

## Two Clinical Presentations of One Basic Pattern: Lichenoid and Granulomatous Reaction

Pinar Incel Uysal<sup>1</sup>, MD, Neslihan Akdogan<sup>1</sup>, MD, Onder Bozdogan<sup>2</sup>, MD  
Ayse Ciftci<sup>2</sup>, MD, Basak Yalcin<sup>2</sup>, MD

Address: <sup>1</sup>Ankara Numune Training and Research Hospital, Dermatology Department, Ankara

<sup>2</sup>Ankara Numune Training and Research Hospital, Pathology Department, Ankara, Turkey

E-mail: pinarincel@hotmail.com

\*Corresponding Author: Dr. Pinar Ince Uysal, Talatpasa Bulvarı, Ankara Numune Training and Research Hospital, Dermatology Department, Altindag, Ankara

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### Abstract

**Observation:** Lichenoid and granulomatous reaction pattern is a rare histopathological pattern which may present with variable clinical pictures. Although numerous triggering factors have been implicated, this pattern commonly occurs as a result of reactive process of a drug reaction. There are also reports in the literature on the association of lichenoid granulomatous dermatitis with infectious diseases, endocrinopathies, rheumatoid arthritis or inflammatory bowel diseases. We report two additional cases of lichenoid granulomatous dermatitis including granulomatous lichen and granulomatous pigmented purpura in association with hyperlipidemia.

### Introduction

Lichenoid and granulomatous dermatitis (LGD) term also describes lichenoid tissue reaction admixed with a granulomatous component [1]. The clinical presentation of lichenoid and granulomatous dermatitis varies. Lichenoid dermatitis, erythematous and squamous papules and plaques, pigmented purpuric macules and papules, zosteriform eruption, annular erythema, hyperkeratotic violaceous papules, miliary skin colored pinhead size papules are the main clinical impressions. Among these, erythematous patches and plaques induced with drug exposure is the most common clinical picture. Nevertheless, in the literature various types of causative factors have been associated with LGD [1, 2]. Here, we describe unusual clinical cases of lichenoid granulomatous dermatitis in two patients with hypertriglyceridemia.

### Case Report-1

51-year old woman was presented to our department with an eruption on her face, neck and dorsal hands for four months. Dermatologic examination revealed multiple miliary purplish, brown, confluent macules and papules in reticular configuration on her forehead, cheeks, jawline, anterior neck and dorsal hands (Figures 1a and b). Lesions were asymptomatic and slowly spreading in previous months. Systemic examination was normal and lymph nodes were non-palpable. Skin scrape was negative for Demodex mites. Dermoscopic examination was unremarkable. Impaired glucose tolerance and depression were noted in her past medical history. She was taking metformin (orally, 850 mg) for two years. There was no history of chemical or cosmetic product use. Routine laboratory examinations were in normal limits except hypertriglyceridemia (344 mg/dL). Erythrocyte sedimentation rate (ESR), C reactive protein levels, anti-streptolysin O, serum calcium and angiotensin-converting enzyme levels were normal. There



**Figures 1a and b.** Confluent brownish maculopapular lesions on the face of case 1 at initial presentation (A). After 3 months of therapy, almost completely improvement of the lesions (B).

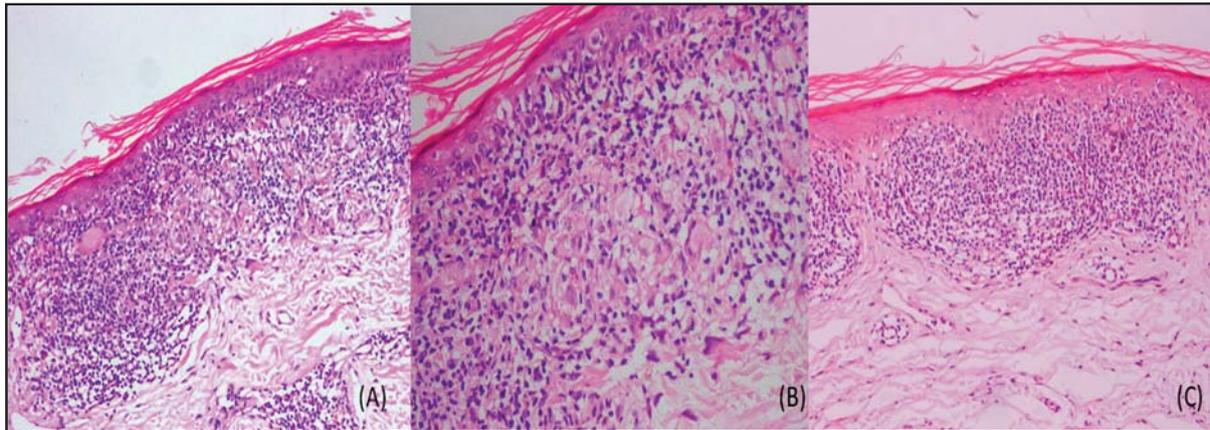
was no abnormality in thyroid hormone levels. Owing to involvement of sun-exposed sites, lupus serological profile was performed. Antinuclear antibody (ANA) and syphilis serology were normal. Skin biopsies were performed from both facial and acral lesions with the presumptive diagnosis of pigmented lichen. Microscopic examination revealed lichenoid infiltration with loose formed granulomas (**Figures 2a and b**). A few giant cells were seen. Second biopsy also showed significant pigment incontinence (**Figure 2c**)

Based on clinicopathological findings, the patient was considered as an actinic variant of lichen planus with granulomatous infiltration. She was screened for other granulomatous disorders including sarcoidosis and tuberculosis. Chest X-ray, tuberculin skin test, serum calcium and angiotensin-converting enzyme levels were unremarkable. Because of her hyperlipidemia and prediabetic status systemic steroids were not given.

Hydroxychloroquine sulphate (400mg/day, orally) was started. After three months of antimalarial therapy and sunscreen use lesions were considerably improved with residual pigmentation (**Figure 1b**). She is still on follow-up without recurrence for a year period.

### Case Report-2

52-year old man was referred to our clinic with asymptomatic eruption that had been present for 18 months on the dorsa of hands. The lesions were slowly spreading and enlarging. Physical examination was normal. Numerous millimetric violaceous, cayenne pepper like red papules were present on the dorsal hands (**Figure 3a**). Nails were normal. The medical history included a diagnosis of essential hypertension and hypertriglyceridemia. No medications had been prescribed prior to the eruption. Laboratory examinations (complete blood count, biochemistry, urinalysis) were within



**Figures 2 a,b and c.** Lichenoid infiltration with loose granuloma formation. Second biopsy from acral area shows lichenoid infiltration with pigment incontinence (A-B). A giant cell easily detected (C). (A, Hematoxylin and eosin, original magnification; x 10, B, Hematoxylin and eosin, original magnification; x 20, C, Hematoxylin and eosin, original magnification; x 10)

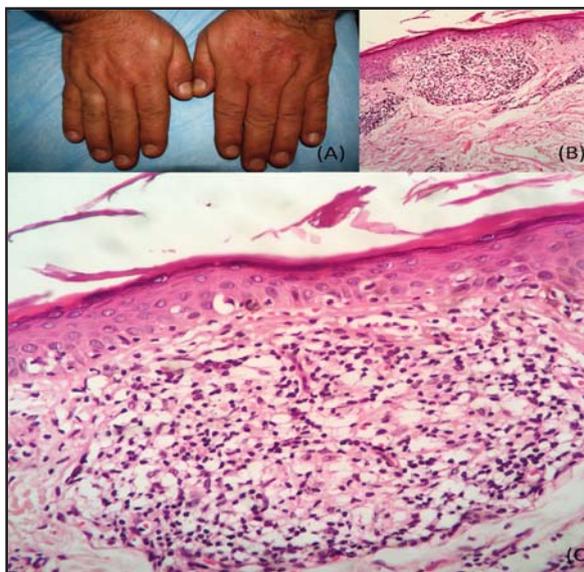
normal limits. Chest X-ray and tuberculin skin test was normal. Pigmented purpuric dermatosis, acne rosacea and sarcoidosis were included in presumptive diagnosis.

Skin biopsy specimen of the dorsal hand showed hyperkeratosis, hypergranulosis, focal vacuolar degeneration of basal membrane. Papillary dermal lymphohistiocytic granulomatous infiltration and concomitant superficial perivascular infiltration were identified (**Figures 3b and c**). Extravasated

red blood cells and thickening of vessel walls were also noted. On the basis of clinical and pathological findings we established the diagnosis of granulomatous pigmented purpura of dorsal hands. He was treated with mometasone furoate 0,1 % cream. After two months of topical therapy, lesions resolved without new lesion development. Relapse was not noted during one year follow-up.

**Discussion**

SLGD and interstitial granulomatous dermatitis (IGD) are uncommon microscopical entities and they belong to same ‘reactive’ granulomatous disorders. Both disorders have been associated with same underlying factors including drugs and systemic disorders [2]. Also, LGD and IGD have quite heterogenous clinical manifestations According to the report of Margo et. al, LGD is mostly present with lichenoid papules and only one third of 21 patients have additional characteristic microscopic or clinical features favouring the diagnosis of lichen planus[1]. Our patient (case 1) with skin phototype IV was unique because of photodistributed millimetric brownish maculopapules in reticular array and ‘lichenoid’ appearance of the lesion. The clinical picture was quite different from classical lichen planus, lichen striatus and lichen nitidus. Furthermore, the lesions were not compatible with any other classical photodermatoses. Photosensitivity was not noted in our patients but we could not identify the reason of sun-exposed localization.



**Figures 3 a,b and c.** Multiple millimetric erythematous papules located on the dorsal hands of case 2 (A). Prominent vacuolar epidermal degeneration and granulomatous infiltrate of lymphocytes and histiocytes in the superficial dermis (B-C). (B, Hematoxylin and eosin, original magnification; x 20, Hematoxylin and eosin, original magnification; x 40)

In the literature granulomatous infiltration admixed with lichenoid tissue reaction was re-

ported in the context of keratosis lichenoides chronica, mycosis fungoides, pigmented purpuric dermatosis, drug eruptions[3, 4, 5, 6, 7] Granulomatous pigmented purpura is very rarely reported variant of pigmented purpuric dermatosis which had been described in 1996 [8, 9]. The disorder commonly affects dorsum of feet [7, 10, 11]. There is no similar patient presenting with isolated lesions on dorsal hands in previous reports. Clinical and histopathological characteristics of our patient (case 2) suggested the diagnosis of granulomatous PPD. PPD has been associated with a wide range of systemic disease including hyperlipidemia, diabetes mellitus, thyroid dysfunction, malignancies or collagen diseases[6]. In agreement with these findings our patient (case 2) had the diagnosis of hypertriglyceridemia.

As some authors have suggested previously, drug associated lichenoid granulomatous dermatitis may reflect granulomatous koebnerization of lichenoid drug reaction in patients with underlying medical conditions including diabetes, Crohn's disease or rheumatoid arthritis[1]. In addition, Wolf et. al described a multiple myeloma patient with erythropoietin induced LGD presenting with erythrodermia[12]. Medications in association with LGD were reviewed but we were unable to identify any evidence for causative drug use in our patients. In addition, on biopsy specimen, any suggestive findings including tissue eosinophilia was not observed in our patients.

Some infectious organisms acting as superantigens have the capacity of inducing T-helper 1 immune response and lymphohistiocytic infiltration[13]. After the association with infections including mycobacteria, syphilis, herpes, hepatitis C has been largely described by Margo et al., causative relationship with atypical mycobacterium infections were discussed a few times[14]. In addition, sarcoidosis is a well reported condition that has lichenoid granulomatous infiltrate[15]. Notably, our patients were physically healthy without any sign of clinic-pathological infectious disease. Thus we did not perform further laboratory analyses including special stains or tissue cultures regarding tuberculosis or sarcoidosis.

However, laboratory investigations for systemic illness revealed hypertriglyceridemia in both of our patients. Also impaired fasting glucose was noted in case 1. Interestingly, hyper-

lipidaemia was commonly found in patients with granulomatous PPD [6, 11]. Thus, we believe pre-diabetic state and/or impaired lipid profile may play role in altered immune response and type IV skin reaction in our patients. Antimalarial drugs are well known agents with high efficacy and safety for both granulomatous and lichenoid skin conditions. Of note, rapid improvement of the lesions of with hydroxychloroquine therapy (case 1) was supportive for our diagnosis.

**Conclusion:** LGD is a distinct histopathological pattern. Lichen planus, lichen striatus, lichen nitidus, mixed connective tissue disease, subacute lupus and lichenoid drug reactions are main clinical forms representing LGD microscopically. Currently it is unclear whether presence of both lichenoid and granulomatous infiltration leads to improved or worsened prognosis of the relevant dermatosis. Here, our patients provide a demonstrative example of LGD presenting with extraordinary clinical features. In conclusion, this report highlights that dermatologists and pathologists should be aware of this reaction pattern. We believe this report will lead better understanding of microscopic picture of LGD and potential clinical implications and associations. Finally, further studies are required to explain the link between hypertiglyceridemia and immune dysregulation in patients with LGD.

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