Necrobiotic Xanthogranuloma in Two Chinese Women: Case Reports and Review of the Literature

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ABSTRACT

Necrobiotic Xanthogranuloma (NXG) is a rare histiocytic disease characterised by destructive cutaneous lesions and subcutaneous nodules. NXG may involve multiple cutaneous regions and is frequently associated with multisystem involvement, including ocular, cardiac, or splenic manifestations. This report details two cases of middle-aged Chinese women with NXG presenting with periorbital plaques and swelling as predominant manifestations. After low-dose prednisone therapy, both patients exhibited amelioration of periocular symptoms with varying efficacy. To date, there are only limited reports of NXG in the Asian population, particularly cases without overt systemic manifestations. The authors describe two such cases, underscoring the importance of recognising NXG in under-represented populations.

Key Words: *Necrobiotic xanthogranuloma, Dermatopathology, Prednisone*.

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INTRODUCTION

Necrobiotic xanthogranuloma (NXG) is a rare, multisystem histiocytic disorder characterised by progressive cutaneous lesions, including indurated plaques and subcutaneous nodules, often accompanied by systemic involvement such as ocular, cardiac, or haematological abnormalities.[1] First described in 1980, NXG is strongly associated with paraproteinaemia, particularly monoclonal IgG gammopathy, and exhibits a predilection for middle-aged to elderly individuals.[1,2] While the majority of reported cases originate from European and American populations, data on Asian cohorts remain scarce, potentially resulting in under-recognition or misdiagnosis in non-Western populations.

This report presents two cases of NXG in middle-aged Chinese women with isolated periorbital manifestations, highlighting the clinical and histopathological features of NXG in Asian populations. By integrating these cases with a literature review, this study seeks to improve recognition of NXG in under-represented demographics and to inform tailored therapeutic strategies.

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CASE 1:

A 39-year woman presented with gradually progressive cutaneous manifestations over 10 years, including firm, beige-coloured plaques with well-demarcated borders, and periorbital oedema. The periocular skin demonstrated prominent bulging compared to adjacent unaffected areas. And a palpable subcutaneous mass was noted in the left mandible (Figure 1A). A diagnostic skin biopsy was performed on the periocular plaque adjacent to the right eye. Histopathological examination revealed extensive dermal necrobiosis with alternating xanthogranulomatous infiltrates, consistent with NXG (Figure 1B-D). Immunohistochemistry demonstrated a diffuse positivity for CD163 (indicating M2 macrophage activation), alongside expression of Vimentin (confirming mesenchymal origin), and CD68 (marking histiocytic infiltration), collectively supporting the diagnosis of NXG and differentiating it from histiocytic mimics. Serological analysis indicated elevation in cholesterol (total cholesterol 6.42 mmol/L, normal <5.2; low density lipoprotein cholesterol 3.97 mmol/L, normal <2.6), immunoglobulin light chains (light chains κ 17.50 g/L, normal range 6.29-13.50; light chains λ 9.46 g/L, normal range 2.8-6.5), IgG (22.3 g/L, normal range 7.5-15.6), and IgG4 (965.6 mg/L, normal range 160.3-635.0). Thyroid function, adrenocorticotropic hormone, immunofixation electrophoresis, and other tests revealed no significant abnormality.

The patient was initiated on oral prednisone acetate at a dose of 0.5 mg/kg/day. At two-month follow-up, significant reduction in periorbital swelling was observed (Figure 1E) with normalisation of immunoglobulin light chains (κ: 7.10 g/L; λ: 4.38 g/L). The prednisone dose was tapered to 0.3 mg/kg/day,

with a plan to gradually discontinue therapy within one year (target: 5 mg/day). No recurrence of facial swelling has been reported during ongoing treatment.

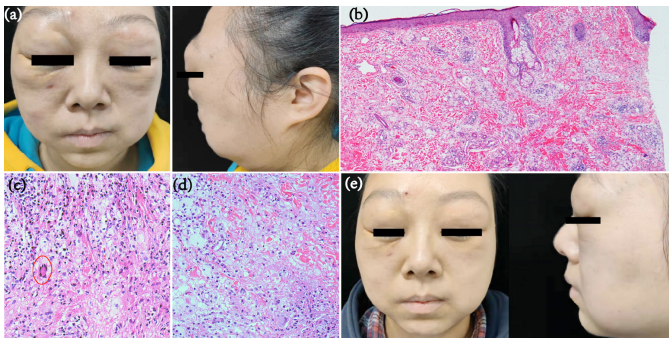

Figure 1: Facial manifestations and H&E-stained sections of a periorbital skin in Case 1. (A) Before two months of treatment. (B) The dermis is infiltrated by dense inflammatory cell infiltration (×50). (C) Touton giant cell (red circle) and foamy histiocytes (×400). (D) Palisading granulomas with lymphoplasmacytic infiltrate and zones of necrobiosis (×400). (E) After two months of treatment.

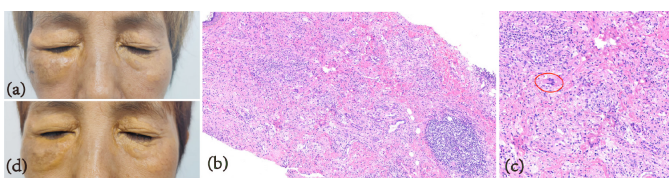

Figure 2: Facial manifestations and H&E-stained sections of the periorbital skin in Case 2. (A) Before two weeks of treatment. (B) The dermis is infiltrated by mixed inflammatory cells and necrobiotic areas. A lymphocyte germinal center can be seen in the lower right corner (×50). (C) Touton giant cell (red circle) (×400). (D) After two weeks of treatment.

CASE 2:

A 54-year woman presented with firm plaques and periocular oedematous tissue persisting for over five years. The lesions manifested as orange-red indurated nodules with irregular borders and no tenderness on palpation (Figure 2A). Histopathological examination of the right periocular biopsy revealed palisading granulomas surrounding necrobiotic zones and Touton giant cells with foamy cytoplasm, confirming the diagnosis of NXG (Figure 2 B, C). Immunohistochemistry demonstrated strong positivity for CD163, and focal CD30 expression (marking activated lymphocytes), and negativity for S-100 (excluding Langerhans cell histiocytosis) and ALK-1 (excluding ALK+ lymphomas). Serological investigations revealed no abnormalities in immunoglobulin kappa light chain, IgE, IgA, and immunofixation electrophoresis results.

The patient was commenced on oral prednisone at a dose of 0.5 mg/kg/day. After two weeks of therapy, significant resolution of periocular swelling and plaques was observed (Figure 2D). Ongoing prednisone therapy is maintained, with a planned tapering regimen mirroring case 1 to achieve sustained remission.

DISCUSSION

NXG is a rare multisystem disorder. Published cases predominantly involve the European and American populations, with limited reports in the Asian cohorts. Kunikata *et al*. documented a 65-year-old Japanese woman with NXG manifesting solely as cutaneous lesions in 2006.[3] Another Japanese case described a 69-year-old woman with NXG exhibiting haematological and musculoskeletal involvement alongside cutaneous manifestations.[4] Notably, case 1 (39 years) was significantly younger than the reported age range (54-61.6 years), while case 2 (54 years) aligned with the lower limit.[1,2] These findings enhance the understanding of NXG diagnosis and management in Asian populations.

NXG exhibits a robust association with paraproteinaemia, particularly IgG gammopathy.[1] Approximately, 80% of patients present with monoclonal gammopathy, predominantly IgG kappa subtype.[5] Emerging evidence suggests a link between NXG and elevated IgG4 levels,[6] reinforcing its classification as a systemic immune-mediated disorder. However, NXG with isolated periorbital symptoms is often misdiagnosed as adult orbital xanthogranuloma, xanthelasma, and plane xanthoma. NXG is distinguished by necrobiotic collagen zones, palisading histiocytes, and Touton giant cells on histopathology, alongside systemic associations such as paraproteinaemia. In contrast, adult orbital xanthogranuloma lacks necrobiosis and systemic involvement;[7] xanthelasma presents as lipid-laden foam cells without granulomatous inflammation,[8] and plane xanthoma shows diffuse cutaneous lesions devoid of necrosis or paraproteinaemia.[9] Immunohistochemistry (CD68+/CD163+ in NXG) and serum paraprotein screening further aid differentiation.

A recent systematic review indicates that intravenous immunoglobulin (IVIG) and glucocorticoids may represent the most effective treatment options for NXG,[10] demonstrating superior efficacy compared to alternatives such as thalidomide, alkylating agents, antimalarial, rituximab, surgery, or radiotherapy.[1,11] Notably, cladribine and peginterferon α-2a have shown efficacy in refractory cases.[12,13] However, glucocorticoids remain the pragmatic choice for patients with predominantly cutaneous disease, owing to cost-effectiveness and manageable side-effect profiles.

In summary, these cases underscore the clinicopathological heterogeneity of NXG in Asian populations, particularly the potential for younger onset and isolated cutaneous manifestations. The efficacy of low-dose glucocorticoids in our patients highlights the importance of tailored therapeutic strategies for mild presentations lacking systemic complications. However, vigilance for paraproteinaemia-associated malignancies and multi-organ involvement remains critical during long-term follow-up. Further multicentre studies are warranted to elucidate demographic-specific disease patterns and optimise management protocols in under-represented cohorts.

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PATIENTS' CONSENT:
Informed consent was obtained from the patients to publish the data concerning these cases.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

YH: Conceptualised the study, collected clinical data, performed literature review, and drafted the manuscript.
HJ: Assisted in data analysis, contributed to histopathological evaluation, and revised the manuscript critically.
YZ: Participated in the image processing, supported clinical documentation, and edited the final manuscript.
XH: Supervised the research design, provided expert guidance on histopathological interpretation, finalised the manuscript, and approved the submission.
All authors approved the final version of the manuscript to be published.

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