CASE OF THE MONTH

Necrobiotic Xanthogranuloma as the Presenting Manifestation of Smouldering Myeloma

Nayani Makkar[1], Vettakkara Kandy Muhammed Niyas[1], Satish Swain[1], Prayas Sethi[1], Neeraj Nischal[1], Shipra Agarwal[2], M Ramam[3], Naveet Wig[1]

Abstract

Necrobiotic xanthogranuloma is a rare dermatological manifestation of underlying hematological malignancies, in particular, when associated with paraproteinemia. These patients who are clinically symptomatic with chronic papules, nodules or plaques which demonstrate a histopathological pattern suggestive of extensive and frequently confluent areas of necrobiosis with granulomatous infiltration, warrant evaluation for an underlying monoclonal gammopathy.

We present an unusual case of pyrexia of unknown origin. The patient, on evaluation, was found to have nodular lesions on his buttocks and thigh. Biopsy from these lesions demonstrated the histopathological findings of necrobiotic xanthogranuloma. Subsequent evaluation diagnosed the patient with smouldering myeloma. As the patient was not fulfilling the criteria for multiple myeloma and his symptoms were not debilitating it was decided to keep the patient under close follow up.

Necrobiotic xanthogranuloma (NXG) is a rare skin disorder grouped under non – Langerhans cell histiocytosis.[1] This condition is often associated with an underlying haematological disorder especially paraproteinemias. A monoclonal gammopathy is present in about 90% of cases of NXG.[2] We report an interesting case where in which a patient of smouldering myeloma presented as pyrexia of unknown origin and necrobiotic xanthogranuloma.

Case Report

A 50 year old male patient, a BSF Jawan from Rajasthan presented with complaints of recurrent fever and nodules in the buttocks and thigh for four years duration. The fever was episodic and with each episode of fever the patient noticed multiple nodules in the buttocks and thigh. The nodules were red and painful. The fever and swelling used to persist for around a week and subside without any treatment. The patient did not have any history of cough, breathlessness, bone pain or joint pain.

On examination the patient was conscious and oriented, pulse rate was 80/minute and blood pressure was 110/80 mm Hg. There was no pallor, lymphadenopathy or clubbing. There were multiple nodular swellings (2x2 cm) in the gluteal area and thigh which were tender on palpation. The skin surrounding these swelling were thick and indurated. Rest of the physical examination showed no abnormalities.

Blood investigations showed a Haemoglobin of 9.8 g/dL, a total leucocyte count of 8200/mm^3 and a platelet count of 4, 47,000/mm^3. His Erythrocyte sedimentation rate was 40mm in the first hour. Albumin level was 3.2g/dl and globulin level: 4.1 g/dl. Urine microscopy was normal and there was no proteinuria. Test for anti-nuclear antibodies by Immunofluorescence was negative. Rest of the investigations are summarised in Table 1.

A biopsy of the nodule from the gluteal area was done which showed a fragment of panniculus with septal thickening (Figure 1). The lobules showed many foamy macrophages and Touton giant cells with occasional polymorphs and eosinophils. These features were suggestive of xanthogranulomatous panniculitis which is a feature of necrobiotic xanthogranuloma.

In view of the biopsy finding and the reversed Albumin: Globulin ratio an underlying paraproteinemia was suspected. Serum electrophoresis showed a dense and narrow M band in the gamma region. Immunofixation studies showed the M Band to be IgG

Table 1: Laboratory investigations

Hematocrit (%)	29.5
Haemoglobin (g/dl)	9.8
White cell count (per mm^3)	8200
Differential count	Neutrophils:74% Lymphocytes:14% Monocytes:9% Eosinphils:1.8%
Platelet count(per mm^3)	4,47,000
ESR (mm in first hour)	40
Blood Urea (mg/dl)	29
Creatinine (mg/dl)	0.9
Sodium (mEq/L)	132
Potassium (mEq/L)	4.8
Calcium (mmol/litre)	2.4
Bilirubin (mg/dl)	
Total	0.9
Direct	0.2
Alanine aminotransferase (U/Liter)	27
Aspartate aminotransferase (U/Liter)	49
Total Protein (g/dL)	7.3
Globulin (g/dL)	4.1
Serum Free kappa light chains (mg/L)	30.63
S.Free lambda light chains (mg/L)	531.05
S.Free kappa / lambda ratio	0.05
Serum Beta 2 Microglobulin (mg/L)	3.56

g/dl: grams per decilitre; mm^3: cubic millimetre; mg/dl: milligrams per decilitre; mEq/L: milliequivalents per litre; mmol: millimoles; U/litre: units/litre

[1]Department of Medicine, [2]Department of Pathology, [3]Department of Dermatology, All India Institute of Medical Sciences, New Delhi
Received: 26.10.2018; Accepted: 20.01.2019

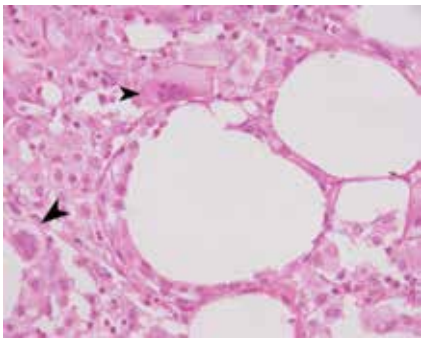

Fig. 1: (Haematoxylin and Eosin): Biopsy from the lesion showing fragment of panniculus with the lobules showing many foamy macrophages, Touton giant cells (arrow heads). Features are of xanthogranulomatous panniculitis

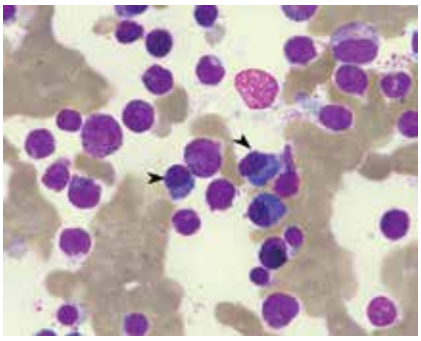

Fig. 2: Bone marrow study showing increase in plasma cells (arrow heads)

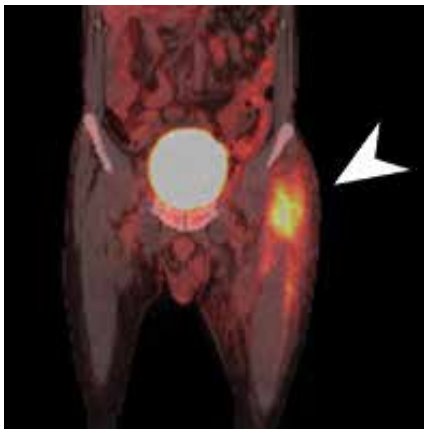

Fig. 3: PET CT scan done showing metabolically active lesion in the region of left quadriceps muscle (arrow head)

Lambda. A bone marrow study done showed 12 % plasma cells (Figure 2). A serum Free Light Chain Assay showed a serum free Kappa light chains of 30.63 mg/L, free lambda light chains: 531.05 mg/L and a serum free kappa/ lambda ratio of 0.05. PET scan done showed metabolically active ill-defined hypodense lesion in the region of left quadriceps muscle (Figure 3). There were no lytic bone lesions.

Patient was thus not fulfilling the criteria of Multiple Myeloma and was diagnosed as Smouldering Myeloma. He was decided to be kept under regular follow up.

Discussion

NXG is a rare skin disorder that occurs in patients with underlying haematological disorders especially paraproteinemia. NXG was first described by Kossard and Winkelman in 8 patients with underlying paraproteinemia.[3] Currently this skin disorder is considered as a non-Langerhans cell histiocytosis.[2]

Clinical presentation of NXG is in the form of chronic papules, nodules and plaques predominantly involving the face and periorbital areas. However the lesions can involve the trunk and extremities as well.[4] Histopathological features include extensive areas of necrobiosis with a prominent granulomatous infiltrate in the dermis and subcutaneous tissue. Within the granulomas foreign body giant cells, Touton-type giant cells and foam cells are characteristically seen.[5] Xanthogranulomatous panniculitis with Touton-type giant cells and palisading cholesterol clefts is a characteristic feature of NXG.[6]

An underlying monoclonal gammopathy should always be investigated in a case of NXG. In a series of NXG patients, 86% had underlying paraproteinemia. 26% of patients in this series had an underlying hematologic malignancies at the time of NXG diagnosis or during followup. Multiple myeloma was present in 11% of the patients.[4] In another series 71% had an underlying monoclonal gammopathy while 18% met the criteria for multiple myeloma.[5]

Many peculiarities of our case mark it as a rather atypical clinical presentation. The first is the presentation of our patient as a case of pyrexia of unknown origin. He had presented to multiple health care facilities with the chief complaint of intermittent fever over the prior four years, with no evident cause on extensive evaluation including imaging. the systemic manifestation of pyrexia in the absence of overt systemic disease (while the patient demonstrated laboratory evidence for a plasma cell disorder, the absence of target organ damage led to the designation of a smouldering multiple myeloma) is an uncommon presentation not only of NXG but also of plasma cell dyscrasia.

The second is the unusual presentation of the dermatological disorder itself. The exclusive involvement of the lower limbs in the absence of facial of trunk lesions, while reported, is infrequent.[5] Furthermore, the skin manifestations presented with a rather indolent course, marked by recurrent, spontaneously healing nodular swellings with no evidence of local infiltration or destruction, as well as no extracutaneous organ involvement over the four year symptomatic period.

Given the rarity of NXG, there exists no definite clinical guideline to direct management of the cutaneous manifestation. The treatment of the underlying plasma cell dyscrasia, hence takes precedence and the cutaneous manifestation has been seen to respond to treatment of multiple myeloma.[7] Our patient, however, did not have significantly debilitating cutaneous manifestations or end organ manifestations from his plasma cell dyscrasia. On discussion with a panel of medical oncologists, physicians, dermatologists in conjunction with the patient, it was decided to continue close monitoring and regular follow-up with the subsequent initiation of therapy in the event of worsening of clinical and/ or laboratory parameters.

References

1. Emile J-F, Abla O, Fraitag S, Horne A, Haroche J, Donadieu J, et al. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. *Blood* 2016; 127:2672–81.
2. Hilal T, DiCaudo DJ, Connolly SM, Reeder CB. Necrobiotic xanthogranuloma: a 30-year single-center experience. *Ann Hematol* 2018.
3. Kossard S, Winkelmann RK. Necrobiotic xanthogranuloma with paraproteinemia. *J Am Acad Dermatol* 1980; 3:257–70.
4. Bhari N, Chiramel MJ, Vedi KK, Nath D, Sandip S, Kumar R, et al. Necrobiotic xanthogranuloma with multiple myeloma. *Clin Exp Dermatol* 2015; 40:811–4.
5. Flann S, Wain EM, Halpern S, Andrews V, Whittaker S. Necrobiotic xanthogranuloma with paraproteinaemia. *Clin Exp Dermatol* 2006; 31:248–51.
6. Finan MC, Winkelmann RK. Histopathology of necrobiotic xanthogranuloma with paraproteinemia. *J Cutan Pathol* 1987; 14:92–9.
7. Efebera Y, Blanchard E, Allam C, Han A, Lee S, Munshi N. Complete Response to Thalidomide and Dexamethasone in a patient with Necrobiotic Xanthogranuloma Associated with Monoclonal Gammopathy A Case Report and Review of The Literature. *Clinical Lymphoma, Myeloma & Leukemia* 2011; 11:298-302.