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Severe Combined Immunodeficiency in a Malaysian Child

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Summary

A 3-month-old Malay male infant presented with multiple infections (candidiasis, *Pseudomonas aeruginosa*, Cytomegalovirus), persistent pneumonia, intractable diarrhoea and failure to thrive. There was lymphopaenia affecting both T and B subsets. He developed Graft versus Host disease weeks following transfusion with non irradiated blood. In spite of aggressive microbicidal and supportive therapy including regular immunoglobulin infusions, the child succumbed to infection before a bone marrow transplant could be instituted.

Key Words: Severe combined immunodeficiency, Recurrent infections, Graft versus host disease

Introduction

Severe combined immunodeficiency (SCID) is probably the rarest of the known entities of the primary immunodeficiencies, with an estimated prevalence of 1 per 50 – 100,000 live births. They can present early in life but classically in the first 3 months with chronic infectious diarrhoea and failure to thrive. Abnormal

low T and B cell numbers and functions support the diagnosis. Early diagnosis is essential as bone marrow transplantation even when the related donor is not fully HLA compatible can be curative.

Case History

Clinical history

MS, a Malay male infant of consanguinous parents was first seen in 6 March 1993 at the Hospital Kuala Lumpur at the age of 3 months having been referred from another hospital in Ipoh. Following an uneventful term pregnancy and a BCG and hepatitis B vaccination at birth, MS remained well until the age of 2 months when he was admitted to hospital with recurrent cough, fever and tachypnoea. At admission he had stridor and an ulcer and whitish membrane over the tonsils and oropharynx. He was treated as a case of diphtheria (administration of diphtheria antitoxin, penicillin and gentamicin was instituted). He continued to be unwell and at 2 weeks of admission at the referring hospital, he developed pneumonia and apnoea requiring ventilatory support. He was extubated but pneumonia persisted in spite of ceftazidime, cloxacillin and amikacin therapy. Within the same period he had diarrhoea which was blood stained on several ocassions. He had also developed a perianal ulceration at this juncture. He received packed red cell transfusion which was unirradiated.

Physical examination

At admission into Hospital Kuala Lumpur, MS was found to be a malnourished child with a stridor but had normal facies. Candidiasis on the neck and ulcers in the oropharynx as well as at the perianal region were also noted. Except for basal bilateral crepitations and a hepatomegaly of 3 cm, the rest of the system examination had been normal. A BCG scar was noted.

Laboratory findings

Laboratory data were as follows: haemoglobin 7.5 g/dl, total white count 2 x 10^9/L, lymphocytes 0.3 x 10^9/L, platelet 31 x 10^9/L (the platelet count improved with therapy reaching the highest level of 116 x 10^9/L); serum calcium 2.37 mmol/L.

Chest X-ray was normal, no rib abnormalities were noted; *Pseudomonas aeruginosa* was cultured from throat swab and *candida albicans* from perianal swab and urine. HIV antibody screening was negative.

Immunological studies

Immunoglobulin (mg/dL), IgG 100 mg/dL (n 142-988), IgA 123 (n 4-90), IgM < 13.1 (n 18-118); Complements (mg/dL), C3 108, C4 92 (normal) ; T and B cell enumeration, T(CD3) 4% (67 ± 13), B (CD19) 0% (13 ± 10)[1]; in vitro lymphocyte proliferative response to mitogens PHA and con A were impaired with a stimulation index (SI) of 9 (normal control 36) and 1 (normal control 70) respectively (SI of > 10 is considered normal).

A diagnosis of severe combined immunodeficiency with septicaemia was made. His initial management was conservative which included antibiotic therapy (ceftazidime, amikacin), irradiated packed red cell transfusion for the anaemia. He was placed in an isolation room.

Progress

On the seventh day of admission he developed respiratory distress and the stridor became more prominent. He required assisted ventilation. A laryngoscopic and bronchoscopic examination showed tracheitis, a swab from which grew *Pseudomonas* and *Enterobacter*. A urine examination showed 'owl's eye cell' which strongly suggest cytomegalovirus infection; gancicyclovir was administered. Chest X-ray showed bilateral patchy pneumonia and in view of a deteriorating clinical condition, cotrimaxozole (as pneumocystis carini pneumonia was a strong probability) and ketoconazole (for candida albicans) were added. During the same period intravenous immunoglobulin was administered at a dose of 400 mg/kg weekly for the first month and reduced to biweekly subsequently.

On the third week of admission, 4 weeks after the first uniradiated blood transfusion, and after a successful extubation and disconnection from the ventilator, maculopapular erythematous rash was noted. Histopathology of biopsied skin lesion showed changes consistent with a graft versus host response. (Diarrhoea

persisted and hepatosplenomegaly was noted). The child was put on cyclosporin A and prednisolone to combat the graft versus host reaction. At this juncture a T depleted haploidentical bone marrow transplant from either of the parents was considered as both of his female siblings were histoincompatible (Table I).

Table I
HLA studies of patient and his family

Family members	Blood group	HLA phenotype
MS (Patient)	O	A2/A30/B44/ B46/CW1/CW7
Father	A	A2/A11/B13/ B38/CW6/CW7
Mother	O	A30/A11/B5/ B15/CW4
Sibling 1	O	A11/B13/B5/ CW4/ CW6
Sibling 2	O	A11/B13/B5/ CW4/CW6

The above showed absence of a compatible sibling donor.

While waiting for bone marrow transplant, he developed methicillin resistant septicaemia as well as candidaemia. In spite of appropriate antimicrobicidal and other supportive therapy (intravenous immunoglobulin, irradiated blood products) he succumbed to an irreversible disseminated intravascular coagulation (DIVC) after a massive gastrointestinal bleed at an age of 7 months.

Discussion

Our patient who unfortunately succumbed before he could be treated with bone marrow transplantation, had all the clinical and laboratory features of severe combined immunodeficiency viz chronic infection, diarrhoea, failure to thrive, lymphopaenia, impaired cellular immune functions and graft versus host disease following transfusion of unirradiated blood. Disseminated BCGiosis are known to complicate BCG in SCID children; however this was uneventful in this patient. The HLA phenotype of the patient who was completely histoincompatible with his female siblings, showed only 1 common antigen with each parent. The HLA phenotype could be due to chimerism as the patient received multiple blood transfusions (unirradiated) before the diagnosis was made. Unfortunately this postulate could not be confirmed by HLA genotyping using DNA methods.

The reported incidence of SCID is one per 50 – 100,000 live births[2]. The genetic and biochemical defects have been characterised in a number of this cases. Adenosine deaminase (ADA) deficient SCID comprised about 20 – 30% of the cases. Autosomal recessive SCID make up about another 30% and X linked form the rest of SCID[3]. The defect in our patient had not been fully characterised. SCID can be successfully treated by bone marrow transplant ; a recent series reported more than 80% success rate in HLA compatible sibling transplant and 56% success rate with HLA non identical transplant[2]. Amongst the adverse prognostic features reported in this paper were, delay in diagnosis, graft versus host disease and pneumonia requiring assisted ventilation. There was further delay in arranging for a bone marrow transplant. It should be possible to diagnose SCID early if there was an awareness of the condition among medical practitioners and a referral to a regional immunology centre for further investigations and management. When SCID or any other cellular immunodeficiency is suspected all blood products should be irradiated.

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Oesophageal Tuberculosis – An Unusual Site of Tuberculous Infection

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Summary

A female patient presenting with post-prandial epigastric pain and weight loss was diagnosed to have oesophageal tuberculosis by endoscopic biopsy. She responded well to standard anti-tuberculosis treatment.

Key Words: Tuberculosis, Oesophagus

Introduction

Tuberculosis is a very ancient disease which is certain to have been present before the beginning of recorded history. In the past decade, there has been a resurgence of tuberculosis in many parts of the world attributed to a number of factors, including the association with HIV infection/AIDS. Tuberculosis remains a major health problem in Malaysia despite effective modern chemotherapy: it is the leading cause of death from any single infectious disease and over 10,000 new cases are treated annually by government hospitals. Tuberculosis is capable of mimicking many disease processes and may involve virtually any anatomical structure. We report a case of oesophageal tuberculosis; to the best of our knowledge, this is the first such case reported in a Malaysian patient.

Case Report

NAB, an 18-year-old Malay girl, was admitted to the surgical ward in January 1995 with a 3-week history of post-prandial epigastric pain and weight loss of 4 kg. There were no other symptoms and no past medical history of note. She worked in a factory and was a non-smoker. Her father had suffered from pulmonary tuberculosis in 1980 and had completed treatment. On examination, she weighed 46.5 kg and had 2 BCG scars. There were no positive findings apart from mild epigastric tenderness on palpation of the abdomen. She was treated symptomatically for gastritis and discharged the following day. Outpatient upper gastrointestinal endoscopy in February 1995 revealed an area of irregularity about 25 cm from the incisor teeth on the right posterior wall of the