CASE REPORT

Severe vitamin B₁₂ deficiency with pancytopenia, hepatosplenomegaly and leukoerythroblastosis in two Syrian refugee infants: a challenge to differentiate from acute leukaemia

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SUMMARY

Megaloblastic anaemia due to vitamin B₁₂ deficiency is rare in childhood. However, as most cases are due to maternal insufficiency, it is mainly seen in breastfed infants especially when the mother's socioeconomic status is low and the nutrition is not adequate. We present case of two Syrian refugee infants with severe vitamin B₁₂ deficiency with pancytopenia, hepatosplenomegaly and leukoerythroblastosis.

BACKGROUND

Megaloblastic anaemia due to vitamin B₁₂ deficiency is rare in childhood.¹ However, as most cases are due to maternal insufficiency, it is mainly seen in breastfed infants especially when the mother's socioeconomic status is low and the nutrition is not adequate.^{2,3} Even consequences of social problems such as war also affect children's health. We present cases of two Syrian refugee infants with severe vitamin B₁₂ deficiency with pancytopenia, hepatosplenomegaly and leukoerythroblastosis.

CASE PRESENTATION

Case 1

A 7-month-old male child was referred from a local hospital near refugee camp to our paediatric haematology clinic, with a possible diagnosis of infantile leukaemia. The patient was born at full term, exclusively breast fed due to low socioeconomic status complicated with the consequences of war and he was staying with his family in the refugee camp in Gaziantep Turkey for 1 month. Physical examination revealed pale mucous membranes and conjunctiva, irritability and petechia in the extremities and trunk. He was not capable of sitting without support; besides, he had diminished deep tendon reflexes.

Investigations

The laboratory evaluation revealed pancytopenia with haemoglobin (Hb) 5.1 gr/dL, haematocrit (Htc) 16.4%, red blood cell count (RBC) $2 \times 10^{12}/L$, mean corpuscular volume (MCV) 88 fL, red cell distribution width (RDW) 37.7%, white cell count (WCC), neutrophils $1.26 \times 10^9/L$ and platelet count $20 \times 10^9/L$. Peripheral smear showed anisocytosis, poikilocytosis, polychromasia, macrocytes, normoblasts, few hypersegmented neutrophils and thrombocytopenia. Biochemical values revealed a lactate dehydrogenase

(LDH) measure of 1995 IU/L (180–430), uric acid 4.2 mg/dL (2–5.5), total bilirubin 1.1 mg/dL and direct bilirubin 0.29 mg/dL. He was suspected to have acute leukaemia and bone marrow examination was performed (figure 1). The bone marrow was markedly hypercellular with a myeloid:erythroid ratio 1:3. The erythroid precursors were increased with giant erythroblasts and megaloblastic changes were seen. Granulocytes were scarce and giant metamyelocytes were present. Megakaryocytes were normal in number but two multinucleated forms were detected. There was no malignant infiltration in the bone marrow. Vitamin B₁₂ level of the patient was 83 pg/mL (normal value 180–914). Methylmalonic acid levels and homocysteine could not be evaluated due to lack of laboratory facilities. Vitamin B₁₂ level in his mother was found to be 150 pg/mL and she was given vitamin B₁₂ treatment.

Differential diagnosis

The patient's condition was referred as acute leukaemia as the patient had pancytopenia, hepatosplenomegaly and leukoerythroblastosis; however, bone marrow and laboratory studies showed that he had vitamin B₁₂ deficiency.

Treatment

The patient was started intramuscular vitamin B₁₂ 500 µg/day for 7 days followed by 500 µg twice a week for a month and then followed by monthly 500 µg injections for 6 months.

Figure 1 Bone marrow findings of case 1.

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Outcome and follow-up

Six days after initiation of the treatment, reticulocyte increased to 5.1%. Hepatosplenomegaly disappeared in 1 week. Neutrophil count and haemoglobin were normalised in 1.5 months; neurological findings were resolved after 4 months.

Case 2

An 18-month-old male child was referred from the refugee camp near our hospital, with failure to thrive, recurrent infections and pancytopenia with the diagnosis of possible acute leukaemia. It was learned from the history that, his father had died and he was living in ruins with his mother and six brothers recently before he was transported to the refugee camp 1 week ago. The patient was born at full term, born from a consanguineous marriage. He was pale, was able to sit but could not walk. Physical examination revealed 4 cm hepatosplenomegaly. His neurological examination revealed decreased deep tendon reflexes and hypotonia.

Investigations

The laboratory evaluation revealed pancytopenia with Hb 5.5 g/dL, Htc 16.9%, RBC $1.76 \times 10^{12}/L$, MCV 96.2 fL, RDW 25.2%, WCC, neutrophils $0.77 \times 10^9/L$, platelet count $102 \times 10^9/L$, LDH 1334 IU/L (180–430), uric acid 4.5 mg/dL (2–5.5), total bilirubin 1.95 mg/dL and direct bilirubin 0.54 mg/dL. His peripheral smear showed anisocytosis, poikilocytosis, polychromasia, macrocytes, normoblasts, hypersegmented neutrophils and mild thrombocytopenia. The bone marrow was markedly hypercellular with a myeloid:erythroid ratio 1:2. The erythroid precursors were increased and megaloblastic changes were seen. Granulocytes were decreased and giant metamyelocytes were present. Megakaryocytes were normal. No blastic infiltration was seen in the bone marrow (figure 2). Vitamin B₁₂ level was 80 pg/mL (180–914). Methylmalonic acid levels and homocysteine could not be evaluated due to lack of laboratory facilities. His mother's vitamin B₁₂ level was also low (110 pg/mL) combined with iron deficiency anaemia.

Differential diagnosis

The patient's condition was referred as acute leukaemia as the patient had pancytopenia, hepatosplenomegaly and leukoerythroblastosis; however, bone marrow and laboratory studies showed that he had vitamin B₁₂ deficiency.

Figure 2 Bone marrow findings of case 2.

Treatment

The patient was started intramuscular vitamin B₁₂ 500 µg/day for 7 days followed by 500 µg twice a week for a month and then followed by monthly 500 µg injections for 6 months.

Outcome and follow-up:

Five days after the initiation of the treatment, reticulocyte count increased to 3.2%.

Hepatosplenomegaly disappeared in 8 days. Neutrophil count and haemoglobin were normalised in 2 months, whereas neurological findings were resolved after 4 months.

DISCUSSION

Nutritional vitamin B₁₂ deficiency is an uncommon disorder mostly due to inadequate feeding especially in breastfed infants.^{4 5} Gaziantep region is the most populated city for refugees in Turkey where 60% of Syrian refugees are residing.⁶ The most important problem of refugee infants is inadequate consumption of animal products due to poverty. Vitamin B₁₂ and iron deficiency anaemia are commonly seen among this population. Although neurodevelopmental delay is a common manifestation of vitamin B₁₂ deficiency, pancytopenia is not frequent. Only two-thirds of vitamin B₁₂-deficient patients may manifest haematological abnormalities.⁷ In a recent study, among children undergoing bone marrow biopsy, 13.2% were found to have megaloblastic anaemia as the underlying cause.⁸ Both of these patients were admitted with pancytopenia accompanied by hepatosplenomegaly and high lactate dehydrogenase levels mimicking acute lymphoblastic leukaemia. Although early studies have shown palpable splenomegaly as a common finding in megaloblastic anaemia, the exact prevalence of hepatosplenomegaly in severe vitamin B₁₂ deficiency is not known.^{9 10} Severe vitamin B₁₂ deficiency resulting in pancytopenia, splenomegaly and leukoerythroblastosis in a 46-year-old woman was recently reported.¹¹ The patient in this recent report and our patients had circulating nucleated cells and immature myeloid cells at the peripheral smear named as leukoerythroblastic anaemia by Vaughan¹² previously. As such findings can be solely present in paediatric malignant haematological disorders, our patients were referred to us with the suspicion of acute leukaemia. The peripheral smear of our patients included signs of haemolytic anaemia with anisocytosis, poikilocytosis, polychromasia and nucleated RBCs besides increased LDH. Hepatosplenomegaly of our patients may also be attributed to increased extramedullary haematopoiesis compensatory to mild haemolytic anaemia complicating nutritional vitamin B₁₂ deficiency.

We have described patients with severe nutritional vitamin B₁₂ deficiency who had been presented with pancytopenia, hepatosplenomegaly and leukoerythroblastosis. Caretakers must be aware of these features which are severe enough to be misdiagnosed as acute leukaemia, particularly in undernourished refugee infants. With appropriate treatment measures, persistent neurological sequelae in these patients can be avoided.

Learning points

- ▶ Consider vitamin B₁₂ deficiency in infants with pancytopenia, hepatosplenomegaly and leukoerythroblastosis.
- ▶ Vitamin B₁₂ deficiency can be seen in malnourished breastfed infants.
- ▶ Neurological sequelae can be avoided with appropriate treatment.

Contributors BB was involved in patient care and writing the manuscript. BOH helped in diagnosis of the patient and revised the manuscript. UK revised the manuscript and took pictures of bone marrow aspiration findings.

Competing interests None.

Patient consent None.

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