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Hypoplastic Anemia in an Infant With Human Immunodeficiency Virus (HIV) Infection

To the Editor: Human immunodeficiency virus (HIV) infection is associated with various hematologic disturbances, including thrombocytopenia, leukopenia, and anemia. Pure red cell aplasia is a well-known complication of viral hepatitis and parvovirus infection. We report a case of an infant with congenital hypoplastic anemia and HIV infection.

A black female presented at 12 weeks of age with upper airway congestion and dry intermittent cough. She then developed diarrhea, became lethargic, and was admitted to Texas Children's Hospital. The child was a term product of a gravida I, para I, 23-year-old mother who denied any HIV high-risk behavior. Birth weight and length were small for gestational age.

The physical examination was remarkable for pallor, a heart rate of 160, and a grade II/VI systolic murmur. Laboratory evaluation showed hemoglobin 3.4 g/dl, MCV 102 fl, reticulocyte count 0.5%, and platelet count 906,000/mm^3. Erythropoietin level was 9,200 mU/ml. The bone marrow examination revealed normal cellularity, but erythroid precursors were absent.

A clinical diagnosis of congenital hypoplastic anemia was made, and the patient was treated with prednisone 2 mg/kg per day. She was given an initial red blood cell transfusion, and her hemoglobin stabilized at 10 g/dl (Fig. 1). Three months later, she developed thrombocytopenia (50,000/mm^3). Investigation for HIV was positive. The mother was also HIV-positive, indicating perinatally acquired infection. Three weeks later, the steroids were discontinued; however, the hemoglobin level fell and rose only after prednisone was resumed. The patient was lost to follow-up for 3 months. Upon return, her hemoglobin was 3.5 g/dl, and she has since become resistant to steroids and is transfusion-dependent.

Although identification of HIV and its relationship to the acquired immunodeficiency syndrome were recognized in 1983 [1], the spectrum of hematologic manifestations remains incompletely defined. Thrombocytopenia occurs in 13–33% of pediatric patients [2,3]. Immune-mediated destruction of platelets is postulated as the cause [4,5], although suppression of thrombopoiesis may also play a role.

Leukopenia occurs in one-half of pediatric patients [2]. Granulocytopenia is probably secondary to ineffective myelopoiesis; however, immunoglobulin-mediated destruction may be an additional factor [4].

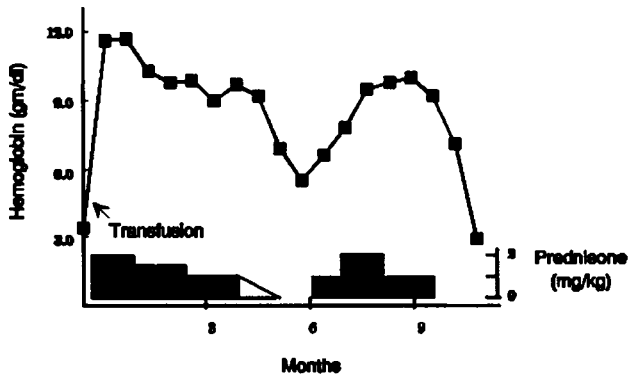

Fig. 1. Response to therapy from diagnosis. Solid squares show hemoglobin levels. Shaded bars indicate the prednisone dose (mg/kg/day); open triangle shows the tapering of prednisone over a period of 3 weeks.

Anemia affects over 90% of children with symptomatic HIV infection [2]. Ineffective erythropoiesis appears to be the major cause [5]. Autoimmune hemolysis has been proposed as a possible etiology [6,7]; however, the direct Coombs test positivity may be secondary to hypergammaglobulinemia [8,9]. Erythroid hypoplasia has been reported in AIDS patients as a result of human parvovirus B19 infection [10] and responds to high-dose gammaglobulin.

Our patient had several features supporting a diagnosis of congenital hypoplastic anemia. She responded initially to prednisone. Relapse coincided with discontinuation of steroids. Upon resuming prednisone, there was a rise in hemoglobin level; however, noncompliance was associated with steroid resistance and transfusion dependence. Thrombocytopenia occurred on only one occasion; however, it prompted a search for an etiology, and HIV positivity was confirmed. With this new finding, investigation for a cause of erythroid hypoplasia was pursued. There was no evidence of parvovirus B19 infection. Moreover, gammaglobulin infusion (400 g/kg per day for 4 days) was ineffective.

It is possible that HIV was responsible for erythroid hypoplasia. Perinatally acquired HIV infection is reported in increasing numbers. Infants presenting with erythroid hypoplasia should be investigated for HIV infection.

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Efficiency of Alteplase in the Treatment of Venous and Arterial Thrombosis in Neonates

To the Editor: The use of vascular catheter in neonates has increased the frequency of venous and arterial thrombosis. While urokinase [1] and streptokinase [2] have been widely used in the treatment of occluded central

catheters, there are few documented reports concerning alteplase [3,4]. Alteplase, because of its clot-selective activity and its short elimination half-life, seemed to us particularly interesting in the treatment of central catheter thrombosis in neonates, who generally present coagulation abnormalities with high risk of bleeding. In that no recommended doses were available for alteplase in neonates, we used a range between 0.05 mg/kg/hr and 0.2 mg/kg/hr as reported for adults (Actilyse; Boehringer Ingelheim, France).

Case 1

A 2.860 kg female infant was born after 37.5 weeks of gestation by caesarian section because of a giant omphalocele, diagnosed at 18 weeks of gestation and operated on day 1. A catheter was inserted into the left subclavian vein, and the clinical course was satisfactory. On day 20, left pleural collection occurred, and, although no abnormal opacification of the pleural cavity was detected after injection of the catheter with an aqueous constrast, the catheter was removed and reinserted into the right subclavian vein. Pleural effusion continued, despite daily puncture and pleural drainage with clinical deterioration. On day 42, a bilateral superior vena cava syndrome complicated the clinical course. Unilateral left antecubital venography disclosed complete left subclavian vein occlusion, and color doppler-flow mapping did not reveal any filling of the superior vena cava on the right innominate vein. Alteplase was administered at a dose of 0.1 mg/kg/hr, over two 12-hr periods, along with continuous IV heparin infusion (20 U/kg/hr) for 10 days. The superior vena cava syndrome clearly waned in 2 days, and on day 48 doppler-flow studies revealed complete repermeability of the deep venous system. Chylothorax disappeared gradually, and the pleural drain was removed on day 49. No bleeding was observed, and coagulation tests and platelet count, which were normal before fibrinolytic therapy, remained normal thereafter.

Case 2

This 1-day-old neonate was born after 33 weeks of gestation by caesarian section, required for fetal distress. Birth weight was 1.300 kg. Pregnancy had been complicated by sever eclampsia first noted a few weeks before delivery. An umbilical catheter was inserted 15 hr after birth, and radiographic control showed the tip at the fourth lumbar vertebra. The leg became cold and cyanotic 2 hr after insertion, without palpable femoral pulse. Capillary refill time was markedly decreased, and no detectable blood pressure was present in the left lower limb. The catheter was immediately removed. After continuous IV heparin infusion at a dose of 20 U/kg/hr, and xylocaine (1 mg/kg), the leg became pinker, but the pulse remained undetectable. After color echo-doppler studies confirmed an iliac artery thrombosis, alteplase treatment was added. Doses of 0.05 and 0.1 mg/kg/hr failed to dissolve the clot, while 0.2 mg/kg/hr for 20 hr allowed a complete clot dissolution, with, 12 hr after the end of the treatment, a palpable femoral pulse and detectable blood pressure. Left iliac arterial filling was detectable by color echo-doppler-flow mapping. Heparin was infused simultaneously for 8 days. No hemorrhagic signs were observed. During and after fibrinolytic treatment, cranial ultrasounds cans remained normal. At age 2.5 months, no necrosis was observed on the left lower limb.

In these 2 cases, alteplase was obviously effective, with absence of bleeding and perfect tolerance. It is probably a useful thrombolytic agent in the neonatal period. Nevertheless, further studies are necessary to determine the exact doses range that can be used in such cases.

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Pseudohyperkalemia and Platelet Count in Thrombocythemia

To the Editor: Pseudohyperkalemia is an in vitro rise of the serum potassium concentrate during whole blood coagulation in the presence of normal renal function and normal plasma potassium levels [1]. For the diagnosis of pseudohyperkalemia, both serum and plasma potassium determinations are warranted in order to exclude true hyperkalemia.

Pseudohyperkalemia was prospectively studied in 26 patients with primary thrombocythemia and 18 patients with polycythemia vera and thrombocythemia not receiving any medication. Potassium levels were measured at the time of increased platelet count and at the time of normal platelet count after treatment with busulphan. The reference ranges for potassium concentration in serum of normal controls were 2.6–5.1 mmol/liter and for creatinine concentration in serum 60–110 μmol/liter. Elevated serum potassium concentrations exceeding the upper reference limit in the presence of a normal renal function and normal plasma potassium levels were recorded at whole blood platelets counts in excess of 600×10^9/liter (Fig. 1). At platelet counts between 600 and 800×10^9/liter serum potassium levels were in the very upper range of normal values or increased. At platelet counts in excess of 800×10^9/liter, serum potassium concentrations were always significantly elevated. An increment of 0.15 mmol serum potassium was found for every 100×10^9/liter rise in platelet count, with a correlation coefficient of 0.82 between the serum potassium concentrations and the whole blood platelet counts. In patients with thrombocythemia and high platelet counts, normal potassium concentrations were always found in platelet-poor plasma (Fig. 1), in platelet-rich plasma, in platelet-rich plasma after aggregation induced by collagen or adenosine diphosphate (ADP), and in serum samples derived from platelet-poor plasma. However, the potassium levels were always significantly increased in the serum samples after coagulation of whole blood or platelet-rich plasma. This indicates that potassium is released from the platelets during the coagulation and clot retraction phases but not during the aggregation phase of platelets.

Since potassium plays an essential role in cardiac function, it is important that erroneous interpretation of increased potassium be avoided. Awareness of pseudohyperkalemia in disease conditions with increased platelet counts [2,3] will lead to the withholding of potentially harmful treatment, which is not needed. In conclusion, pseudohyperkalemia is a feature of high platelet count in the peripheral blood and therefore a clue to the diagnosis of thrombocythemia or reactive thrombosis.

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