Published in final edited form as:

Am J Dermatopathol. 2015 July ; 37(7): 523–529. doi:10.1097/DAD.0000000000000357.

Histopathologic features of cutaneous acute graft-versus-host disease in T-cell-depleted peripheral blood stem cell transplant recipients

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Abstract

T-cell-depleted (TCD) allogeneic hematopoietic stem cell transplantation demonstrates similar efficacy and reduced incidence and severity of graft-versus-host disease (GVHD) in appropriately selected patients versus T-cell-replete transplantation. The histopathology of cutaneous acute GVHD (aGVHD) following TCD peripheral blood stem cell transplants (PBSCT) is not described.

We identified 13 cases of patients post TCD-PBSCT, with definitive aGVHD, and 20 cases of non-aGVHD skin rash in patients after TCD-PBSCT, during multidisciplinary review by a dermatopathologist, dermatologist and transplant physician, incorporating clinical presentation, therapeutic response, and histopathology data. Histopathologic features of aGVHD and non-aGVHD skin rash in TCD-PBSCT patients were compared to each other, and also to features recently reported for non-TCD transplant recipients.

AGVHD and non-aGVHD skin rash in TCD-PBSCT patients' biopsies had similar rates of epidermal acanthosis, dermal melanophages, neutrophils, plasma cells, eosinophils and extravasated erythrocytes. While satellitosis, exocytosis and adnexal involvement slightly favored

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Conflicts of Interest

For the remaining authors none were declared

aGVHD, more notable differential findings favoring aGVHD, were diffuse (versus focal/absent) basal vacuolization (77% aGVHD vs 25% non-aGVHD rash), involvement of the entire epidermis (versus partial thickness) by necrotic keratinocytes (42% aGVHD vs 0% non aGVHD rash), and non-dense (rather than exuberant) inflammatory infiltrates (77% vs. 20%).

After filtering features seen in all TCD samples (epidermal acanthosis, dermal melanophages, neutrophils, plasma cells, eosinophils and extravasated erythrocytes), the most distinct features belonging to aGVHD-positive TCD samples were diffuse basal vacuolization, slight rather than dense inflammatory infiltrates, and necrotic keratinocytes involving the entire epidermis. Awareness of these features may help when evaluating a skin rash occurring after a TCD transplant.

Keywords

T-cell depletion; Graft-versus-host disease; peripheral blood stem cell transplant

Introduction

For patients with hematologic malignancies, T cell-depleted (TCD) bone marrow transplants (BMT) and peripheral blood stem cell transplants (PBSCT) from related and unrelated donors have proven to be effective, and have demonstrated decreased incidence and severity of graft versus host disease (GVHD).¹⁻⁵ Although a variety of methods of TCD have been studied over the years for bone marrow and PBSC, automation of ex vivo CD34 positive selection of stem cells has facilitated its wider application⁶. Given its success, the FDA recently approved the use of this technology for patients with acute myelogenous leukemia (AML) in first complete remission undergoing matched related donor transplantation. It is expected that the spectrum of patients and diagnoses will expand. While GVHD is indeed reduced in TCD transplant recipients, it still occurs. Acute GVHD (aGVHD), a diagnosis that is no longer limited to the first 100 days post-transplant,⁷ most commonly affects the skin and classically presents as a maculopapular rash with associated pruritus and erythema.

While controversial, pathologic evaluation by cutaneous biopsy continues to be a routine part in the diagnostic workup of patients who develop rashes following hematopoietic stem cell transplantation (HSCT). The histopathologic features of acute cutaneous GVHD have been generally described, but not the findings specific to TCD PBSCT recipients.⁸

In our study, we specifically describe the histopathologic features of cutaneous aGVHD in TCD PBSCT recipients, and we compare the frequencies of these features to their frequencies in TCD PBSCT recipients with non aGVHD skin rashes. We further compare the findings of our aGVHD TCD PBSCT patients to previously reported findings of both aGVHD and non-aGVHD skin rashes in recipients of T-cell (T) replete transplants.

Materials and Methods

Patient selection

Data was gathered under an Institutional Review Board and Privacy Board (IRB/PB) approved waiver of authorization. Using a clinical research database, adult patients were identified who had received allogeneic TCD PBSCT at our cancer center between 2008 and 2011. These patients were cross-referenced with a pathology database and slide archive, identifying 37 patients who had undergone skin punch or shave biopsies for rashes that were clinically concerning for aGVHD, and for which histopathologic slides were available for review. Each patient's case was reviewed by a multidisciplinary team that included a dermatopathologist, dermatologist, and BMT physician. Consensus diagnoses were based on clinical presentation, therapeutic responses, and histopathology with case by case consideration of additional organ involvement. Based upon consensus diagnosis, patients for whom a definitive interpretation was possible were divided into two groups, aGVHD (n=13) and non-aGVHD skin rash (n=20). The remaining four patients showed intermediate, non-diagnostic features.

Histopathological analysis

Hematoxylin and eosin stained sections were evaluated at least twice, each time by a different expert dermatopathologists (MPP, TH, KJB) including once at initial evaluation, once at a clinical management meeting, and then again in the context of the multidisciplinary meeting by one dermatopathologist, resulting in either a single or differential diagnosis at each evaluation. Histopathologic findings were classified according to standard criteria.⁹

Prior to final consensus diagnosis, slides were evaluated by 2 dermatopathologists (MPP and TH), who were blinded to the patients' clinical data and prior histopathologic diagnoses, for presence and quantification of the following histopathologic features: epidermal thickness, intercellular edema (spongiosis), dermal-epidermal interface alteration (basal vacuolization), epidermal keratinocyte necrosis (number and localization), adnexal epithelial necrosis, intraepidermal lymphocyte "satellitosis", lymphocytic exocytosis, inflammatory infiltrate (density, pattern, and composition), and extravasated erythrocytes. Specifically, the presence of eosinophils, neutrophils, plasma cells and melanophages in the dermis were noted. Adnexal involvement was reported when excretory ducts of sweat glands, follicular epithelium and sebaceous glands demonstrated basal cell vacuolization with single necrotic keratinocytes. Inflammatory patterns were described as perivascular, lichenoid, or mixed. Interface alteration was assigned a grade from 0–3, with grade 0 representing absence of significant histopathologic changes; grade 1 indicating focal or diffuse vacuolar changes of epidermal basal cells and keratinocytes of the upper epidermis; grade 2 demonstrating basal vacuolar degeneration, single cell dyskeratosis and spongiosis; and grade 3 corresponding to the same changes as grade 2, with separation of the dermoepidermal junction secondary to clefts and spaces in the basal and suprabasilar layers of the epidermis, as previously described.¹⁰

Descriptive Analysis

First we assessed agreement between pre-consensus and consensus diagnosis, by direct comparison, having excluded cases for which no definitive consensus diagnosis was possible. We then compared frequencies of each histopathologic feature between TCD aGVHD and non-aGVHD skin rash TCD PBSCT recipients as percentages. Specifically, we looked for abnormal skin alterations that were shared by aGVHD and non-aGVHD skin rash TCD cases, to elucidate baseline changes that might be induced by the T-cell-depleted graft itself. We then assessed for features that appeared to be markedly different between aGVHD and non-aGVHD skin rash TCD cases, which would be helpful to confirm or exclude an aGVHD diagnosis.

Finally, we compared our aGVHD data, as percentages, to previously reported frequencies of the same features in specimens from BMT recipients of HLA-matched sibling donorgraft recipients⁹ diagnosed with aGVHD, looking for shared or discrepant features of aGVHD between the two patient populations. We further compared histologic features of skin rash specimens (not attributable for aGVHD) from our TCD patients to those from previously reported T replete transplant patients¹⁰ to see if we could find any shared baseline characteristics among non-GVHD rashes of the entire cohort of transplant recipients that might be helpful in ruling out aGVHD.

Results

Clinical data

Following multidisciplinary review, consensus diagnosis was reached for 33 of the 37 patients, with aGVHD diagnosed in 13 patients, and 20 patients determined not to have aGVHD. For 4 patients with complicated clinical courses and comorbid conditions, a consensus diagnosis could not be reached following thorough review. The remaining patients included in this study developed rashes in the post-transplant period that were clinically concerning for aGVHD.

Patients' ages ranged from 28 to 68 years (median 53.1 years), and included 25 male and 12 female patients. Among the aGVHD patients, 3 (23%) died of complications from GVHD. Biopsy specimens were obtained on different days post-transplant depending on when patients presented with skin rash, and ranged from day +10 to >2 years (overall median 152 days; aGVHD group median 121 days; non-aGVHD skin rash median 155.5 days; equivocal group median 180 days). The documented clinical differential diagnoses for patients most commonly included GVHD (37 biopsies, 100%), hypersensitivity to drug/adverse drug reaction (11 biopsies (30%)), viral exanthem (5 biopsies (14%)), and dermatitis of other or unknown etiology (5 biopsies (14%)).

Histopathologic data

See table 1 for details

Histopathologic features of aGVHD vs non-aGVHD skin rash in TCD PBSCT recipients (table 2)

Similar frequencies of the following features were seen in aGVHD and non-aGVHD skin rash specimens: marked epidermal acanthosis (54% and 65%), dermal neutrophils (31% and 25%), plasma cells (39% and 35%) and melanophages (100% and, 90%). Extravasated erythrocytes in the dermis were common in both groups, but slightly more frequent in aGVHD (69% vs 55%). Adnexal involvement was slightly increased in aGVHD (77% vs 45%). Eosinophils were common to both groups, but slightly less frequent in aGVHD (31% vs. 65%).

Features more common to aGVHD TCD samples versus non-aGVHD samples included presence of diffuse basal vacuolization (77% vs 25%), presence of any single necrotic keratinocytes per high-power field (HPF) (92% vs 45%), and >3 single necrotic keratinocytes per HPF (31% vs 5%). The site of necrotic keratinocytes was evaluated in biopsies from 12 aGVHD and 9 non-aGVHD skin rash patients. The aGVHD group showed more full thickness epidermal involvement by necrotic keratinocytes (42%) while the non-aGVHD skin rash group demonstrated necrotic keratinocytes limited to the basal and suprabasilar layers of the epidermis (100%). Satellitosis was increased in aGVHD patients (77% vs 30%). Exocytosis was also increased in aGVHD (92% vs 65%). aGVHD biopsies showed an increased presence (100% vs 65%) and severity (grade 2, 77% vs 25%) of interface dermatitis. Finally, a slight inflammatory infiltrate was more common in aGVHD TCD patients than in non-aGVHD skin rash patients (77% vs. 20%) which showed more marked infiltrates.

We controlled for shared features seen in all TCD samples (epidermal acanthosis, dermal melanophages, neutrophils, plasma cells, eosinophils and extravasated erythrocytes). Without these features, the most strikingly distinct features belonging to aGVHD-positive TCD samples were diffuse basal vacuolization, slight rather than dense inflammatory infiltrates, and necrotic keratinocytes involving the entire epidermis.

Histopathologic features of aGVHD in TCD vs T replete transplant recipients (table 3)

Comparison of our 13 TCD aGVHD cases with a previously reported T replete aGVHD cohort of 38 cases¹⁰ confirms that, as expected, there are features common to aGVHD regardless of whether or not the graft is T-cell depleted. Other features appear to be unique to cutaneous aGVHD following TCD.

Common features of aGVHD in TCD and T replete specimens included the presence of any necrotic keratinocytes per HPF (92% vs. 87%), slight to absent (rather than marked) lymphocytic infiltrate (77% and 79%), spongiosis (54% and 55%), >3 single necrotic keratinocytes per HPF (31% vs 34%). Slightly differential features included a lichenoid pattern of the infiltrate (46% and 34%), diffuse basal vacuolization (77% vs 50%), and full thickness epidermal necrosis (42% vs 25%). Features seen most frequently in the TCD group included adnexal involvement (77% vs 16%), satellitosis (77% vs 24%), lymphocytic exocytosis (92% vs 37%), epidermal acanthosis (54% vs 8%), dermal melanophages (100% vs 37%), dermal neutrophils (31% vs 0%), dermal plasma cells (39% vs 3%), dermal

eosinophils (31% vs 3%), and extravasated erythrocytes (69% vs 13%). When comparing TCD aGVHD cases, TCD non-aGVHD skin rash cases, and T replete aGVHD cases, we found notable differences in adnexal involvement (77% vs 45% vs 16%), satellitosis (77% vs 30% vs 24%) and lymphocyte exocytosis (92% vs 65% vs 37%) respectively.

Histopathologic features of non-aGVHD-skin rash in TCD vs T replete recipients post transplant

Biopsies from non-aGVHD skin rashes in TCD and T replete patients demonstrated that the presence of any necrotic keratinocytes per HPF (45% and 58%), necrotic keratinocytes limited to the basal/suprabasilar layers versus full-thickness epidermis (100% and 96%), and a perivascular pattern of the inflammatory infiltrate (85% and 88%) were seen in similar frequencies in both cohorts.

In regards to distinguishing features, TCD non-aGVHD skin rashes showed a notably increased presence of inflammatory infiltrates (100% vs 40%). The majority of these were marked (80%). In contrast, all of the T replete non-aGVHD skin rashes which showed inflammation, all had only slight/mild infiltrates (100%). TCD vs T replete non-aGVHD skin rashes also showed a markedly increased frequency of dermal eosinophils (65% vs 5%). Unlike TCD specimens, epidermal acanthosis, diffuse basal vacuolization, adnexal involvement, satellitosis, lymphocyte exocytosis, extravasated erythrocytes, dermal neutrophils, melanophages, and plasma cells, (all frequently observed in any TCD specimens), were either absent or infrequent in the T replete non-aGVHD skin rashes.

Histopathologic features in biopsies from patients with equivocal diagnoses

Samples from our TCD patients in whom a consensus diagnosis could not be reached demonstrated a mixed distribution of the histopathologic parameters. As with the other biopsy samples from TCD patients, there was epidermal acanthosis (75%), spongiosis (75%), adnexal involvement (50%), satellitosis (50%), lymphocyte exocytosis (50%), extravasated erythrocytes (75%), dermal neutrophils (75%), melanophages (100%), and plasma cells (75%). Fifty percent of the cases had diffuse basal vacuolization. In only one case were there any single necrotic keratinocytes identified, and these involved only the basal/suprabasal epidermis.

Discussion

Randomized trials have shown that the transplantation of T cell replete filgrastim-mobilized PBSCs from HLA-identical donors accelerates engraftment but have variably shown increased acute and/or chronic GVHD, as compared with transplantation of bone marrow. TCD transplantation at this center and in a multicenter trial has demonstrated decreased incidence and severity of GVHD compared to T replete transplantation, even when used as the sole method of GVHD prophylaxis¹. The incidence of acute grade II-IV GVHD in the largest multicenter study has reported to be ~23%.

Furthermore, *ex vivo* TCD has not resulted in decreased antitumor activity. Recent FDA approval of the automated technology for CD34 selection, the most frequently used method of *ex vivo* TCD, has made TCD transplantation a reality for a greater number of transplant

centers, and is now being used for alternative grafts such as haplo-matched transplants alone or in combination with cord blood grafts. As a consequence, in order to assist new investigators in this field to understand potential differences in the presentation of transplant complications such as acute GVHD for these TCD transplants, we undertook this study.

Beyond the few cases which exhibit specific histopathologic features that may enable prompt diagnosis, the utility of skin biopsies in diagnosing and managing patients with suspected aGVHD in the post-transplant period is controversial.^{11–13} For example, one study in allogeneic BMT recipients reported that early histopathologic evaluation provided little value, and that clinical assessment was more useful in determining prognosis.¹⁴ Contradictory conclusions were drawn by a separate multicenter retrospective study of patients after reduced-intensity conditioning regimens, who reported that histopathologic diagnosis influenced clinical management and correlated with survival, ultimately recommending the continued use of skin biopsies in assessing patients for GVHD.⁸ Even when skin biopsies are performed, immunosuppressive therapy may be initiated before histopathologic review is complete, because of the adverse effect of GVHD on patients' quality of life and survival.

It has been shown that transplant recipients who do not develop clinically definable aGVHD may exhibit aGVHD-like histologic changes in their skin. Vassallo et al. studied biopsy samples obtained on day 100 post-transplant from seemingly normal-looking skin of BMT recipients, and demonstrated that 76% of patients had subtle histopathologic changes. They characterized 31% as having GVHD-like patterns including basal vacuolization, a perivascular infiltrate, scattered necrotic keratinocytes in the epidermis and follicular epithelium, and occasional satellitosis.¹⁵

To address this phenomenon, we first compared biopsies from our TCD transplant recipient cohorts, with and without aGVHD, to identify common histopathologic changes attributable to the TCD PBSCT and graft effect in the skin. We found that both aGVHD and non-aGVHD skin rashes post TCD exhibited significantly elevated rates of epidermal hyperplasia (acanthosis), dermal melanophages, neutrophils, plasma cells, eosinophils and extravasated erythrocytes. This was in contrast with traditionally reported features of biopsies from T replete transplant recipients, which have been described as exhibiting epidermal atrophy, and only minimal inflammation.¹⁰ One hypothesis to explain this finding is that the acanthosis and dermal inflammation post-TCD may be related to an imbalance in the T-reg/T_H17 axis. A model for this can be seen in psoriatic patient's skin, in which the effector cytokines IL-17 and IL-22 produced by T_H17 cells have been implicated in the development of both acanthosis and dermal inflammation.¹⁶

Fortunately, from a diagnostic perspective, in aGVHD post TCD, there are a number of features which we found to be more common when compared to non-aGVHD skin rashes post TCD, allowing for diagnostic distinction. These included *diffuse* basal vacuolization, *>3* necrotic keratinocytes per high power field, *full thickness* epidermal necrosis, satellitosis, exocytosis, interface changes beyond grade 2, and *slight* rather than marked inflammation. Conversely, the absence of diffuse basal layer vacuolization, satellitosis, and interface alteration, *<3* necrotic keratinocytes per high power field, increased spongiosis, dermal

eosinophils and the presence of a marked rather than slight inflammatory reaction supported the diagnosis of a non-aGVHD skin rash. The findings were not independently predictive. For example, eosinophils were common to both groups post TCD transplantation, but slightly less frequent in aGVHD. As with other studies^{12,13}, we observed the presence of necrotic keratinocytes, including some within skin adnexal structures, in TCD non-aGVHD skin rashes, confirming that this feature alone cannot be used to make a diagnosis of GVHD.

When comparing our findings favoring aGVHD post-TCD with a historical control, TCD and T replete aGVHD shared the following features: diffuse basal layer vacuolization, any single necrotic keratinocytes, >3 necrotic keratinocytes per high power field, full thickness epidermal involvement by necrosis, satellitosis, exocytosis, and slight rather than marked inflammatory infiltrates. These conserved features are consistent with a cytotoxic effector T cell response in which T-cells expand, release inflammatory cytokines and damage host tissue (target epidermal keratinocytes) upon recognition of host antigens in aGVHD pathogenesis.¹⁷ Altogether, the aggregate of these features continues to be helpful in distinguishing TCD aGVHD from non-aGVHD skin rash.

However, when we compared TCD aGVHD, TCD non-aGVHD skin rash, and T replete aGVHD, we found that some features were more common in TCD non-aGVHD than reported in T replete aGVHD, e.g. adnexal involvement, satellitosis and lymphocyte exocytosis. Biologically, these findings may also relate to an altered immunologic milieu (e.g. greater cytotoxic activity post TCD). Clinically, the finding of these features, particularly in the TCD non-aGVHD group, is important to note, as they are features typically used to favor aGVHD in a T replete transplant recipient's skin⁹, but may have less significance in a TCD-transplant patient's biopsies. This observation should be validated in a larger group of patients.

In conclusion, there appear to be histopathologic changes that are common to all patients who have received a TCD PBSTCT, which may confound the evaluation of aGVHD. Specifically, in TCD-transplanted patients, assessment for features such as diffuse basal layer vacuolization, full thickness keratinocyte necrosis, and lack of exuberant inflammation, should be performed when considering the diagnosis of aGVHD. Non-aGVHD rashes in recipients of TCD vs T replete transplants, as with aGVHD in recipients of TCD vs T replete transplants, show more extensive inflammation, which is more marked, and more eosinophils. Adnexal involvement, satellitosis and lymphocyte exocytosis and single necrotic keratinocytes should not be used to favor aGVHD over non-aGVHD in the TCD graft recipient population. Close clinicopathologic correlation may not be adequate when assessing patients with many comorbidities and complicated clinical presentations. In these cases, clinical judgment and experience should guide appropriate management.

This study was limited by its small sample size, but provides valuable preliminary findings that must be confirmed in a larger sample of patients, as TCD transplantation acquires a more prominent role in the treatment of hematologic malignancies. Further analysis of this question should follow, in order to improve patient care and prognosis, while avoiding possible overtreatment of GVHD with systemic immunosuppression.

Acknowledgments

Source of Funding.

AMD received funding from the Canadian Dermatology Foundation. MEL has a speaking, consultant or advisory role with Advancell, AstraZeneca, Aveo, Bayer, BergPharma, Bristol-Myers Squibb, Galderma, Genentech, Genzyme, GlaxoSmithKline, Helsinn, Imclone, Lilly, LindiSkin, Merck, Novocure, Novartis, Onyx, Pfizer, Roche, Sandoz, Sanofi Aventis and Wyeth.

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Table 1

Histopathologic features of biopsies from transplant patients

Feature	aGVHD-positive		aGVHD-negative		Equivocal
	TCD/+aGVHD (total n=13)	n (%) T replete/+aGVHD (total n=38)	n (%) TCD/- aGVHD (total n=20)	n (%) T replete/- aGVHD (total n=40)	
Interface Dermatitis					
Grade 0	–	NA	7 (35)	NA	2 (50)
Grade 1	3 (23)		8 (40)		1 (25)
Grade 2	9 (69)		5 (25)		–
Grade 3	1 (8)		–		1 (25)
Epidermal Thickness					
Normal	5 (38)	7 (18)	5 (25)	16 (40)	–
Atrophy	1 (8)	28 (74)	2 (10)	24 (60)	1 (25)
Acanthotic	7 (54)	3 (8)	13 (65)	–	3 (75)
Spongiosis					
Absent	6 (46)	17 (45)	6 (30)	32 (80)	1 (25)
Present	7 (54)	21 (55)	14 (70)	8 (20)	3 (75)
Basal Vacuolization					
Absent	1 (8)	3 (8)	6 (30)	9 (22)	2 (50)
Focal	2 (15)	16 (42)	9 (45)	28 (70)	–
Diffuse	10 (77)	19 (50)	5 (25)	3 (8)	2 (50)
Single necrotic keratinocytes (HPF)					
Absent	1 (8)	5 (13)	11 (55)	17 (42)	3 (75)
3	8 (61)	20 (53)	8 (40)	21 (52)	–
>3	4 (31)	13 (34)	1 (5)	2 (5)	1 (25)
Site of necrotic keratinocytes					
Basal/suprabasal	n=12	n=33	n=9	n=23	n=1
Entire epidermis	7 (58)	25 (76)	9 (100)	22 (96)	1 (100)
Adnexal Involvement	5 (42)	8 (24)	–	1 (4)	
Adnexal Involvement					
Absent	3 (23)	32 (84)	11 (55)	39 (98)	2 (50)
Present	10 (77)	6 (16)	9 (45)	1 (2)	2 (50)

Feature	aGVHD-positive		aGVHD-negative		Equivalent
	n (%) TCD/+aGVHD (total n=13)	n (%) T replete/+aGVHD (total n=38)	n (%) TCD/- aGVHD (total n=20)	n (%) T replete/- aGVHD (total n=40)	
Minor	6 (46)	NA	7 (35)	NA	1 (25)
Major	4 (31)	NA	2 (10)	NA	1 (25)
Satellitosis					
Absent	3 (23)	29 (76)	14 (70)	40 (100)	2 (50)
Present	10 (77)	9 (24)	6 (30)	—	2 (50)
Inflammatory Infiltrate					
Absent	—	1 (3)	—	24 (60)	—
Slight	10 (77)	29 (76)	4 (20)	16 (40)	3 (75)
Marked	3 (23)	8 (21)	16 (80)	—	1 (25)
Disposition of Inflammatory Infiltrate		n=37		n=16	
Perivascular	7 (54)	21 (57)	17 (85)	14 (88)	4 (100)
Lichenoid*	6 (46)	16 (43)	3 (15)	2 (12)	—
Perivascular +Lichenoid*	5 (42)	NA	2 (10)	NA	—
Lymphocyte exocytosis					
Absent	1 (8)	24 (63)	7 (35)	38 (95)	2 (50)
Present	12 (92)	14 (37)	13 (65)	2 (5)	2 (50)
Eosinophils					
Absent	9 (69)	37 (97)	7 (35)	38 (95)	2 (50)
Present	4 (31)	1 (3)	13 (65)	2 (5)	2 (50)
Neutrophils					
Absent	9 (69)	38 (100)	15 (75)	40 (100)	1 (25)
Present	4 (31)	—	5 (25)	—	3 (75)
Plasma cells					
Absent	8 (62)	37 (97)	13 (65)	40 (100)	1 (25)
Present	5 (38)	1 (3)	7 (35)	—	3 (75)
Melanophages					
Absent	—	24 (63)	2 (10)	35 (88)	—
Present	13 (100)	14 (37)	18 (90)	5 (12)	4 (100)
Extravasated erythrocytes					

Feature	aGVHD-positive		aGVHD-negative		Equivocal
	n (%) TCD/+aGVHD (total n=13)	n (%) T replete/+aGVHD (total n=38)	n (%) TCD/- aGVHD (total n=20)	n (%) T replete/- aGVHD (total n=40)	
Absent	4 (31)	33 (87)	9 (45)	37 (92)	1 (25)
Present	9 (69)	5 (13)	11 (55)	3 (8)	3 (75)

aGVHD, acute graft versus host disease, TCD, T cell depleted, HPF, high power field

Table 2

Features of aGVHD vs non-aGVHD skin rash in TCD graft recipients

Histopathologic feature	TCD aGVHD (%)	TCD non-aGVHD (%)
Diffuse basal vacuolization	77	25
Any single necrotic keratinocyte/HPF	92	45
>3 single necrotic keratinocytes/HPF	31	5
Full thickness necrotic keratinocyte	42	0
Satellitosis	77	30
Exocytosis	92	65
Slight (rather than marked) inflammation	77	20

TCD, T-cell depletion, aGVHD, acute graft versus host disease, HPF, high power field

Table 3

Features of aGVHD in TCD vs T replete graft recipients

Histopathologic feature	TCD aGVHD (%)	T replete aGVHD (%)
Any necrotic keratinocytes per HPF	92	87
Slight (rather than marked) lymphocytic infiltrate	77	79
Spongiosis	54	55
>3 single necrotic keratinocytes per HPF	31	34
Adnexal involvement	77	16
Satellitosis	77	24
Exocytosis	92	37
Acanthosis	54	8

TCD, T-cell depleted, aGVHD, acute graft versus host disease, HPF, high power field