

**Letter TJH-2018-0057.R1**

Submitted: 6 February 2018

Accepted: 2 July 2018

DEMODOCIDOSIS ACCOMPANYING ACUTE CUTANEOUS GRAFT-VERSUS-HOST DISEASE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

Pelin Aytan

Baskent University Teaching and Research Hospital Bone Marrow and Stemcell Transplantation Center - Hematology

Dadaloglu mah. 2591 sk. No:4/A Yuregir/ADANA Adana 01250 Turkey

T: (322)3272727-2028

drpelinaytan@gmail.com

Pelin Aytan

Baskent University Teaching and Research Hospital Bone Marrow and Stem cell Transplantation Center - Hematology Dadaloglu mah. 2591 sk. No:4/A

Yuregir/ADANA , Adana 01250 Turkey

MAHMUT YERAL

Baskent Ü. adana araştırma ve uygulama hastanesi. hematoloji kliniği . yüreğir /ADANA , Adana 01250 Turkey

CİGDEM GEREKLİOĞLU

Baskent University, faculty of medicine - family medicine Adana, Turkey

Nazim Emrah Kocer

Baskent Üniversitesi Tıp Fakültesi Adana Uygulama ve Arastirma Merkezi-Pathology Adana, Turkey

Nurhilal BUYUKKURT

Baskent University Adana Education and Research Centre - Hematology  
Baskent Universitesi Adana Egitim ve Arastirma Merkezi Yuregir , Adana  
01240, Turkey

ILKNUR KOZANOGLU

Baskent University Medical Faculty - Physiology  
Baskent University Adana Hospital , Adana 01250 Turkey  
Baskent University - Adana Adult Bone Marrow Transplantation and Stem  
Cell Therapy Cen-ter

Hakan Ozdogu

Baskent University - Hematology Yuregir Hospital , Adana 01250, Turkey

Can Boga

Baskent University Faculty of Medicine - Hematology  
Baskent University Hospital Yuregir , Ankara 01250, Turkey

A thirty-nine year old woman with acute myeloid leukemia presented to the Stem Cell Transplantation Center Day Care Unit with a non-pruritic face eruption. She developed the eruption 28 days after undergoing an allogeneic hematopoietic stem cell transplantation (SCT). She was allografted with  $6.12 \times 10^6$  non-manipulated CD34+ cells from her full-matched sibling after conditioning with busulphan ( $12.8 \text{ mg/m}^2$ ), fludarabine ( $150 \text{ mg/m}^2$ ), anti-thymocytoglobulin ( $30 \text{ mg/kg}$ ) and total body irradiation ( $400 \text{ Gy/day}$ ). Graft-versus-Host prophylaxis included methotrexate  $12 \text{ mg/day}$  for 3 days and cyclosporin A  $75 \text{ mg}$  twice daily. There had been no recent changes of the medication. The patient was engrafted with neutrophils and with thrombocytes on day 11. Regimen related toxicity was mild with first grade for oral mucosa according to Bearmanscale (1). The findings of the physical examination were patchy and confluent erythema of the face, suspicious for cutaneous acute GVHD. There was no other skin involvement except palms and soles. Also neither intestinal nor hepatic acute GVHD occurred. Laboratory evaluation revealed a WBC count of  $12000/\mu\text{L}$ , a hemoglobin level of  $11.5 \text{ g/dl}$ , a platelet count of  $158000/\mu\text{L}$  and an absolute neutrophil count  $8400/\mu\text{L}$ . A skin  $4 \text{ mm}$  punch biopsy was performed (2). There were lymphocytes and polymorphic neutrophils that attack hair follicles and two civatte bodies. Histochemically demodex folliculorum was diagnosed with PAS staining within the hair follicles (Figure 1A-1B). Even lymphocytes attacking hair follicles and civatte body preoccupy GVHD, demodex folliculitis can mimic acute GVHD (Figure 1C-1D). Demodicidosis was treated successfully with local 1% metronidazole and 5% permethrin. Methylprednisolone was also administered from the beginning of the symptoms and the dosing was reduced  $8 \text{ mg}$  every week. The skin eruptions on the face and the neck resolved on day +52.

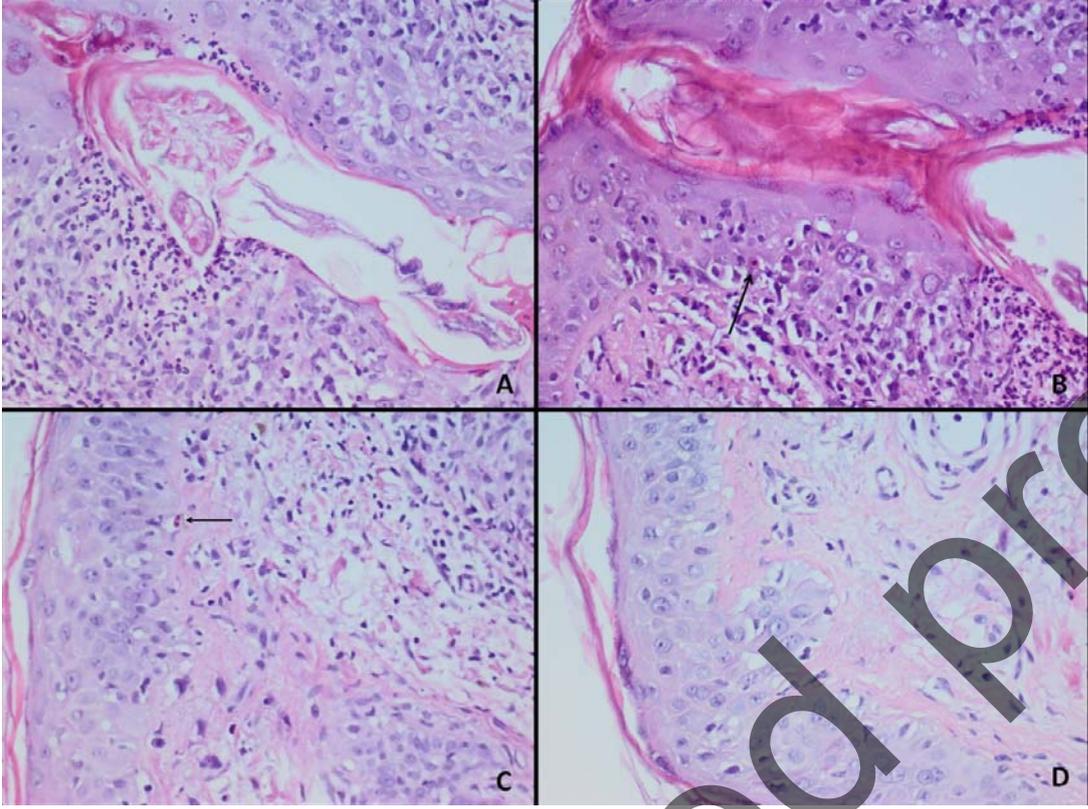
Demodex folliculitis after allogeneic SCT is seen rarely and as far as we know, our case is the sixth reported case (3-6). The most important differential diagnosis of Demodex folliculitis within the first 100 days after allogeneic SCT is acute GVHD. The infestation by Demodex can be associated with immune suppression. The differential diagnosis of facial erythema after bone marrow transplantation includes acute GVHD, drug eruptions, systemic lupus erythematosus, viral exanthema, toxic erythema of chemotherapy, drug induced photosensitivity and photodermatitis (3). In the present case there were eruptions on the cheek, forehead and jaw regions which all can be seen in both acute GVHD and demodex folliculitis. However there was also palmar erythema of upper extremities which is not a feature of demodicidosis. As confirmed with pathological examination, there were both findings of acute GVHD (presence of civatte bodies, lymphocyte exocytosis, diffuse basal vacuolization in epidermis) and demodicidosis (presence of demodex follicularum).

It should be kept in mind that GVHD may be associated with demodicidosis and Demodex infestation should be included in the differential diagnosis of eruptions in patients with hematological malignancies receiving chemotherapy and after SCT. Therefore when the diagnosis of acute GVHD is uncertain, early skin biopsy has to be performed after allogeneic SCT because early treatment of a possible demodex infestation would prevent progression of GVHD.

#### REFERENCES

1. Bearman SI, Applebaum FR, Buckner CD, Petersen FB, Fisher LD, Clift RA, Thomas ED. Regimen related toxicity in patients undergoing bone marrow transplantation. *J Clin Oncol* 1988;6:1562-1568.
2. Hillen U, Häusermann P, Massi D, Janin A, Wolff D, Lawitschka A, Greinix H, Meyer R, Ziemer M. Consensus on performing skin biopsies, laboratory workup, evaluation of tissue samples and reporting of the results in patients with suspected cutaneous graft-versus-host disease. *J Eur Acad Dermatol Venereol.* 2015;29:948-54.
3. Jonathan Cotliar. Demodex Folliculitis Mimicking Acute Graft-vs-Host Disease. *JAMA Dermatol.* 2013;149:1407-1409
4. Lotze C, Krüger WH, Kiefer T, Swensson O, Herbst EW, Schüler F, Busemann C, Dölken G. Facial rash mimicking cutaneous acute graft-versus-host disease after allogeneic stem cell transplantation for osteomyelofibrosis: was Demodex the culprit? *Bone Marrow Transplant.* 2006;37:711-712.
5. Aisa Y, Mori T, Tanikawa A, Takae Y, Kato J, Ikeda Y, Okamoto S. Demodicidosis as a cause of facial eruption developing early after allogeneic hematopoietic stem cell transplantation. *Transplant Int.* 2008; 21:1192-1193.
6. Román-Curto C, Meseguer-Yebra C, Cañueto J, Fraile-Alonso C, Santos-Briz A, Vázquez L, Fernández-López E. Demodicidosis stimulating acute graft-versus-host disease after allogeneic stem cell transplantation in one patient with acute lymphoblastic leukemia. *Transpl Infect Dis.* 2012;14:387-390.

Figure 1. A) Demodex mite B) Civatte body in the follicle epithelium containing demodex and lymphocyte exocytosis C) Civatte body in the epithelium far from the follicle D) Diffuse basal vacuolisation in epidermis (PAS staining, magnification x40)



Uncorrected proof