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Diamond Blackfan Syndrome in a Nigerian Child: a Case Report

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Abstract

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We report the case of a 21-month-old girl with a rare congenital anaemia. Born on July 8, 2005, BE was first seen with severe anaemia necessitating blood transfusion at the age of eight weeks. The anaemia recurred with subsequent transfusions within three months of the first transfusion. She was eventually referred to the paediatric haematology unit when she was five months old. At presentation, her packed cell volume was 10 percent. Peripheral blood film revealed normal white cell and platelet counts and macrocytosis, but the reticulocyte count was low. Bone marrow aspiration and biopsy showed paucity of red cell precursors with normal white cell precursors and megakaryocytes. Serum electrolytes, urea and creatinine levels were normal. A diagnosis of Diamond Blackfan syndrome was made with a differential of transient erythroblastopaenia of childhood. She received transfusion of packed red cells. Thereafter, prednisolone at a dose of 2mg/kg/day in three divided doses, was commenced. From then on, she maintained a packed cell volume of between 32 and 37 percent until two months after the commencement of steroid when, in an attempt to reduce the steroid to 2.5mg on alternate days, her packed cell volume (PCV) dropped to 19 percent. The steroid was recommenced at 2mg/kg/day until the PCV normalized within three weeks. Thereafter, the steroid was gradually reduced. She is currently on 2.5mg twice daily, a dose that has maintained her PCV at between 28 and 37 percent.

Introduction

DIAMOND Blackfan anaemia (DBA), otherwise referred to as pure red cell aplasia is a rare congenital disorder that affects the red cells, while sparing the white cells and platelets.[1-3] It is characterized by a low reticulocyte count, the absence of, or severe reduction in haemoglobin containing cells in the bone marrow, and normal megakaryocyte and granulocyte differentiation.[1-3] It affects 5-7.3 per million live births in Europe[4,5] and 600-700 people are believed to have the disease worldwide.[6] There is no ethnic predisposition and both sexes are equally affected. The cause of the disease is not known. Most cases are sporadic but inheritance is observed in 10-25 percent of cases.[7] In cases where hereditary pattern is described, it is largely autosomal dominant with variable penetrance[8] although a recessive pattern of inheritance has also been described.[9] The genetic basis for DBA is said to be heterogeneous. A mutation in chromosome 19q13.3 which codes for a ribosomal protein, RPS 19 is associated with 25 percent of the autosomal dominant cases and 25 percent of the sporadic cases.[7,10,11] In 10-20 percent of cases, there is no family history of this disorder but linkage to different chromosomes have been implicated.[11-14] One third of children born with this disorder, have physical defects including short stature, craniofacial, neck and thumb malformations, and cardiac defect.[2,3,6,12] Seventy percent of them respond to steroid but the disorder may later become resistant to the drug[4] requiring life long blood transfusions leading to infectious complications or iron overload.[2,3,6,12] Definitive treatment is bone marrow transplant.[2,6,12,15-17] Other treatment modalities include the use of androgen, cyclosporine, interleukin 3[2,3,6,12,18-20] and metoclopramide.[21] Recently, a 19-year-old girl with this syndrome was reported to have achieved normal haematocrit levels while on sodium valproate for control of her seizure disorder.[22] However, further

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studies will need to be conducted on the role of sodium valproate in the treatment of DBA. The apparent rarity of this condition in Nigeria prompted this report.

Case report

BE, a 21-month-old child, was delivered at term to a 36-year-old para 4+0 mother by spontaneous vertex delivery. Pregnancy and delivery were uneventful and she cried immediately after birth. She was apparently well until the age of eight weeks when the mother noticed that she was pale and sucking poorly from the breast. Her packed cell volume (PCV) at the initial admission was five percent and she was transfused with packed cells. Within a period of three months following the first transfusion, she received three other blood transfusions for severe anaemia with PCVs of 13, 15 and 15 percent, respectively. At five months of age, she was referred to the haemaotolgy unit. On admission, she was pale, anicteric, tachypnoiec. There was no peripheral lymphadenopathy, no digital anomalies and no cardiac murmurs were heard. She had tender hepatomegaly. Her PCV was 10 percent, total white cell count 11.4 x 10^9/L with a differential of 59 percent neutrophils, 40 percent lymphocytes, and 1 percent monocyte, Reticulocyte count was 1.5 percent, platelet count was 315.0 x 10^9/L. The peripheral film revealed anisocytosis, macrocytosis, and poikilocytosis. Bone marrow aspiration revealed a slightly hypocellular particulate marrow with increased myeloid erythroid ratio, depressed erythropoiesis with very few normoblasts and moderate amounts of dying cells. Granulopoiesis was increased with normal morphology. Lymphopoiesis and megakaryopoiesis were normal as were blood electrolytes and urea. Chromosomal studies and red cell deaminase levels could not be done because facilities to do these tests were not available in our centre. A diagnosis of Diamond Blackfan syndrome, with a differential of transient erythroblastonia of childhood was made. She received blood transfusion and was commenced on prednisolone at 2mg/kg/day in three divided doses. Thereafter, she did not require further transfusions as she maintained her PCV at 32-38 percent. However, three months later, in an attempt to reduce the steroid to 2.5mg on alternate days, her PCV dropped to 19 percent for which she had to be transfused as she had cardiovascular decompensation. Thereafter, the steroid was stepped up and she is currently on 2.5mg twice daily. She has maintained her PCV at between 32-38 percent. Growth monitoring revealed that her height has been persistently low for her age. At the age of 21 months, her height was 70cm which is below the third centile for her age. Study of both parents and her three older siblings revealed normal haematocrits and no physical abnormalities. The mother has been counselled on the need to maintain the child on the drug without which her PCV would drop. The effects of steroid therapy has also been explained to her and the need for regular follow up in the clinic was emphasized.

Discussion

Diamond Blackfan anaemia (DBA), otherwise called congenital pure red cell aplasia, was first described by Diamond and Blackfan in 1938,[1] although similar cases had earlier been reported by Joseph at John Hopkins Hospital in 1936.[23] It is a rare congenital disorder. It is believed to affect 600-700 people worldwide and has no racial or sex predilection.[6] Although this disorder has been reported in several parts of Europe, United States of America,[4-6] and the Middle East,[24] cases have not been as commonly reported in African countries. As far as we know, the disorder has not been reported in Nigeria but 22 cases were reported in Egypt.[25] The disease may present at birth but 72.5 percent of cases present in infancy as was the case in this child. However, 95 percent of them are diagnosed by the age of seven years, while it has been diagnosed in adults including elderly patients.[26] The clinical features are those of easy fatiguability which usually manifests as poor suck and increasing pallor as was the case in this patient. Thirty percent of patients with DBA have physical anomalies including short stature, craniofacial dysmorphism and skeletal defects, particularly abnormalities of the thumb.[2,3,6,12] Most of these anomalies were not present in our case except that she had a short stature as her height was below the 5th centile for her age.

Twenty five percent of cases of DBA are familial[7,10,11] although most cases are sporadic.[4] The disease has been linked to an abnormality in chromosome 19 in 25 percent of familial and sporadic cases.[2] The disorder is inherited as autosomal dominant with variable penetrance although recessive pattern of inheritance has also been established. A possible genetic pattern could not be established in this patient as facilities to carry out chromosomal studies were not available. Also red cell adenosine deaminase levels (ADA) which is usually elevated in patients with this disorder and affected relations or sibling[27,28] could not be determined due to lack of necessary facilities. However, the early presentation of the disease, short stature, steroid dependence for erythropoiesis ruled out transient erythroblastopenia of childhood. Furthermore, the child responded promptly to

treatment with steroids and has remained steroid dependent till date. Studies have shown that 72.5 percent respond to steroid although they may later become resistant.

Since commencement of steroid, the child has only had one blood transfusion in 12 months. The need for the blood transfusion arose from attempts to reduce the steroid to the minimum effective level. The mother has been couselled about the disorder and the side effects associated with prolonged use of steroids.

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