

Congenital Leukaemia – A case report

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Introduction

Congenital leukaemia which is characterised by proliferation and extrahaemopoietic infiltration of immature leucocyte precursor cells is a rare disorder encountered in the neonatal period. Although more than 100 cases of congenital leukaemia have been reported in the literature, the experience of most general paediatricians with this condition is very likely to be limited. Thus a patient presenting with congenital leukaemia admitted to Alor Star General Hospital is reported.

Key words: Congenital leukaemia, Clinical features and Diagnosis.

Case history

A Chinese girl ten days of age was referred on June 25, 1987 to the Paediatric Unit Alor Star General Hospital, (ASGH) Kedah for further investigation. She was admitted to a private hospital a day earlier because of prolonged bleeding after a vesicular lesion on the gums was pricked. The bleeding had started about ten hours prior to the admission and was subsequently controlled by pressure applied on the gums. The patient was noted to be pale with haemorrhagic lesions on the skin. She also had two episodes of loose stools which were not blood stained. She was apparently still fairly active, feeding well with no vomiting or fever.

She was born by normal delivery on 16.1.87. The weight at birth was 3.5 kg. She appeared normal at birth and was discharged after one day in hospital. She was then readmitted the next day for physiological jaundice with a serum bilirubin was 180 $\mu\text{mol/l}$.

She is the first child of the family. Mother had history of molar pregnancy in March 1985. She was well during this pregnancy with no history of fever or rash. She was not on any drugs nor had any exposure to X-ray examination.

Physical examination revealed a fairly active infant. She was noted to be pale but there was no evidence of elevated temperature or jaundice. There were multiple haemorrhagic vesicles over the body. A small haematoma was seen over the gums with petechiae over the palate and buccal mucosa. Slight bleeding from the umbilical stump was noted. The liver was palpable three centimetres below the right subcostal margin and the spleen was palpable two centimetres below the left subcostal margin along the mid-clavicular line. No significant enlargement of the lymph nodes was noted. Examination of the fundus of both eyes revealed no abnormality. A provisional diagnosis of congenital infection or bacterial septicaemia was made. The following preliminary investigations were done: Full blood counts, peripheral blood film, prothrombin time, blood culture, urine for culture and blood serology for syphilis, rubella, toxoplasmosis, cytomegalic inclusion disease and herpes simplex.

She was treated with a course of intravenous penicillin and gentamicin. Blood transfusions were given on three occasions. Investigations done manually revealed a haemoglobin of 75g/L, total white cell counts was $140 \times 10^9/\text{L}$ and platelets were $40 \times 10^9/\text{L}$ on admission. The peripheral blood film was

reported as showing predominantly blasts cells. Bone marrow aspiration which was done subsequently revealed a hypercellular marrow with a monotonous population of blast cells. This is consistent with a diagnosis of acute leukaemia. Prothrombin time was 36 seconds compared with the control of 14 seconds which when repeated after giving vitamin K was normal. Blood culture revealed a growth of *Bacillus subtilis* which was probably due to contamination. Urine culture showed no growth. Mother's blood group was AB and rhesus positive. Direct Coomb's test was negative. Serology tests for syphilis, rubella, toxoplasmosis, cytomegalic inclusion disease and herpes simplex were negative.

She remained stable with no further bleeding while in the ward. She was then referred to the University Hospital, Kuala Lumpur (UHKL) on the 8.7.1987 for further management. On admission to the Paediatric unit UHKL (10.7.1987), she was noted to be pink. Examination of the mouth showed the presence of oral thrush and an erythematous rash was noted over the neck, trunk and groin areas. The liver was three centimetres below the right subcostal margin and the spleen was five centimetres below the left subcostal margin. The haemoglobin was then 113g/L, total white cell count was $476.8 \times 10^9/L$ and the platelets were $24 \times 10^9/L$. Bone marrow aspiration was repeated on the 13.7.1987 and the fragments were noted to be hypercellular with normal haemopoiesis markedly depressed. More than 95% of the nucleated cells were blast cells mostly having scanty cytoplasm and inconspicuous nucleoli. The cytochemical evaluation on the leukaemic cells were negative to peroxidase, acid phosphatase, esterases and PAS stain.

The patient was later noted to be bleeding from the bone marrow site and the umbilicus. Investigations done then showed that the haemoglobin was 68g/L total white cell count was $845 \times 10^9/L$, the platelets were $20 \times 10^9/L$, prothrombin time 16.5 seconds compared with control of 12 seconds, partial thromboplastin time was 55.4 seconds with control of 28 seconds and thrombin times was 200 seconds compared with control of 17.7 seconds. She then expired on the same day. However no postmortem examination was done.

Discussion

It has been customary to categorise leukaemia as congenital when it is diagnosed within a few days after birth, and neonatal when it manifests itself during the first four to six weeks of life.¹ The incidence of congenital leukaemia is not well known. However, in a study in USA it was reported as 4.7 per million live births in newborns less than 29 days old.² It is most often myelogenous in sharp contrast to the predominance of lymphoblastic leukaemia in older children.

Clinical features are due to the result of replacement of normal bone marrow cells by blast cells and the invasion of leukaemic cells into various organs. Cutaneous manifestations are the most frequent clinical findings noted at birth. In addition to petechiae and purpura, leukaemic skin nodules have been observed in approximately 50% of cases of congenital leukaemia. These skin nodules vary in size from 0.2–3.0 centimetres, are bluish to slate-gray in colour, may appear in all sites and palpated as fibroma like tumours of the deep skin. These skin nodules were not seen in this patient. Hepatosplenomegaly is common but lymphadenopathy is not a frequent finding as in this patient. Other nonspecific symptoms include lethargy, pallor poor feeding and bleeding.

A variety of disorders in the neonatal period can imitate leukaemia.¹ The newborn's bone marrow response to infection, hypoxaemia or severe haemolysis is commonly associated with a leukaemoid reaction, and the presence of circulating nucleated red blood cells. This leucoerythroblastic reaction frequently has been confused with congenital leukaemia, although careful physical examination and judicious laboratory studies usually can distinguish between these entities. However, in infants with Down's syndrome an intriguing transient myeloproliferative disorder has been described, where

complete clinical and haematological recovery occurs within weeks to months of diagnosis without specific anti-leukaemic treatment.

Congenital leukaemia has been noted to have a statistical correlation with Down's syndrome.³ Reports of congenital leukaemia associated with other chromosomal abnormalities have also been noted as in a patient where a deleted chromosome in the A3 set was detected.⁴ However, the chromosomal analysis for the ASGH patient is not available.

The diagnosis of leukaemia is confirmed by examination of the bone marrow aspirate. Both morphological and cytochemical studies should be performed so that the origin of the cell types involved can be defined more precisely as its morphological characteristics alone may be misleading.⁵ In the ASGH patient as most of the blast cells have scanty cytoplasm and inconspicuous nucleoli, and the negative cytochemical reactions to peroxidase, acid phosphatase and esterases were all consistent with acute lymphoblastic leukaemia. However, the PAS stain, which is usually positive in acute lymphoblastic leukaemia was negative in this patient. Thus further marker studies such as immunological or cytogenetic studies need to be done in order to classify the exact type of acute leukaemia in this patient.⁶

Reviews of treatment of congenital leukaemia are limited to case reports. Thus treatment programmes should be modelled after established childhood programmes for acute lymphoblastic leukaemia and acute myelogenous leukaemia. This is done with the necessary modification so that complications of treatment are avoided e.g. adjustment of dosages and avoidance of radiotherapy. The prognosis of the newborn with acute leukaemia receiving similar therapy is not known.¹ Regrettably this patient expired before treatment could be given.

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