this opportunist infection. In addition, it was noted during cross-matching that he had a high titre of cold haemagglutinins in his serum. In such patients cyanosis of the digits and other parts may develop on exposure to cold, and gangrene may supervene (Marshall, Shepherd, and Thompson, 1953).

Despite the uncertain aetiology of idiopathic scrotal gangrene, the finding of a plasma cell dyscrasia with its concomitant diminished resistance to infection in the presence of cold agglutinins suggests possible aetiological factors in this case.

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