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Scalp Biopsy and Diagnosis of Common Hair Loss Problems

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1. Introduction

Patients presenting with hair loss (alopecia) is a very common problem and is often a cause of great concern for cosmetic and psychological reasons and this has several causes; as it may be an important sign of systemic disease.

2. Causes of alopecia

Alopecia can be either scarring or non-scarring. Non-scarring alopecias tend to have preserved follicular ostia, with no clinically visible inflammation in most presentations, although histologic inflammation may be present. The common types of non-scarring alopecias are androgenic alopecia, telogen effluvium, alopecia areata, trichotillomania and traction alopecia. Scarring alopecias, also known as cicatricial alopecia, refers to a collection of hair loss disorders that have loss of follicular ostia, or atrophy, with permanent and irreversible destruction of hair follicles and their replacement with scar tissue. The histologic confirmation is the best method to confirm the presence of a fibrosing/scarring process with loss of hair follicles.

Scarring alopecias can be classified as lymphocytic (discoid lupus erythematosus (DLE), lichen planopilaris (LPP), central centrifugal cicatricial alopecia, pseudopelade of Brocq), neutrophilic (folliculitis decalvans, dissecting folliculitis), and mixed (acne keloidalis) entities [1].

Many alopecia types are biphasic. For example, androgenetic alopecia eventually results in loss of ostia and thus may appear like a scarring alopecia.

To establish the cause of the hair loss, one requires a history to identify known triggers, scalp examination, biochemical investigations and in many cases histology to identify the earliest stages of some types of alopecias esp scarring alopecia.

3. Indications of scalp biopsy in diagnosis of hair loss

Scalp biopsies can be used to make or confirm a diagnosis of alopecia. Scalp biopsy is considered mandatory in all cases of scarring alopecia. The interpretation of the histopathological findings of primary scarring alopecias without known clinical history may be difficult and this is especially true if the biopsy specimen is inadequate.

In non-scarring type, it is not difficult to diagnose these disorders. However, scalp biopsy can be needed in few cases of:

- Lack of identifiable triggers.
- Severe hair loss (as in some cases of alopecia areata which does not present in a well defined bald area, but as severe hair loss (Fig 1).
- Acute hair loss.
- Telogen effluvium does not occur in an acute way after a known triggering factor.
- Some cases of female androgenetic alopecia pattern; the clinical presentation may be similar to other types of non-scarring alopecias.



Figure 1. year old female patient presented with diffuse, acute severe hair loss and with localized patch of alopecia areata as it demonstrated by red arrow.

4. Technique of scalp biopsy

It is a crucial to determine the appropriate site of a scalp biopsy to have a correct diagnosis of alopecia, and this approach is different in scarring and non-scarring types. For a scarring process, the biopsy should be taken from the active border of hair loss where some hairs still remain and are more likely to display diagnostic findings. For non-scarring alopecias, the preferred site of biopsy is generally the border of a lesion (positive exclamation marks in alopecia areata), or from the site of a positive pull test in the setting of a diffuse alopecia. In the setting of evaluating a possible androgenic alopecia, two biopsies, one from the involved scalp (often vertex) and one from the uninvolved scalp (often occiput; serves as a positive control) may be beneficial.

The current gold-standard for a scalp biopsy specimen is the use of a 4-mm punch and must include subcutaneous fat to ensure sampling of the entire follicular unit and any anagen follicles; the specimen may be sectioned vertically or transversely [2]. Although a combination of the two may be optimal, the pathologist is frequently only provided with a single specimen.

5. Vertical sections

Vertically-sectioned punch biopsy specimen is adequate for assessing alopecias associated with interface changes, lichenoid infiltrates, and subcutaneous pathology [3]. However, vertical sectioning will show only 10% of the follicles present in the specimen [4] because the hair follicles, which grow at an angle, cannot be visualized in their entirety in conventional vertical sections.

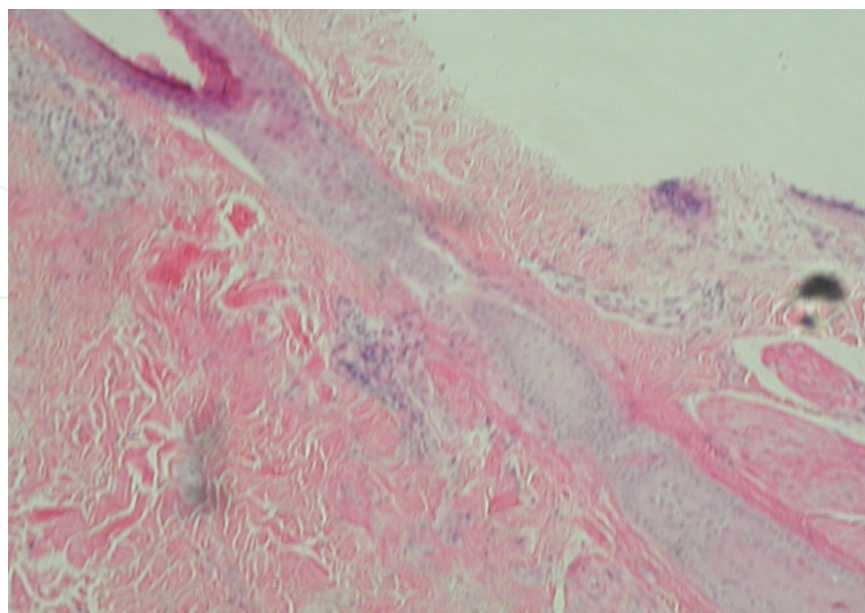


Figure 2. Vertical section of a scalp biopsy from a patient with DLE.

6. Horizontal sections

Horizontal sections are becoming the method of choice as they offer the advantage of evaluating large numbers of follicles simultaneously, determining hair density, location of inflammatory infiltrate and anagen to telogen ratio [5]. A transversely sectioned specimen will include all the hair follicles present in the biopsy, and in the same section. Although the clinical impression is very important in diagnosing alopecia, transversely sectioned biopsy specimens can greatly aid the diagnosis and management of patients with alopecia [6].

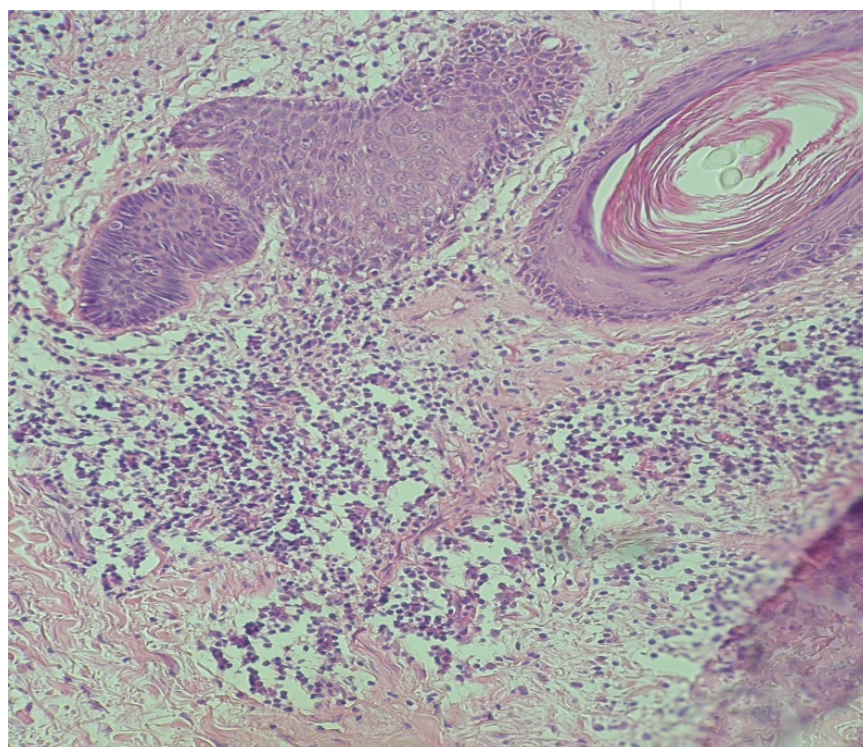


Figure 3. Transverse section from a scalp biopsy from a patient with DLE.

7. Hematoxylin and eosin staining of scalp biopsy

The histological findings in many forms of hair loss may be similar, and an accurate diagnosis of hair loss depends on distinguishing abnormal from normal follicular architecture. It is important to identify the normal hair follicle structure, the number, size and distribution of hair follicles within a biopsy specimen. Hematoxylin and eosin staining of the scalp biopsies is the usual stain in most of the cases of hair loss, but in some of the alopecias (such as DLE), immunofluorescence staining may be needed to add in diagnosis. In addition, the pathologist may use additional special stains to narrow a differential diagnosis or confirm an initial impression and one of these is immunohistochemistry which is dependent on the localization

of antigens in tissue sections by the use of labeled antibody as specific reagents through antigen-antibody interactions that are visualized by a marker such as peroxidase.

8. Histopathological findings in different types of hair loss

Specimens are categorized as scarring or nonscarring alopecia, and further diagnostic criteria discussed herein assist the pathologist in making specific diagnoses of nonscarring and scarring alopecias.

9. Scarring alopecia

Histologically, cicatricial alopecia is characterized by dermal scarring, along with absent or reduced hair follicles and reduced number of erector pili muscles. But taking skin biopsy from the active area will be more informative about the diagnosis.

This scarring alopecia may be secondary, and due to numerous etiologies (such as due to infectious causes (Fig 4), or primary, where the cause and pathogenesis are largely unknown, but the target is the hair follicle itself (such as DLE and LPP).

The discussion in following sections is about the primary type as the skin biopsy is more informative about the diagnosis.



Figure 4. Scarring alopecia in a child secondary to tinea capitis.

10. Lupus erythematosus

Lupus erythematosus is an autoimmune disease that can affect one or more internal organs as well as the skin. This disease is a clinical spectrum ranging from mildly affected patients with only localized skin disease to those at risk of dying from systemic manifestations. The skin involvement is among the most frequent symptoms; and is characterized by its natural history of relapsing and chronicity. The scalp (Fig 5) is a common area of involvement, and permanent alopecia may result with the following morphological features; sclero-atrophy, erythema, follicular hyperkeratosis, plugging and telangiectasia. The irreversible, scarring alopecia differs from the reversible non scarring alopecia that is seen in patients with systemic lupus erythematosus.

Scarring alopecia in DLE may mimic other types of scarring alopecia seen in some dermatoses, the most common differential diagnosis of this is lichen planopilaris (LPP) and the differentiation between them is possible by early clinical and histological changes. Both LPP and DLE show perifollicular erythema and keratotic follicular papules, but the distinctive clinical features of DLE of the scalp are the presence of erythema, scaling, telangiectasia, and mottled hyperpigmentation within the areas of scarring alopecia and the presence of hyperkeratotic papules in the central part of the bald area in DLE, while in LPP it presents at the margin of the alopecia patch [7].



Figure 5. Discoid lupus erythematosus of the scalp. The typical scaling is evident.

DLE is a scarring disease and so early treatment is needed to control existing cutaneous lesions and limit scarring and to prevent the development of the disease. Patients with DLE lesions should have regular clinical evaluation accompanied by simple laboratory studies to evaluate the possible progression from the primary cutaneous disorder to the disorder accompanied by systemic involvement. Therapy begins with general measures such as the use of sun-

protective measures, including sunscreens, protective clothing and medical therapy includes corticosteroids (topical or intralesional) and antimalarials.

Routine histologic examination of lesional skin from CLE patients is necessary, as the diagnosis of CLE generally requires clinicopathologic correlation and the distinction between different types of CLE based on histological findings without clinical correlation is difficult; all forms of CLE are similar histologically in broad terms. Histopathological features (Fig 6) include pilosebaceous atrophy, hyperkeratosis, parakeratosis, basement membrane thickening, subepidermal oedema and vasodilatation. A perivascular and peri-appendageal superficial and deep lymphoid cell infiltrate with plasma cells are other histopathological findings.

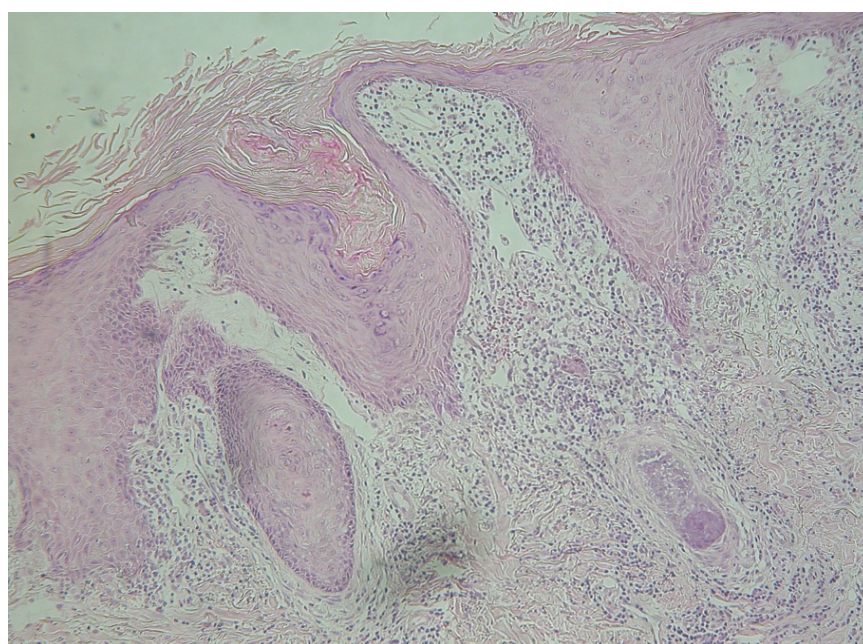


Figure 6. DLE pathology. Note the hyperkeratosis, basal cell degeneration and heavy inflammatory infiltrate.

Direct immunofluorescence (DIF) of lesional skin in CLE is an adjunctive test; it helps to confirm the diagnosis when the routine histological findings are equivocal. The test is positive only in some of lesional skin biopsies; so light microscopy should be carried out before DIF. For DIF, the optimal lesion of LE should be an established, erythematosus lesion, and of at least 6-8 weeks in duration. The most suggestive findings are the presence of multiple immunoreactants typically IgG and IgM, in a special pattern (bright in intensity, continuous, perifollicular, and granular) [8]. Sometimes complement components may be present including C3b and C1q. Scalp lesions have been reported to show the highest frequency of the DIF test (83 %), the immunoreactants deposits occur around hair follicles, an important feature not seen in other types of scarring alopecia.

Using immunohistochemistry [9], there were significant alterations in the basement membrane zone (BMZ) in patients with active DLE and this explain the previous histological findings of thickened BMZ in DLE. There was an increase in the expression of the anchoring fibril and

collagen component antigens in the BMZ with gross thickening and protrusion into the dermis in active DLE lesions (Fig 7).

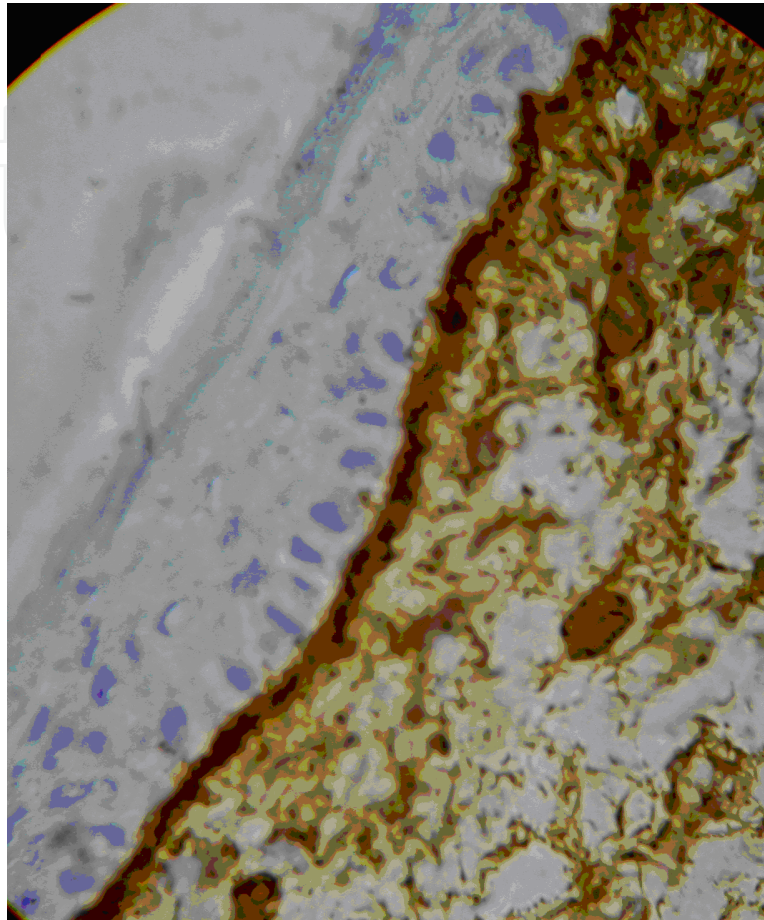


Figure 7. Anti-type IV collagen staining in DLE with an exaggerated expression as demonstrated by thickness of the basement membrane and protrusions.

11. Lichen Planopilaris (LPP)

LPP is a rare type of lichen planus which characteristically affects the scalp (Figure 8) with perifollicular erythema, keratotic follicular spines and with patchy or diffuse hair loss which may result in scarring alopecia as its end stage. Scalp lesions can be associated with characteristic flat topped violaceous papules of lichen planus (LP) on the limbs in 50 % of cases [10]. LPP of the scalp is a scarring disease and it is difficult to treat comparing to the glabrous LP and this has major psychological consequences for the affected patients. The therapeutic management often is quite challenging, as relapses are common after local or systemic treatments. The recommended treatments are ultrapotent topical or intralesional injections of corticosteroid. Some cases may need systemic treatment including oral corticotherapy and cyclosporine.



Figure 8. LPP of the scalp.

Histologically (Fig 9) has been reported to show two different patterns [11], each pattern characterized by the presence of specific histological features that reflects the specific stage of the progression of the disease. In the first pattern, hair follicles and the perifollicular dermis were mainly involved in the pathologic process, with no involvement of the interfollicular structures. In the second pattern, the pathologic changes extended to the interfollicular epidermis and the papillary dermis.

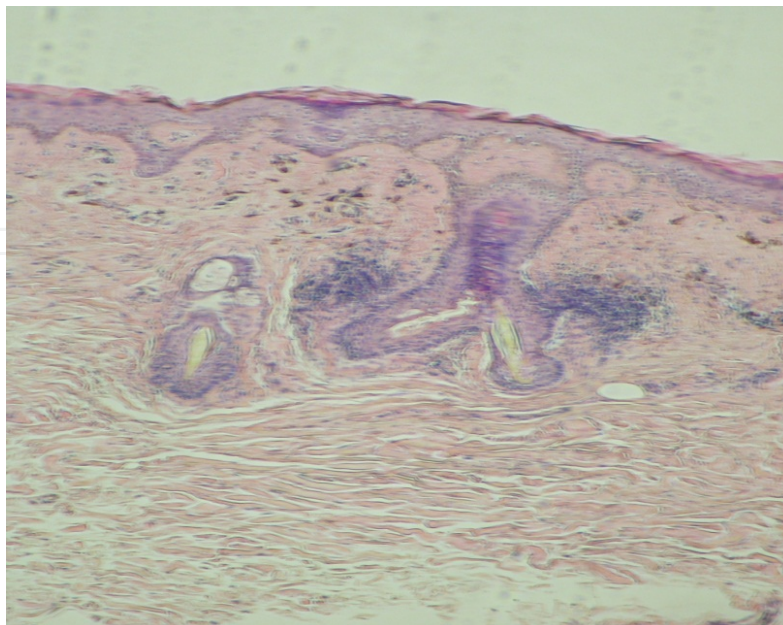


Figure 9. LPP pathology. The inflammation is mainly perifollicular with some involvement of the basal cell layers which also show basal cell degeneration.

Direct immunofluorescence highlights the presence of colloid bodies in the peri-infundibular area staining with IgM (less frequently with IgG, IgA and C3).

By immunohistochemistry staining [12], there is a significant alteration in the basement membrane structure in lesions of LPP which could differentiate it from active lesions of scalp DLE lesions.

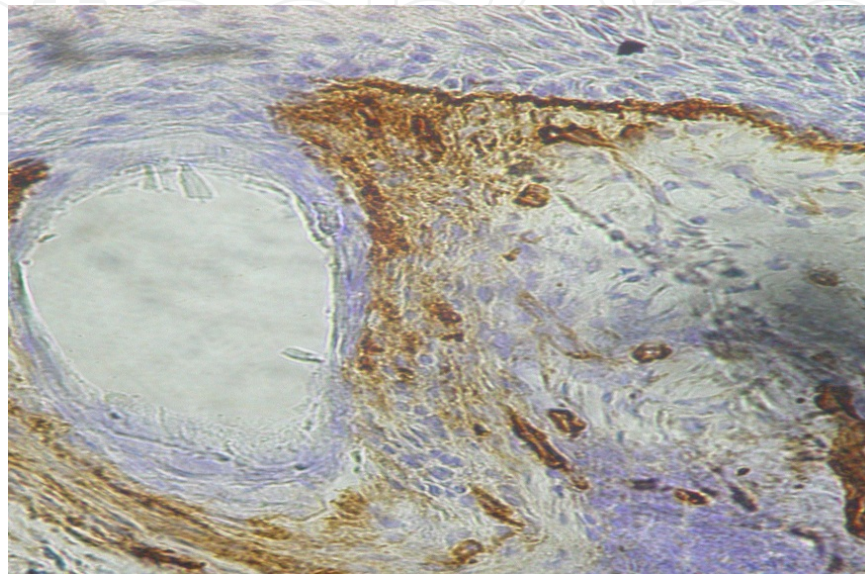


Figure 10. Anti-type IV collagen staining in LPP. Interrupted expression of type IV collagen in an affected hair follicle in an LPP lesion with projections into the underlying dermis, with the adjacent epidermis showing normal expression of the collagen

12. Non scarring alopecia

The diagnosis of this type of alopecia is usually based on a thorough history and a focused physical examination. In some patients, punch biopsy may be necessary if the cause of hair loss is unclear as has been described previously. The focus in the following discussion will be on alopecia areata and androgenetic alopecia (the skin biopsies will be needed in some of cases).

13. Alopecia Areata

Alopecia areata (Fig 11) is one form of non-scarring alopecia characterize by patchy hair loss of autoimmune origin. It usually presents as a single or multiple confluent patches of non-scarring alopecia. Spontaneous regression of the disease is common in this disease and the hair may grow back if the affected region is small. Topical treatment is effective including corticosteroids clobetasol or fluocinonide, corticosteroid injections, or cream, steroid injections,

topical minoxidil, irritants (anthralin or topical coal tar), and topical immunotherapy. Oral corticosteroids decrease the hair loss, but only for the period during which they are taken.

Diagnostic pathological findings (Fig 12) are more prominent in this type of alopecia which characterize by peribulbar lymphocytic inflammation which is usually considered to be an essential finding in establishing the diagnosis [13]. The lymphocytic

infiltrate is rich in helper T cells, which are considered to be evidence of an autoimmune process. Despite this, it may be absent in many scalp biopsy specimens. In the acute stage; a moderate to dense inflammatory cell infiltrate (mainly lymphocytes and langerhans cells) [14] develops around anagen hair and this leads finally to anagen arrest and inhibition which weakens the lowest portion of the

hair shaft. Using follicular counts [15] related to the stage of disease is a useful way to establish the histologic features of alopecia areata in scalp biopsy specimens taken from different types of alopecia areata; alopecia areata should be suspected when high percentages of telogen hairs are present, even in the absence of a peribulbar infiltrate [15].



Figure 11. Alopecia areata in a child presented with diffuse hair loss.

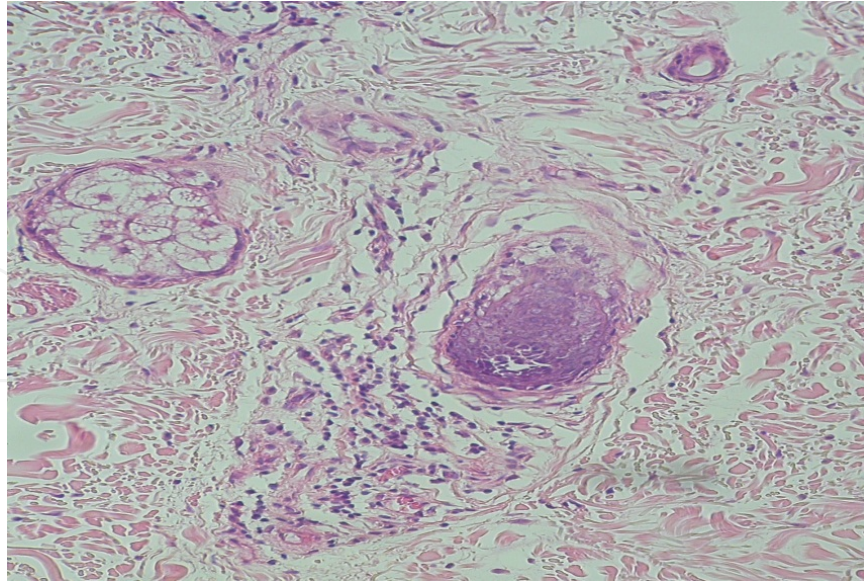


Figure 12. Skin biopsy from a patient with alopecia areata demonstrating perifollicular lymphocytic infiltrate.

14. Androgenetic alopecia

Androgenic alopecia is the most common type of hair loss. Clinically, it is a patterned alopecia, in that it is characterized by bitemporal recession and vertex balding in men, and in women (female pattern hair loss) by diffuse hair thinning of the crown with an intact frontal hairline. Histopathologically, the use of transverse sections is the most valuable method to reach a diagnosis [16], as all the hair follicles can be visualized.

The terminal (T) to vellus (v) ratio is T: V= less than 4:14. Normal scalp ratio is T: V= 7:1). A ratio of T: V= 3: 1 or less is considered to be diagnostic [16], [17].

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