Histology of hidradenitis suppurativa

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Background: Hidradenitis suppurativa is traditionally classified as a disease of the apocrine gland. However, different histologic descriptions exist.

Objective: Our purpose was to describe prospectively the histopathologic characteristics of hidradenitis.

Methods: We systematically described and classified 60 consecutive biopsy specimens from patients with hidradenitis and compared them with 33 specimens from clinically noninvolved regional controls.

Results: A heterogeneous histologic picture was found. Apocrine glands were involved in a minority of the 60 specimens, 17 showed poral occlusion, 17 simple folliculitis without poral occlusion, 9 sinus tracts, 6 epithelial cyst, 5 abscess, 3 apocrinitis, 2 diffuse dermal inflammation, and 1 pyogenic granuloma and scarring. Secondary involvement of apocrine glands was found in 12% of all specimens, and secondary involvement of eccrine glands was found in 25%. Sinus tracts were found significantly more often in the presence of poral occlusion or epithelial cysts. Control specimens frequently revealed changes compatible with early stages of follicular involvement. Apocrine glands were observed significantly more often in the axillae than in the groin.

Conclusion: The clinical picture of hidradenitis suppurativa covers a broad histologic spectrum. This may help explain the therapeutic problems posed by this disease. The disease appears to be predominantly follicular, and apocrine glands appear to be primarily involved in only a minority of axillary lesions.

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In some studies hidradenitis is described as an inflammation of the apocrine gland; other studies have suggested that it is a form of acne inversa and associated with the pilosebaceous unit rather than the apocrine gland.1-5 This study was undertaken to clarify its histologic features.

MATERIAL AND METHODS

A total of 93 biopsy specimens from patients with hidradenitis as well as from patients without any clinical evidence of hidradenitis were studied. Sixty specimens of hidradenitis were obtained from 36 patients (8 men and 28 women; mean age [SD]: 33.2 years [9.5]; mean age of men [SD]: 39.6 years [10.6], of women: 31.4 years [8.5]). The sites of the lesions from which biopsy specimens were taken were axilla, 24; breast, 3; groin, 32; and buttocks, 1. Control specimens were taken from patients requiring minor surgery in the axillae and from the axillae and groin of cadavers. A total of 33 specimens from 23 persons (9 men, 14 women, mean age [SD]: 39 years [13.7]) were studied.

All specimens were fixed in formaldehyde 4% and embedded in paraffin. Sections were stained with hematoxylin and eosin. Each slide was assigned a number and evaluated by both authors. Control specimens were viewed first to assess the normal regional histologic features, and lesional specimens were viewed without any information about the clinical presentation. The following features were described: parakeratosis, pilosebaceous unit, poral occlusion (lesional/paralesional), folliculitis, inflammation of eccrine glands, inflammation of apocrine glands, sinus tracts, and fibrosis. Additional features were described if present. Parakeratosis, poral occlusion and folliculitis were graded 0, +, ++, and ++++, and only specimens with ++ or +++ features were included (Fig. 1).

In the classification, the following definitions were applied:

1. Poral occlusion/ acne vulgaris: Infundibular hyperkeratosis in excess of that seen in control specimens. Changes range from pronounced hyperkeratosis without distortion of the general architecture (inflammation may be present) to pronounced infundibular hyperkeratosis with a milia-like appearance and a general distortion and distention of the pilosebaceous unit (inflammation is often pronounced) (see Fig. 2).

2. Folliculitis: Infundibular hyperkeratosis not in ex-
cess of that in control specimens. Inflammation originating in a follicle, involving the follicular epithelium as well as lumen. The cellular infiltrate is dominated by neutrophils and giant cells and often contains free hairs, but other cells may be present. Inflammation was classified as slight, moderate, or severe. Surrounding fibrosis is often present (Fig. 3).

3. Apocrinitis: Apocrinitis was present when apocrine glands showed cellular infiltrates primarily involving the gland and were surrounded by tissue without inflammation. Inflammation must be at least intraepithelial and preferably intraluminal (Fig. 4).

4. Eccrinitis: Eccrinitis occurred when eccrine glands showed cellular infiltrates primarily involving the gland and were surrounded by tissue without inflammation. Inflammation must be at least intraepithelial and preferably intraluminal.

5. Epidermal cyst: Space in the dermis or subcutis, lined with squamous epithelium of even thickness. The surrounding collagen/fat often appears concentric as a sign of distention from expansive growth. Inflammation may or may not be present. The wall of the cyst may contain rudimentary skin appendages.

6. Abscess: A focus of acute inflammation surrounded by a pyogenic layer and granulation tissue.

7. Diffuse dermal inflammation: Diffuse dermal infiltration without signs of a primary focus associated with the structures of epidermis or dermis. Appears with scarring of the tissue.

8. Sinus tract: Irregular space, often an elongated cavity in the dermis or subcutis lined by squamous epithelium of uneven thickness. The epithelium often extends into the surrounding dermis in a leaflike pattern. Surrounding collagen or fat does not appear compressed, suggesting infiltrative rather than expansive growth. Inflammation may or may not be present.

**Statistical methods**

For contingency tables the chi-square test was used, except where any cell contained less than six patients or

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### Fig. 1. Hidradenitis suppurativa: Flow chart for classification of biopsy specimens (n = 60) according to dominant histologic feature. See “Material and Methods” section for definitions used. Specimens may display other features as secondary changes. n, Number of biopsy specimens in which the given feature was histologically dominant.
specimens; in such cases Fisher’s exact test was used. For continuous data the $t$ test was used, except when the SD of the two groups was different; in such cases Welch’s alternate $t$ test was used.

**RESULTS**

Examining specimens from clinically uninvolved skin formed the basis for assessing variation in normal regional histologic features (Table I). A tentative diagnosis was made in eight control specimens: of minimal papillomatosis of the epidermis in three, perifollicular fibrosis in two, perifolliculitis in one, perivascular inflammation in one, and milia in one. Parakeratosis was present in two control and two lesional specimens.

In the paralesional or lesional specimens a heterogeneous picture was found. In 17 moderate or severe paralesional specimens poral occlusion was found, suggesting the diagnosis of acne. Folliculitis without signs of poral occlusion was found in 17. Nine specimens showed sinus tracts as their main feature; six were diagnosed as epithelial cysts. Five specimens showed frank abscess formation, apocrinitis was diagnosed in three, and two showed diffuse dermal inflammation of unknown origin in connection with widespread scarring. Only one specimen fell outside the proposed classification by displaying a pyogenic granuloma and fibrosis.

The specimens often had additional features as can be seen in Table II. Intral glandular inflammation was found associated with dermal inflammatory foci in several: 7 of 57 showed secondary involvement of apocrine glands, and 15 of 60 showed secondary involvement of eccrine glands. Secondary involvement of apocrine or eccrine glands was not significantly greater in any of the groups. The diagnostic groupings of poral occlusion and epithelial cysts contained sinus tracts significantly more often ($p = 0.04$). There was no significant difference in the age or sex between different diagnostic groups.

**DISCUSSION**

Our results show that the majority of lesions clinically compatible with a diagnosis of hidradenitis suppurativa appear to be of follicular origin, and only a minority are without a follicular component. Fol-
icular lesions, lesions compatible with poral occlusion, or possible epithelial cysts account for some 67% of all lesions. Several other features are often present, but the dominant histologic feature is follicular involvement. Apocrinitis, originally suggested as the typical histologic appearance of hidradenitis, was the dominant histologic feature in only 5% of all lesions. This may result from the scarcity of apocrine glands in the genitofemoral area where lesions are often found (Table I). Secondary apocrine involvement in connection with poral occlusion was more common (12%; 7 of 57) but not as common as secondary involvement of eccrine glands (25%; 15 of 60). This may be because of the greater number of eccrine glands in the specimens.

The remaining 28% of the lesions presented more obscure findings such as scarring, sinus tracts, and abscess formation. These appear to be more suggestive of later stages of disease.

Sinus tract formation has been considered the hallmark of hidradenitis and used to underline further the similarities between hidradenitis and other forms of acne. It is not clear whether sinus tract formation is a general response pattern to any severe inflammation or a specific feature of hidradenitis. Sinus tracts were seen significantly more often in the specimens in which the dominant feature was perilesional follicular occlusion (acne), suggesting these two diseases share a common pathogenic pathway.

Historically, the concept of hidradenitis suppurativa has caused considerable debate in dermatology. After the original clinical descriptions of the disease by Velpeau in 1832 and Verneuil in 1864, subsequent histologic studies showed the apocrine gland to be involved in producing characteristic lobular abscesses. The concept of apocrine involvement, however, appears to have been developed only because of the presence of inflamed apocrine glands as a part of an often mixed histologic picture and because of the overlapping location of hidradenitis and apocrine glands. On the basis of visualization of bacteria in the lesions, it was hypothesized that the disease was caused by staphylococci or streptococci entering the apocrine glands; a debate developed over the way bacteria reached the glands. Maintaining the central role of the apocrine glands, some authors argued that the glands were the target of lymphatic or hematogenous spread of bacteria, whereas others argued that follicular involvement was necessary. Experimental studies by Shelley and Cahn showed that follicular plugging could reproduce lesions that were clinically and histologically compatible with hidradenitis; however, these results were not universally accepted, and the notion of primary apocrine gland involvement therefore continued. More recently, specific studies of the follicular orifice have found changes suggestive of follicular plugging, thereby supporting the earlier experimental evidence. It has been speculated that follicular plugging can cause deep inflammation with associated or secondary intraglandular abscesses of the apocrine glands where these are present. The current study found this histologic picture in 2 of 17 specimens (12%). If similar abscesses of the more prominent eccrine glands are considered, this histologic picture is found in approximately 25% of specimens.

Local irritation of the skin from shaving, deodorants, and hyperhidrosis has been suggested as a possible causal mechanism for hidradenitis. However, the absence of parakeratosis in our sample suggests that irritation of the skin surface is not a major factor.

The life-time prevalence of hidradenitis has been estimated to be as high as 4% in women. The study of control biopsy specimens suggests that low-grade poral occlusion is common in the regions where hidradenitis occurs, offering a possible explanation for the apparently high incidence of the disease. Control specimens also revealed that apocrine glands,

<table>
<thead>
<tr>
<th>Table I. Histologic findings in control biopsy specimens*</th>
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<tbody>
<tr>
<td><strong>Rating</strong></td>
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<td>------------</td>
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<tr>
<td>Poral occlusion</td>
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<tr>
<td>Severe</td>
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<tr>
<td>Moderate</td>
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<tr>
<td>Slight</td>
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<tr>
<td>None</td>
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<tr>
<td>Apocrine glands</td>
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<tr>
<td>Many</td>
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<tr>
<td>Moderate</td>
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<tr>
<td>Few</td>
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<td>None</td>
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*Histologic findings in clinically uninvolved skin of control biopsy specimens. Findings suggest apocrine glands are predominantly found in axillae, whereas genitofemoral regions contain very few or no apocrine glands (many/moderate vs few/none; p < 0.0001; odds ratio: 97.5; 95% confidence interval 7.9-1203.8). A low degree of poral occlusion appears to be a common finding in clinically normal skin of regions studied.
Fig. 4. Apocrine gland involvement classified as apocrinitis. Note predominantly intraluminal infiltrate of polymorphonuclear leukocytes.

Table II. Histologic findings in classified lesional biopsy specimens

<table>
<thead>
<tr>
<th>Classification</th>
<th>Secondary features</th>
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<tbody>
<tr>
<td>Poral occlusion (n = 17)²,³</td>
<td>Two showed associated intraglandular abscesses in apocrine glands and four in the eccrine glands. One biopsy specimen showed an associated cyst; sinus tracts were found in 16.</td>
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<tr>
<td>Folliculitis without poral occlusion (n = 17)</td>
<td>One showed associated intraglandular abscesses in apocrine glands and three in the eccrine glands. One biopsy specimen showed an associated cyst; sinus tracts were seen in eight.</td>
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<tr>
<td>Apocrinitis (n = 3)</td>
<td>Associated ecrinitis was seen in two specimens, and sinus tracts were found in one.</td>
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<tr>
<td>Ecrinitis (n = 0)</td>
<td>This feature did not appear as a main finding in any biopsy specimen.</td>
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<tr>
<td>Epithelial cyst (n = 6)</td>
<td>One biopsy specimen showed associated ecrinitis, and one showed sinus tracts.</td>
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<tr>
<td>Abscess (n = 5)</td>
<td>Associated apocrinitis and ecrinitis were each found in one specimen.</td>
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<tr>
<td>Diffuse dermal inflammation (n = 2)</td>
<td>Both specimens showed sinus tract formation and associated eccrine gland abscesses; one showed an associated apocrine gland abscess.</td>
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<tr>
<td>Sinus tracts (n = 9)</td>
<td>Two biopsy specimens showed associated intraglandular abscesses of eccrine glands, and two showed intraluminal abscesses of apocrine glands.</td>
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<td>Other (n = 1)</td>
<td>Pyogenic granuloma and fibrosis</td>
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</table>

*Histologic findings in biopsy specimens studied after their classification. Classified according to dominant histologic features, but presence (partial or secondary) of other features was also noted and is listed for each of the major groups (e.g., of the 17 biopsies classified as poral occlusion, two showed apocrine gland involvement interpreted as secondary to poral occlusion).
²Parakeratosis was graded 0 (none), + (focal), ++ (extensive), and +++ (confluent); only biopsy specimens rated ++ or +++ are included.
³Poral occlusion classified as 0, +, ++, or +++; only biopsy specimens rated ++ or +++ are included.

hitherto associated with hidradenitis, are rare in the genitofemoral area where hidradenitis appears. This finding supports the view that hidradenitis is not pathogenetically linked with the presence of apocrine glands and that the observed apocrine involvement is secondary.

REFERENCES