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Survival of a Severe Combined Immunodeficiency Patient from Transfusion-associated Graft-versus-host Disease: A Case Report

Seyed Hesamodin Nabavizadeh [1], Hossein Esmaeilzadeh [2], Soheila Alyasin [3], Abbas Avazpour [4], * Aida Askarisarvestani [5]

[1] Department of Pediatrics, Allergy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.

[2] Department of Pediatrics, Allergy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.

[3] Department of Allergy and Clinical Immunology, Shiraz University of Medical Sciences, Shiraz, Iran.

[1] Professor of Allergy and Clinical Immunology, Shiraz University of Medical Sciences, Shiraz, Iran.

[2] Associate Professor of Allergy and Clinical Immunology, Shiraz University of Medical Sciences, Shiraz, Iran.

[3] Professor of Allergy and Clinical Immunology, Shiraz University of Medical Sciences, Shiraz, Iran.

[4] Division of Pediatric Gastroenterology and Hepatology, Department of Pediatrics, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

[5] Division of Allergy and Clinical Immunology, Department of Pediatrics, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

Abstract

Patients with Severe Combined Immunodeficiency are at high risk of Transfusion Associated Graft Versus Host Disease (TAGVHD) if they receive a non-radiated blood product that has a high mortality rate. This Case study reports on the case of a premature baby who had anemia of prematurity with a normal level of WBC. He received packed red blood cells, but after a while, he developed severe nausea and skin lesions. Endoscopy was done and the biopsy from the gastrointestinal lesions as well as the biopsy from the skin lesions showed graft versus host disease when he was 6 months old. However, he has received Hematopoietic Stem Cell Transplantation and is well now after about 4 months from his transplant.

Key Words: Blood Transfusion, GVHD, Hematopoietic Stem Cell Transplantation, Severe Combined Immunodeficiency (SCID), Transfusion Associated Graft Versus Host Disease (TAGVHD).

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Corresponding Author:

Aida Askarisarvestani, Subspecialty fellow of Allergy and Clinical Immunology, Shiraz University of Medical Sciences, Shiraz, Iran. Email: drhesamnabavi@yahoo.com

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1- INTRODUCTION

Severe Combined Immunodeficiency (SCID) is defined as a serious defect in B-cell and T-cell functions (1). Since the SCID patients suffer from a suppressed immune system, blood transfusion, just like any other organ transplantation, can cause Graft-versus-host Disease in such patients. To reduce the rate of GVHD in these patients, blood products must be irradiated to inactivate the Leukocytes in the product which are to be blamed for GVHD responses.

GVHD mostly involves the skin, the gastrointestinal tract, and the liver. Typical cases of GVHD are mostly present with skin manifestations, diarrhea, and hyperbilirubinemia; however, other symptoms such as hematemesis and hematochezia could be seen in fewer numbers of patients (2).

2- CASE REPORT

The patient was a 2-month-old boy who was born with a gestational age of 34 weeks and a birth weight of 2450 grams. In his initial course of hospitalization, after performing routine lab tests, anemia of prematurity was diagnosed for him. Therefore, non-irritated packed cells were transfused for him twice. Another complication observed during his course of hospitalization was wheezing, alongside cough and poor feeding. Hence, he was admitted to NICU and received Intravenous antibiotics with the impression of pneumonia. After being discharged from the hospital in a good condition, he was returned to hospital after only 5 days with the same symptoms. This process was repeated a few times; consequently, he was admitted to Namazee hospital for evaluation regarding tracheoesophageal fistula and diaphragmatic hernia by barium swallow and chest sonography studies. These tests did not yield any results concerning the underlying causes of his recurrent symptoms. Although the patient's first Complete Blood Count (CBC) had a WBC count of 8900/mm3 with 43% of them being lymphocytes, flow cytometry samples were sent due to his recurrent infections. After investigating the results of his flow cytometric studies, the diagnosis of Combined Immunodeficiency was made for him. However, no SCID-related mutation was found in his whole exome sequencing (a mutation in lipopolysaccharide (LPS)-responsive and beige-like anchor protein (LRBA) for common variable immunodeficiency was found though). In his workup, we sent stool samples for calprotectin and Cytomegalovirus (CMV) which returned negative. The blood samples were also sent for PCR for Candida, Aspergillus, CMV, Epstein Barr Virus (EBV), all negative again, and COVID-19 PCR which came back negative as well. He received prophylactic Vancomycin, Meropenem, Acyclovir, Fluconazole, and cotrimoxazole. Since the patient was hospitalized most in his life, he had not received the BCG vaccine; hence, he did not need prophylactic Isoniazid and Rifampin. Since the patient was in respiratory distress and was dependent on supplemental oxygen, lung HRCT was taken from him which revealed faint ground-glass opacities in peripheral aspects of his left upper lobe, and subsegmental atelectasis in posterior and basal segments of both lower lobes of the lungs, suggestive for bronchopulmonary dysplasia. The patient was in his usual state of health until 90 days after the blood transfusions, after which he developed generalized maculopapular erythematous skin lesions. At first, we suspected that the patient was experiencing Red Man Syndrome, as an adverse effect of Vancomycin; therefore, the Vancomycin was discontinued, but the patient's symptoms did not resolve. The next supposal for the patient was GVHD. In order to check the patient for GVHD, skin biopsies were taken from the lesions, the

results of which came back to be suggestive for Acute GVHD. As a result, oral glucocorticoids were added to his drug regimen. The patient then developed non-bloody diarrhea and intractable vomiting to a degree that he could not tolerate oral drugs. Due to this problem, an endoscopy was done in which ulcerative lesions were found in his esophagus and stomach which were not much like the ones seen in typical GVHD cases; after taking multiple biopsies, those lesions were found to be ulceration and granulation tissue formations with few apoptotic bodies in squamous epithelium, suggestive for GVHD. However, during this phase of the disease, the patient's liver function tests came back normal.

Table 1: The results of flow cytometric studies

Parameter	Date		
	4/10/2020	7/10/2020	28/10/2020
CD3	19%	14%	5.37% (160.93)
CD4	1%	1%	0.51% (15.28)
CD8	15%	12%	2.90% (86.91)
CD16	12%	24%	28.20%
CD19	69%	62%	60.79% (1821.87)
CD45	85%	92%	-
CD56	12%	24%	21.75%
CD4/CD8	0.07	0.08	0.17
CD20	69%	60%	61.02% (1828.76)
CD11b	Normal	Normal	-
CD14	15%	8%	-
CD16/CD56	-	-	19.22% (576.02)

Table-2: CBC results

Parameter	Date		
	7/10/2020	30/11/2020	30/12/2020
WBC (*1000/mm3)	8.9	3.5	3.4
Neutrophil (%)	52	70	78
Lymphocyte (%)	43	18	11
Monocyte (%)	3	9	9
Eosinophil (%)	1	0	2
Basophil (%)	1	0	0
Band (%)	0	3	0
RBC (*106/mm3)	2.92	2.80	3.16
Hb (g/dL)	8.9	7.9	9.1
HCT (%)	27.2	27,2	29.5
MCV (fL)	93.2	97.1	93.4
MCH (pg)	30.5	28.2	28.8
MCHC (g/dL)	32.7	29.0	30.8
Plt (*1000/mm3)	302	108	307
RDW (%)	16.0	17.6	16.6
PDW (fL)	17.6	24.9	14.9
MPV (fL)	12.2	12.8	11.3
P-LCR (%)	40.8	44.9	33.7

Table-3: Biochemical studies

Parameter	Date		
	12/11/2020	28/12/2020	9/1/2021
BUN (mg/dL)	10	-	4
Cr (mg %)	0.3	-	0.23
AST (unit/L)	90	89	63
ALT (unit/L)	50	33	28
Alk.P (unit/L)	1139	194	247
Total bilirubin (mg/dL)	0.2	0.2	0.3
Direct Bilirubin (mg/dL)	0.1	0.1	0.1
Total protein (gr %)	4.2	4.5	5.7
Albumin (gr %)	3.3	3.4	3.6
P (mg %)		2.4	

On February 11th 2021 he received a hematopoietic stem cell transplantation from his sister, after which his flow cytometry started to resolve. His last flow cytometry results are presented in **Table 4**.

Table-4: The results of the patient's flow cytometry after HSCT

CD marker	Relative count (%)	Absolute count (/µl)
CD3	61.65	1726.02
CD4	20.15	564.02
CD8	25.73	720.44
CD4/CD8 ratio	0.78	-
CD19	5.05	141.40
CD20	4.93	138.04
CD16	26.87	-
CD56	22.05	-
CD16/56	20.23	566.44

The fact that he had shown significant improvement in his flow cytometry results, despite the results of his whole exome sequencing, proved his diagnosis to be Severe Combined Immunodeficiency (SCID). The patient had not shown any signs of GVHD in the 90-day-period after the HSCT. He also had gained weight properly.

3- DISCUSSION

Although in patients with dermal and gastrointestinal GVHD, skin lesions and gastrointestinal symptoms appear more or less at the same time, in this patient, the gastrointestinal symptoms developed later than the skin manifestations of GVHD. Moreover, the appearance of his gastrointestinal lesions was not similar to that of the other patients with gastrointestinal GVHD. **Tables 1**, **2**, and **3** show the results of the paraclinical tests performed for him. As found by the patient's lab results, his initial leukocyte count, and his lymphocyte count were normal. He had received non-irritated packed cells based on his normal leukocyte count which started to drop in his course of hospitalization and turned out to be due to SCID. Therefore, quantifying T-cell Receptor Excision Circles (TRECs) might be a better way of predicting

immunodeficiency than a simple CBC in our nurseries, where the first decision for blood transfusion is made; because its sensitivity for diagnosis of SCID is 100% (3). Moreover, Transfusion-associated Graft-versus-host Disease (TAGVHD) in SCID patients has a mortality of about 90% in less than a month after non-irradiated blood transfusion (4), however this patient developed TAGVHD very late after the incident of Blood Transfusion; and fortunately, he survived the transfusion which could cost him his life.

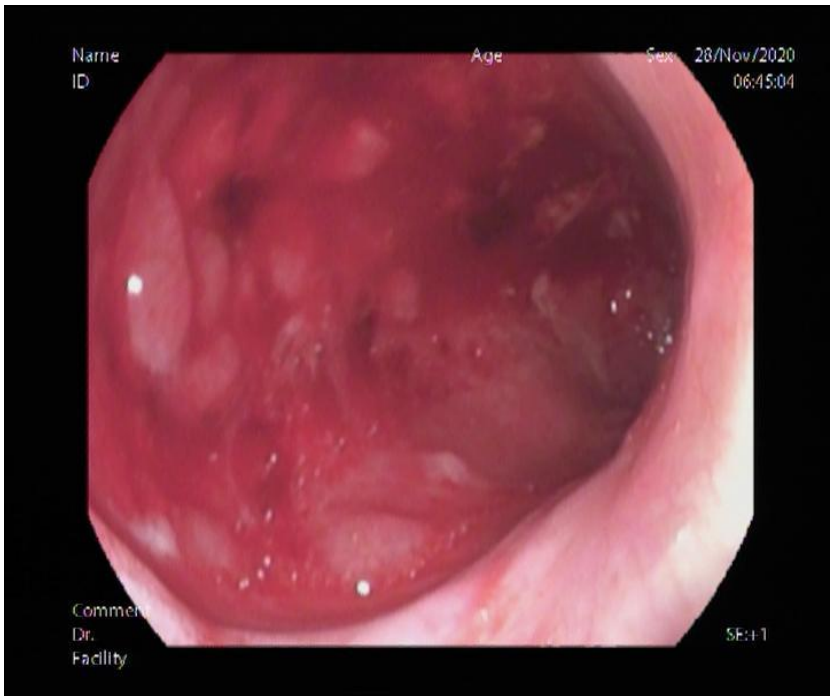

Fig. 1: The endoscopic view of the patient's esophagus.

4- CONCLUSION

This case report suggests that although the mortality rate of TRGVHD in SCID patients is extremely high, it is not 100%; therefore, a proper screening method is needed to rule out SCID in newborns. TREC might be an eligible screening test to do so.

5- ACKNOWLEDGMENTS

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6- CONFLICT OF INTEREST

None.

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