Histopathologic Spectrum of Connective Tissue Diseases Commonly Affecting the Skin

Alvaro C. Laga, MD, MMSc[a,*], Allison Larson, MD[b], Scott R. Granter, MD[a]

KEYWORDS

• Histopathology • Connective • Lupus • Scleroderma • Dermatomyositis • Patterns • Neutrophilic

Key Points

- Connective tissue diseases affecting the skin may show the following histologic patterns: interface alteration, vasculitis, vasculopathy, neutrophilic dermatosis, and dermal sclerosis.
- The main role of histopathology in the diagnosis of connective tissue disorders is to confirm, exclude, or alert clinicians of connective tissue disease as a diagnostic category rather than specific entities.
- Clinical and serologic correlation is needed to arrive at the correct diagnosis.
- Neutrophilic dermatosis may be the initial (presenting) manifestation of connective tissue disease.

ABSTRACT

Connective tissue disorders (CTDs), also known as collagen vascular diseases, are a heterogeneous group of diseases with a common pathogenic mechanism: autoimmunity. Precise classification of CTDs requires clinical, serologic, and pathologic correlation and may be difficult because of overlapping clinical and histologic features. The main contribution of histopathology in the diagnosis of these disorders is to confirm, rule out, or alert clinicians to the possibility of CTD as a disease category, rather than producing definitive diagnoses of specific entities. This article discusses the histopathologic spectrum of 3 common rheumatologic skin disorders: lupus erythematosus, dermatomyositis, and morphea (localized scleroderma).

OVERVIEW

Connective tissue disorders (CTDs), also known as collagen vascular diseases, are a heterogeneous group of diseases with a common pathogenic mechanism: the loss of self-tolerance and development of so-called autoimmunity. Although the exact cause is unknown, it is generally accepted that genetic predisposition and environmental factors such as infection play an important role in unmasking self-antigens that are then recognized by autoreactive clones with consequent target cell/organ injury.[1] Autoimmune disorders can be broadly categorized into organ-specific disorders (eg, diabetes mellitus [DM] type 1, Hashimoto thyroiditis, localized scleroderma, chronic cutaneous lupus erythematosus) and systemic disorders (eg, systemic lupus erythematosus [SLE], dermatomyositis, systemic

Disclosure: The authors have nothing to disclose.

[a] Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Amory-3, 75 Francis Street, Boston, MA 02115, USA; [b] Department of Dermatology, Boston University School of Medicine, 609 Albany Street, J202, Boston, MA 02118, USA

* Corresponding author.

E-mail address: alaga@partners.org

Surgical Pathology ■ (2017) ■–■

http://dx.doi.org/10.1016/j.path.2017.01.012

sclerosis).[2,3] Precise classification of CTDs requires clinical, serologic, and pathologic correlation and may be difficult at times because of overlapping clinical and histologic features. Although there are classic or characteristic histopathologic changes of CTD, the main contribution of histopathology in the diagnosis of these disorders is perhaps to confirm, rule out, or alert clinicians to the possibility of CTD as a disease category, rather than producing definitive diagnoses of specific entities. Although some histologic patterns (eg, vacuolar interface alteration) are readily associated with CTD by pathologists, there are other patterns (eg, neutrophilic dermatosis) that, despite having characteristic histopathologic features, only recently have emerged as distinctive manifestations of CTD.[4–7] This article discusses the histopathologic spectrum of 3 common rheumatologic disorders involving the skin: lupus erythematosus, dermatomyositis, and morphea (localized scleroderma).

LUPUS ERYTHEMATOSUS

CLINICAL FEATURES

Lupus erythematosus is an inflammatory disease with a protracted clinical course and potential for multiorgan disorder. Skin involvement is seen in more than 80% of patients.[3] Although severity and clinical manifestations vary from patient to patient, multiple clinical and pathologic patterns of skin disease may be encountered and should alert clinicians and pathologists to this diagnosis.

Lupus erythematosus is predominantly observed in young women, but can occasionally affect men and may occur at any age. Cutaneous manifestations of lupus can be divided into acute, subacute, and chronic cutaneous lupus. Chronic cutaneous lupus, in turn, can be subdivided into discoid lupus (the most common form), lupus panniculitis, chilblain lupus (lupus perniosis), and tumid lupus, this last form being controversial.[8–10]

Acute cutaneous lupus erythematosus (ACLE) is a manifestation of SLE and presents with the classic malar erythema (butterfly rash) spreading over the cheeks and bridge of the nose, with sparing of the nasolabial folds, which are relatively sun protected. ACLE manifests in up to 50% of patients with SLE after sun exposure and can be confused with sunburn. Subacute cutaneous lupus erythematosus (SCLE) is characterized by annular, polycyclic, or psoriasiform scaly papules and plaques on photosensitive areas of the chest, upper back, and arms. The central face is typically spared and most patients have anti-Ro (SSA) antibodies. SCLE is frequently induced by medications but can be idiopathic; both forms are indistinguishable clinically, serologically, and by histopathology. Permanent pigmentary changes and scarring do not occur. Discoid lupus erythematosus (DLE) presents with indurated pink, violaceous, or hyperpigmented plaques that may develop central hypopigmentation and scarring. Scale is frequently seen, and follicular plugging may be evident. Involvement of the scalp is common and results in scarring alopecia. The head and neck are most frequently involved. There is minimal risk of systemic involvement. Long-standing DLE lesions are at increased risk for squamous cell carcinoma formation, and these squamous cell carcinomas confer a higher rate of recurrence, metastasis, and death. Lupus panniculitis presents with indurated nodules, most frequently on the head, neck, and arms, and heals with depressed scars. Lupus panniculitis may represent purely cutaneous disease or may be a manifestation of SLE. Bullous lupus erythematosus occurs in patients with SLE and presents with tense vesicles and bullae on both sun-exposed and sun-protected sites.[8–13]

MICROSCOPIC FEATURES

The key features of histologic patterns encountered in lupus erythematosus, dermatomyositis, and morphea are summarized in **Box 1**.

HISTOLOGIC PATTERNS SEEN IN LUPUS ERYTHEMATOSUS

INTERFACE DERMATITIS

Vacuolar interface alteration, consisting of vacuolar or hydropic degeneration of the epidermal basal cell layer, is the most common histologic pattern in lupus erythematosus and can be seen in the acute, subacute, and chronic forms of cutaneous lupus. Early lesions of ACLE may show subtle, nonspecific findings such as dermal edema and sparse mononuclear inflammation. Well-developed lesions show vacuolar interface alteration, indistinguishable histologically from SCLE (**Fig. 1**A). In SCLE, there is vacuolar interface dermatitis, sometimes associated with colloid bodies in the papillary dermis and edema. There is a lymphocytic inflammatory infiltrate, but it tends to be less conspicuous than in DLE (**Fig. 1**B). SCLE is also the most frequent pattern seen in neonatal lupus erythematosus. In DLE, there is interface dermatitis and prominent mononuclear inflammatory infiltrates near the dermal-epidermal