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Case Report

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Transfusion-Associated Graft *vs* Host Disease in a Post-Coronary Artery Bypass Graft Patient

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Abstract

TA-GVHD is a rare, usually fatal complication of transfusion of blood and blood products containing viable T lymphocytes. Very rarely it may arise in an immunocompetent individual. There is an increased risk of TA-GVHD following bypass grafting and other surgical procedures where blood transfusion are required. Here we present a case of a 57 old patient who received 5 units of whole blood from his close relatives perioperatively and manifested unexplained anaemia, fever, skin rash which later became desquamating & cheilitis on his 19th POD. His CBC report suggested pancytopenia indicating bone marrow failure. Skin biopsy confirmed the diagnosis as chronic TA-GVHD, lichenoid type. His liver function deteriorated and he died subsequently on his 32nd POD. TA-GVHD develops when immunocompetent T lymphocytes of transfused blood able to engraft in the recipient's lymphoid tissues that fail to reject them. Those lymphocytes mediate immune response causing damage and dysfunction of the skin & other organs. Our patient showed all features of TA-GVHD that was complicated by sepsis and multiorgan failure despite aggressive management. Pathologists, surgeons, physicians and transfusion centers must be aware of this sinister complication of perioperative blood transfusion in any surgery, including CABG. Though fatal in >90% cases, it can be prevented by using irradiated blood. Patient parties must also be discouraged to donate blood to avoid this grave outcome.

Keywords: TA-GVHD, Post-CABG, Prevention, Blood transfusion

Introduction

Graft Versus Host Disease (GVHD) is a condition that can occur after Hematopoietic Stem Cell Transplantation (HSCT). It happens when the transplanted T-cells recognize the recipient's body as foreign and attack it. Solid organ transplantation, particularly bone marrow or stem cells, and transfusion of non-irradiated blood or blood products are the major risk factors of GVHD. In TA-GVHD, the donor T-cells (T lymphocytes) in a transfused blood or blood product attack the recipient's tissues including the skin, intestine, liver, and bone marrow. TA-GVHD is a clinical diagnosis and should be suspected if the recipient develops a fever, skin rash, and pancytopenia following a BT. Most common symptoms include erythematous, maculopapular skin rash, fever, elevated liver enzymes, hepatomegaly, and jaundice, in addition to nausea, vomiting, and diarrhea. Many transfusion reactions are not readily recognized, perhaps because signs and symptoms mimic other clinical conditions. TA-GVHD is probably underreported and the incidence in Bangladesh is perceived to be too low to warrant routine irradiation of cellular products for this group of patients. TA-GVHD usually occurs 5-10 days after the process of BT. However, symptoms of TA-GVHD can develop as early as three days and as late as 30 days. TA-GVHD first reported in immunocompromised patients and later was described even in immunocompetent hosts following transfusion when the donor was a first or second-degree relative with partially-HLA-matched. Here we present case where perioperative transfusion of blood from his 1st degree relative during OP-CABG gave rise to chronic TA-GVHD, which ultimately lead to his death [1-3].

Case Summary

A 57-year-old businessman presented on the 19th Post-Operative Day (POD) of Off-Pump Coronary Artery Bypass Graft (OP-CABG) surgery with the complaints of high-grade continued fever, skin rash, oral ulcer and vague abdominal pain for 11 days. He also had significant weight loss. The patient had received 5 units of non-

irradiated packed red cells (1 from his brother, 1 from nephew, others from unrelated donors) perioperatively. His past medical history included chronic coronary disease, hypertension and diabetes mellitus.

At admission, the patient had generalised erythroderma, morbiliform pruritic rash involving face, abdomen, and limbs (Figure 1). There was cheilitis and oral thrush. He was febrile (103° F) and mildly anaemic. Bibasal end-inspiratory crackles were found. There was no evidence of wound infection. Broad-spectrum antibiotics, antifungal and antiviral drugs were started.

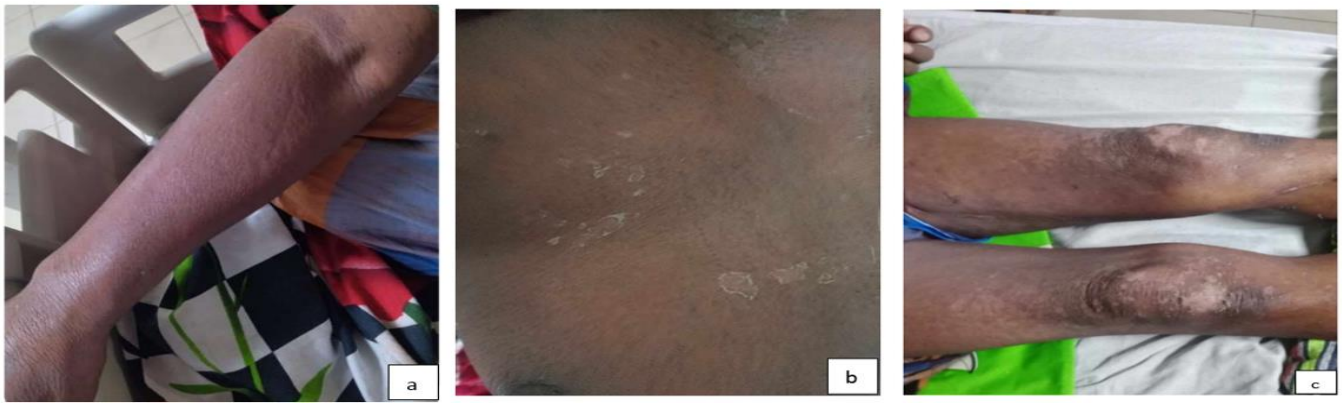

Figure 1: a) Rash on admission, b) and c) Rash 1 week later.

On investigation, CBC showed pancytopenia with low reticulocyte count, hepatic enzymes were elevated; but other tests including repeated blood and urine cultures, Dengue serology, viral markers, X-ray chest, echocardiography, ultrasonography of abdomen, procalcitonin revealed no evidence of infection (Table 1,2).

Parameters	**12th Aug 23**	**13th Aug 23**	**14th Aug 23**	**15th Aug 23**	**16th Aug 23**
Haemoglobin (g/dL)	9	8.6	8.7	9.2	9.2
Total WBC count (/cmm)	500	310	210	130	240
Neutrophil (/cmm)	80	30	30	20	20
Lymphocyte (/cmm)	305	280	170	110	210
Eosinophil (/cmm)	100	0	10	10	0
Plateletes (/cmm)	1,90,000	1,34,000	73,000	46,000	20,000
ESR (mm in 1st hr)	25	8	11	7	5

Table 1: Complete blood count of the patient.

Test	**Result**
ICT for Malaria	Negative
Triple Antigen Test	Negative
Dengue Ig M, Ig G	Negative
CRP	24 mg/dL
Blood C/S (FAN method)	No growth
Urine RME	Normal study
Fibrinogen	203.6 mg/L
FDP	87.19 µg/mL
D-Dimer	12.56 µg/mL
Lactate	21 mg/dL
Serum Procalcitonin	0.38 ng/mL 0.29 ng/mL (0.05-0.5: Local bacterial infection possible)
Serum Ferritin	456 micro g/L

Table 2: Other investigation profile of the patient.

Despite all those medications, the pancytopenia worsened and fever never subsided. The rash transformed to generalized desquamation with intense itching (Figure 1).

Skin biopsy was sent for histopathological examination. Skin histopathology report stated the diagnosis as-Chronic TA-GVHD, lichenoid type (Figure 2-4).

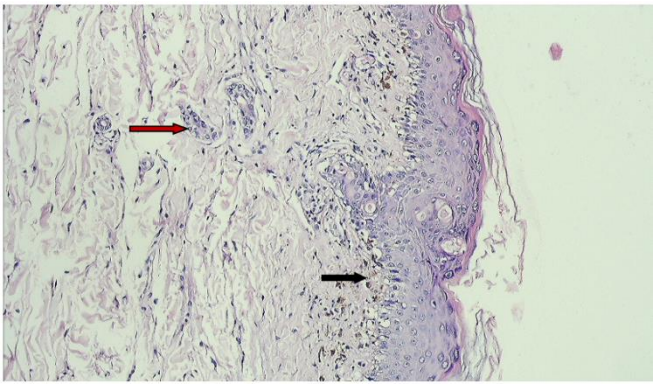

Figure 2: H&E staining of skin biospy showing perivascular lymphocytic infiltrate (Red arrow) and interface dermatitis (Black arrow) (10X).

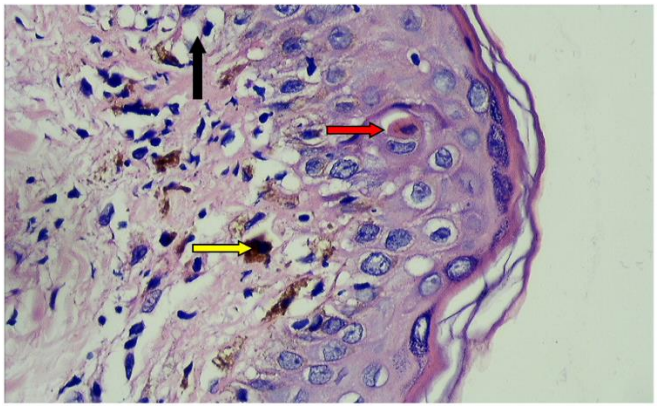

Figure 3: H&E staining of skin biospy showing dyskeratotic keratinocytes (red arrow), basal layer vacuolar degeneration (black arrow) and melanophages (yellow arrow) (40X).

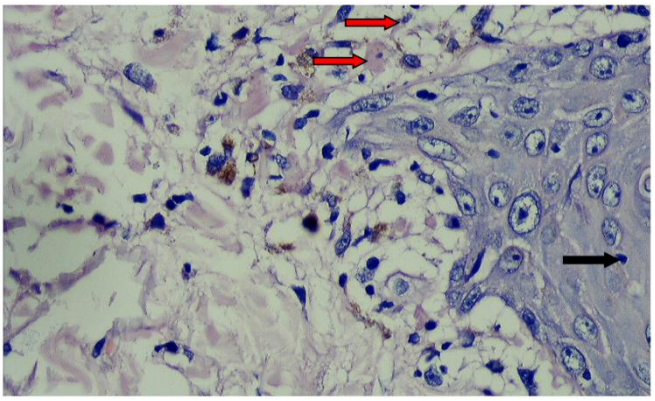

Figure 4: H&E staining of skin biospy showing satellite cell necrosis (red arrow) and exocytosis (black arrow) (40X).

While preparing for bone marrow studies and urgent allogenic Hematopoietic Stem Cell Transplantation (HSCT), the patient expired on the 32nd POD of his successful OP-CABG surgery.

Discussion

Likelihood of developing TA-GVHD is dependent upon the number and viability of the transfused lymphocytes in cellular blood components, and also upon the extent of immunosuppression and degree of HLA antigen sharing between donor and recipient. It is suggested that the presence of a shared HLA haplotype in blood donors and recipients may be more important in the development of TA-GVHD than the patient's immune status, which happened in our case [4]. Typically seen in immunocompromised individuals, TA-GVHD in immunocompetent individuals appears most commonly following CABG and other cardiovascular surgery. This is thought to be due to the use of relatively fresh blood with more viable lymphocytes- increasing the chance of engraftment. Diagnosis may remain elusive. Important differential diagnoses to be considered were acute viral infection, hypersensitivity to drugs (Maculopapular drug eruption or lichenoid drug eruption) and dengue fever, but such intense exfoliation of skin and oral thrush are unlikely in all of them [5]. Management of TA-GVHD is difficult and administration of immunosuppressive therapy poses a risk of aggravation or invitation of infection. Diagnosis can be confirmed histologically by skin biopsy. Acute GVHD usually affects skin: ears, palms, soles, lateral neck, cheeks and upper back. Acute extracutaneous GVHD involves liver, gastrointestinal tract, lungs and lymphoid tissue. Chronic GVHD affects primarily the skin; however, nearly all organ systems can be involved (mucous membranes, liver, lung, eye, joints and fascia, gastrointestinal tract, genitalia). The most important findings in Acute TA-GVHD are superficial perivascular lymphocytic infiltrate, exocytosis, basal vacuolation, interface dermatitis, melanin incontinence & eosinophilic keratinocytes with pyknotic nuclei at all levels of the epidermis. In Chronic TA-GVHD, the histological features may be or 3 types- lichenoid, sclerodermoid or rarely psoriaform/poikiloderma. The most important clues are: satellite cell necrosis and absence of eosinophils (though it can be rarely present). HLA typing and other molecular methods can also be used to demonstrate donor lymphocyte engraftment. Death follows in >90% of TA-GVHD cases as, in majority of the scenarios the possible cure by allogenic HSCT is nearly impossible to arrange before time runs out.

Conclusion

Pathologist should make meticulous diagnosis correlating with patient history & clinical features, as skin biopsy can be used as an important tool identifying TA-GVHD in patients. Awareness among doctors, proper counseling of patients and attendants before blood transfusion, and use of irradiated blood products are the most feasible options for prevention of TA-GVHD in CABG as well as in other surgical or nonsurgical indications of blood transfusion.

Author's contributions

Dr. Sayedatus saba: Conceptualization, writing, editing, final draft, investigations

Dr. Noshin Tabassum: Editing, clinical information of the patient, patient treatment, investigation

Prof. Dr. Mohammed Kamal: Investigation, supervision, final draft

Prof. Dr. Md. Khalequzzaman: Clinical information of the patient, patient treatment, investigation

Dr. Md. Mazharul Islam: Clinical information of the patient, patient treatment, investigation

Dr. Md. Mustain Billah: Assisted in CABG surgery, editing.

Declaration of conflicting interests

There are no conflicting interests.

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Research ethics statement

Approval of the research protocol by an institutional reviewer board: N/A.

Informed consent: Informed written consent was taken from the patient

Registry and the registration no. of the study/trial: N/A.

Animal Studies: N/A