

Granuloma formation in discoid lupus erythematosus: a novel microscopic feature

Rifat Yasmin, Ikramullah Khan, Anwar Ul Haque, Syed Afaq Ahmad

Department of Dermatology and Pathology, Pakistan Institute of Medical Sciences Islamabad

Abstract *Background* Lupus erythematosus is an autoimmune disease with marked pleiotropism. If several systems are involved then the disease is named as systemic lupus erythematosus (SLE) and if skin is exclusively involved the term discoid lupus erythematosus (DLE) is used. One of the several histopathological features of DLE includes periappendageal inflammation. This may at times completely wipe out sebaceous glands forming sebaceous granulomas.

Objective To determine the frequency of sebaceous granulomas formation in discoid lupus erythematosus.

Materials and methods In this prospective observational study was conducted at the Departments of Dermatology and Pathology, Pakistan Institute of Medical Sciences, Islamabad. 100 cases of DLE spanning over two years and with the age range of 3 years to 70 years were examined for the presence of sebaceous granuloma. Other features of DLE like hyperkeratosis, follicular plugging, epidermal atrophy, basal layer vacuolization, basement membrane deposits, pigmentary incontinence, perivascular inflammation, periappendageal inflammation, and collagen damage were also noted.

Results Out of these 100 cases, 8 cases contained sebaceous granulomas. These granulomas were composed of epithelioid cells, foreign body giant cells containing partially digested sebaceous material and a few lymphocytes.

Conclusion Sebaceous granulomas formation was seen in 8% cases of DLE cases. This feature must be recognized both by dermatologists and pathologist so that diagnosis of DLE may not be distracted and erroneous diagnosis due to presence of granulomas may not be rendered.

Key words

Discoid lupus erythematosus (DLE), sebaceous granulomas.

Introduction

Discoid lupus erythematosus (DLE) is a chronic, scarring, atrophic, photosensitive dermatosis. DLE may occur in patients with systemic lupus erythematosus (SLE), and <5% patients with DLE progress to SLE.¹

The primary lesion is an erythematous papule or plaque with slight-to-moderate scaling. As the lesion progresses, the scale may thicken and become adherent, and pigmentary changes may develop. Patients with DLE rarely fulfil four or more of the criteria used to classify SLE.² Serologic abnormalities are uncommon³. Therapy with sunscreens, topical corticosteroids, and antimalarial agents is usually effective.

This study was based on a hitherto undescribed sebaceous granulomas as a feature of DLE in some cases which we observed in our weekly

Address for correspondence

Dr. Rifat Yasmin
Registrar, Department of Dermatology,
PIMS, Islamabad
E-mail: rifat_chaudhary@yahoo.com

dermatopathological conference held in our institution. The sebaceous granulomas are apparently formed due to destruction of sebaceous glands from intense chronic periappendageal inflammation. The liberated lipid and fat vacuoles initiate and promote phagocytic activity, epithelioid cell differentiation and giant cell formation finally culminating in well-formed granulomas. This feature was, of course, not seen in all cases but observed in some cases. The purpose of this study was to determine the frequency of the sebaceous granulomas and to create awareness among dermatologists and pathologists about this feature which may otherwise lead to erroneous diagnoses.

Material and methods

This observational study was carried out at Dermatology and Pathology Departments of Pakistan Institution of Medical Sciences, Islamabad based on our observations in weekly dermatopathological conferences. 100 cases of DLE patients of both gender and age range of 3 years to 70 years, spanning over two years period were examined specifically for the presence or absence of well formed sebaceous granulomas. All cases with the clinical suspicion of cutaneous LE were biopsied, which were routinely processed and stained in the department of pathology using formalin fixation and hematoxylin and eosin (H&E) staining. The slides were seen jointly in the weekly dermatopathology session held every Friday together with consultant dermatologist and pathologist along with the whole dermatology department on multihead microscope attached with TV monitors and overhead projector. We observed that along with other features like hyperkeratosis, follicular plugging, epidermal atrophy, basal layer vacuolization, basement membrane deposit, pigmentary incontinence

Table 1 Frequency of histopathological features of patients (n=100).

<i>Histopathological feature</i>	<i>N & %</i>
Hyperkeratosis	100
Basal cell vacuolization	100
Collagen damage	100
Epidermal atrophy	97
Perivascular inflammation	96
Periappendageal inflammation	94
Follicular plugging	65
Acanthosis	40
Pigmentary incontinence	30
Parakeratosis	20
Sebaceous granulomas	8

perivascular inflammation, periappendageal inflammation, and collagen damage, some cases had complete effacement of the sebaceous glands with their replacement with well formed granulomas comprising of lymphocytes, many epithelioid cells, few neutrophils and giant cells along with vacuolated macrophages containing lipid droplets derived from sebaceous glands.

Results

Out of these 100 cases, 8 cases contained sebaceous granulomas. The cases were associated with absence of normal sebaceous glands. Remnants of hair follicles and/or erector pylorum muscles provided the clue to the true nature of the granulomas. Another useful clue was clear cut punched out vacuoles in the cytoplasm of the giant cells (**Figures 1-4**). These granulomas comprised of epithelioid cells, foreign body-type giant cells and a few lymphocytes.

Other histopathological features included hyperkeratosis, keratin plugging, epidermal atrophy, basal cell vacuolization, perivascular inflammation, and collagen damage (**Table 1**).

Discussion

DLE is a chronic dermatological disease that can

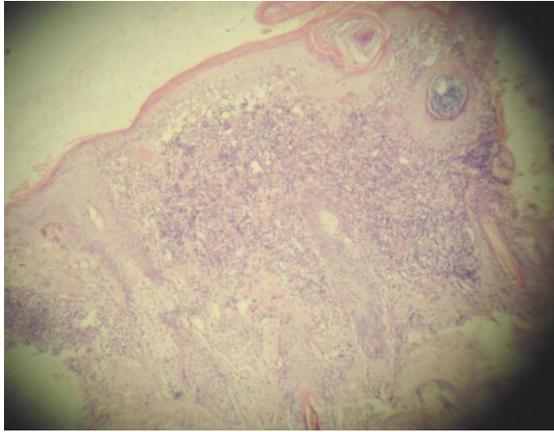


Figure 1 Skin biopsy from a discoid lesion: hyperkeratosis, keratin plugging, epidermal atrophy, basal cell vacuolization and several sebaceous granulomas (H&E X 100) .

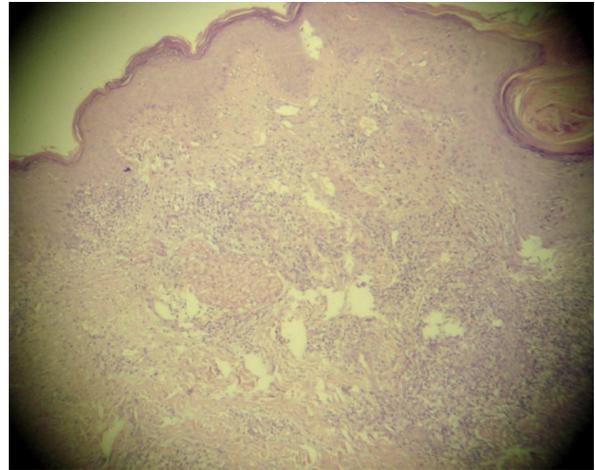


Figure 2 Low power view showing sebaceous granulomas with destroyed sebaceous gland visible as white vacuoles.

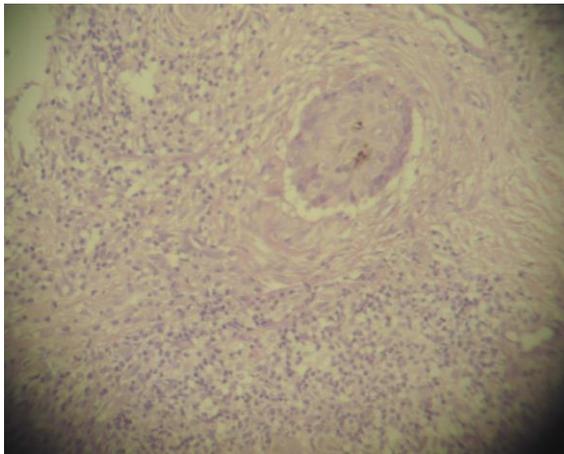


Figure 3 Sebaceous granulomas visible with giant cell. Destroyed sebaceous glands are visible as white holes.

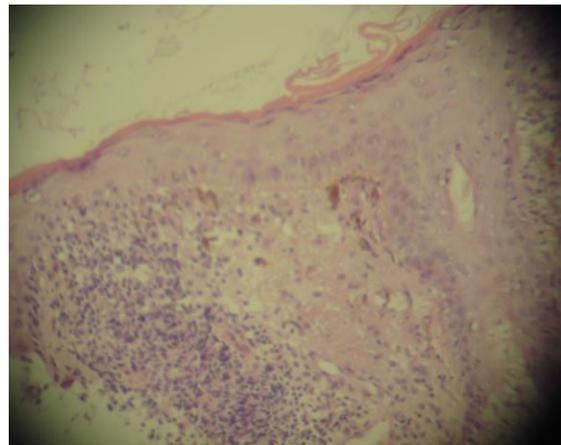


Figure 4 Pigmentary incontinence with sebaceous granulomas.

lead to scarring, hair loss, and hyperpigmentation changes in the skin if not treated early and promptly, can have a considerable effect on quality of life.¹ The prevalence is between 17 and 48 per 100,000 people. Women are affected about thrice as often as men, compared with 9-10 times the frequency for SLE. The usual age of onset is between 20 and 40 years.

LE is thought to be an autoimmune disease among other connective tissue diseases like scleroderma, rheumatoid arthritis, polymyositis, and mixed connective tissue disease. Within

the spectrum of diseases included in LE, at one end is a disease confined mainly to the skin and referred to as DLE and at the other end is a florid disease with systemic involvement of heart, lungs, brain, kidneys and other organs called SLE. In between the 2 ends of the spectrum are disorders like subacute cutaneous lupus erythematosus (SCLE). SCLE has a rather sudden onset with annular or psoriasiform plaques erupting on the upper trunk, arms, and/or dorsa of hands, usually after exposure to sunlight.¹

Early recognition and treatment improves the prognosis. The diagnosis is usually made by clinical examination. In some cases histopathology³ may be required to confirm the diagnosis. The histology is that of a lichenoid tissue reaction with changes at the dermo-epidermal junction that include thickening of the basement membrane (best demonstrated by periodic acid-Schiff staining) and vacuolar degeneration of the basal cells along with perivascular and periappendageal lymphohistiocytic infiltrate of a variable degree in the reticular dermis. Hyperkeratosis is more evident and follicular plugging may be seen in more mature lesions.^{4,5} Often, an abundance of mucin is seen within the dermis.¹⁰ The histopathological features differ depending upon the type and age of the lesion.¹¹

DLE tends to run a less severe course than SLE and has a better prognosis.⁶ It is important for family physicians to recognize DLE because it is a potentially scarring disease. Early referral and institution of treatment by dermatologists increases the hope of minimizing the progression of the disease and consequent socioeconomic impact on the individual.

In this study histopathological features included hyperkeratosis, basal cell damage and collagen damage as most common features with presence in 100% of cases. Epidermal atrophy was seen in 97% of cases and periappendageal and perivascular inflammation in 96% and 94% of patients, respectively. Acanthosis was found in 40% of cases. Parakeratosis was the least found feature with percentage of only 20 (**Table 1**).

Total number of cases which were examined over period of two years was 100. Out of these 100 cases, 8 cases showed formation of sebaceous granulomas. This finding has not previously been discussed with the

histopathological findings of DLE. Another important finding in this study was the earlier destruction of sebaceous glands than hair follicle. This was shown in the form of lymphocytic infiltration of sebaceous glands, disruption of glandular structure and formation of sebaceous granulomas comprising foreign body giant cells as well as partially digested sebaceous material.

These findings raise the possibility that in DLE, immune attack might be primarily directed towards sebaceous glands that is responsible for their destruction. Sebaceous glands seem to be destroyed earlier than the hair follicles and hence persisting hair follicles and erector pylorum muscle may provide a clue to the true nature of sebaceous granulomas.

Skin is host to many different types of granulomas.¹² Like tuberculosis and leprosy where the lipid coat of the mycobacteria serve as an inciting factor, lipid of sebaceous gland may lead to granuloma formation. Granuloma formation may result from simple lipids in some cases (cholesterol granuloma).¹³ Apart from infectious agents such as Leishman-Donovan bodies and fungi, dead hair and myriad of foreign bodies may result in granuloma formation. Endogenous substances such as mammary gland secretions (granulomatous mastitis), sperm (spermatocytic granuloma), dead or damaged collagen (granuloma annulare, cutaneous laxa) may result in granuloma formation.¹⁴ Endogenous hemorrhages (giant cell tumour of bone) and in present study lipid of sebaceous glands may cause granuloma formation. Evaluation of each and every microscopic feature is necessary to further delineate the etiology and clinical course of the disease.¹⁵

More studies should be conducted to evaluate the changes on larger scale as this might have some relationship to the duration or severity of clinical features of DLE and may be involved in some way in the treatment and prognosis of these patients.

Conclusion

Sebaceous granuloma formation is an important dermatopathological finding which can be occasionally encountered in DLE. Both dermatologists and pathologists must be aware of this infrequent feature (8% in our study) in order not to be distracted from the diagnosis of DLE and from making an erroneous diagnosis based on the granulomas.

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