

## Partial Exchange Transfusion for Hyperviscosity and Necrotizing Enterocolitis after Complication of Intravenous Immunoglobulin in a Late Preterm Infant: Case Report and Review of the Literature

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### Abstract

Thrombocytopenia is not rare haematologic finding in the sick newborn infants, it occurs frequently in patients who were admitted to newborn intensive care units. Use of intravenous immunoglobulin (IVIG) in newborn infants has brought some amelioration to primary and secondary immune deficiencies, haemolytic disease of newborn, autoimmune thrombocytopenias and sepsis. There have been reports of thrombotic events in especially in adults and children after usage of high dose IVIG. However some unexpected adverse effects started to be reported by the increasing usage of IVIG. In this case we described a late preterm infant with necrotizing enterocolitis after IVIG treatment of neonatal isoimmune thrombocytopenia. After IVIG treatment, necrotizing enterocolitis began to occur and high blood viscosity was detected. We performed partially exchange transfusion. Thrombocyte numbers did not increase but significant improvement of clinical status occurred.

**Keywords:** Immune thrombocytopenic purpura; IVIG; Necrotizing enterocolitis

### Introduction

Thrombocytopenia is not rare hematologic finding in the sick newborn infants, it occurs frequently in patients who were admitted to newborn intensive care units. Thrombocytopenia can be also found apparently healthy newborn infant on the first day of life. Classification of thrombocytopenia in a newborn infant is made by underlying causes which are increased destruction, including consumption, or decreased production.

Use of intravenous immunoglobulin (IVIG) in newborn infants has brought some amelioration of primary and secondary immune deficiencies, hemolytic disease of newborn, autoimmune thrombocytopenia and sepsis. There have been some reports of thrombotic events especially in adults and children after usage of higher dose of IVIG. The use of IVIG in neonates has been extensively studied and has been shown to be safe and well tolerated. However some unexpected adverse effects have been also reported after IVIG treatment in newborn infants.

In this report, we described a late preterm infant with necrotizing enterocolitis after IVIG treatment of neonatal isoimmune thrombocytopenia.

### Case

A late preterm (35 weeks, 2080 g), appropriate for gestational age; male infant was born to a 26-years-old mother who has chronic immune thrombocytopenic purpura for 6 years and had splenectomy operation 3 years ago. Infant was born in 35 weeks gestational age with emergency cesarean section because of oligohydramnios. Apgar score was 8 and 9 at the 1<sup>st</sup> and 5<sup>th</sup> minute respectively. After birth, physical examination performed and generalized purpura and ecchymoses on lower quadrants of abdomen were noted. Blood count showed platelet count was 45,000/mm<sup>3</sup>, 12100/mm<sup>3</sup> leukocytes, 19.7% hemoglobin and 57% haematocrit with a normal differential count. Cranial ultrasound was normal. IVIG at a dose of 3 gr/kg was started and continued for 6 hours in the hospital where the newborn infant was born. Number of thrombocytes was 46,000/mm<sup>3</sup> one day after IVIG therapy. One gr/kg IVIG treatment was given in 3rd day of life. Following the therapy

thrombocyte number of 45,000/mm<sup>3</sup> was recorded. While the preterm infant receiving only breast milk, after second dosage of IVIG therapy, recurrent vomiting and abdominal distension began occurring. Gastric residuals were noted. When diffuse intestinal edema and suspected pneumotosis intestinalis were determined, enteral feeding of the preterm infant was stopped. Ampicillin 100 mg/kg/day, gentamicin 4 mg/kg/day and metronidazole treatment with total parenteral nutrition was started then infant was referred to our hospital. The patient was admitted to Baskent University Ankara Hospital, Neonatal Intensive Care Unit (NICU) on 3<sup>rd</sup> day of life. Gase appearance in portal vein was shown by abdominal ultrasound. Patient's blood culture sample was obtained then *Streptococcus* spp. was found. We changed ampicillin and gentamicin to vancomycin and meropenem. We evaluated protein electrophoresis and revealed that gamma globulin level was 33 (normal range: 5-20). Plasma viscosity was determined using Vilastic Bioprofiler (Vilastic scientific, Inc, Austin, U.S.). According to this method, the patient's plasma viscosity was between 7.5-8 centipoises (normal range: 1.18 ± 0.17) [1]. We performed partial exchange transfusion with normal saline and then transferred erythrocyte transfusion. Thrombocyte numbers did not increase but the patient's abdominal distention started getting better, stool passage progressively occurred. After all, full enteral feeding was tolerated by patient who was discharged from the NICU on 13<sup>th</sup> day of life.

### Discussion

IVIG is a purified, concentrated solution of immunoglobulins

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derived from plasma. It is primarily used in replacement therapy for patients with primary and secondary immune deficiencies characterized by absence or deficiency of antibody production [2,3]. There are many studies to show that IVIG is an effective treatment in the field of neonatal medicine for isoimmune haemolytic disease of newborn, alloimmune and autoimmune thrombocytopenia and sepsis. This therapy reduces frequency of exchange transfusion, phototherapy duration, hospital stay and treating thrombocytopenia [4,5]. But IVIG usage caused some adverse effects [6,7]. These adverse events after IVIG usage are pyrogenic, allergenic reactions and tachycardia and hypertension due to volume overload [8,9]. Hemolysis can also be a complication together with renal failure and necrotizing enterocolitis [10,11]. Some reports about occurrence of necrotizing enterocolitis were published after IVIG therapy. One of these studies was made by Merlob et al. The author reported that usage of IVIG therapy in isoimmune autoimmune thrombocytopenia caused necrotizing enterocolitis. They suggested that sudden increase in thrombocyte numbers and character of newborn infant's intestinal microcirculation to take part in necrotizing enterocolitis formation [12]. In another retrospective study, Figueras-Aloy J et al. [13] examined a total of 492 live born infants who had severe isoimmune haemolytic anemia and showed that 2.2% of patients treated with IVIG were diagnosed as necrotizing enterocolitis. In a case report, Lalitha Krishnan et al. [14] reported necrotizing enterocolitis occurred in a term newborn just 5 hours after the completion of the IVIG therapy. Intestinal perforation and massive hemorrhagic acites were determined in the term baby as signs of NEC. The baby died because of this complication. Roig JC et al. [15] have shown that severe hemolytic anemia itself may be a risk factor and NEC can occur even before an exchange transfusion. Go et al. [16] reported deep vein thrombosis as an adverse effect of IVIG in adults. Thrombosis related to hyperviscosity and hyperproteinemia after IVIG therapy may increase risk for necrotizing enterocolitis. It is especially attributable to intestinal ischemia due to mesenteric venous thrombosis. Tarcan et al. [17] defined pseudohyponatremia as an adverse effect after IVIG therapy which also occurred due to hyperviscosity and hyperproteinemia. They performed partial exchange transfusion with serum physiologic solution and transferred erythrocyte suspension. After this procedure, hyponatremia improved gradually. When we defined necrotizing enterocolitis after IVIG therapy, initial procedures of treatment started immediately. After elevation of serum viscosity was confirmed we performed partially exchange transfusion with normal saline. Significant improvement of clinical status occurred.

IVIG therapy is usually used in infants who had severe illness like haemolytic disease of newborn, primary and secondary immune deficiencies and isoimmune thrombocytopenia. High-dose IVIG therapy is found to be associated with a higher incidence of NEC in late-preterm and term infants. In these circumstances, clinicians should be cautious when prescribing IVIG to a newborn. If it is considered to be necessary, the infusion should be monitored very carefully.

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