

Necrobiotic xanthogranuloma (NXG) co-occurring with plane xanthoma in IgG kappa monoclonal gammopathy patient: A case report.

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ABSTRACT :

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Necrobiotic xanthogranuloma (NXG) is a rare non-Langerhans cell histiocytic disease characterized by firm papules, nodules and plaques with various color from violaceous to red-orange or yellow. Periorbital area, face, trunk and extremities are commonly involved. The pathogenesis of NXG is unknown. The histopathology shows characteristic cholesterol cleft within necrobiosis area, surrounded by palisading granuloma. NXG is reported to be accompanied by monoclonal gammopathy of IgG type up to 80% of cases and about 10% of the patients developed multiple myeloma. There had been some previous reports of xanthoma and NXG derived in the same patients. We herein report a case of necrobiotic xanthogranuloma with normolipemic plane xanthoma and IgG kappa monoclonal gammopathy.

Key words: Necrobiotic xanthogranuloma, non-Langerhans cell histiocytic disease, plane xanthoma, multiple myeloma, IgG kappa monoclonal gammopathy

บทคัดย่อ :

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Necrobiotic xanthogranuloma (NXG) เป็นโรคที่พบน้อยในกลุ่ม non-Langerhans cell histiocytosis ซึ่งมักจะมาด้วยผื่นสีม่วง แดง ส้ม หรือเหลือง ตำแหน่งที่พบได้บ่อย คือ บริเวณรอบดวงตา ใบหน้า ลำตัว และแขนขา พยาธิกำเนิดของโรคนี้ยังไม่ทราบแน่ชัด เมื่อตรวจทางพยาธิวิทยาพบลักษณะเฉพาะ คือมี cholesterol cleft ภายในบริเวณ necrobiosis ล้อมรอบด้วย granuloma มีรายงานการพบภาวะ IgG monoclonal gammopathy ในผู้ป่วย NXG ได้ถึง 80% และ 10% ของผู้ป่วยพบเป็นโรค multiple myeloma นอกจากนี้ยังมีรายงานว่าสามารถพบร่วมกับ xanthoma ได้ ผู้เขียนได้รายงานผู้ป่วย NXG ร่วมกับ plane xanthoma ที่มีระดับไขมันในเส้นเลือดปกติ และมีภาวะ IgG kappa monoclonal gammopathy

คำสำคัญ: Necrobiotic xanthogranuloma, non-Langerhans cell histiocytic disease, plane xanthoma, multiple myeloma, IgG kappa monoclonal gammopathy

Introduction

Necrobiotic xanthogranuloma (NXG) is a rare non-Langerhans cell histiocytic disease which has a characteristic clinical manifestations and histopathology. Pathogenesis of NXG remains unclear. Most of the NXG patients were reported to be accompanied by monoclonal gammopathy of IgG type with either kappa or lambda. There had been few previous reports of xanthoma and NXG derived in the same patients. We reported a case of NXG co-occurring with plane xanthoma and IgG kappa monoclonal gammopathy in the same patient.



Figure 1 Indurated erythematous plaque at V-shape of neck with background of yellowish papules and plaques on the neck and anterior chest wall

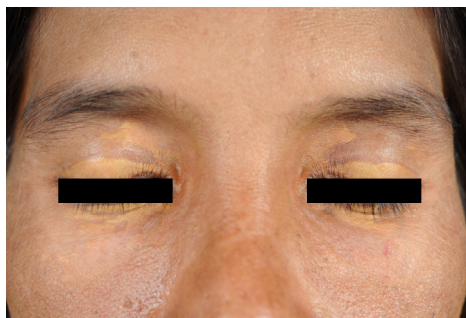


Figure 2 Bilateral yellowish patches and plaques on eyelids and periorbital area

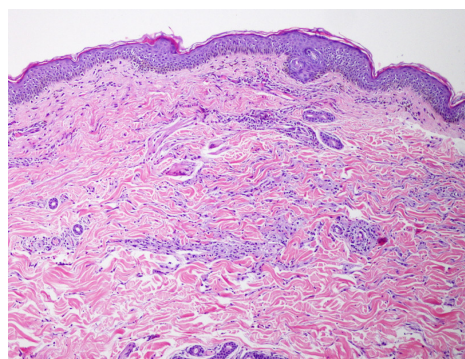


Figure 3a Histopathology from yellowish papule on the neck shows interstitial infiltration of foamy histiocytes in upper to mid dermis. (Hematoxylin-Eosin, x40)

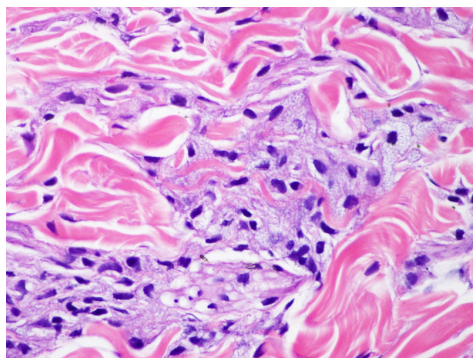


Figure 3b Higher magnification of figure 3a reveals interstitial infiltration of foamy histiocytes without other inflammatory cells infiltrate. (Hematoxylin-Eosin, x400)

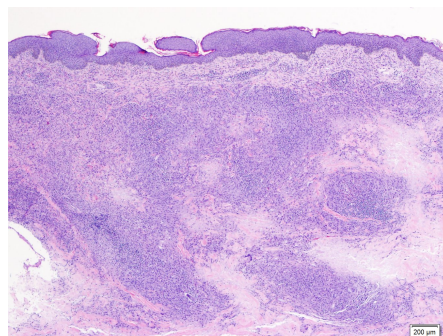


Figure 4a Histopathology from erythematous plaque on chest wall shows extensive necrobiosis admixed with cholesterol clefts, surrounded by foamy histiocytes, Touton's giant cells, lymphocytes and eosinophils. (Hematoxylin-Eosin, x40)

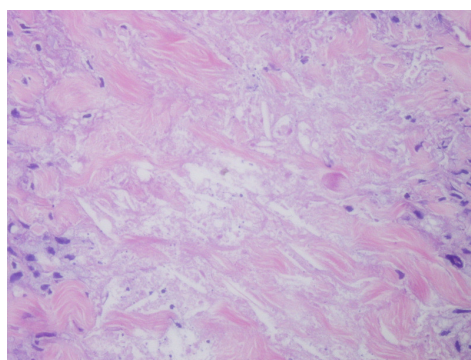


Figure 4b Higher magnification of figure 4a shows the area of necrobiosis admixed with cholesterol clefts and nuclear debris. (Hematoxylin-Eosin, x400)

Case report

A 43-year-old Thai female presented with a 6-month history of asymptomatic plaques on the chest wall. She also has asymptomatic yellowish plaques on eyelids for 10 years. The skin biopsy was done from the lesion on the chest wall from the other hospital and the pathological report was poorly formed granuloma.

She was treated with trimethoprim and sulfamethoxazole for three weeks. The lesions were partially subsided. Later on, she developed a severe drug allergy with generalized skin rashes and the medication was discontinued. She was then referred to Siriraj hospital for proper investigation and management. There were neither other abnormal systemic symptoms nor familial history of similar skin condition.

Dermatological examination revealed well-defined indurated erythematous plaque at V-shape of neck with background of yellowish papules and plaques at neck and anterior chest wall (figure 1), some yellowish patches and plaques at both upper and lower eyelids (figure 2). Others physical examinations were unremarkable.

In this patient, we had done two skin biopsies from the yellowish papule on the chest wall which revealed normal epidermis with interstitial infiltration of foamy histiocytes in the upper to mid dermis devoiding of other inflammatory cells. The findings were compatible with plane xanthoma (figure 3a, b). Another skin biopsy was done from erythematous plaque on chest wall which revealed nodular and diffuse infiltrations composing of foamy histiocytes, Touton's giant cells, with lymphoplasmacytic cells and eosinophils in some areas. The intervening tissue separating the granulomas showed extensive necrobiosis admixed with cholesterol clefts (figure 4a, b). This section was compatible with NXG.

Other investigations were done in this patient; complete blood count showed Hb12.7 g/dL, Hct 43.5%, WBC 8,290 cells/mm³ (N 45.6%, L 29%, E 17.2%), Platelet 345,000 cells/mm³. Liver function and lipid profile were normal. Serum protein electrophoresis revealed free kappa light chain of 32.20 (3.30-19.40) mg/L, free lambda light chain of 17.00 (5.71-26.30) mg/L, kappa: lambda ratio 1.89 (0.26-1.65) and immunofixation showed IgG kappa monoclonal gammopathy.

Discussion

Necrobiotic xanthogranuloma (NXG) is a rare non-Langerhans cell histiocytic disease characterized by firm papules, nodules and plaques with various color from violaceous to red-orange or yellow.^{1,2} Most NXG lesions firstly appear on the trunk or extremities and subsequently involve the periorbital area with majority of 80-85%. The lesions usually are asymptomatic but sometimes may spontaneously ulcerated.¹ Pathogenesis of NXG remains unclear. There had been some previous reports of xanthoma and NXG derived in the same patients.³ In our case, we had done two skin biopsies from the yellowish papule and the erythematous plaque on the chest wall which histopathological results were compatible with plane xanthoma and NXG respectively.

NXG had been reported to be accompanied by monoclonal gammopathy of IgG type with either kappa or lambda light chain in up to 80% of cases and about 10% of the patients developed multiple myeloma.⁴

Most common extracutaneous site of involvement is respiratory tract and the second most common site is cardiac tissue.⁵ Ophthalmologic findings had been variably reported including burning, itching, painful eye, diplopia, scleritis, proptosis, blepharoptosis and restricted ocular motility.⁶ Other hematologic malignancies including Hodgkin lymphoma, non-Hodgkin lymphoma and chronic lymphocytic leukemia were also reported.⁷ However, the most common association is monoclonal gammopathy of uncertain significance (MGUS). Hematological disorders can occur anytime during the course of the disease. Therefore, patients with NXG require lifelong follow-up care.⁶

Histologically, NXG shows granulomatous inflammations in the dermis that can extend to subcutaneous tissue. The most distinct features are large zone of necrobiosis surrounded by well-formed, palisading granuloma composing of foamy histiocytes, lymphocytes, foreign body-type multinucleated giant cells and Touton-type giant cells.¹ Cholesterol clefts in the areas of necrobiosis are characteristic and helpful clues for the diagnosis of this condition.⁸ No correlation between clinical presentations and specific histological findings such as necrobiosis, plasma cells or atypical giant cells infiltrations.⁹ Differential diagnosis of NXG includes necrobiosis lipoidica diabetorum, granuloma annulare, foreign-body granuloma, juvenile xanthogranuloma, rheumatoid

nodules, xanthoma disseminatum and Erdheim-Chester disease.^{6,8}

Our patient also has plane xanthoma co-existed with NXG. Both normolipemic plane xanthoma and NXG were associated with monoclonal gammopathy, multiple myeloma and other lymphoproliferative disorders. There were reported cases that had histological proven lesions of plane xanthoma and NXG at the same time³ and progression of plane xanthoma to NXG had also been observed.¹⁰ Plane xanthoma and NXG had some common histological findings. Previous studies suggested a common physiopathology of these forms of xanthomatous reactions. They represent part of a spectrum of responses to monoclonal immunoglobulin that interfere with lipoprotein deposits in monocytes and macrophages.¹¹

For long term outcomes, NXG was usually slowly progressive and showed variable response to chemotherapeutic agents. No specific treatment of choice is recommended.⁶ Recurrence after surgery is high.⁴ Treatment modalities including topical, intralesional or systemic corticosteroids, alkylating agents such as cyclophosphamide, chlorambucil and melphalan had been used with limited success.⁴ There were reports that NXG patients with monoclonal gammopathy completely responded and well-tolerated to a combination of dexamethasone with oral cyclophosphamide and a combination of thalidomide with dexamethasone. The clinical severity and

prognosis are not associated with the level of the monoclonal gammopathy.^{7,12} Long term follow up study in NXG patients, especially when co-occurring with normolipemic plane xanthoma is crucial for early detection of monoclonal gammopathy and hematologic malignancy.

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