Case Report

GVHD after LT

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Graft versus host disease after liver transplantation: A case report

Sencan Acar[1], Mutlu Arat[2], Tulay Tecimer[3], Kamil Yalcin Polat[4], Murat Akyildiz[5]

[1]Department of Gastroenterology and Organ Transplantation Center, Sakarya University Faculty of Medicine, Sakarya, Turkey; [2]Department of Haematology and Bone Marrow Transplantation Unit, Bilim University Faculty of Medicine, Sisli Florence Nightingale Hospital, Istanbul, Turkey; [3]Department of Pathology, Acibadem University Fculty of Medicine and Nisantasi Pathology Center, Istanbul, Turkey; [4]Department of General Surgery and Organ Transplantation Center, Memorial Atasehir Hospital, Istanbul, Turkey; [5]Department of Gastroenterology and Organ Transplantation Center, Koc University Faculty of Medicine. Istanbul, Turkey

Abstract

Graft Versus Host Disease (GVHD) is a severe immunological-clinicopathological condition mediated by healthy T-lymphocytes in donor tissue against the immunosuppressed host tissue and rarely seen after solid organ transplantation (SOT). A 72-year old male patient underwent cadaveric liver transplantation. On day 34 of the postoperative follow-up, the patient developed fever, generalized skin rash and hemorrhagic lesions in the oropharynx. Skin biopsy was consistent with GVHD. Despite high-dose corticosteroid treatment, he died on postoperative day 51. Although it is seen rarely after liver transplantation, GVHD is an important clinical entity for which early diagnosis is critical due to its high rates of mortality.

Keywords: Graft versus host disease; hemorrhagic lesions; liver transplantation; pancytopenia; rash.

Introduction

Graft versus Host Disease (GVHD) is a rare complication of hematopoietic stem cell transplantation. It is a clinical syndrome mediated by healthy T-lymphocytes in the donor tissue, which indicates severe immunological reaction against host tissues and consequent organ dysfunction. This rare condition may develop much less frequently after liver transplantation (LT). The incidence is 0.06-2% with a mortality rate over 75%. It usually develops 2 and 6 weeks after LT.[1–3] It gives clinical symptoms with fever, rash, diarrhea and cytopenia. Generally, liver function tests are not affected. Currently, high-dose corticosteroids are usually administered, although there is no effective treatment. The report herein presents a patient with GVHD who developed following deceased donor LT (DDLT).

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Corresponding author: Sencan Acar; Sakarya Universitesi Egitim ve Arastirma Hastanesi, Gastroenteroloji Anabilim Dali, Sakarya, Turkey
Phone: +90 533 769 71 96; **e-mail:** sencanacar@yahoo.com

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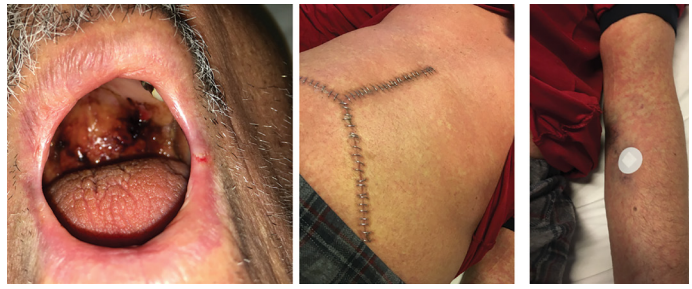

Figure 1. Generalized skin rash and haemorrhagic lesions in oropharynx.

Case Report

A 72-year old male patient underwent cadaveric liver transplantation in March 2018 due to cryptogenic liver cirrhosis and hepatocellular carcinoma (HCC). The donor was a 56-year old AB Rh (+) female with a history of surgery due to a lesion in the posterior fossa (pathology consistent with epidermal cyst). Brain death had occurred due to sudden-onset increased intracranial pressure and her liver had been transplanted. The recipient's explant pathology revealed moderately differentiated nodular-infiltrative HCC of 2 cm and autoimmune hepatitis in the non-tumor areas of the liver.

On day 34 of the recipient's postoperative follow-up under ongoing tacrolimus and steroid treatment, the fever, generalized skin rash and hemorrhagic lesions in the oropharynx developed (Fig. 1). Pancytopenia developed and gradually deepened. He was not receiving mycophenolate mofetil therapy. Also, CMV DNA was negative. Skin biopsy revealed parakeratosis in focal epidermis regions, mild acanthosis, abundant dyskeratotic cells, occasional apoptotic cells in the basal layer, hydropic degeneration, vascular proliferation in the upper dermis, pigment-loaded macrophages and few lymphocytes around some of the vessels. PAS-AB staining was insignificant. The available findings and clinical presentation of the patient, along with hematology and dermatology consultations, led to a GVHD-Grade II result.

Pulse steroid treatment and plasmapheresis were administered due to the presence of GVHD. Tacrolimus treatment was discontinued. Diarrhea developed in the follow-up of the patient and no significant findings were noted in the stool analysis. PRA Class I and II antigens were found to be negative in the patient. The patient's blood test results after LT are shown in Table 1. Despite the high-dose steroid treatment and supportive treatments (G-CSF, erythrocyte or platelet replacement), the patient died on the postoperative day 51.

Table 1. The patient's post-LT blood test results

Post-LT	AST	ALT	LDH	CRP	HB	PLT	WBC	NEUT	LYMP
Day 0	438	206	588	33.9	10	59	3020	1790	610
Day 7	8	24	165	30.4	11.4	107	11110	8740	900
Day 14	11	19	145	27.2	11.4	313	13300	10720	1120
Day 21	7	9	132	8.2	11	261	11520	9670	1120
Day 28	10	9	135	11.9	11	139	9220	7930	400
Day 34	74	19	892	116.4	10.4	53	4320	3000	780
Day 35	56	17	1121	115.2	8.1	34	2780	1250	900
Day 36	36	15	981	54.2	7.2	23	1580	710	830
Day 37	70	31	914	53.6	7.4	25	1040	470	520
Day 38	156	93	1091	70.9	7.7	27	250	50	200
Day 39	48	62	806	240.1	7.5	22	110	10	100
Day 40	20	44	629	139.9	9.2	23	50	0	40
Day 41	13	31	483	126.5	8.7	17	40	10	40
Day 42	10	19	423	118	8.1	14	30	0	40
Day 43	8	12	377	70	7.1	7	30	0	40
Day 44	9	8	392	40.1	7.7	43	70	0	0
Day 45	9	7	498	63.3	9.5	22	70	0	0
Day 46	8	6	512	101.7	9.2	11	50	0	0
Day 47	9	6	461	50	8.9	33	20	0	0
Day 48	6	3	337	25.6	7.1	14	30	0	0
Day 49	6	2	289	21.8	6.6	24	70	0	0
Day 50	6	4	310	48.1	8.1	11	20	0	0
Day 51	21	2	371	337.9	8.2	10	30	0	0

LT: Liver transplantation; AST: Aspartat aminotransferase; ALT: Alanin aminotransferase; LDH: Lactate dehydrogenase; CRP: C-reactive protein; Hb: Hemoglobin; PLT: Platelet; WBC: White blood cell; Neut: Neutrophil; LYMP: Lymphocyte.

Discussion

Graft Versus Host Disease (GVHD) is a severe immunological-clinicopathological condition mediated by the healthy T-lymphocytes in donor tissue against the immunosuppressed host tissue. GVHD was first described by Billingham in 1966. Immunocompetent cells of the donor are defined as cells that react against the recipient antigen. There are 3 conditions required for GVHD to develop; in order for the graft to generate an antigenic stimulus in the recipient. It must contain immunoblot cells, contain foreign tissue compatibility antigens, the recipient must be immunosuppressed and unable to respond to foreign lymphoid cells.[4]

In the pathogenesis of GVHD after solid organ transplantation, donor suppressive and cytotoxic T cells as well as lymphocyte-secreting helper T lymphocytes are involved in response to receptor cells. The possibility of GVHD development after SOT varies depending on the amount of lymphoid tissue present in the organs. Accordingly, GVHD is more common in the pancreas-spleen and small intestine after more lymphoid tissue.[5]

Tissue compatibility antigens are glycoprotein structures on the surface of nucleated cells. These antigens are encoded by various genes on different chromosomes. The major tissue compatibility antigens, the most important ones, are encoded in the HLA region on the short arm of chromosome 6. It's stated that graft versus host disease can develop even in transplants performed between individuals with fully compatible HLA antigens. This suggests that minor tissue antigens also play a role in graft versus host reaction.[6]

The probability of GVHD development in solid organ transplantation varies depending on the amount of lymphoid tissue present in the organs. According to this, GVHD is more common in the pancreas-spleen and small bowel transplantation where lymphoid tissue is abundant.[5]

The risk of GVHD increases as the recipient age increases. Thymus tissue is more deficient in elderly patients than in younger patients, allowing the formation of GVHD-inducing T cell clones. The risk of GVHD is higher in male patients who receive bone marrow, especially from a female donor. The role of the mechanism of the Y antigen in male patients.[7]

In acute GVHD, on immunofluorescent examination, 39% of cases had IgM deposition in the dermo-epidermal region, as well as Ig and C3 deposition in the perivascular region. Biopsy specimens of patients with acute GVHD showed significant CD4 and CD8 T lymphocytes as well as CD 56 NK cells.[8]

Although studies in the literature are mostly on post-bone marrow transplantation and it is stated that CMV seropositivity in both donor and the recipient increases the risk of GVHD development.[5,9]

In a review of 61 studies covering 87 patients, pancytopenia showed that the age difference between donor and recipient, the diagnosis of initial symptoms, or the time to start of treatment was statistically significant.[10]

Glucocorticoids reduce the number and function of lymphocytes. In

the treatment of acute GVHD, it is generally recommended to initiate high-dose pulse therapy or at a dose of 2 mg /kg /day in moderate to advanced patients. Approximately 50% of patients with Grade II and IV respond to systemic corticosteroid therapy and 25% of patients had a complete recovery. Cyclosporine and ATG can be added to the treatment in patients without steroid response.

Conclusion

Although seen rarely after liver transplantation, GVHD is an important clinical entity for which early diagnosis is critical due to the high rates of mortality. Our case is presented to raise awareness because of the development of GVHD after SOT, its confusion with other rare post-transplant conditions, and the need for early treatment. Studies to continue to reduce the mortality rate with the effectiveness of the new generation of drugs.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

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Conflict of Interest: The authors have no conflict of interest to declare.

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