



Abstract

Primary Lymphocytic Cicatricial Alopecia: A Retrospective Analysis of 36 Patients

Neslihan Akdoğan¹, Ayşen Karaduman², Sibel Ersoy Evans², Aslı Hapa³, Gonca Elçin², Gül Erkin⁴, Nilgün Atakan²

Introduction: Cicatricial alopecia (CA) is a group of disorders that lead to permanent hair loss due to irreversible damage to hair follicles. The aim of this study is to examine clinical and demographic characteristics of patients diagnosed with primary lymphocytic cicatricial alopecia (PLCA).

Methods: Patients admitted to our outpatient clinic between 2000 and 2010 and who were diagnosed with PLCA were retrospectively evaluated for demographic characteristics, dermatologic findings, personal and family history, histopathologic results, therapeutic options given to the patients, and patient responses to the treatments.

Results: Thirty-six patients were included in this study. Histopathological examination of scalp hair samples revealed that findings were concordant with lichen planopilaris (LPP) in 26 patients, discoid lupus erythematosus (DLE) in 7 patients, pseudopelade de Brocq (PB) in 3 patients. The main first-line treatment most commonly reported was intralesional corticosteroid injection (ILCS, n=16, 44.4%), which was followed by hydroxychloroquine (n=10, 28%). Nineteen of the 36 patients responded to the first-line treatments, whereas 17 patients needed another treatment. Treatments that patients were most likely to respond to were hydroxychloroquine and ILCS for LPP patients; hydroxychloroquine for DLE patients; hydroxychloroquine, systemic corticosteroid, and topical corticosteroid treatments for PB patients.

Conclusion: PLCA is an entity widely observed in middle-aged women and is mostly encountered in the form of LPP. In the current study, patients most likely benefited from ILCS and hydroxychloroquine treatments.

Keywords: Alopecia, cicatricial, epidemiology

Introduction

Cicatricial alopecias (CAs) are a group of diseases that cause irreversible loss of hair follicles (1). The folliculocentric attack is common in all CAs, which can be divided into 2 groups as primary and secondary CAs. While the hair follicle is targeted and damaged mainly in primary CAs, the primary event in secondary CAs is cutaneous, and when cutaneous inflammation involves the hair follicles, the follicle is damaged; in other words, they are not specifically folliculocentric. According to the predominant inflammatory cell type, primary CAs are divided into four subgroups as lymphocytic, neutrophilic, mixed inflammatory, and nonspecific (2). Infections, severe burns, tumors, and exposure to radiation are among the causes of secondary CAs. As a result, the hair follicles are permanently damaged irrespective of whether they are primary or secondary; CAs are clinically characterized by the loss of follicular ostium and histopathologically by the loss of hair follicles, which are substituted with fibrous tissue (3).

Hair loss is the most frequent cause of hospital applications of the patients with CAs, and patients may also have symptoms such as itching, burning, sensitiveness, and pain. The most common clinical finding is cicatricial alopecia patches. In the histopathologic examination, findings such as perifollicular concentric fibrosis, mild peripheral perifollicular and perivascular lymphoid cell infiltration (if it is a lymphocytic type), destruction of follicular epithelium, and complete loss of follicles may be seen at terminal phase. The disappearance of the sebaceous glands is also considered as a marker indicating CAs (3).

The purpose of this retrospective study is to examine clinical and demographic characteristics, the treatment options applied, and the responses to treatment in 36 patients who were histopathologically diagnosed with primary lymphocytic cicatricial alopecia (PLCA).

Material and Methods

In this study, 36 patients who visited the dermatology polyclinic of our hospital between 2000 and 2010 and who were histopathologically diagnosed with PLCA were included. The age, gender, history and family characteristics, systemic diseases and drugs they used, histopathologic diagnoses,

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¹Clinic of Dermatological and Venereal Diseases, Ankara Numune Training and Research Hospital, Ankara, Turkey

²Clinic of Dermatological and Venereal Diseases, Hacettepe University School of Medicine, Ankara, Turkey

³Department of Dermatological and Venereal Diseases, Şifa University School of Medicine, Izmir, Turkey

⁴Clinic of Dermatological and Venereal Diseases, Güven Hospital, Ankara, Turkey

Address for Correspondence:

Neslihan Akdoğan
E-mail: nslakdogan@gmail.com

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location of lesions, dermatological examination findings, patient complaints for the hospital application, the presence of other skin findings other than on the scalp, the treatments applied as the first choice, the treatments applied to the patients who did not benefit from the first-option treatment, and the treatment options that the patients most benefited from were recorded at the time of hospital application. The response to the treatment was accepted as the cessation of hair loss, appearance of hair follicles, as well as the decrease in the symptoms of follicular and perifollicular erythema, purple plaque, and follicular plugs, if the patient had these symptoms. The data related to the patients were obtained retrospectively from the patient files. Because the information of the patients diagnosed with lichen planopilaris (LPP), discoid lupus erythematosus (DLE), and pseudopelade of Brocq (PB) was obtained adequately when the files were scanned retrospectively, these patients were included in the study.

The ethics committee approval for this study was obtained from the Ethics Committee of the Medical Faculty of Dicle University. Since this study was conducted by retrospectively examining the patient records after the ethics committee approval was received, informed consent was not received from the patients in this study.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for Social Sciences version 21.0 (IBM Corp.; Armonk, NY, USA). The numerical variables were expressed as mean±standard deviation, median and minimum–maximum values, and the categorical variables as number and percentage. The limit of statistical significance was accepted as $p < 0.05$ in all comparisons.

Results

Demographic Characteristics

A total of 36 patients (25 females, 69%; 11 males, 31%) who were histologically diagnosed with PLA were included in the study. The female/male ratio of patients was 2.3. The mean age of the patients was 44.5 ± 10.94 (mean±standard deviation). According to age distribution, 21 patients (58%) were between the ages 40 and 60, 12 patients (33%) were between the ages 20 and 40, and 3 patients (8%) were over 60 years old (Figure 1). The mean duration of disease was 7 ± 5.7 months (range: 2–35 months).

Clinical Features

Histopathologic findings of the scalp were found to be compatible with LLP in 26 patients (72%), DLE in 7 patients (20%), and PB in 3 patients (8%). Considering the age distribution according to the diagnoses, 54% ($n=4$) of patients with LPP, 57% ($n=4$) of patients with DLE, and 3 (100%) of patients with PB were between 40 and 60 years of age (Figure 1). In all three groups, the number of female patients was higher than male patients, but this difference was not statistically significant ($p > 0.05$).

The most frequent reason for visiting a doctor was hair loss (94%, $n=34$). Considering the patients for whose disease location sufficient information was found, while the alopecia was limited to vertex in 7 (26.9%) of the LPP patients, 7 (26.9%) patients had diffuse alopecia in the scalp. There was diffuse alopecia in the scalp in 2 (28.6%) of the DLE patients and limited alopecia in 2 (28.6%) patients in the vertex and occiput regions. Alopecia was in the

vertex region in 1 of the PB patients, in the frontal region in 1 patient, and it was limited to the vertex and parietal regions in 1 patient. Dermatological examination revealed DLE in 23 (88.5%) of the LPP patients and atrophic alopecic patches in all PB patients. In 8 LPP patients (30.8%), follicular plugs were observed in addition to atrophic alopecic areas, and in 4 patients (15.4%), perifollicular erythema was observed in addition to atrophic alopecia area and follicular plugs. Non-scalp skin findings were found only in 1 patient out of all patients who participated in the study, and this patient was followed up with LPP diagnosis, and there were clinical findings compatible with lichen planus in addition to LPP findings in the patient. There were no systemic diseases in the history of 26 patients (72%) and in the family history of 32 patients (88%). While 72% ($n=26$) of the patients did not use any systemic medication due to a non-skin disease, there was a continuous use of medication in 28% ($n=10$) of them.

The Treatments That Were Applied

The most common first-line therapy was intralesional corticosteroid injection (ICSI) ($n=16$, 44.4%), and it was followed by hydroxychloroquine therapy ($n=10$, 28%). While 13 LPP patients (50%) benefited from the first treatment, other treatment regimens were used in the remaining 13 patients. While no additional treatment was given to 4 (57%) DLE patients because they benefited from the treatment, other treatments were used in 3 patients. While 2 of the PB patients (66.7%) benefited from the first treatment, 1 patient received another treatment. As a result, while 19 of the patients (52.8%) benefited from the first treatments, 17 patients were treated with another treatment option. The most frequently used second treatment option was hydroxychloroquine (47%, $n=8$), and oral isotretinoin (29%, $n=5$) was in the second place (Table 1).

When the treatments that patients most benefit from are considered, 12 of LPP patients (46.2%) benefited from hydroxychloroquine, 9 patients (34.6%) from the ICSI application, 2 patients (7.7%) from oral isotretinoin, 2 patients from topical corticosteroids and 2 patients from systemic corticosteroids. While the most beneficial

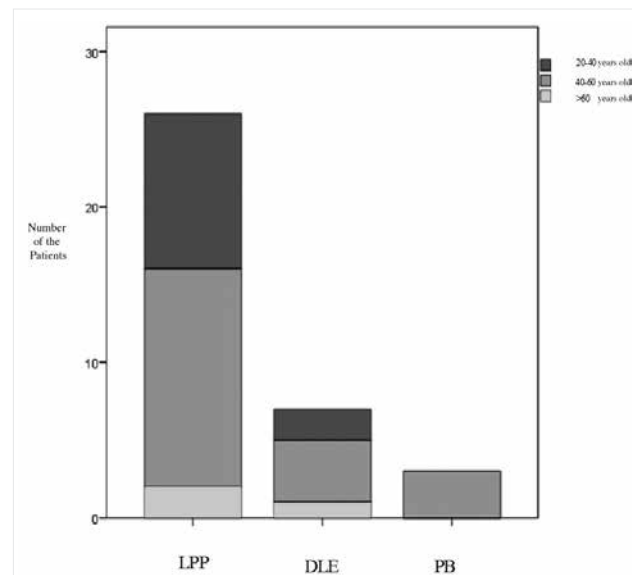


Figure 1. The distribution of patients by age range
LPP: lichen planopilaris; DLE: discoid lupus erythematosus; PB: pseudopelade of Brocq

Table 1. The treatments that our patients received and the treatment options that the patients most benefited from

Options	Distribution of the Most Beneficial Treatments According to Diagnosis		
	LPP (n=26)	DLE (n=7)	PB (n=3)
ICSI	9	1	-
Topical Corticosteroids	2*	-	1
Hydroxychloroquine	12*	5	1
Oral Isotretinoin	2	1	-
Systemic Corticosteroids	2	-	1

*A patient with the diagnosis of LPP has benefited from the combination of topical corticosteroids and hydroxychloroquine.
LPP: lichen planopilaris; DLE: discoid lupus erythematosus; PB: pseudopelade of Brocq; ICSI: intralesional corticosteroid injection

treatment for DLE patients was hydroxychloroquine (n=5, 71.4%), PB patients benefited from hydroxychloroquine (n=1, 33.3%), systemic corticosteroid (n=1, 33.3%), and topical corticosteroid (n=1, 33.3%) treatments, respectively (Table 1).

Discussion

CAs are a rare group of diseases in which follicular ostia disappear after an attack targeting the hair follicle, which is followed by atrophy. They can be divided into two groups as primary and secondary CAs (3). In 2001, a primary CA classification was made by the North American Hair Research Society (2). This classification was based on histopathological examination, and primary CAs were divided into subgroups according to the dominant inflammatory cells located inside and outside the hair follicles. According to this classification, primary CAs are divided into 4 groups as lymphocytic, neutrophilic, mixed, and nonspecific (2).

The etiopathogenesis of CAs is not exactly known. In studies, peroxisome proliferator-activated receptor dysfunction (4), psycho-emotional stress (5), trauma, increased susceptibility to *Staphylococcus aureus* (6), drugs and vaccines (5), genetic factors (7, 8), and immunological mechanisms (9) are implicated as the triggering factors in pathogenesis. However, primary CAs are involved in the autoimmune disease spectrum all over the world (10). In primary CAs, the condensation of inflammatory infiltrate in the stem cells of the bud region of the hair follicle, the cytotoxic T-cell-mediated tissue damage, the vulnerability of the bud region to immune damage as a result of the increase in the expression of MHC-1, MHC-2, and β 2-microglobulin in the bud region, and the apparent increase of apoptosis are among the mechanisms that are implicated in the formation of the disorder (10).

In the clinic, CAs can lead to complaints such as hair loss, thinning in the hair, sometimes burning sensation, itching, pain, and susceptibility. In our study, hair loss was the most common cause for visiting the clinic. In our study, only 2 patients came to our clinic with a complaint other than hair loss, which were itching (n=1) and the formation of acne and roughness in hair roots (n=1). Scarred alopecic patches are the most common dermatologic finding expected in CAs. The most common finding in our study was atrophic alopecic patches (n=33, 91.7%). As is known, alopecic, and sometimes atrophic patches, and perifollicular erythema at the borders of these alopecic regions, follicular hyperkeratosis,

and plugs in the scalp are typical for LPP. In our study, there were 15 patients (41.7%) who had atrophic alopecic patches in the scalp and in whom perifollicular erythema and/or follicular plugs were observed, and 12 (80%) of these patients received LPP diagnosis. LPP is a disease that often affects middle-aged women, in which the lesions tend to widen from the periphery and leave scarring in the middle. In our study, supporting this knowledge, more than a half of the LPP patients (n=14, 53.8%) were between 40 and 60 years of age. According to the literature, lichen planus is found in 30%–50% of LPP patients (11). However, in our study, lichen planus was found in only 1 of the LPP-diagnosed patients.

DLE is a disease that frequently affects 20- to 40-year-old women, which causes application to clinic due to hair loss and burning in the scalp and which is seen as discoid erythematous plaques accompanied by follicular plugs. Of the DLE patients in our study, 4 (57.1%) were between 40 and 60 years of age, and 2 (28.6%) were between 20 and 40 years of age; the patients came to the clinic due to hair loss. However, in addition to this complaint, 2 patients complained of itching, and 1 patient had rash in the scalp. In all the DLE patients, while atrophic alopecic patches were observed in the dermatological examination, 2 patients had follicular plugs and purple plaques in addition to this finding.

PB was first described by Brocq (12) in 1888. It is not clear whether it is a specific entity or whether it is the last point of other CAs. The diagnosis of the disease is a diagnosis of exclusion, made by eliminating other diagnoses (13). It is multifocal and asymptomatic, and it is characterized by alopecic patches in the skin color. Its appearance was thought to look like “footprint in the snow.” The patches are usually atrophic and have no inflammation (14). In our study, atrophic alopecic patches were seen in all PB patients, and the patients came to our clinic with the complaint of hair loss.

Potent topical corticosteroids or ICSI applications are the first-choice treatment options for LPP (14, 15). Oral corticosteroids, oral cyclosporine, and oral tetracycline are the second-line treatment options that can be used in patients who do not benefit from these treatments (14). In our study, ICSI application was used in 57.7% (n=15) of the LPP patients, hydroxychloroquine in 15.4% (n=4), and systemic corticosteroids in 15.4% (n=4) of the patients, and each of the remaining 3 patients received topical corticosteroid treatment, the combination of topical corticosteroid and hydroxychloroquine treatment, and the combination treatment of topical corticosteroids and phototherapy, respectively. Of the LPP patients, 12 (46.2%) benefited from hydroxychloroquine, 9 patients (34.6%) from the ICSI application, 2 patients (7.7%) from oral isotretinoin, 2 patients from topical corticosteroids, and 2 patients (7.7%) benefited from systemic corticosteroids. Because half of the LPP patients did not benefit from the first treatment choices, hydroxychloroquine treatment was started in 7 (53.9%) of these patients, oral isotretinoin treatment in 2 (15.4%) patients, topical corticosteroid treatment in 2 (15.4%) patients, oral isotretinoin and topical corticosteroid treatment in 1 patient (7.7%), and ICSI, topical corticosteroids, and oral isotretinoin treatments were started in 1 patient (7.7%). It is known that oral corticosteroids are very effective, especially in rapid and progredient disease (16). Systemic corticosteroid therapy was successfully used in 5 (19.2%) of 26 LPP patients (first choice in 4 patients, second choice in 1 patient) in this study. Oral isotretinoin, oral antimalarials, thalidomide, griseofulvin, mycophenolate mofetil, and excimer laser are the third most common agents in LPP treatment (14).

In the treatment of DLE, patient exposure to ultraviolet radiation should be reduced, and sunscreen creams should be used at each step of treatment and along with other treatments. Potent topical corticosteroids or ICSI applications are the first-choice treatment methods of the disease (14). One of the 7 DLE patients included in the study received ICSI application as the first treatment option, 1 patient received ICSI and hydroxychloroquine combination, and 5 patients received hydroxychloroquine treatment as the first treatment option. Apart from these treatments, systemic corticosteroids are not preferred except for their temporary use during the active period of the disease due to the side effects that may occur in long-term use. Systemic isotretinoin or oral antimalarials are the second-choice agents in the treatment of the disease (14). Because 2 of the 7 DLE patients who were included in the study did not benefit from oral antimalarial therapy given as first-line treatment, oral isotretinoin treatment was started in these patients as the second-option treatment. One patient received oral antimalarial therapy because he/she did not benefit from ICSI treatment. Additional treatment was not considered in 4 patients because they benefited from the first-line treatments. There was no significant difference between systemic isotretinoin and oral antimalarial treatments in terms of efficacy in DLE treatment (17). However, as far as the side effects are concerned, systemic isotretinoin can lead to dose-dependent telogen effluvium, and therefore oral antimalarials are superior to systemic isotretinoin. Thalidomide, oral vitamin E, oral gold, topical immunomodulators, dapsone, and clofazimine are the third-choice treatment modalities for DLE treatment. Other than these, there are the uses of topical imiquimod, topical 5-fluorouracil, topical tazarotene, sulfasalazine, interferon-alpha, methotrexate, azathioprine, phenytoin, oral beta-carotene, cyclophosphamide, colchicine, isoniazid, mycophenolate mofetil, chloramphenicol, danazol, cyclosporine, UVA1 phototherapy, cryotherapy, and the anecdotal use of biological agents (14).

There is not any definitive treatment scheme in PB treatment. One option is to implement the protocol that is followed in the classical LPP. Potent topical corticosteroids, hydroxychloroquine, and thalidomide are the agents used in the treatment (14). In the study, oral antimalarial was applied in one of the 3 patients diagnosed with PB, topical corticosteroids in 1 patient, and systemic corticosteroid treatment in another patient. Because the patient receiving systemic corticosteroid treatment did not benefit from the treatment, oral isotretinoin was started in this patient; however, other patients benefited from treatment.

Conclusion

As a consequence, PLCAs are a group of diseases mostly seen in middle-aged people in the form of LPP, which cause patients to apply to clinics with the complaint of hair loss and which cause atrophic alopecic patches in the scalp. After the subgroup of the disease is identified, it is required that the most appropriate treatment according to the situation should rapidly be chosen without any delay, and unnecessary treatments should not be applied in patients who are at the last stage of the disease.

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Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

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