Blistering Skin Diseases—Part I: A Systematic Approach
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Blistering lesions can be a burdensome clinical finding, carrying a laundry list of potential diagnoses and an impending battery of daunting unfamiliar testing procedures. Prompt diagnosis can be critical because some of these blistering diseases have the potential to become severe and even life threatening.1,2 With the right approach, this historically intimidating area of dermatopathology can be broken down into easily manageable parts to help guide the physician toward the correct diagnosis.

The first step in approaching a blistering skin disease is to obtain a thorough patient history. Next, identify what type of blister you are dealing with. Blisters are categorized into two groups: 1) vesicles are blisters that are less than 0.5 cm in diameter, and 2) bullae are blisters larger than 0.5 cm. Blistering disorders tend to predominately present with one or the other type of blister. For example, herpes gestationis consists of small vesicles, while bullous pemphigoid is composed of larger bullae. Additional characteristics to assess include:

- Is the blister tense or flaccid?
- Are there single or multiple lesions?
- Is the distribution localized or diffuse?
- Is there involvement of the skin, mucus membranes, or both?
- Is the Nikolsky sign positive?

Once a clinical picture is established, open and clear communication with the pathologist is essential for proper patient care. Clinicopathological correlation is always a necessity in dermatopathology, but it can be particularly important in the diagnosis of blistering diseases.

After benign and self-limited etiologies have been ruled out clinically, performing a biopsy is the next step. The proper biopsy site for a vesiculobullous skin lesion is extremely important, and the right type of biopsy must be obtained in order to produce the most promising diagnostic specimen for the pathologist to evaluate. This includes taking a punch biopsy of the border of an intact early lesion that includes both lesional and adjacent perilesional skin.3 A punch biopsy helps keep the roof of the blister intact so that a pathologist can properly evaluate it. The tissue should be submitted for routine hematoxylin and eosin staining.

Evaluation for autoimmune vesiculobullous skin diseases requires an additional biopsy for immunofluorescence testing. To do this, obtain a punch biopsy from normal-appearing skin near a fresh blister.4 The areas where a blister has formed are involved by an intense inflammatory reaction that interferes with the detection of antibodies. The normal-appearing tissue is ideal for this testing because it contains the antibodies of interest but lacks the inflammatory component, allowing for optimal testing environment.

A microscopic examination will help further classify the lesion depending on three key features: 1) plane of separation, 2) mechanism of blister formation, 3) type of inflammatory infiltrate. Ancillary testing, commonly used to further differentiate autoimmune vesiculobullous disorders, includes immunofluorescence and more recently, enzyme-linked immunosorbent assay (ELISA).1 Historically, direct immunofluorescence has been the gold-standard ancillary test in the workup for autoimmune vesiculobullous disease.4,5
The presence or absence of fluorescence will alert you if there is immune activity in the skin. Particular patterns of fluorescence help establish a diagnosis.

Classification of autoimmune vesiculobullous skin disease can be both complex and intimidating to those attempting to make a diagnosis. A stepwise approach should begin with the plane of separation to split blisters into two groups: 1) intraepidermal or 2) subepidermal. Upcoming articles will focus on autoimmune vesiculobullous skin disease, including the intraepidermal blistering skin disorders, known as the pemphigus group, which is the clinically similar-appearing pemphigoid (pemphigus-like) group of subepidermal blistering disorders.

References:


