Hemolysis After Administration of High-Dose Immunoglobulin in a Patient with Myocarditis

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ABSTRACT

The use of high-dose intravenous immunoglobulin (IVIG) has greatly increased in the last years. With broader use of immunoglobulin, the numbers of reported side effects are also growing. IVIG have also been used in the treatment of myocarditis and dilated cardiomyopathy. Here we reported a child with presumed acute myocarditis who has developed severe hemolytic anemia following high-dose IVIG administration. As our knowledge, this is the first case report with myocarditis or dilated cardiomyopathy who developed hemolytic anemia following high-dose IVIG administration.

Key Words: Cardiomyopathy, Anemia, Hemolytic, Immunoglobulin therapy.

ÖZET

Miyokardit Olgusunda Yüksek Doz İmmünglobulin Uygulanmasını İzleyen Hemoliz

Son yıllarda yüksek doz intravenöz immünglobulin (IVIG) kullanımı artmaktadır. Kullanımın artması ile bildirilen yan etkiler de artmaktadır. IVIG miyokardit ve dilate kardiyomiyopati tedavisinde de kullanılmaktadır. Bu yazıda akut miyokardit tedavisi için yüksek doz IVIG kullanılan bir çocukta gelişen ciddi hemolitik anemi bildirilmektedir. Bilgimiz dahilinde bu olgu miyokardit ve dilate kardiyomiyopatide yüksek doz IVIG kullanımı sonrası bildirilen ilk hemolitik anemi olgusudur.

Anahtar Kelimeler: Kardiyomiyopati, Anemi, Hemolitik, İmmünglobulin tedavisi.

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INTRODUCTION

During the recent years high-dose intravenous immunoglobulin (IVIG) has been used increasingly in the treatment of myocarditis and dilated cardiomyopathy with encouraging results[1,2]. However, many side effects of the high-dose IVIG treatment have been reported[3]. Hemolysis is one of the well known side effects of IVIG therapy[4]. It may be self limited but if it occurs in patients with compensated congestive heart failure, it can worsen hemodynamic disturbance and cause decompensation of congestive heart failure[5]. We describe a patient with presumed acute myocarditis who developed severe autoimmune hemolytic anemia and deterioration of hemodynamic findings following high-dose IVIG administration.

A CASE REPORT

An eleven-year-old boy was admitted to Pediatric Cardiology Unit of Selçuk University on February 2000 with a two-week history of dyspnea, palpitation, syncope, fatigue, nausea, and vomiting. Medical and family history of the patient was unremarkable. His physical examination revealed rapid and labored respiration, tachycardia, gallop rhythm, muffled heart sounds, II/ VI pansystolic murmur at the apex, hepatomegaly and distention of the neck veins. Blood pressure was normal. The electrocardiogram showed sinus tachycardia, low-voltage QRS complexes and T wave inversion in the left chest leads. The radiological investigation revealed cardiomegaly (cardiothorasic ratio was 0.59). On echocardiographic examination, left ventricle end-diastolic and end-systolic dimensions were larger than normal. Left ventricular systolic functions were depressed (ejection fraction: 27%, fractional shortening: 12%). Doppler examination of mitral valve showed mild mitral regurgitation. Both coronary arteries originated from the aorta. Complete blood and urine analysis, and also immunoglobulin A (IgA) level were within normal limits. Owing to the technical and economic difficulties, attempts on the identification of the etiologic agent were unsuccessful and the patient's family refused invasive diagnostic procedures. After starting anticongestive therapy (a combination of digoxine, furosemide, and captopril) symptoms of congestive heart failure ameliorated. In addition to anticongestive therapy, he received IVIG (Octagam 5Gm, Berk) 400 mg per kg daily for a total of five days. Each IVIG dose was infused over at least 4 hours. After five days of IVIG therapy he felt unwell and he had chest pain, nausea, jaundice, and dark urine. His hemoglobin levels decreased from 11.4 g/dL to 7.3 g/dL and unconjugated bilirubin increased to 3.3 mg/dL. Reticulocyte count also increased from 0.1% to 8%. Although it was negative previously, direct Coombs test was positive during two weeks. Serum haptoglobin decreased to 5 mg/dL. Glucose-6-phosphate dehydrogenase activity was normal. Osmotic fragility and sucrose lysis test were normal. Cold antibodies, Donath-Landsteiner hemolysin, antinuclear and anti-DNA antibodies were negative. The serologic tests for Epsteine-Barr virus, cytomegalovirus and parvovirus were negative. Since the hemodynamic status of the patient deteriorated owing to anemia a transfusion of packed red blood cell was administered two times (each 5 mL/kg). He responded to transfusions with hemodynamic improvement and hemolysis did not recur. When he was discharged with anticongestive therapy he had no anemia but his left ventricular systolic function was still depressed (ejection fraction: 35%, fractional shortening: 17%).

DISCUSSION

It has been suggested that IVIG administration improves ventricular function and the probability of survival in children with myocarditis and dilated cardiomyopathy[1,2]. In an animal study, IVIG therapy completely suppressed acute coxsackievirus B3 myocar-

ditis by transferring the neutralizing antibody into the host in acute viremic stage[6]. Myocarditis is an inflammation of the muscular walls of the heart. Depressed ventricular functions with dilation of one or more chambers, in the absence of any structural abnormality, help to establish the diagnosis. However, these echocardiographic findings are not specific for myocarditis and can also be detected in cases with dilated cardiomyopathy and anomalous origin of the left coronary artery. The differential diagnosis from dilated cardiomyopathy depends on histological and immunocytochemical examination of endomyocardial biopsies. However, this lack of information did not change our strategy of therapy since both disease share the same mode of therapy. Recent advances in echocardiography have helped to define the origin of coronary artery noninvasively[7]. As it was demonstrated by echocardiographic examination, both coronary arteries were originated from the aortic root in our patient.

Although, Drucker and co-workers observed no adverse effects during IVIG administration, many side effects of this mode of treatment have been reported[1,3]. Hemolytic anemia is a rare but severe complication of IVIG treatment[4]. Our patient was considered as having hemolytic anemia owing to the development of anemia without bleeding in conjunction with reticulocytosis, unconjugated hyperbilirubinemia and decreased level of serum haptoglobin. The development of hemolytic anemia following IVIG administration with positive direct Coombs test confirmed the diagnosis of hemolysis as a complication following IVIG administration. As reported previously, this complication occurred as a result of antibodies against to human blood cell antigen which can be found in IVIG preparations[4,8]. In a study, commercial human plasma preparation products were examined and found to contain A and/or B antibodies of the IgM or IgG type with titers of 1 to 1024[9]. It is concluded that performance of a minor cross matching procedure prior to immunoglobulin use will prevent the occurrence of hemolysis[10]. In our case, cross matching procedure was not performed prior to IVIG administration. Since that time cross matching has been performed before IVIG administration in our institution. Even mild reduction in hemoglobin level can cause decompansation of heart failure in patients with myocarditis or dilated cardiomyopathy as in our patient. In general, pediatric cardiologists are not familiar with this kind of complication. Here, we reported this patient in order to warn pediatric cardiologists about this serious complication of IVIG therapy. As our knowledge this is the first case report which has demonstrated the occurrence of hemolytic anemia following high-dose IVIG administration in a patient with myocarditis or dilated cardiomyopathy.

REFERENCES

1. Drucker NA, Colan SD, Lewis AB, Beiser AS, Wessel DL, Takahashi M, Baker AL, Perez-Atayde AR, Newburger JW. Gamma-globulin treatment of acute myocarditis in the pediatric population. Circulation 1994;89:252-7.
2. McNamara DM, Rosenblum WD, Janosko KM, Trost MK, Villaneuva FS, Demetris AJ, Murali S, Feldman AM. Intravenous immune globulin in the therapy of myocarditis and acute cardiomyopathy. Circulation 1997;95:2476-8.
3. Stangel M, Hartung HP, Marx P, Gold R. Side effects of high-dose intravenous immunoglobulins. Clin Neuropharmacol 1997;20:385-93.
4. Wilson JR, Bhoopalam N, Fisher M. Hemolytic anemia associated with intravenous immunoglobulin. Muscle Nerve 1997;20:1142-5.
5. Salama A, Mueller-Eckhardt C, Kiefel V. Effect of intravenous immunoglobulins in immune thrombocytopenia. Lancet 1983;11:193-5.
6. Takada H, Kishimoto C, Hiraoka Y. Therapy with immunoglobulin suppresses myocarditis in a murine coxsackievirus B3 model. Antiviral and anti-inflammatory effects. Circulation 1995;92:1604-11.
7. Friedman RA, Schowengerdt KO, Towbin JA. Myocarditis. In: Garson A, Bricker JT, Fisher DJ, Neish SR (eds). The Science and Practice of Pediatric Cardiology. 2nd ed. Philadelphia: Williams & Wilkins, 1997:1933-82.

8. Copelan EA, Strohm PL, Kennedy MS, Tutschka PJ. Hemolysis following intravenous immune globulin therapy. Transfusion 1986;26:410-2.
9. Okubo S, Ishida T, Yasunaga K. Hemolysis after intravenous immune globulin therapy: relation to IgG subclasses of red cell antibody. Transfusion 1990; 30:436-8.
10. Tamada K, Kohga M, Masuda H, Hattori K. Hemolytic anemia following high-dose intravenous immunoglobulin administration. Acta Paediatr Jpn 1995;37:391-3.

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