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### Case report/Kazuistyka

# Transfusion-associated graft-vs-host disease – A case report



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#### ABSTRACT

Transfusion-associated graft-vs-host disease (TAGVHD) is a rare complication of blood transfusion. Unlike GVHD associated with hematopoietic stem cell transplantation TAGVHD involves the patient's bone marrow and leads to bone marrow aplasia. We report a case of TAGVHD in a 45-year-old post-hysterectomy patient after packed red blood cell transfusion from a sibling donor. The patient had fever, maculopapular rashes all over the body, elevated transaminases, and hyperglycemia after a week of the blood transfusion. Severe pancytopenia and bone marrow aplasia followed and she succumbed to her disease after 3 weeks of onset.

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## Introduction

Transfusion-associated graft-vs-host disease (TA-GVHD) is a rare and almost always a fatal complication of blood transfusion and develops 4 days to a month after a blood transfusion. It results from an attack by viable immunocompetent donor lymphocytes on the recipient's antigen presenting tissues. This immunologic assault is manifested clinically by dysfunction of the skin, liver, gastrointestinal tract and bone marrow. Normally the donor lymphocytes are destroyed by the recipient's immune system before they can mount a response against the host. This response does

not occur when the recipient is immunodeficient or when there is a specific type of partial HLA matching between the donor and the recipient even in immunocompetent persons; in the latter group of blood recipients who are heterozygous for a HLA haplotype for which the donor is homozygous (partial or one way HLA matching as in direct transfusion from a first-degree relative); the T lymphocytes from donor initiate an immune response against the lymphoid tissue of recipient. These engrafted donor T cells mediate a cellular immune response against host tissues, resulting in damage to the skin, liver, gastrointestinal tract, and bone marrow [1]. All blood components containing viable lymphocytes potentially can cause TAGVHD. Whole blood, red cells,

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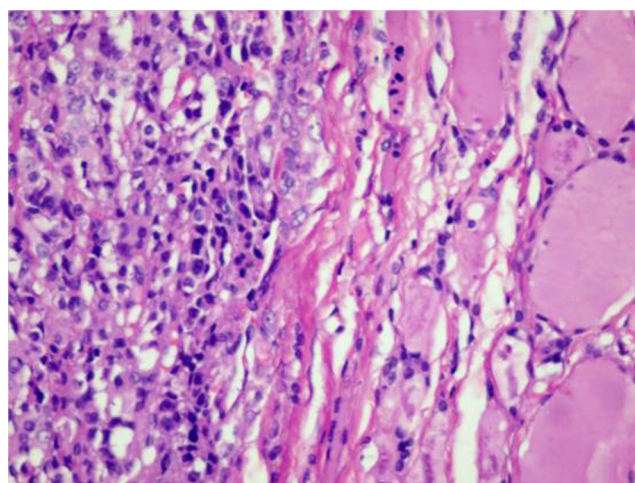
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**Fig. 1 – Erythroderma on back**



**Fig. 2 – Skin biopsy showing lymphocytic infiltration**

platelets and granulocytes have been implicated as causes of TA-GVHD. Frozen components and fractionated components have not been implicated in TA-GVHD [2]. Fatal case of TA-GVHD in the United States [3] caused by blood from an unrelated and proven HLA homozygous donor to an immunocompetent host and few others from India from a related donor to an immunocompetent host [4–6] and unrelated donor to immunocompromised host have been reported recently [7].

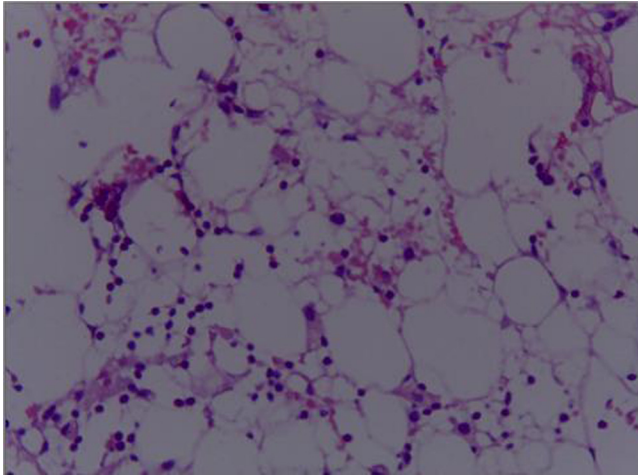
### Case report

A 45-years-old non-diabetic, non-hypertensive, otherwise healthy female nurse, who had recently undergone hysterectomy, was referred to us on 15th post-operative day with diffuse erythematous skin rashes over her face, trunk and extremities. Her operation had been uneventful. She was apparently asymptomatic for about a week after her

discharge from the hospital. She started having fever with chills and rigors and maculopapular skin rashes over her face and trunk on day 7 of her discharge from the hospital. Assuming it to be drug allergy, she took symptomatic treatment before being referred. When she came to us she had generalised maculopapular skin lesion along with pancytopenia and raised transaminases. Over the next few days her skin rashes (Fig. 1) developed into erythroderma and then into toxic epidermal necrolysis along with appearance of jaundice which deepened over the next few days; her cell counts also continued to drop. Suspecting TA-GVHD, a transfusion history was taken when she revealed that post-operatively on the day of her discharge, she was transfused a unit of freshly collected whole blood as her hemoglobin was found to be 8 g/dl; it was 9 g/dl before the surgery. As she was having menorrhagia before the surgery, her anemia was attributed to the blood loss that she had. Further it was revealed that the donor of the blood unit that she received was her own sister. The blood investigations at

**Table I – Various parameters on day of admission, day 6 and day 15 post admission**

Parameter	At admission	Day 6 post-admission	Day 15 post-admission
Hemoglobin	8	8.6	6
Total leukocyte count	450	200	45
Platelet	104 000	84 000	5000
DLC	N12%, L83%, M05%	N05%, L85%, M10%	N06%, L90%, M09%
Fasting blood sugar	290	204	211
Post-prandial blood sugar	324	277	249
C reactive protein	66.5	–	–
Sr Na	125	141	138
Total bilirubin	1.5	2.1	3.2
AST	542	792	819
ALT	467	620	714
Total proein	6.8	6.2	6.1
Albumin	2.9	2.7	2.9
RFT	0.4	0.6	0.9
Prothrombin time	16s	14s	16s
USG W/A	Hepatomegaly		
Chest X-ray	WNL	WNL	Mild pleural effusion
ECG	WNL	WNL	WNL



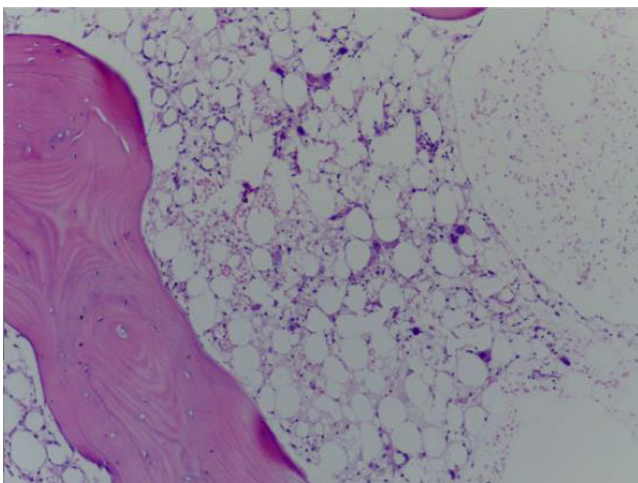
**Fig. 3 – Bone Marrow Aspiration showing decreased cellular elements**

diagnosis and on subsequent days has been shown in Table I. A bone marrow aspiration and biopsy was carried out which showed aplasia (Figs. 3 and 4) and the skin biopsy (Fig. 2) showed infiltration by lymphocytes, consistent with GVHD.

She was put on immunosuppressants and was given aggressive supportive care. Her disease progressed over the next few days. Her cytopenia progressed with the nadir TLC of 40/cmm and platelet count of 5000/cumm. She started having septicemia, developed multi organ failure and succumbed to her disease on 25th post-transfusion day. Consent for autopsy was not given by the family members. HLA typing could not be done because of unavailability of resources.

## Discussion

TA-GVHD is one of the most severe adverse reactions of transfusion and greatly feared because more than 95% of the victims die within 2–4 weeks of transfusion.



**Fig. 4 – Bone Marrow Biopsy showing aplasia**

The diagnosis of TA-GVHD is based on the evaluation of clinical manifestations in combination with relevant laboratory findings, where the gold standard tests are biopsy of the skin, liver or bone marrow [8]. Febrile illness and skin manifestations are the usual initial presenting features. Skin lesions can range from erythematous macules to hemorrhagic bullae. Fever is the first symptom, with an average onset of 10 days after transfusion. After fever, an erythematous maculopapular skin rash appears on the trunk and spreads to the palms and soles. Associated gastrointestinal problems are elevated liver enzymes, often with associated hepatomegaly and jaundice, in addition to the usual gastrointestinal symptoms, i.e. nausea, vomiting, and diarrhea [9]. Our patient developed erythematous skin rash, fever and abnormal liver function one week after the transfusion was given to her.

The main requirement for the development of GVHD is that of shared HLA types between the recipient and the donor. In a normal recipient, immune cells will far outnumber donor-derived T cells, which are therefore eliminated by a host-vs-graft reaction. However, if a small number of functional T lymphocytes are transfused which derive from a donor who is homozygous for one of the recipient's HLA haplotypes, the recipient will not recognize these cells as foreign. The donor T cells will, however, recognize the host as foreign, undergo clonal expansion and establish TA-GVHD. This situation is referred to as a one-way HLA match [3]. Besides one way HLA-matched transfusions, TA-GVHD is also seen when there is intrauterine and exchange transfusions, patients with congenital immunodeficiency syndromes, stem cell transplantation, or malignancies like lymphomas, etc. [4]. Our patient received blood from her own sister and it is possible that one way HLA matching was responsible for the grave outcome.

The difference between GVHD associated with stem cell transplantation and TA-GVHD is that in the former the bone marrow being that of the donor is spared whereas in the latter, the bone marrow being that of the recipient is attacked by the donor T-cells resulting in fatality of almost all the cases [10].

Very few cases of TA-GVHD have been reported worldwide and Indian data could be under reported due to lack of awareness about this condition. Ours is the first case being reported from the North Eastern part of India. Sohi et al. reported TA GVHD in a 5mth old male infant after he received two units of blood transfusion for anemia from his father [5]. Gupta et al. reported 3 cases of TAGVHD in immunocompromised patients (a 5 year ALL girl on chemotherapy and two 6 year and 4 year boys with severe aplastic anemia on ATG and cyclosporine respectively) all of whom had received blood transfusions from unrelated donors. While the ALL child recovered post-immunosuppressive therapy, the two males succumbed to the disease [7]. Clinicians should always consider TA-GVHD in the differential diagnosis if a patient develops a skin rash, diarrhea, liver failure, and bone marrow aplasia shortly after blood transfusion. A high index of suspicion is required to make a diagnosis of TA-GVHD.

As it is almost always a fatal complication, efforts must be placed on prevention. Using properly irradiated blood

components would prevent this disease; gamma irradiation of cellular blood components is the standard method of preventing TA-GVHD. The dose mandated by FDA is 2500 cGY, which renders T lymphocytes incapable of replication, without affecting the function of red cells, platelets and granulocytes [11]. Directed transfusion should be discouraged and the recipient at risk should be given only irradiated blood. The reported frequency of one way matching or sharing HLA haplotype in a non-first degree relative in Japan ranges from 1 in 312 to 1 in 874, which increases the risk of developing TA-GVHD in immunocompetent individuals even after receiving transfusion from unrelated donors [12]. This accounts for the high incidence of TA-GVHD in the Japanese population and as a result it has been made a national policy to irradiate all blood components before transfusion in Japan. Similar steps are also being considered in USA after the death of a patient with TA-GVHD who was given unrelated blood transfusion.

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#### Authors' contributions/Wkład autorów

According to order.

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#### Conflict of interest/Konflikt interesu

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#### Ethics/Etyka

The work described in this article have been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments

involving humans; EU Directive 2010/63/EU for animal experiments; Uniform Requirements for manuscripts submitted to Biomedical journals.

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