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Isolated Bilateral Periocular Lupus Miliaris Disseminatus Faciei: A Clinicopathological Mimicker of Granulomatosis With Polyangiitis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Male, 19-year-old
Final Diagnosis: Lupus miliaris disseminatus faciei
Symptoms: Periocular papules
Clinical Procedure: —
Specialty: Dermatology

Objective: Challenging differential diagnosis

Background: Lupus miliaris disseminatus faciei (LMDF) is a rare idiopathic granulomatous dermatosis that presents as discrete yellow-brown, erythematous, or skin-colored papules on the central face, with a recognized preference for the eyelids and periorbital region.

Case Report: We report a case of isolated bilateral periocular LMDF in a healthy young adult man whose initial eyelid biopsy revealed suppurative necrotizing granulomatous inflammation, raising histopathological concern for granulomatosis with polyangiitis and other systemic granulomatous diseases. Autoimmune, vasculitic, infectious, urinary, orbital, and thoracic evaluations were otherwise negative, apart from only mild inflammatory marker elevation, with an erythrocyte sedimentation rate of 21 mm/h (reference range, 0-20 mm/h) and C-reactive protein level of 0.94 mg/dL (reference range, 0.1-0.5 mg/dL). The final diagnosis was supported by the clinicopathological combination of symmetrical folliculocentric periocular papules, perifollicular necrobiotic suppurative granulomas, absence of true vasculitis, negative infectious studies, and absence of systemic disease. After 1 month of extended-release oral minocycline, the patient had marked flattening of papules and near-complete resolution of crusted inflammatory lesions. Adverse effects were monitored clinically during routine follow-up after completion of the 1-month treatment course; the patient reported no treatment-related adverse effects, and no adverse effects were observed.

Conclusions: Clinicopathological correlation and comprehensive systemic evaluation are necessary to differentiate this rare dermatosis from infectious or vasculitic mimics. In this patient, oral minocycline was associated with marked short-term clinical improvement after 1 month, but this single observation does not establish broader therapeutic efficacy for LMDF.

Keywords: Minocycline • Granulomatosis with Polyangiitis

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Introduction

Lupus miliaris disseminatus faciei (LMDF) is a rare idiopathic granulomatous dermatosis that presents as discrete yellow-brown, erythematous, or skin-colored papules on the central face, with a recognized preference for the eyelids and periorbital region [1]. Reliable population-based incidence and prevalence estimates are not well established; therefore, the condition should be described as rare without assigning an unsupported numerical frequency.

While described, sometimes, as acne agminata and once regarded as a tuberculid, LMDF is now considered a diverse clinicopathological entity rather than a manifestation of cutaneous tuberculosis [2]. The histopathological hallmark of LMDF is a perifollicular epithelioid granulomatous infiltrate, often with central necrosis or necrobiosis, which may overlap with histological findings seen in infection, sarcoidosis, granulomatous rosacea, and vasculitic disorders [3-5].

We report a case of isolated bilateral periocular LMDF in a healthy young adult man whose initial eyelid biopsy revealed suppurative necrotizing granulomatous inflammation, raising concern for granulomatosis with polyangiitis (GPA) and other systemic granulomatous diseases. This case illustrates how periocular LMDF with necrotizing suppurative granulomatous histology can closely mimic systemic vasculitic disease. It also shows that accurate diagnosis relies on close clinicopathological correlation, once infectious and systemic causes have been thoroughly excluded.

Case Report

An 18-year-old previously healthy adult man presented with a 6-month history of persistent, asymptomatic papules involving the bilateral periocular region. The lesions were 3 to 5 mm, skin-colored to brown, and symmetrically distributed over the upper and lower eyelids and adjacent periorbital skin (**Figure 1**). Some papules showed focal crusting, and the distribution was predominantly folliculocentric. There was no ulceration, scarring, telangiectasia, conjunctival involvement, mucosal disease, extrafacial involvement, or cervical lymphadenopathy. He denied fever, weight loss, respiratory symptoms, arthralgia, ocular pain, visual disturbance, and oral ulceration. His past medical, medication, and family histories were unremarkable.

Because of the isolated periocular distribution, he was initially evaluated by the ophthalmology department. Eyelid biopsy demonstrated suppurative dermatitis with focal necrotizing granulomatous inflammation, raising concern for systemic granulomatous or vasculitic disease, particularly GPA. A comprehensive evaluation was therefore performed. Autoimmune and vasculitic testing, including antineutrophil cytoplasmic antibodies (ANCA), negative anti-myeloperoxidase (MPO), anti-proteinase 3 (PR3), anti-dsDNA, anti-Smith, anti-SSA/SSB, anti-RNP, anti-Scl-70, anti-CCP, thyroid autoantibodies, HLA-B27, and HLA-B51, was negative or unremarkable. The erythrocyte sedimentation rate (ESR) was mildly elevated at 21 mm/h (reference range, 0-20 mm/h), and the C-reactive protein (CRP) level was mildly elevated at 0.94 mg/dL (reference range, 0.1-0.5 mg/dL); these findings were interpreted in the context of an otherwise negative systemic work-up. HIV, hepatitis B, and hepatitis C serologies were negative. Urinalysis, urine culture, skin swab culture, and tissue cultures were also negative. Orbital imaging, chest radiography, and high-resolution computed tomography of the chest showed no evidence of systemic granulomatous or vasculitic disease.

Dermatopathological review demonstrated perifollicular suppurative granulomatous inflammation involving the mid-to-deep dermis. The granulomas consisted of epithelioid histiocytes

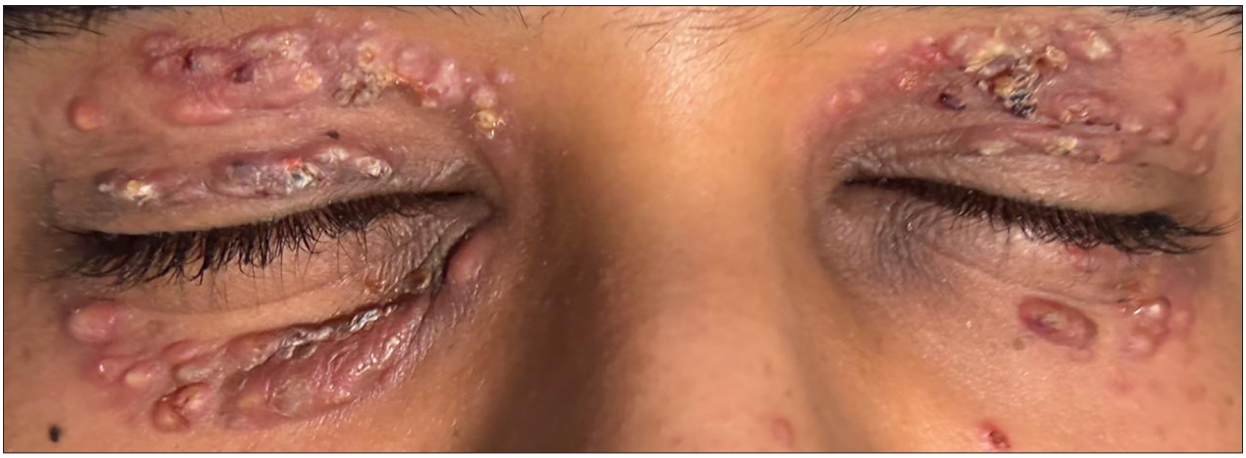

Figure 1. Baseline clinical presentation. Several erythematous to brownish papules and small nodules symmetrically affecting the bilateral periocular region (upper and lower eyelids). Multiple lesions with superficial crusting and focal erosion.

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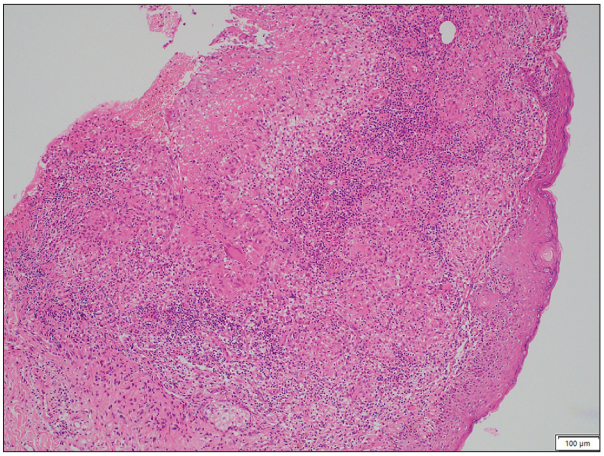

Figure 2. Low-power histopathological findings. Discrete dermal granulomatous inflammatory infiltrate with focal necrosis. Hematoxylin and eosin staining, × 10.

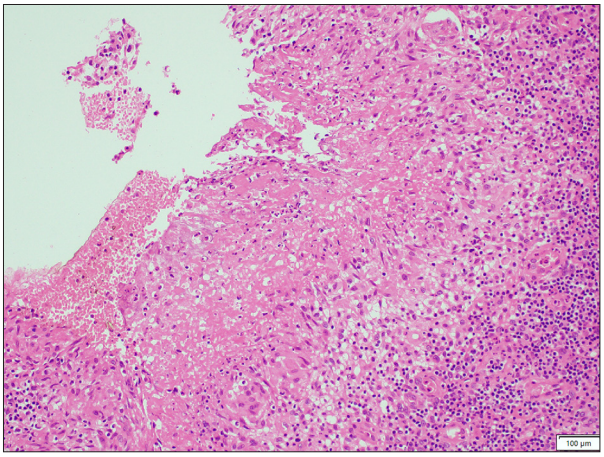

Figure 3. Histopathology at higher magnification. Necrotizing granulomatous inflammation consisting of epithelioid histiocytes and multinucleated giant cells around a focus of necrosis, with associated lymphohistiocytic inflammation. Hematoxylin and eosin staining, × 20.

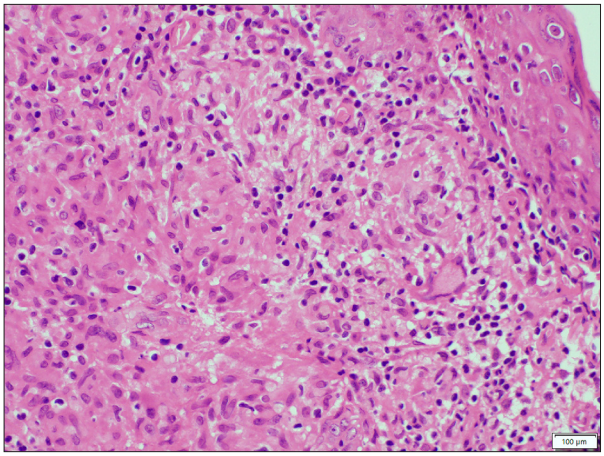

Figure 4. High-power histopathology. Compact aggregates of epithelioid histiocytes with scattered inflammatory cells. Hematoxylin and eosin staining, × 40.

and multinucleated giant cells surrounding focal necrosis and necrobiosis, with neutrophils concentrated around the necrotic foci (**Figures 2-4**). There was no true vasculitis or prominent plasma cell infiltrate. Periodic acid-Schiff, Gomori methenamine silver, acid-fast bacilli, Giemsa, and Warthin-Starry stains were negative, and CD1a immunostaining was also negative. In view of the characteristic periocular folliculocentric papules, perifollicular necrobiotic suppurative granulomas, and negative systemic and infectious evaluation, an LMDF diagnosis was made.

The patient was treated with extended-release oral minocycline 105 mg extended release once daily without additional topical or systemic therapy. Minocycline was selected because tetracycline-class antibiotics, including minocycline, have been used for LMDF in the published literature, while the extended-release formulation was chosen because it was the only minocycline formulation available in our clinical setting [6-8]. Adverse effects were monitored clinically during routine follow-up after completion of the 1-month treatment course; the

Figure 5. Appearance at 1 month after minocycline treatment. Follow-up clinical image 1 month after starting oral minocycline therapy showing interval flattening of most periocular papules and nodules, with remaining erythematous to brown macules.

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patient reported no treatment-related adverse effects, and no adverse effects were observed. At 1-month follow-up, there was marked clinical improvement (**Figure 5**), with flattening of the papules and near-complete resolution of crusted inflammatory lesions. Mild residual periocular erythema and post-inflammatory changes persisted.

Discussion

The value of this manuscript is incremental, mainly to reinforce a particular boundary condition in the clinical spectrum of LMDF. The general characteristics of LMDF are well known. This case highlights a diagnostic dilemma, as isolated bilateral periocular LMDF may have a necrotizing suppurative granulomatous histology that closely mimics GPA. The clinical importance is not in the description of a new entity, but in the description of the integrated diagnostic pathway necessary to work through this severe histological mimic. The diagnostic dilemma in this case was the presence of isolated bilateral periocular papules with necrotizing granulomatous inflammation on eyelid biopsy. This pattern was appropriate to raise concern for severe systemic granulomatous or vasculitic disease, particularly GPA, and warranted the thorough systemic evaluation carried out in this patient. However, the final diagnosis of LMDF was confirmed by the combination of clinical morphology, folliculocentric distribution, dermatopathological findings, negative infectious studies, and absence of systemic disease. Therefore, careful clinicopathological correlation was required to prevent the misdiagnosis of LMDF as systemic vasculitis or infection.

LMDF is generally established through clinicopathological correlation rather than by a single definitive or gold-standard examination. Compatible clinical morphology and distribution, supportive histopathology, and exclusion of relevant infectious, granulomatous, and vasculitic mimics are all required to make the diagnosis defensible [1,4,5]. The clinical manifestations in this patient are consistent with the known spectrum of LMDF, a rare, idiopathic granulomatous inflammatory dermatosis, which was formerly thought to be a tuberculid but is now accepted as a separate clinicopathological entity [9]. The disease typically affects the central face and often the eyelids and surrounding periorbital skin [4].

A recent clinicopathological review similarly found facial involvement in all reviewed cases, frequent eyelid/periocular involvement, and pilosebaceous-unit association in many cases, supporting the relevance of this patient's folliculocentric periocular distribution [5]. The clinical spectrum of LMDF is reported to be discrete, asymptomatic, skin-colored to brown periocular papules, which was the morphology observed in this patient [1]. This diagnosis was supported by the predominantly folliculocentric distribution.

LMDF is characterized by perifollicular granulomatous inflammation, often involving the mid-to-deep dermis [10]. The presence of epithelioid histiocytes and multinucleated giant cells surrounding foci of necrosis or necrobiosis, with an associated neutrophilic infiltrate, closely paralleled the dermatopathological findings in this case [9]. Necrosis is a recognized feature of LMDF, but its prominent suppurative nature in this periocular distribution was the main reason for the GPA mimicry. Published clinicopathological series support that LMDF granulomas may show central caseous necrosis and follicular or pilosebaceous association, but the specific reason for a markedly suppurative necrotizing pattern in an isolated periocular presentation remains uncertain [5]. No true vasculitis was identified in the present patient. Although necrosis within granulomas can suggest infection, vasculitis, or systemic granulomatous disease, the necrosis or necrobiosis observed in LMDF should be interpreted in the context of the overall clinicopathological pattern rather than in isolation [11].

The main diagnostic mimics in this case included GPA, cutaneous tuberculosis, deep fungal infection, atypical mycobacterial infection, leishmaniasis, sarcoidosis, granulomatous rosacea, and Langerhans cell histiocytosis. GPA was considered because of the necrotizing granulomatous pattern; however, the absence of true vasculitis, negative testing for ANCA, MPO, and PR3, normal urinalysis, and lack of sinonasal, pulmonary, renal, or orbital involvement made this diagnosis unlikely. The mild ESR and CRP elevations were nonspecific and did not outweigh the otherwise negative systemic, urinary, serological, microbiological, and imaging evaluation. Negative tissue cultures and special stains, including Gomori methenamine silver, periodic acid-Schiff, acid-fast bacilli, Giemsa, and Warthin-Starry stains, provided no evidence of fungal, mycobacterial, leishmanial, or spirochetal infection. Negative CD1a immunostaining also argued against Langerhans cell histiocytosis. The absence of diffuse centrofacial erythema, flushing, telangiectasia, systemic features, and radiologic abnormalities made granulomatous rosacea and sarcoidosis less likely.

Ophthalmic and orbital GPA can involve structures from the eyelid and orbit to the ocular globe and optic nerve, and a systematic review of published ocular and orbital GPA cases reported necrotizing granulomatous disease in this diagnostic spectrum [12]. Cutaneous findings in ANCA-associated vasculitis may also overlap clinically and histopathologically, and facial lesions can occur in GPA, which supports why GPA was considered despite the localized presentation [13]. In this patient, however, the absence of true vasculitis on biopsy, negative ANCA-related testing, and lack of renal, pulmonary, sinonasal, orbital, or other systemic involvement supported histopathological mimicry rather than clinically evident GPA.

Evidence for the therapeutic management of LMDF is still limited and mostly comes from case series and case reports.

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Table 1. Differential diagnoses considered in this patient.

Differential diagnosis	Reason considered	Findings arguing against the diagnosis
Granulomatosis with polyangiitis	Necrotizing granulomatous inflammation in a periocular biopsy	No true vasculitis; negative ANCA, anti-MPO, and anti-PR3; no renal, pulmonary, sinonasal, or orbital disease
Infectious granulomatous disease	Necrosis and suppurative inflammation can suggest mycobacterial, fungal, leishmanial, or spirochetal infection	Negative tissue cultures and negative PAS, GMS, AFB, Giemsa, and Warthin-Starry stains
Sarcoidosis	Granulomatous facial lesions can overlap clinically and histologically	No systemic features or radiologic abnormalities; necrobiotic suppurative folliculocentric pattern favored LMDF
Granulomatous rosacea	Facial papules can resemble LMDF	No diffuse erythema, flushing, telangiectasia, or typical rosacea background
Langerhans cell histiocytosis	Periocular papules and crusted lesions can enter the clinical differential	CD1a immunostaining was negative

Abbreviations: ANCA, antineutrophil cytoplasmic antibodies; MPO, myeloperoxidase; PR3, proteinase 3; PAS, periodic acid–Schiff; GMS, Gomori methenamine silver; AFB, acid-fast bacilli; LMDF, lupus miliaris disseminatus faciei.

Antibiotics of the tetracycline group, such as minocycline, are often used, but responses have been inconsistent [6,7]. This limited and inconsistent evidence was the reason minocycline could be justified as a reasonable reported option, but not as an evidence-proven therapy. In this instance, extended-release oral minocycline (105 mg once daily) was correlated with significant improvement after 1 month, with flattening of papules and almost complete resolution of crusted inflammatory lesions. The extended-release formulation was used because it was the only available minocycline formulation in the authors' clinical setting. No treatment-related adverse effects were reported by the patient or observed during clinical follow-up. However, causality cannot be inferred from a single case, and the short follow-up period does not allow conclusions to be drawn about sustained remission, relapse prevention, or reduction in the risk of pitted scarring, a recognized sequela of LMDF [8].

Conclusions

This case illustrates the need for careful clinicopathological correlation and thorough systemic evaluation to differentiate this rare dermatosis from infectious or vasculitic mimics (**Table 1**). Such evaluation is important both to recognize LMDF and to avoid overlooking consequential systemic or infectious diseases in patients with localized periocular granulomatous lesions. In this patient, oral minocycline was associated with marked short-term clinical improvement after 1 month, but this single observation does not establish broader therapeutic efficacy for LMDF.

Department and Institution Where Work Was Done

Patient was treated at: Imam Abdulrahman Bin Faisal University Hospital

Informed consent

Written informed consent was obtained from the patient.

Declaration of Figures' Authenticity

All figures submitted have been created by the author who confirms that the images are original with no duplication and have not been previously published in whole or in part.

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