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Hodgkin's disease in siblings: a case report

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Summary

Two male siblings (ages 12 and 16 years) presenting with Hodgkin's disease are reported. They were both diagnosed as stage IVB with identical histological type — lymphocyte depleted. The presence of identical sex, shared environment and the closeness of the time of onset suggested a combination of both environmental and genetic factors in the aetiology of the disease in these siblings.

Résumé

Nous avons étudié le cas de deux frères (12 et 16 ans) qui souffrent de la maladie de Hodgkin's. La diagnostique des deux a permis d'identifier l'étape IVB avec type histologique identique — réduction sensible des lymphocytes. Le sexe identique, le même cadre et la proximité de la phase initiale pourraient donner à croire qu'une combinaison des facteurs de l'environnement et la génétique conditionnent l'étiologie de la maladie chez ces frères.

Introduction

Hodgkin's disease occurs commonly in Nigeria as in other parts of the world [1]. However, the incidence in childhood is much higher in Nigeria and other developing countries of the world than in the Western countries [2–4].

The aetiology of this disease remains largely unknown. It is postulated that several factors, including genetic, environmental and infective, may be responsible [5–9]. Patients with Hodgkin's disease have been found to share the same HLA antigens, notably HLA-A1 and HLA-A5 [10,11], thus supporting the genetic basis. Several cases of familial Hodgkin's disease have been reported involving parent–child and siblings, including identical twins [5,6,8,9,11].

However, cases of familial Hodgkin's disease have not been reported in Nigeria. We present a concurrent occurrence of Hodgkin's disease in two brothers.

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Case reports

AS (IUTHC No. 101257)

A 16-year-old boy from Ondo, Nigeria presented on 18/12/86 with a 13-month history of weight loss, recurrent fever with night sweats, tiredness and progressive abdominal swelling. He also had a cough that produced a whitish sputum. There was no pruritus. On examination he was cachectic, pale, febrile (38.5°C) and had evidence of hypoproteinaemia (i.e. fluffy hair and bilateral pitting pedal oedema with dry and scaly skin). He was 162 cm tall and weighed 38 kg (Fig. 1). There were palpable lymph nodes in the cervical and right axillary regions. The nodes were rubbery, non-tender and varied in size from 2 to 4 cm in diameter. Chest auscultation revealed poor air entry with rhonchi on the left base. He was in sinus rhythm with a pulse rate of 100 per minute. His blood pressure was 100 mmHg systolic and 60 mmHg diastolic. There were no cardiac murmurs. He had a massive splenomegaly (15 cm below the costal margin) with a tender and smooth hepatomegaly (6 cm below the costal margin) and minimal ascites.

He had a pancytopenia with haematocrit of

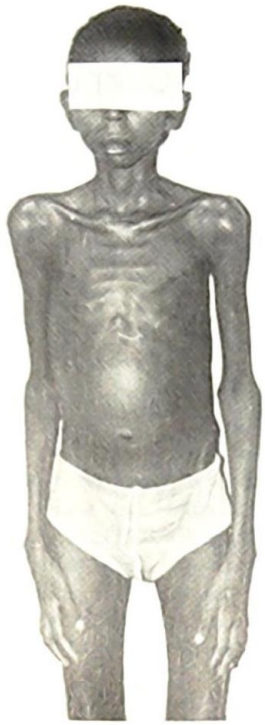

Fig. 1. Sixteen-year-old boy with Hodgkin's disease (stage IVB). Note marked cachexia and hepatosplenomegaly.

0.23 l/l, platelets of 70 × 10^9/l and leucocytes of 1.65 × 10^9/l with normal differentials. The erythrocyte sedimentation rate (ESR) was 75 mm/h (Westergreen). Serum electrolytes and urea, including uric acid and creatinine were essentially normal, but serum calcium was reduced at 1.9 mmol/l (7.6 mg/dl). His serum albumin was reduced (24 g/l), however, serum globulins, bilirubin and liver transferases (i.e. glutamic oxaloacetic transaminase, GOT; and glutamic pyruvic transaminase, GPT) were all within normal limits. He was blood group O/Rh-positive and had normal adult haemoglobin, i.e. type A. The direct antihuman globulin test (DAGT) was negative. Chest radiography showed consolidation in the left upper zone and multiple ill-defined opacities in the right lung field (Hodgkin's disease?).

Bone marrow aspiration was essentially normal but for the negative Perl's stain. Trephine biopsy showed infiltration of the marrow by Hodgkin's disease. The histology of lymph node biopsy was consistent with Hodgkin's disease of the lymphocyte depleted type.

He was clinically staged IVB, and died on day 35 of admission despite chemotherapy.

AB (IUTHC No. 102067)

The 12-year-old brother of AS. While visiting his brother in hospital, he was noticed to have marked bilateral cervical lymphadenopathy (Fig. 2).

He had a 2-year history of progressive painless generalized peripheral lymph node enlargement, starting in the left cervical region but soon involving the right side, submental, supraclavicular, both axillae and the groin. Two months prior to admission, he developed abdominal swelling with no associated pain. The illness was associated with recurrent fever and progressive weight loss. He denied any history of night sweats, pruritus or cough.

Examination revealed a chronically ill-look-

Fig. 2. Twelve-year-old boy with Hodgkin's disease (stage IVB). Note gross cervical peripheral lymphadenopathy and hepatosplenomegaly.

ing and underweight boy with fluffy hair, pallor and a tinge of jaundice. He was 128 cm tall and weighed 22 kg. He was febrile (38.9°C) and had generalized peripheral lymphadenopathy. The nodes were discrete, tender, rubbery and varied in size from 2 to 6 cm. He had bilateral coarse crepitations on chest auscultation. There was tachycardia of 100/min but no cardiac murmurs. The abdomen was distended with a tender, smooth and soft hepatomegaly extending to 7 cm below the costal margin, and a splenomegaly of 8 cm below the left costal margin.

Laboratory results showed anaemia with haematocrit of 0.25 l/l. Platelet counts and total leucocyte counts (and differentials) were essentially normal. ESR was 108 mm/h (Westergreen). Serum electrolytes and urea, including uric acid and creatinine were essentially normal, as were the serum calcium, phosphate and globulins. His serum albumin was reduced at 24 g/l and the liver transferases (GOT and GPT) were slightly elevated at 23 IU/l (normal up to 18 IU/l) and 52 IU/l (normal up to 23 IU/l) respectively. His blood group was A/Rh-positive and he had normal adult haemoglobin, i.e. type A, and DAGT was negative. Chest radiography revealed bilateral lung involvement with a right paratracheal lymph node enlargement and infiltrative changes in the right perihilar region and left apex. Bone marrow aspiration and trephine biopsy were essentially normal. Lymph node biopsy confirmed Hodgkin's disease of the lymphocyte depleted type.

He was clinically staged IVB and he continues to improve on chemotherapy 5 months after diagnosis.

Discussion

The modes of presentations of these patients would confirm the general observation in Nigeria that the majority of our patients with Hodgkin's disease present rather late for treatment and often with the more aggressive histological types, i.e. mixed cellularity and lymphocyte depleted [2,3,4,12].

A genetic basis for this disease is suggested by its occurrence in siblings, as in this report. Significantly, there is sex concordance and both had the same histological subtypes. This is in support of the observations of other workers [8].

However, genetic factors would not explain why Hodgkin's disease is present in married couples who are 'genetically' unrelated [13], or why the disease occurs at about the same time in sibs of similar age groups sharing the same environment. In such cases environment may be of greater importance than anything else [8,9,13]. The finding of a cluster of Hodgkin's disease in some pupils from the same school in a study in the USA [7] also suggests an environmental influence. However, it is difficult to say with certainty which factor is responsible for familial Hodgkin's disease.

It is conceivable that the aetiology of this disease in our patients is both genetic and environmental. Both of them were within the same age group, they were sex concordant and they had identical histological subtypes — lymphocyte depleted. In addition, they were sharing the same environment, probably having a common source of exposure and the disease manifested at about the same time in both. We would therefore agree with Fraumeni's conclusion [14] that both genetic and environmental factors are important and it is only meticulous laboratory studies of high risk families that may delineate which is the more important factor. Such investigations should of course include HLA-typing, which we could not do on these patients.

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