Case Report

Surgical debridement of infected necrobiotic xanthogranuloma: a case report and review of the literature

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ABSTRACT

Necrobiotic xanthogranuloma (NXG) is a rare skin disorder characterized by the development of large violaceous plaques all over the body. Rarely, these plaques become infected and require surgical debridement. The current literature is lacking on outcomes of surgical intervention in this patient population. Hence this case report aims to describe surgical management for a patient with NXG presenting to The Shoalhaven District Memorial Hospital and review the literature on the pathophysiology and current treatment modalities for this condition. A 61-year-old man presented to The Shoalhaven District Memorial Hospital with an infected NXG plaque on his left calf unresponsive to intravenous antibiotics. He has had a previously infected lesion on his right shin debrided by our surgical team in 2015, with plaque recurrence on the superior-medial aspect. His current infection was managed with surgical excision of the necrotic core of the NXG plaque while sparing the healthy surrounding plaque tissue. This is in accordance to the current literature which demonstrates poor cosmetic outcomes with complete surgical resection of healthy plaques, with a 42% recurrence with increased size and nodularity.1, 2 NXG appears to be related to autoimmune monoclonal paraproteinemia and associated with hematological malignancy. Therefore, management is primarily medical with surgical resection only indicated in cases of severe infection. NXG presents a rare challenge to the general surgeon given the lack of evidence for surgical debridement. Understanding the underlying pathophysiology, treatment options and healing patterns in this disorder will allow the surgeon to assess and manage infected lesions with minimal cosmetic disfigurement.

Keywords: Necrobiotic xanthogranuloma, Necrobiosis, Surgical excision, Debridement, Infection

INTRODUCTION

Necrobiotic xanthogranuloma (NXG) is a rare skin disorder that results in cutaneous eruptions of yellow to red plaques across the face, trunk and extremities. While the pathogenesis is not well understood, NXG is associated with monoclonal paraproteinemia and haematological diseases such as multiple myeloma, Hodgkins and non-Hodgkins lymphoma.1-3 Due to the rarity of the disease, there is no consensus on first-line therapy.1,2 However, these cutaneous lesions are prone to infection.2 There is currently no data in the literature on patients presenting with infected NXG lesions. Hence, we present the case of a 61-year-old man presenting to The Shoalhaven District Memorial Hospital with an infected NXG lesion on his left lower limb with surrounding cellulitis.

CASE REPORT

A 61-year-old man presented to The Shoalhaven District Memorial Hospital with two days of left lower limb pain, swelling, tenderness and erythema spreading from an ulcerated NXG lesion on his left calf. He had been diagnosed with NXG 11 years prior and was currently not receiving any treatment, having previously trialed radiotherapy and steroid injections with no success. The
patient reported that prior to the development of NXG he worked for 35 years as an electroplater with exposure to chromic acid, silver cyanide and cadmium oxide without personal protective equipment. The development of skin lesions occurred shortly after he retired. Around the same time, he was also diagnosed with autoimmune neutropenia and monoclonal gammopathy of unknown significance (MGUS). He is otherwise healthy, active, does not smoke and does not consume alcohol.

Figure 1: NXG plaques over chest and abdomen. Round and violaceous, various sizes and textures.

Figure 2: NXG plaques over back. Variation in size and shape.

Figure 3: NXG plaques extending to the neck and base of skull with central pitting.

The patient has over twenty raised violaceous plaques covering his back, abdomen, chest, neck, upper and lower limbs (Figure 1-3). The lesions initially developed on his back before progressing to the rest of his body over the course of three years. He has had a lesion on his left forearm previously excised for cosmetic reasons, however six months post excision it had regenerated with increased nodularity and size (Figure 4). He also has a lesion on his right shin which became infected with staphlococcus aureus in 2015. This was managed with shallow debridement of the necrotic tissue, oral probenecid and intravenous cephalasin. The infection destroyed the original plaque leaving a flat scar with plaque recurrence on the superior-medial aspect (Figure 5).

Figure 4: Left arm with prominent raised plaque with pitted centre. This plaque had been excised years prior, now recurred with increased nodularity compared to flat plaque below.

Figure 5: Right shin scar where previous plaque was destroyed by Staphylococcus infection. There is a new plaque arising from superior-medial aspect.

Figure 6: NXG plaque on left leg with necrotic centre surrounded by cellulitis extending into the popliteal fossa onto the back of the thigh.

The current infected lesion had developed 11 years ago but only started to ulcerate over the last 48 hours. He had been
commenced on cephazolin by his Infectious Diseases specialist with no improvement and had been asked to present to the Emergency Department due to worsening cellulitis.

On examination, the patient was haemodynamically stable and afebrile. He had a white cell count (WCC) of 9.4 and a C-reactive protein (CRP) of 295. On the posterior aspect of his left calf, there was a 4 cm x 4 cm raised fleshy pink plaque with a central area of ulceration and necrosis (Figure 6). There was a surrounding area of erythema extending to the popliteal fossa and down to the ankle, which was tender to touch and swollen (Figure 7). Other NXG lesions were dispersed over his abdomen, back, both upper limbs and lower limbs. These were violaceous, well circumscribed, slightly raised and non-tender with a central area of pitting without ulceration.

On advice by his Infectious Diseases’ specialist, the patient was commenced on intravenous meropenem and vancomycin. He was admitted under the General Surgical team and taken to the operating theatre for surgical debridement. During the operation, the necrotic centre of the plaque was excised and devitalized tissue removed with curette. The cavity was washed out with saline, then packed with Vasgauze (Figure 8 and 9). A swab and tissue sample were sent to the pathology lab for histology, microscopy, culture and sensitivity testing. Histologically, the specimen contained keratin squames and a focal area of skin showing spongiosis with underlying abscess and macro-inflammatory change. The culture grew group. Streptococcus pyogenes that was pansensitive to penicillin.

The patient’s antibiotics were changed to cephazolin and he completed 10 days of intravenous antibiotics. His cellulitis resolved and he was discharged home with a plan for daily community nursing dressing changes and 5 days of oral cephalexin.

DISCUSSION

NXG is a rare skin disorder that can be challenging to manage due to the lack of consistent evidence on first-line therapy. It was first reported in the 1980s, where Kossard and Winkelmann biopsied a number of cutaneous lesions which histologically comprised of necrobiosis surrounded by prominent granulomatous infiltrate in the dermis and subcutaneous layers of the skin. These granulomas consisted of foamy histiocytes, foreign type giant-cells, cholesterol clefts, lymphoid aggregates and giant touton cells. While the majority of these lesions are cutaneous, in the aggressive form of NXG there can be systemic involvement of multiple organs such as the liver, spleen, kidney, heart and lungs.

NXG occurs in the fifth and sixth decades of life with equal rates in men and women. There are reports of lesions initially developing in areas related to trauma or radiation, or within previous scars. Borrelia burgdorferi infection and other spirochetal microorganisms are proposed to play a role in the development of some cases of NXG but the pathogenesis is largely unknown.

NXG is associated with monoclonal paraproteinemia. Approximately 80% of patients with NXG have Monoclonal gammopathy of undetermined significance (MGUS) with IgG kappa paraproteinemia. Other common associations include smoldering multiple myeloma and chronic lymphocytic leukemia. Less commonly associated haematological disorders include Hodgkins and non-hodgkins lymphoma and lymphoplasmacytic lymphoma. NXG appears to be a separate entity rather than a manifestation of the aforementioned diseases as the majority of patients with MGUS and multiple myeloma...
will not have NXG. Lesions are reported to occur up to 8 years prior to the development of haematological malignancy or up to 11 years after the development of haematological malignancy. Due to this association, it is recommended that patients diagnosed with NXG be closely monitored for the development of haematological malignancy.

Although there is no data linking exposure to industrial chemical compounds to the development of NXG, there is some evidence linking occupational exposure to plasma cell disorders. This is seen mainly in agricultural workers, who have a 2-fold increased prevalence of MGUS compared to the normal population. Industrial workers who have exposure to chemicals such as aromatic hydrocarbons also show varying degrees of increased risk of development of multiple myeloma. Like NXG, the pathogenesis of MGUS is poorly understood, however it is likely that the damage to cellular deoxyribonucleic acid (DNA) from exposure to chemical compounds is similar in both MGUS and NXG. Further studies on the impact of occupational exposure on disease development is challenging due to the variation in levels of exposure between different individuals and different workplaces. The available case-control studies published all demonstrate conflicting reports.

There are a number of theories that postulate why this condition can occur with plasma cell dyscrasias. It is proposed that serum immunoglobulins bind to lipids and deposit in the skin where the complexes are engulfed by macrophages that undergo foreign body giant-cell reaction, or become foam cells and xanthomatous cells. Another theory is that the paraproteins in MGUS are similar in structure to lipoproteins and thus bind to histiocyte lipoprotein receptors on macrophages to induce granuloma giant-cell formation. This however does not explain why only an extremely small number of patients with MGUS develop NXG, therefore other unknown factors likely play a role.

Treatment modalities range from immunomodulators, protease inhibitors, corticosteroids, immunosuppression, alkylating agents and autologous stem cell transplantation. Of these, the most commonly used are immunomodulators and protease inhibitors, however even when multiple modalities of treatment are utilized, very few patients have improvement of their disease state. In a case series by Whittaker et al two out of four patients had no response to therapy. The other two showed improvement with topical steroids and chlorambucil respectively. Data from the Mayo Clinic suggests that the greatest impact in disease improvement is when NXG is treated with systemic therapy directed against co-existing haematological malignancy. In the Whittaker et al study, the patient who reported disease improvement with chlorambucil was also receiving this therapy for chronic lymphocytic leukemia. It is proposed that chemotherapy in the form of alkylating agents such as chlorambucil reduces paraprotein load which thus improves cutaneous disease. Our patient had been offered to trial chemotherapy but he had declined. Chemotherapy also adds an additional challenge in managing infection in these patients, as the impact on healing and response to infection will be hindered.

Excision of non-infected plaques are discouraged due to high recurrence rates of 42% within the first 6-12 months, as well as worsening severity of disease and cosmetic disfigurement. This is apparent in figure 4, where a previously excised plaque recurred with greater size and nodularity compared to the other plaques on the patient’s body. However, there is no data on how to manage infected lesions that may necessitate surgical debridement. In 2015, our patient had a staphylococcus infection of a plaque on his right shin. This was managed with surgical debridement and antibiotics that resolved the infection and left only mild scarring, however there was plaque recurrence (Figure 5). The infected plaque on his left leg was managed with attempts to spare all healthy tissue and debride only what was non-viable in hopes that the plaque will not change in size. The histopathology of the excised infected plaque reassures us that resected necrotic components contains tissue that behaves like a normal abscess.

Minimizing the degree of plaque resection will avoid anatomical disruption and the risk of larger, more fleshy plaques forming over the area. Furthermore, patients on immunosuppressant therapy for NXG will have delayed healing time and be prone to infection, therefore large surgical defects are not ideal. Although cutaneous plaques can become ulcerated during the development of NXG, we recommend resection only if the patient has signs of infection such as surrounding cellulitis, fevers and pain with no response to intravenous antibiotics. Other indications for surgery include lesions over the eyelid impacting vision, which can be managed by resection and reconstruction with local flaps.

**CONCLUSION**

NXG presents a rare challenge to the general surgeon given the lack of evidence for surgical debridement in the literature. Understanding the underlying pathophysiology, associated haematological diseases, treatment options and healing patterns in this disorder will allow the surgeon to perform an adequate assessment and enable management of infected lesions with minimal cosmetic disfigurement. Appropriate follow up and involvement of specialty teams is vital to ensure appropriate long-term care.

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