Alopecia is a clinical and histologic challenge. Much of the difficulty arises from the perceived obvious clinical presentation, coupled with few treatment options and/or poor therapeutic response. As a result of the seemingly obvious clinical nature of alopecia, biopsies rarely are performed. The goal of this study was to evaluate the role of biopsies in evaluation of patients with hair loss with differential diagnoses of alopecia areata and/or telogen effluvium.

Pattern mimics may be more prevalent than previously thought, and an alopecia pattern may not necessarily lead to a diagnosis, as some diagnoses may mimic several patterns. Overall, these mimics and overlap cases are a large percentage of difficult-to-manage clinical presentations of alopecia that result in biopsy. Further research is critically needed to advance the physician’s diagnostic criteria and capability as well as management of these alopecia mimics in both clinical and histologic terms.

Diagnosing alopecia can be challenging for both patients and physicians. Because alopecia areata is perceived to be the most clinically obvious presentation of the disease, biopsies rarely are performed; however, physicians sometimes will biopsy because of an atypical presentation, progression, or treatment response; suspicion of overlap with another form of alopecia; or persistence of a patient who wants a definitive diagnosis.

Overall, the rampant potential for clinical mimicry among different forms of alopecia may explain why many patients are unresponsive to treatment or demonstrate atypical presentations. These challenges are augmented by the scarcity of large evidence-based studies on most alopecias and their subtypes.

The goal of this retrospective study was to develop a better understanding of the implications of histologic samples from patients with hair loss with differential diagnoses of alopecia areata and/or telogen effluvium.

Methods
A search was performed using the dermatopathology database for tissue biopsies (January 2007 to July 2009). The search did not include patient data, except for any clinical history that was provided by the physician for the pathologist’s use. Submitted tissue samples were limited to those taken from dermatologists who were trained by US dermatology residency programs accredited by the Accreditation Council for Graduate Medical Education. None of the samples came from physicians at formal alopecia clinics, which are rare in most dermatology training programs. Samples were selected based on the inclusion of alopecia areata in the differential diagnosis submitted by the physician. When alopecia areata was the only clinical diagnosis provided, these samples were placed in a separate category. A repeat search was conducted using the aforementioned criteria to identify samples whose differential diagnosis included telogen effluvium. When telogen effluvium was the
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only clinical diagnosis provided, these samples were placed in a separate category.

On histologic evaluation, classic findings were used to diagnose the formally characterized disease processes as described by Sperling. Some samples did not demonstrate unequivocally normal histology findings or classic pathology findings; thus samples with nonspecific abnormal findings were characterized as nonspecific active inflammatory (mild to moderate inflammatory infiltrate of predominantly lymphocytes [>10 lymphocyte cells per high-power field]) with absence of eosinophils; neutrophils; or more specific/diagnostic histologic changes that would suggest vasculitis, mucin deposition, pigment incontinence, or interface change. Also included in this group was nonspecific burnt-out scarring (presence of parallel collagen bundles/streaks with decreased numbers of folliculosebaceous units), again with absence of more classically diagnostic findings pertaining to other pathologies.

**Results**

A total of 33 tissue biopsies that included alopecia areata in the clinical differential were collected. The biopsies had been performed by 8 physicians in private practice and 4 physicians in academic practice. The patient age range was 8 to 72 years, and all 33 samples came from females. For cases submitted with alopecia areata and multiple forms of alopecia among the differential diagnoses (26 cases), the most common alternate differentials indicated by physicians were telogen effluvium (23%), scarring alopecia (19%), and discoid lupus erythematosus (15%). The most common histologic diagnoses were normal histology (19%) and lichen planopilaris (12%). Overall, 50% of cases showed nonspecific inflammatory and/or scarring forms of alopecia on histologic evaluation (Table).

In 18% of tissue samples, the differential diagnosis included alopecia areata only. In this data set, histologic results showed 14% were androgenic alopecia, 14% had signs of chronic inflammation, and 72% were alopecia areata (Figure).

In a similar data set, a total of 17 tissue biopsies were collected in which the clinical differential included telogen effluvium. The biopsies had been performed by 5 physicians in private practice and 3 physicians in academic practice. The patient age range was 29 to 87 years, and 88% of samples came from females. For cases submitted with telogen effluvium and multiple forms of alopecia among the differential diagnoses (14 cases), the most common alternate differentials indicated by physicians were alopecia areata (47%), androgenic alopecia (33%), and discoid lupus erythematosus (20%). The most common histologic diagnoses were mild nonspecific scarring (29%) and androgenic alopecia (21%). Overall, 43% (6/14) of cases showed inflammatory and/or scarring forms of alopecia, and 14% showed telogen effluvium on histologic evaluation.

In 24% of samples (4 cases), the differential included only telogen effluvium. Of these samples, 50% were scarring alopecia and none of the cases were read as telogen effluvium despite the physician’s differential diagnosis (Figure).

**Comment**

This data analysis demonstrates the value of biopsy and histologic evaluation in the diagnosis of alopecia. In many cases, the histologic results provided

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### Analysis of Samples Provided With Multiple Differentials

<table>
<thead>
<tr>
<th>Alopecia Type</th>
<th>Most Common Alternative Clinical Differentials, %</th>
<th>Histologic Diagnoses, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alopecia areata</td>
<td>Telogen effluvium, 23%; scarring alopecia, 19%; discoid lupus erythematosus, 15%</td>
<td>Nonspecific inflammatory/scarring alopecia, 50%; normal histology, 19%; lichen planopilaris, 12%</td>
</tr>
<tr>
<td>Telogen effluvium</td>
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</tr>
</tbody>
</table>

*Results show total percentage of the most common alternate diagnoses provided in the clinical differentials for both the alopecia areata and telogen effluvium data sets. Further depicted are percentages for the most common histologic diagnoses in the same category.*
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Evaluation of these data also revealed the importance of considering the information provided by the physician. As many pathologists know, clinical differentials submitted by physicians often are abbreviated or absent. This lack of an expansive differential often is a result of years of experience and well-honed skills that allow physicians to narrow down 1 or 2 differentials as possible diagnoses. For alopecia biopsies, clinical suspicions and/or differentials always are submitted. This broad differential may be a reflection of the challenges that are presented in managing alopecia, which prompts discussion and relay of information between the physician and the dermatopathologist.

This data analysis revealed 2 important points: how often physician and patient suspicions of atypical alopecias were proven correct by biopsy (Table), and how often cases of alopecia that initially appeared clear-cut with 1 diagnostic consideration ultimately were proven by histology to be atypical (Figure). Overall, the data emphasize common areas of clinical deception that arise when diagnosing different forms of alopecia. For example, when alopecia areata was the only differential diagnosis, the strongest clinical-pathologic correlation was noted. In these cases, a delay in biopsy may or may not adversely affect disease management. However, in cases of telogen effluvium, a biopsy should be considered at an early stage of management, as it is likely the patient has an alternate diagnosis that will require treatment, rather than using the wait-and-watch approach to telogen effluvium management.

Ultimately, even with few unique histologic descriptors available, notation of scarring alopecia can be enough to substantially alter a patient’s treatment, morbidity, and outcome. Thus clinical examination of pattern presentation rarely is reliable on its own as an approach to diagnosis. There also is the potential for overlap in histologic findings that previously were seen as specific to certain forms of alopecia. For example, miniaturized hairs are characteristic of both patterned alopecia and alopecia areata; hair casts from traction also have been described in alopecia areata.

Despite the many unique aspects of the data, this study was limited by the retrospective nature of the results. The diagnostic criteria also were subjective. However, this study does reflect the natural setting of the majority of general dermatology clinics. Increased research funds should be allocated to the study of alopecia because of the difficulty of its clinical management and well-established morbidity. Also, many patients may present in nondiagnostic stages, and further research may be able to determine if these cases are early-stage alopecia without defining characteristics, late-stage and near burnt-out inflammatory alopecia, or simply a new category in which the mild inflammation may or may not play an actual role in the alopecia. Further discoveries may be noted in addition to recently revitalized and expanded concepts, such as the use of elastin stain in diagnosing lichen planopilaris.

Conclusion

Clinical mimicry among different forms of alopecia may be more common than previously thought, though the number and variety of instances remain unclear. Furthermore, a thorough list of clinical and histologic criteria must be devised to more accurately identify mimicry in the clinical signs of alopecia. Although most clinicians heavily rely on clinical evaluation to establish diagnoses, the need for biopsy in patients with hair loss must not be underemphasized.

REFERENCES


