

Clinico-histopathological Study of Cicatricial Alopecia in a Tertiary Care Center

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Abstract

Introduction: Cicatricial alopecia (CA) comprises a group of disorders characterized by permanent destruction of the hair follicle and fibrosis on histopathologic examination. The similarities in the clinical presentation of various types of this disorder cause difficulty in prompt diagnosis, so histopathological assessment plays a pivotal role in the diagnosis. This study aimed to assess the clinical variants of cicatricial alopecia and compare the histopathology of the various subtypes.

Materials and Methods: In this cross-sectional study, 22 patients of cicatricial alopecia were enrolled and punch biopsies from the active site were taken for histopathological examination. Statistical analysis and correlation of clinical and histopathological features were done.

Results: Out of the 22 patients, 10 cases (45.45%) were confirmed as lichen planopilaris (LPP), seven (31.81%) as discoid lupus erythematosus (DLE), two (9%) as morphea, one (4.5%) each as pseudopelade, central centrifugal cicatricial alopecia (CCCA) and dissecting cellulitis (DC). There was a fair agreement between clinical and histopathological diagnoses (Kappa=0.384). The age ranged from 10 years to 60 years with the mean age of 32.32 ± 15.51 years.

Conclusion: There is high clinical and histopathological variability and similarities among the variants of CA, which represents a true diagnostic challenge. A precise and early diagnosis is possible if the clinico-histopathological correlation is employed.

Key words: Alopecia; Cicatrix; Pathology

Introduction

Cicatricial alopecia comprises a group of disorders characterized by permanent destruction of the hair follicle and irreversible hair loss. The diagnostic hallmarks on histopathologic examination are visible loss of follicular ostia and destruction of the hair follicle.^{1,2} The exact incidence and prevalence of CA are unknown; however it represents approximately 7% of patients in hair loss clinics.³ Pseudopelade, discoid lupus erythematosus (DLE), lichen planopilaris (LPP) and folliculitis decalvans (FD) are the predominant clinical types of CA.^{3,4} The commonly observed features in histological examination are perifollicular fibrosis, basal cell vacuolization, perifollicular lymphocytic infiltrate, epidermal atrophy and hyperkeratosis.⁵

CA is a trichologic emergency and accurate diagnosis is dependent on clinical and pathological evaluation. So, this study helps identify clinical and histopathological features which aids in diagnosing CA. The primary objectives of this study were to assess the clinical variants of CA and compare the histopathology of various subtypes. The secondary objective was to determine the relative frequency of each variant of CA.

Materials and methods

This was a descriptive prospective cross-sectional study where all consecutive patients with CA attending

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Dermatology Department of BPKIHS, Dharan from September 2018 to August 2019 were included. The Institutional Review Committee approved the study.

All the consecutive patients with biopsy-proven cicatricial alopecia fulfilling the inclusion criteria were included in the study.

Participant's selection criteria: CA was defined as skin disorder characterized by permanent destruction of the hair follicle and irreversible hair loss clinically seen as smooth, shiny skin over the area of alopecia, loss of follicular ostia and atrophy of overlying skin.

Exclusion criteria

- Patients not willing to participate in the study
- Patients with comorbidities, not fit to undergo biopsy

A detailed history and thorough clinical examination of scalp was performed. At least one 4 mm punch biopsy was taken from a clinically active area for histopathological analysis.

Data was entered in MS Excel 2010 and converted into Statistical Package for Social Science (SPSS) version 10 for statistical analysis. For descriptive data analysis, mean, median, standard deviation, proportion and percentage were calculated. The clinico-histopathological correlation was done using Cohen's kappa test.

Results

A total of 22,578 patients attended Dermatology OPD, out of which 495 patients were diagnosed as having alopecia. 24 patients were diagnosed as CA, but 2 patients refused biopsy so were not included in the study.

Twenty-two histologically proven cases of CA were enrolled in the study. Out of the 22 patients, 10 were females, and 12 were males with a male to female ratio of 0.83: 1. The age of patients enrolled in our study ranged from 10 years to 60 years with a mean age of 32.32 ± 15.51 years.

The most common site of onset for hair loss was vertex (68.18%). The disease duration ranged from 1 month to 15 years, with the majority having a duration of more than 6 months (15, 68.2%) followed by a sub-acute course with a duration of 6 weeks to 6 months (5, 22.7%) and only 2 patients (9.1%) with acute onset, i.e., less than 6 weeks.

Pruritus was the most common associated symptom (72.72%), 8 patients of LPP, 4 of DLE, 1 each of CCCA, DC, Morphea and Pseudopelade. The most common clinical pattern was a single patch (9 cases). LPP presented as a single patch and 'fingerprint in snow' pattern in 60% of the cases (3 cases each). Other clinical patterns of marginal (2 patients), follicular (1 patient) and diffuse (1 patient) were also observed. In DLE, the most common pattern observed was also single patch seen in 4 patients (57.14%), multiple patches in 2 patients (28.57%) and marginal in 1 patient (14.28%). Central Centrifugal Cicatricial Alopecia (CCCA) presented with a large single patch and DC with the marginal pattern (Figure 1). Among the 2 cases of morphea, 1 showed with single patch and 1 with diffuse pattern.

Perifollicular erythema was seen in 50% of LPP, 57.14% of DLE and 1 case of Morphea. Perifollicular hyperkeratosis was observed in 60% of LPP, 28.57% of DLE (Figure 2 & Figure 3) and 1 case of Morphea. Telangiectasia was a feature exclusively seen in DLE (3 cases). Pigmentary change was observed in 71.42% of DLE, 50% of LPP and 1 case of Morphea. Perifollicular scaling was seen in 85.71% of DLE, 70% of LPP, 2 cases of Morphea and 1 case of pseudopelade.

The histopathological findings observed in the study are summarized in Table 1. Follicular plugging was a common feature for LPP and DLE (Figure 4). On histopathological analysis of inflammation, most cases had mild (10, 45.4%) to moderate (9, 40.9%) inflammation, while only one had severe inflammatory infiltrates. The lymphocyte to neutrophil ratio was found to be 19:1. Inflammation extending to deeper reticular dermis was seen in 57.14% DLE, 20% LPP, and 1 cases of morphea and DC. Similarly, inflammation involving subcutaneous tissue was seen in single cases of DLE and DC each. The perifollicular and periadnexal inflammation were features common to both LPP and DLE. Interstitial inflammation was more common in DLE (71.42%) than in LPP (40%).

Concentric fibroplasia was observed in 70% LPP, 42.85% DLE and one case of DC, CCCA and pseudopelade. Interfollicular mucin deposition was observed in 57.14% DLE and 10% LPP. Basement membrane thickening highlighted by PAS stain was seen in 85.71% DLE.

After histopathological examination, 10 cases (45.45%) were confirmed as LPP, 7 (31.81%) as DLE, 2 (9%) as morphea, 1 (4.5%) as pseudopelade and 1 (4.5%) as DC. Table 2 shows clinical diagnosis correlates with histopathological diagnosis in 12 out of 22 patients while the remaining 10 patients did not match

with histopathology. Among nine patients clinically diagnosed as LPP, histological diagnoses were consistent with 5, while 3 had a histological diagnosis of DLE and one as morphea. Four patients were clinically and histologically diagnosed as DLE. Similarly, one patient had a clinical and histological diagnosis as DC. There were 2 patients clinically diagnosed with CCCA, but histopathological features were consistent in only 1 of them (Figure 5a and 5b), the other had features of LPP. Likewise, out of six patients with the clinical presentation supporting Pseudopelade, only one was histopathologically confirmed, while four had histopathological features suggestive of LPP (Figure 6) and one of morphea.

Clinical diagnosis made by a dermatologist was compared with the histopathological diagnosis at the same center using Cohen's kappa test, which shows statistically significant fair agreement between clinical and histopathological diagnosis (Kappa=0.384).⁶ The main reason for disagreement between the two diagnoses is that clinical evaluation solely cannot make the diagnosis of CA. It requires clinico-histopathological correlation as well as additional investigations like immunofluorescence studies and none of the investigations are 100% specific by themselves.

Table 1: Histopathological features of various types of cicatricial alopecia

Features	LPP (n=10) (%)	CCCA (n=1) (%)	Dissecting cellulitis (n=1)(%)	DLE (n=7)(%)	Morphea (n=2) (%)	Pseudopelade (n=1)(%)
Follicular plugging	7 (70)	0 (0)	0 (0)	5 (71.42)	0 (0)	0 (0)
Inflammation extending to reticular dermis	2 (20)	0 (0)	1 (100)	4 (57.14)	1 (50)	0 (0)
Inflammation extending to subcutaneous tissue	0 (0)	0 (0)	1 (100)	1 (14.28)	0 (0)	0 (0)
Perifollicular inflammation	8 (80)	1 (100)	1 (100)	5 (71.42)	0 (0)	0 (0)
Interstitial inflammation	1 (10)	0 (0)	0 (0)	3 (42.85)	0 (0)	0 (0)
Periadnexal inflammation	7 (70)	0 (0)	1 (100)	5 (71.42)	1 (50)	0 (0)
Perivascular inflammation	4 (40)	0 (0)	1 (100)	5 (71.42)	2 (100)	0 (0)
Concentric fibroplasia	7 (70)	1 (100)	1 (100)	3 (42.85)	0 (0)	1 (100)
Mucin deposition	1 (10)	0 (0)	0 (0)	4 (57.14)	0 (0)	0 (0)
Basement thickening	0 (0)	0 (0)	0 (0)	6 (85.71)	0 (0)	0 (0)

Table 2: Correlation of clinical and histo-pathological diagnosis. (n = 22)

Histopathological diagnosis	Clinical diagnosis					Total
	LPP	CCCA	Dissecting cellulitis	DLE	Pseudopelade	
LPP	5	1	0	0	4	10
	55.6%	50.0%	0.0%	0.0%	66.7%	45.5%
CCCA	0	1	0	0	0	1
	0.0%	50.0%	0.0%	0.0%	0.0%	4.5%
Dissecting cellulitis	0	0	1	0	0	1
	0.0%	0.0%	100.0%	0.0%	0.0%	4.5%
DLE	3	0	0	4	0	7
	33.3%	0.0%	0.0%	100.0%	0.0%	31.8%
Morphea	1	0	0	0	1	2
	11.1%	0.0%	0.0%	0.0%	16.7%	9.1%
Pseudopelade	0	0	0	0	1	1
	0.0%	0.0%	0.0%	0.0%	16.7%	4.5%
Total	9	2	1	4	6	22
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%



Figure 1: Central Centrifugal Cicatricial Alopecia showing centrifugal spread of alopecic patch over the vertex

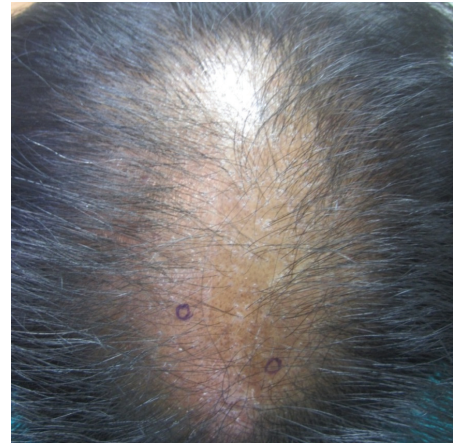


Figure 2: Lichen Planopilaris showing perifollicular hyperkeratosis and scaling



Figure 3: Discoid Lupus Erythematosus showing peri-follicular hyperkeratosis and scarring with dyspigmentation

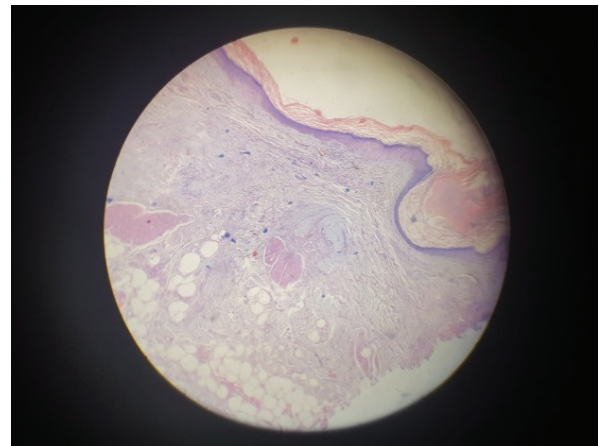


Figure 4: Discoid Lupus Erythematosus showing follicular plugging and mucin deposition (H and E stain, X10)

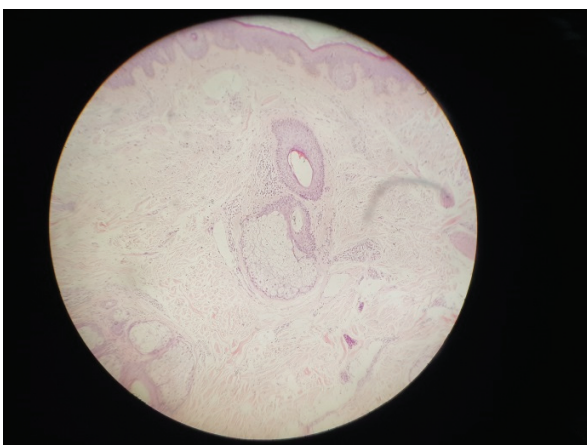


Figure 5a: Histopathology of CCCA showing presence of ghost follicle and concentric lamellar fibrosis (H and E stain, X10)

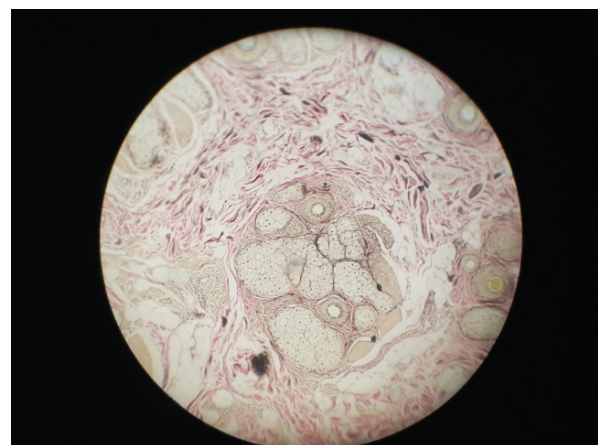


Figure 5b: Histopathology of CCCA showing elastin positive (VVG stain, X40)

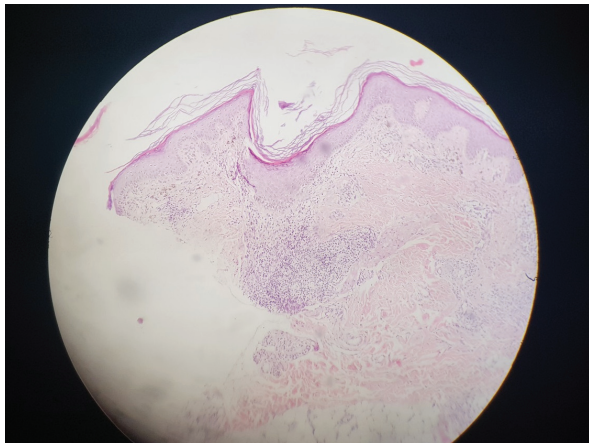


Figure 6: Histopathology of LPP showing follicular plugging with dense inflammation comprising of lymphocytes (H and E stain, X10)

Discussion

CA is a relatively rare dermatological condition with scarce studies published worldwide. Clinical and pathological analysis play an essential role in the precise diagnosis of CA. Our study aimed to assess the clinical variants of CA and compare the histopathological characteristics of those variants.

In our study, the prevalence of CA accounted for 4.8% of alopecia patients. In a study conducted by Tan E et al., from 1997 to 2001, 3.2% of patients with trichologic consultations were diagnosed as having CA.⁴ Similarly, another 10 years study conducted by Whiting DA from 1989 to 1999 showed the prevalence of CA of 7.3% among the patients with hair disorders.³

In our study, we followed the most accepted classification of CA given by the North American Hair Research Society (NAHRS) in 2003.⁷ However, we did not categorize CA as non-specific CA. We tried to classify the disorder into the most probable diagnosis considering even the subtle clinical and histopathological findings. After histopathological evaluation, 10(45.45%) cases were confirmed as having LPP, 7 as DLE (31.81%), 2 morphea and 1 each of CCCA, DC and pseudopelade. This is similar to the recent studies where LPP was found to be the commonest type of CA in the studies by Villablanca S et al., and Puri N et al.^{5,8} However, it varies from the earlier studies by Tan E et al., and Whiting DA where the most frequent type of alopecia was found to be DLE and nonspecific alopecia.^{7,8} Owing to the fact that many cases of lupus erythematosus (LE) may present with cutaneous lesions earlier than scalp involvement, many cases diagnosed earlier with LE especially DLE may not have been included in our study. This could

explain the lower number of DLE cases in our study. After histopathological review, four cases clinically diagnosed as pseudopelade and one case clinically diagnosed as CCCA were later diagnosed as LPP. This highlights that pseudopelade can be an end-stage of other forms of CA, and primary diagnosis may not be obvious on clinical examination. Similarly, three cases clinically diagnosed as LPP were reclassified later as DLE based on histopathological features. This could be because of the similar clinical picture of both variants like perifollicular erythema, perifollicular hyperkeratosis, dyspigmentation and scaling, which may be present in both but are not specific either. The specific features of DLE like telangiectasia, carpet tack sign, and LPP like follicular violaceous papules may not be present in all cases. So, some cases' lack of these specific features and similarities in clinical picture could have led to diagnostic confusion between the two conditions. An interesting finding in our study was that two cases clinically diagnosed as LPP and pseudopelade were found to have histopathological diagnosis of morphea. Hence, it shows that it is not always possible to classify CA solely based on clinical judgement and clinico-histopathological correlation is an important tool for the classification.

The most common site of onset for hair loss was vertex, followed by frontal, temporal, occiput, and midline region. The most common site of onset for LPP was vertex, followed by temporal, frontal and midline. Similarly, the most common site of onset for DLE was also vertex, and there was one case with the frontal region as onset site. This was similar to the findings from the Baylor Study by Whiting DA.³

In our study, 12(54.54%) out of 22 patients were males and 10(45.45%) were females in contrast to the previous study by Tan E et al., where females outnumbered males.⁴ The age in our study population ranged from 10 years to 60 years with a mean age of 32.32 years, and most patients belonged to the age group of 21 to 30 years, which was similar to the study carried out by Whiting DA where the mean age was 36 years but not in parallel to other studies by Puri N et al., and Fatemi-Neini F et al., where the most common age range was 41-50 and 30-39 years respectively.^{3,5,9}

There were 15 cases (68.2%) with a chronic course of disease with disease onset of more than 6 months duration, 5 patients with subacute onset with 6 weeks to 6 months and 2 patients with acute onset, i.e. less than 6 weeks. The chronic course of the disease was present in most DLE cases, i.e. 6 out of 7, LPP, i.e. 5 out of 10 cases, and 1 each of morphea, pseudopelade,

CCCA and DC. Subacute course was seen in 3 cases of LPP and 1 each of DLE and morphea. The acute onset was seen in only 2 cases of LPP. This was partially consistent with the study Villablanca S et al., where the subacute-chronic form was seen in lymphocytic CA in par with our study, but the acute-subacute form was seen in neutrophilic CA.⁸ This could be explained by the small number of neutrophilic CA in our study.

In patients with LPP, the symptoms seen were pruritus (80%), pain (10%) and burning sensation (10%). These findings were similar to the study by Tan E et al.⁴ Similarly, in DLE, pruritus (57.14%), pain (14%), burning sensation (14%), and discharge (14%) were seen. This was again similar to the study by Tan E et al., where pruritus was the commonest symptom in 65% of DLE. The patient of DC had symptoms of pruritus, pain, and discharge. The patients of CCCA and morphea both had pruritus only.

The distinct clinical pattern of the presentation was analyzed in our study, and the most common clinical pattern was found to be single patch (9 patients) followed by marginal (4 patients), footprint in snow (4 patients), diffuse (2 patients), multiple patches (2 patients) and follicular pattern (1 patient). LPP presented as a single patch and footprint in snow in 3 patients each. However other patterns of marginal, follicular and diffuse were also observed. Hence, the pattern conventionally thought of as a characteristic of pseudopelade i.e., footprint in snow could be a presentation of other forms of CA as well. This was similar to the finding in Tan E et al.'s study where 6 patients initially diagnosed as pseudopelade were later classified as other entities.⁴ This supports the idea that pseudopelade could be an end-stage of other forms of CA, so histopathological evaluation can help us find the primary diagnosis. Similarly, the most common clinical pattern observed in patients of DLE was a single patch followed by multiple patches and marginal. CCCA presented as a large single patch, and DC presented as a marginal pattern. Amongst the 2 cases of morphea, 1 presented as a single patch and 1 as a diffuse pattern. This finding slightly deviated from the common finding where multiple patches are most commonly seen in LPP, great central patch in DLE, marginal in FFA or traction alopecia and footprint in snow pattern in Classic pseudopelade of Brocq. The study by Villablanca S et al. LPP followed the common clinical pattern of multiple patches and follicular pattern and the great patch pattern corresponding to LE.⁸ Similar to our findings, in this study, the clinical cases classified as Pseudopelade based on the characteristic clinical

pattern of 'footprints in snow' were later diagnosed as LPP or LE after further investigations.

The clinical findings in our study were similar to the findings in the study by Puri N et al.⁵ Erythema was present in 55% of cases as compared to 45.45% in our study, telangiectasia in 27.5% as compared to 13.63% in our study and hyperpigmentation in 20% as compared to 50% in our study. However, in the study by Puri N et al., the features have not been categorized into an individual variant of CA, unlike in our study.⁵

On histopathological evaluation, it was found that mild to moderate inflammation was present in 95% of cases, and severe inflammation was present in only 1 case. The ratio of lymphocyte to neutrophil infiltrates was 19:1 which was higher as compared to previous studies by Tan E et al. and Villablanca S et al. where the ratio was 4:1.^{4,8} It could be explained by the low sample size in our study so even a small difference in the number of patients could display a large variation in the ratio and also 2 cases of neutrophilic CA were not included in our study due to refusal by the patients. The inflammation extending to the reticular dermis and interstitial inflammation was present in 8 patients (36.36%). It was predominantly present in DLE patients i.e. 4 out of 7, followed by 2 LPP patients. In our study, inflammation extending till the subcutaneous tissue was observed in only 1 patient. The perifollicular and periadnexal inflammation was observed in LPP as well as DLE. However, perivascular inflammation was more common in DLE than in LPP (71% vs. 40%).

It was found that follicular plugging was seen in 70% of LPP and DLE. In the study performed by Thakur BK et al., this feature was seen in 88.88% of DLE patients and 66.67% of LPP patients.¹⁰

The main differentiating features between DLE and LPP were mucin deposition and basement membrane thickening. Mucin deposition was present in 4 DLE cases and 1 LPP. However, mucin deposition in LPP was present in the perifollicular area only in contrast to DLE which was present in the interstitial region. This is supported by the study by Nambudiri VE et al.¹¹ Basement membrane thickening highlighted by PAS stain was specifically seen in DLE only (6 cases). Concentric fibroplasia was another feature that helped us distinguish between the two conditions. It was more commonly seen in LPP (7 out of 10) than in DLE (3 out of 7). This is a more specific feature of CCCA and was present in the single patient of CCCA.

Conclusion

There is a high clinical and histopathological variability and similarities among the variants of CA which, is well demonstrated in this study. This represents a true

diagnostic challenge, especially at late and advanced stages of the disease. A precise diagnosis is possible in such cases if the clinico-histopathological correlation is employed.

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