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Acute cutaneous graft-versus-host disease (aGVHD) has a variety of clinical presentations. In the early posttransplantation setting, histologic confirmation of aGVHD via skin biopsy is frequently equivocal. Additional clinical information may be necessary to differentiate aGVHD from its clinical mimickers such as viral exanthema, morbilliform drug eruptions, engraftment syndrome (ES), pre-engraftment syndrome (PES), and in severe cases, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) [1–3].

Diagnosing and Staging/Grading Acute GVHD

Chapter 6 outlines the diagnosis and staging/grading of aGVHD.

Clinical Manifestations of Acute GVHD

The skin is the most common site of involvement of aGVHD, whether or not extracutaneous features develop. In addition, cutaneous aGVHD is typically the earliest presenting feature of the disease. No systematic prospective studies have been rigorously conducted to determine the most common clinical presentation or anatomic site of distribution for aGVHD, but numerous case series have elucidated the heterogeneity with which aGVHD may present at the bedside. The many different morphologies that may develop in aGVHD are illustrated in the rest of this chapter.

Erythema

Erythema in aGVHD may be patchy or confluent, and may have associated pruritus or dysesthesia [4]. Frequently, erythema develops first on the ears, the hands (palmar or dorsal surface), or both. It may later generalize to the rest of the body (Figs. 3.1, 3.2, 3.3, 3.4, 3.5, 3.5, and 3.7).



Fig. 3.1 Erythema of the face with accentuation of the ear

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Fig. 3.2 Erythema of the ear



Fig. 3.3 Palmar erythema



Fig. 3.4 Palmar erythema (Note microvesicles that herald edema.)



Fig. 3.5 Erythema of the palm



Fig. 3.6 Patchy erythema of the trunk and arms



Fig. 3.7 Confluent erythema of the back

Follicular Accentuation

Prominence of hair follicles (whether overlying erythema is present or not) is typical of aGVHD [5]. Such prominence is often misdiagnosed as folliculitis, but it typically heralds the involvement of aGVHD within the follicular epithelium (Figs. 3.8 and 3.9).



Fig. 3.8 Erythema of the arm with follicular accentuation



Fig. 3.9 Erythema with follicular accentuation of the leg

Morbilliform Lesions

Morbilliform aGVHD is among the most common presentations [6]. Eruptions are erythematous macules and papules that may coalesce into larger papules and plaques, which are symmetric and are often pruritic. This presentation may clinically mimic viral exanthema or drug eruptions (Figs. 3.10, 3.11, 3.12, and 3.13).



Fig. 3.10 Morbilliform lesions on the dorsal forearms/hands



Fig. 3.12 Morbilliform lesions on the thighs



Fig. 3.13 Morbilliform lesions diffusely located on the trunk



Fig. 3.11 Morbilliform lesions on the chest and abdomen

Erythroderma

Erythrodermic aGVHD presents with confluent erythematous patches that mimic severe viral exanthema, drug reactions, psoriasis, eczematous dermatitis, cutaneous T-cell lymphoma, or staphylococcal scalded skin syndrome (SSSS) (Fig. 3.14). When mucous membrane lesions are present, there are no clinical or histologic differences between skin stage 4 aGVHD and toxic epidermal necrolysis (TEN) [7–9]. If extracutaneous features of aGVHD are present, diagnosis may be possible via tissue confirmation at involved sites. If extracutaneous features of aGVHD are absent, review of clinical symptoms and their development in relation to initiation of medications is mandatory. Viral serologies and/or quantification of viremia via polymerase chain reaction (PCR) testing of the blood may aid in the diagnosis of an erythrodermic viral exanthem, such as those caused by HHV-6. Concurrent empiric treatment of aGVHD, viral infection, and TEN may be necessary if a clear diagnosis cannot be rendered.



Fig. 3.14 Confluent erythema with scale mimicking staphylococcal scalded skin syndrome (SSSS)

Reticulated Patterns

Acute GVHD may present in a reticulated, netlike pattern (Fig. 3.15).



Fig. 3.15 Erythematous, reticulated patches on the distal legs and feet

Desquamation

Superficial desquamation is typical of a variety of inflammatory dermatoses, whether or not patients are hematopoietic stem cell transplantation (HSCT) recipients. In aGVHD, desquamation may develop as skin lesions resolve, or it may appear at presentation. Desquamation may be superficial, deep, focal, or more generalized, in which case it may mimic SJS, TEN, or SSSS (Figs. 3.16, 3.17, 3.18, and 3.19).



Fig. 3.16 Erythema and diffuse superficial desquamation



Fig. 3.17 Erythema with deeper desquamation



Fig. 3.18 Erythema with desquamation of the areolar regions



Fig. 3.19 Erythema with sheet-like desquamation mimicking toxic epidermal necrolysis (TEN)

Bullae

Rarely, bullous aGVHD may develop (Fig. 3.20).



Fig. 3.20 Erythema of the right dorsal hand and fingers with a tense bulla on the fourth finger

Papules

Papular aGVHD may mimic papular eczema or papular urticaria (Figs. 3.21 and 3.22).



Fig. 3.21 Erythematous, scaly papules on the right arm and shoulder



Fig. 3.22 Close-up image of erythematous, scaly papules on the thigh

Conclusion

Familiarity with the many presentations of aGVHD and its clinical spectrum is imperative in the care of patients after HSCT. Recognition of this variability can ensure that accurate and immediate treatment of aGVHD is initiated to improve outcomes for affected patients.

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