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Transfusion associated Graft Versus Host Disease; A 25 years old female- A Case Report

Dr. Md. Maruf Al Hasan[1*], Dr. M. Morsed Zaman Miah[2], Dr. Romena Alam[3], Dr. Masuma Mukta[4], Dr. Md. Maruf Morshed[4], Dr. Tamanna Nourin[5], Dr. Tasnim Mahmud[6]

[1]Registrar, Department of Hematology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh.

[2]Assistant Professor & Dept. Head Rajshahi Medical College & Hospital, Rajshahi, Bangladesh.

[3]Assistant Professor, Dept. of haematology, Rajshahi Medical College & Hospital, Rajshahi, Bangladesh.

[4]IMO, Dept. of Haematology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh.

[5]Assistant Registrar of Oncology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh.

[6]Department of Epidemiology, North South University, Dhaka, Bangladesh.

***Corresponding Author**
Dr. Md. Maruf Al Hasan

Registrar, Department of Hematology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh.

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Abstract: - *This case study aims to explore the difficulties arisen of having transfusion associated graft versus host disease, due to poor prognosis or lack of early diagnosis. A 25 years old non-diabetic, nor-hypertensive female patient from Meherpur Sadar with the chief complaint of fever and anorexia for 10 days along with skin rash for 3 days, received one-unit fresh whole blood advised by the surgeon, the donor was her own brother. After that, she noticed high grade of continued fever along with anorexia and skin rash. The confirmed diagnosis was Transfusion associated Graft Versus Host Disease. Patient was referred to Dhaka Medical College and Hospital. She started having septicemia. Patient was transferred to ICU for her critical condition. At last, the patient expired due to multiple organ failure. The overall survival rate of TA-GVHD is very unsatisfactory. Awareness among people can prevent this disease by enhancing early detection and rapid treatment.*

Keywords: *Graft, host, immune, cell, prognosis, transfusion.*

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Background:

Graft versus host disease (GVHD) is a rare clinical condition caused by reaction of donor immune cells on recipient human body after tissue transplant or transfusion [1]. There are two classes of this disease; one is allograft GVHD (allo GVHD) which results from bone marrow transplant or any other form of tissue transfusion (eg: blood). While allograft GVHD is less critical, has good prognosis and has definitive treatment, transfusion associated GVHD is more fatal, has poor prognosis and no evident treatment options [2].

Transfusion associated graft disease have very few reported cases. A study listed three requirements for the development of GVHD: the graft must contain immunologically competent cells; the recipient must express tissue antigens that are not present in the transplant donor; and the recipient must be incapable of mounting an effective response to eliminate the transplanted cells.

TA GVHD in comparison to allo GVHD has fewer occurrences and significantly high mortality rate, almost 90% of patients diagnosed with the disease do not survive. Immunocompromised individuals are at greatest risk of this acquiring this condition therefore, neonates, fetuses and hematopoietic stem cell transplantation patients are mostly affected [3].

This condition results when blood or any tissue is transfused into host, then the immune cells (T lymphocytes) of the donor initiate immune response against host cells. A possible explanation of which can be antigen-antibody reaction and hence, the proven role of Human Lymphocyte Antigen (HLA) and Major Histocompatibility Complex (MHC) protein in the disease. Japanese protocol strictly mentions about HLA typing and histocompatibility matching before transfusion. Many international guidelines focus on pre-treatment of donated blood by Gamma or X-ray irradiation or other means to suppress the activity of T lymphocytes. [4,5].

Preliminary target organs of this disease are skin, bone marrow, gut and liver causing symptoms like: erythema, diarrhea, hepatitis, aplasia, pancytopenia, hyperbilirubinemia etc. With time multiple sites are affected eventually leading the patient to multi-organ failure. Generally, these cases are diagnosed late due to overlapping symptoms thus it is difficult to save the patient, in most cases thus any new treatment cannot be tried [5].

Patient History:

A 25 years old non-diabetic, non-hypertensive female patient from Meherpur Sadar with the chief complaint of fever and anorexia for 10 days along with skin rash for 3 days admitted to Rajshahi Medical College Hospital on 20th August 2023. She gave birth to a healthy baby. After that, she was passing her post-partum period. She had a history of caesarean section 16 days back.

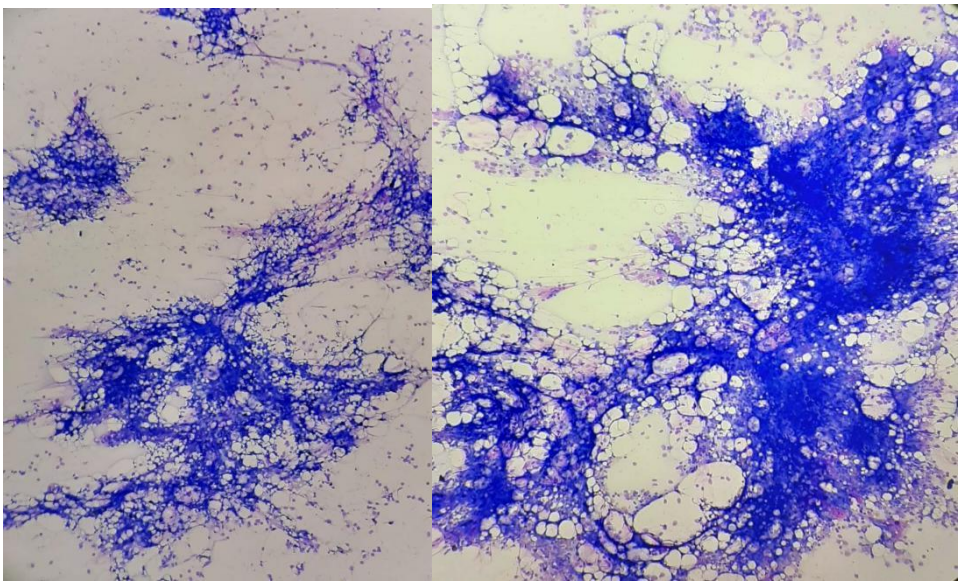
According to her statement, she received one-unit fresh whole blood advised by the surgeon, the donor was her own brother. After 6 days from this transfusion, she noticed high grade of continued fever, however subsided with medications (Paracetamol). She also had anorexia and skin rash which was maculo-papular in nature and distributed whole body started from the chest and abdomen along with mild right upper abdominal pain including loose stool. There was no history of bleeding from any site, polyarthritis, contact with tuberculosis patients or any history of exposure. She was fully immunized according to EPI schedule. Her bladder habit was normal.

Clinical Presentation & diagnosis

On general examination, a 25 years old non-diabetic, non-hypertensive female patient had a record of having anemia and jaundice. In case of systemic examination, no abnormalities were found. Abdomen and Flanks were normal. Umbilicus was centrally placed and inverted. No scar mark, visible peristalsis or engorged veins. Liver and spleen were not palpable. Kidney was not ballotable. Bowel sound was present.

Patient was suggested to undergo with regular routine examinations on 20th August 2023. CBC with PBF revealed normocytosis with moderate rouleaux formation, WBC were mature along with leucopenia (2500/cumm) and lymphocytosis (90%), platelets were decreased in number (1,30,000/cumm). ESR were moderately high. On urine examination, 8-10 pus cells were detected. It was evident that, serum CRP, LDH and D-dimer were also found high. On bone marrow examination, hypocellular marrow with increased fat spaces were found. Overall, peripheral blood film and bone marrow reports were suggestive of pancytopenia and hypoplastic marrow respectively. Ultrasonogram didn't detect any abnormal finding. Serum bilirubin was slightly high above the normal level. So, all the findings strongly indicated the confirmed diagnosis of Transfusion associated Graft Versus Host Disease.

Fig 1: Graft Versus Host Disease: A 25 years old female patient



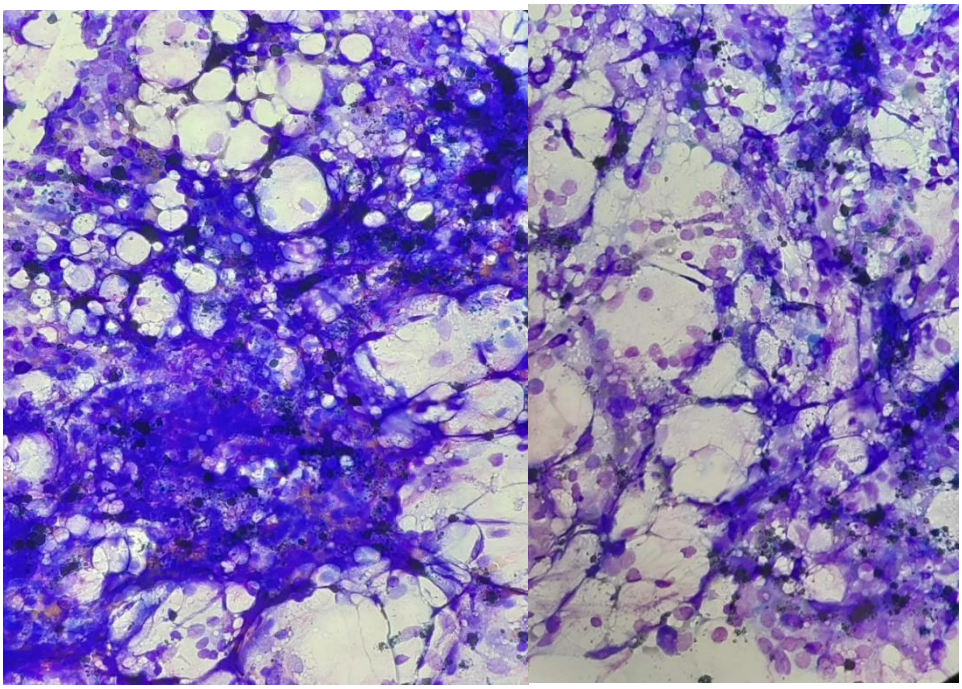


Fig 2: Bone marrow aspiration.

Findings: Hypoplastic marrow

Treatment and Management

Patient was referred to Dhaka Medical College and Hospital. She started having septicemia. Patient was transferred to ICU for her critical condition. At last, the patient expired due to multiple organ failure.

Discussion:

This case of a 25 years old non-diabetic, non-hypertensive female patient enlightens physicians about the crucial, rare condition of transfusion associated graft versus host disorder and its consequences. The primary mode of diagnosis for TA-GVHD is through clinical manifestation followed by detailed investigation. Customary symptoms of this condition include fever, skin rash, pancytopenia following a whole blood transfusion. As the disease progresses, risk of developing liver dysfunction and sepsis increase subsequently which in turn may result in multi-organ failure and septic shock. Hence, most of the times the end result is fatal. This raises questions about the limitations of standard diagnostic methodologies and underscores the need for a more comprehensive diagnostic approach, especially when dealing with rare and complex cases.

TA-GVHD is a renowned fatal adverse reaction, it is evident that more that 95% of patients expire within 2-4 weeks of transfusion. The diagnosis of TA-GVHD depends on relevant clinical manifestations along with significant investigations [6].

Between the year of 2004-2005, four TA-GVHD immunocompetent patients having similar histories of fresh whole-blood transfusion from relatives, fever, rash, liver dysfunction, diarrhea, and pancytopenia- were admitted to the ICU unit within three weeks after transfusions with the diagnosis of sepsis, rapidly progressed to septic shock. Unfortunately, all the patient died due to multiple organ failure [7].

It has been widely accepted that transfusion among first degree relatives should be avoided normally, without prior irradiation treatment and HLA analysis it should not be attempted in the first place. In Bangladesh, blood transfusions are performed without pretreatment and HLA data which doubles the risks while making process blindfolded. The clinic-laboratory features of TA-GVHD and the relative contributions of recipient and component factors remain poorly understood.

The subsequent tests, which included through examinations such as complete blood counts and bone marrow studies, unveiled a more intricate clinical portrait. The presence of hypoplasia in the bone marrow, along with the leucopenia and thrombocytopenia, indicated aplastic anemia. Given the severity of aplastic anemia and the associated complications, immediate intervention is necessary. Treatment may involve supportive care, such as blood transfusions to address low blood cell counts, and medications to stimulate the production of blood cells. In some cases, bone marrow transplantation may be considered as a more definitive treatment option. Treatment options may include blood transfusions to manage low blood cell counts, medications to suppress the immune system (immunosuppressive therapy), and in some cases, a bone marrow transplant. The choice of treatment depends on factors such as the severity of the condition, the underlying cause, and the patient's overall health.

Conclusion:

In Spite of being a rare disease, all the complications arising from TA-GVHD are often fatal. Unfortunately, the prognosis of this disease is very poor. Very few cases are treated successfully with steroids, immunosuppressive drugs, and Hematopoietic stem cell transplantation. In summary, these kinds of clinical case reports can be powerful tools in raising awareness about TA-GVHD,

leading to improved understanding, prevention, and management of this rare but serious condition.

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