GRAFT-VERSUS-HOST DISEASE AFTER EXCHANGE TRANSFUSION
Kan değişimi sonrası gelişen graft- versus - host hastalığı

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Summary: *Post transfusion graft -versus -host disease can occur in children with primary or secondary immunodeficiency, in extremely premature infants or in infants who had intrauterine or postnatal blood transfusion. On the other hand, the disease sometimes can be encountered in immunocompetent children without the presence of a known predisposing factor.We presented a newborn infant with Rh incompatibility who developed graft versus host disease following an exchange transfusion. Post transfusion graft versus host disease is usually severe and the death rate is nearly 100%. Since attempts to treat transfusion associated graft-versus-host disease have not been successful, the primary emphasis has been on prevention. We suggest that all blood and blood products should be irradiated, prior to use in newborn infants.*

Key Words: *Graft-vs- host disease, Exchange transfusion, Newborn infant*

Özet: *Primer ya da sekonder bir immün yetmezlik durumu olanlarda, çok küçük prematürelerde intrauterin veya postnatal kan değişimi yapılan infantlarda kan ya da kan ürünlerinin transfuzyonu sonrasında graft-versus-host hastalığı ortaya çıkabilmektedir. Ancak bazen immün açıdan tamamen yeterli ve bilinen hiçbir predispozan faktör olmayanlarda da görülebilmektedir. Bu yazıda Rh uygunsuzluğu nedeniyle kan değişimi yapıldıktan sonra graft versus host hastalığı gelişen bir yenidoğan bebek bildirildi. Transfuzyon sonrası gelişen graft-verus-host hastalığı çok ciddi seyirli olup ölüm oranı yaklaşık %100'dür.Bu nedenle hastalıktan korunma büyük önem taşımaktadır. Yenidoğan bebeklere verilecek tüm kan ve kan ürünleri muhakkak radyasyona tabii tutulmalıdır*

Anahtar Kelimeler: *Graft vs host hastalığı, Kan değişimi, Yenidoğan*

Transfusion-associated graft-versus-host disease has been reported primarily in adults with immunodeficiency secondary to malignancy and in children with severe combined immunodeficiency, Wiskott-Aldrich syndrome or erytroblastosis after intrauterine transfusion and exchange transfusions(1). There have been reports of post-transfusion graft versus host disease occuring in the absence of a known predisposing factor in extremely premature infants or in healthy infants. It is reported that this risk was increased when donor was a first degree relative (2,3,4). We have recently seen a newborn infant with Rh incompatibility, but otherwise appearently normal, who developed graft versus host disease following an exchange transfusion. In our case, the diagnosis of graft-versus-host disease was based on the clinical and pathological findings.

Transfusion associated graft versus host disease is a rare but hazardous complication caused by transfusion of leucocyte-containing blood. It is not clear why some patients are at risk for transfusion associated graft-versus-host disease while others are not (5).

PATIENT REPORT

A newborn infant with Rh incompatibility who developed graft-versus-host disease following an exchange transfusion was presented.

A 13 -day old infant was brought to hospital with fever and rash. The medical history revealed that the infant was the product of a 27 year old mother's first pregnancy with a normal vaginal birth. The infant underwent an exchange transfusion on

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the eighth day owing to only Rh incompatibility. The infant received one unit of blood from unrelated donor. Complaints of fever, rash, jaundice and irritability began sixth day following the exchange transfusion. There was no personal or family history of immunodeficiency diseases and the infant was not taking any medications but his liver function tests were not evaluated until his deterioration.

Physical examination, on admission to our hospital revealed generalised erythematous rash (Fig. 1), jaundice and hepatomegaly. The results of the laboratory studies were as follows: White blood cell count 22700 /mm3 with 70 % neuthrophils, 24% lymphocytes and 6% immature cells. Haemoglobin 12.5 g/dl, platelet count 138 000 /mm3; aspartate aminotransferase 283 IU/L; alanine amino-transferase 166 IU/L; gamma-glutamyl transferase 1780 IU/L ; total bilirubin 10.9 mg/dl; conjugated bilirubin 6.2 mg/dl; activated partial thromboplastin time 70 " ; protrombin time 55 " ; fibrin degradation products >500 mg/ml ; C-reactive protein 485 mg/dl and seronegative status for the human immunodeficiency virus, cytomegaloviruses and Epstein -Barr virus. Blood and urine cultures were negative. Throat and stool cultures grew flora. Serologic tests for hepatitis A, B and C viruses were also negative.

Despite antibiotic therapy the patient remained febrile and symptoms did not improve. Within the seven days of hospitalization pancytopenia developed, with a white blood cell count of 2000/mm3, platelet count of 23 000 /mm3. The skin biopsy result , along with the clinical profile, was consistent with graft versus host disease(Fig. 2A, B). Our skin biopsy specimen demostrated exosytosis, dermal and epidermal infiltrate composed predominantly neuthrophil cells.This histopathologic state was considered consistent with graft-vs-host reaction. Although the patient received prednisolon intravenously for five days, symptoms persisted and the infant died on 10th day of hospitalization.

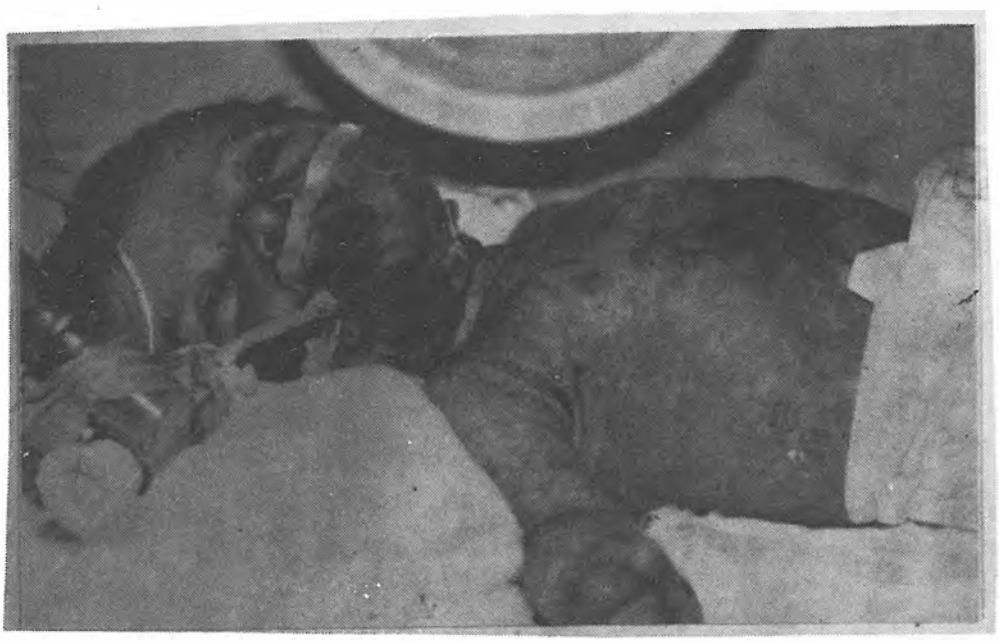

Figure 1. Diffuse erythematous macular rash on the fifth day of hospitalization

Figure 2A. Skin biopsy specimen. Exocytosis,dermal and epidermal infiltrate composed of predominently neuthrophil cells. (Hematoxylin and Eosin, x 100)

Figure 2B. Skin biopsy specimen. Celluler infiltration in the epidermis and upper dermis(Hematoxylin and Eosin, x 40)

DISCUSSION

Intrauterine and exchange transfusions have greatly reduced the mortality and morbidity of hemolytic disease of the newborn. A rare complication of these procedures is graft-versus-host disease (6,7). Graft-versus-host disease has been reported after transfusion of blood products, most

commonly packed red blood cells or whole blood, to immunoincompetent neonates, children and adults (1). There have been reports of post-transfusion graft versus host disease occuring in the absence of a known predisposing factor in extremely premature infants or in healthy term infants.

The critical number of lymphocytes required to induce a graft versus host reaction appears to be 1x107 lymphocytes per kilogram of body weight. For the neonate or young infant, a single transfusion of 10 ml/kg may supply a sufficient number of lymphocytes to initiate engraftment (2).

Post-transfusion graft versus host disease can usually be diagnosed clinically during its florid stage. Hovewer in early stage, it is not easily differentiated from toxic shock syndrome, septisemia, drug reactions or viral infections (1,2,5,8).

Transfusion-associated graft versus host disease typically presents with fever and erythroderma one to two weeks after transfusion. Involvement of the liver and gastrointestinal tract are common, with associated vomiting, profuse diarrhea and abnormal liver enzyme levels. Unlike acute graft-versus-host disease after bone marrow transplantation, transfusion-associated graft-versus-host disease is characterized by bone marrow failure and pancytopenia. Ninety percent of reported cases had fatal outcome within two to three weeks (2,3,4,5).

Fever, diarrhea, skin rash, liver dysfunction, pancytopenia, irritability characteristic of transfusion associated graft-versus-host disease developed in our patient within a week after he underwent an exchange transfusion (1,9). Blood and urine cultures showed no growth, throat and stool cultures grew only normal flora. This has led us to exclude the possibility of septisemia. Similar clinical and laboratory findings can occur also in viral and intrauterine infections. However, since the tests performed in our hospital for this purpose proved to be negative, the possibility of viral infection was also remote. The infant was not taking any medications. The patient may have had immunodeficiency but we did not investigate this possibility before exchange-transfusion; therefore, we could not rule out this possibility as underlying problem of graft -versus- host disease.

Transfusion-associated graft -versus- host disease was strongly suspected on the basis of the clinical course, clinical manifestations and laboratory findings.

Although it is widely accepted that intensive therapy with antithymocyte globulin and steroids in the early phase may be effective for treatment of this potentially fatal condition, our patient died on the fifth day of the steroid therapy (2,10,11,12,13,14,15). For this reason prevention is more important than treatment in graft -versus-host disease (6,1,2,12).

The current popularity of directed donation programs , enabling a first degree family member to donate blood for transfusion to an immediate family member, raises an additional concern. In The United States the estimated frequency of homozygous recipient varies between one in 475 for first degree relatives and one in 7174 for unrelated donors.According to The United States Food and Drug Administration , ten million blood units are transfused each year, of which one third is received from a first degree family member. Irradiation of cellular blood components is essential to prevent this disease but this is still not performed generally (3).

In summary, we have presented a case of graft -versus- host disease following an exchange transfusion in an infant with Rh incompatibility without known risk factors. The clinical constellation of pancytopenia, gastrointestinal or hepatic dysfunction and rash should heighten the physician's index of suspicion for graft -versus- host disease. The diagnosis can be confirmed by skin biopsy (1,8).

The current recommendation for transfusion of blood products to neonates is to irradiate all blood products. Irradiation of cellular blood components may lead complete elimination of this transfusion associated lethal disease (1,2,4,6,8,12).

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