International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Case Report .

Cytological Diagnosis of Multiple Normolipemic Tuberous Xanthoma: An Unusual Occurrence

Ashok Kumar Dash[1], Shushruta Mohanty[2]*, Sujit Manohar Swain[3], Biswajit Padhy[3], Milan Tripathy[3]

[1]Associate Professor, [2]*Senior Resident, [3]Post Graduate,
Department of Pathology, M.K.C.G Medical College, Berhampur, Odisha, India.

ABSTRACT

Xanthomas are lesions characterised by accumulations of lipid laden macrophages within the dermis. Tuberous xanthomas are large nodular lesions those develop in patients with underlying hyperlipoproteinemias. A 26-year-old female presented to our hospital with multiple tuberous swellings on the extensor surface of the body since 15 years. We also incidentally detected presence of Nodular thyroid swelling while examining the patient in our lab. Routine investigations along with Lipid profile were within normal range and serum protein electrophoresis showed normal pattern. FNAC from few Tuberous nodules and multiple sites of thyroid nodule was then performed. Cytosmears in all tuberous nodules showed good number of foamy histiocytes in clusters and discretely admixed with plenty of giant cells and collections of cholesterol crystals over a dirty haemorragic background. Surprisingly FNAC done from thyroid smears shows good number of epithelioid cell clusters, group of benign follicular cells and other features similar to aspiration of tuberous nodules. Thyroid function revealed increased TSH with low normal T3, T4. Histopathology from a single excised nodular lesion showed attenuated epidermal lining with collection of foamy macrophages in the dermis with plenty of giant cell reaction and cholesterol crystals that confirmed our findings to be Tuberous xanthoma. We present a case of normolipemic tuberous xanthomas with its association with thyroid disorder (hypothyroidism), which is an uncommon occurrence.

Keywords: Cutaneous, FNAC, Normolipemic, Tuberous Xanthoma.

***Correspondence to:**

Dr Shushruta Mohanty,
Senior Resident,
Department of Pathology,
M.K.C.G Medical College, Berhampur, Odisha, India.

Article History:

Received: 07-04-2019, **Revised:** 02-05-2019, **Accepted:** 28-05-2019

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2019.5.3.041	

INTRODUCTION

Tuberous xanthomas are not true tumours, but tumour like collections of foamy histiocytes, which is probably due to reactive histiocyte proliferation that occur in response to alterations in serum lipid profile.[1] Xanthomas usually occur in skin and subcutis, but occasionally can involve deep soft tissue such as tendons or synovium.[2] They may be associated with familial or acquired disorders resulting in hyperlipidemia, with lyphoproliferative malignant neoplasms, or with no underlying disorder.[3]

We present a case of multiple tuberous xanthomas in a subject with normal lipid metabolism and with associated thyroid (systemic) disorder, which is uncommon and rare. The aim of this report is to emphasize the importance of considering this disease entity in a patient with normal lipid profile.

CASE REPORT

A 26-year old female presented to the medicine outpatient department with a history of multiple nodular lesions over bilateral elbows, knees and feet for the past 15 years. The lesions first appeared over the extensor aspect of bilateral elbow joints followed by similar nodules over bilateral ankle joints, dorsal aspect of the feet and lastly over bilateral knee joints Fig 1 (a)(b). The patient was otherwise healthy with a family history of similar lesions in one of the four siblings. On physical examination, multiple yellowish, firm, non-tender cutaneous lesions were identified over the extensor aspect of bilateral elbows, ankle and knees, largest measuring 3 cm in size over the right elbow. X ray of the forearm showed no bone/joint involvement with areas of

dystrophic calcification Fig 2 (a)(b). FNAC was performed from multiple tuberous sites with nature of aspirate being thick greyish white. Smears were moderately cellular and showed predominantly foamy histiocytes in clusters and scattered singly, plenty of giant cells and cholesterol crystals in, few foci of fibrous tissue on a haemorragic background Fig 3(a)(b)(c). We also discovered an incidental thyroid swelling on systemic examination Fig 4(a) which on aspiration showed follicular cells in clusters, normofollicular pattern admixed with good number of foamy histiocytes, multinucleated giant cells, clusters of epitheloid histiocytes over a background of thin colloid which was suggestive of granulomatous thyroiditis with evidence of xanthoma cell infiltration Fig 4 (b)(c)(d). She had a normal haemogram. Her biochemical investigations showed normal blood glucose levels, liver function tests, kidney function tests and electrolytes levels, however the lipid profile was within normal limit. Thyroid profile done showed higher TSH levels 16.67 IU/ml with normal T3 and T4 levels s/o (Hypothyroidism). Corroborating with the clinical presentation, X ray findings and with the biochemical findings, a possibility of Tuberous Xanthoma was considered on cytology and an excision for histopathological correlation was advised. Excision of a single tuberous swelling was done under local anesthesia in minor surgical OT and the sample was sent for histopathological examination. Grossly we received a globular grayish white globular structure measuring 4x3 cms, c/s was solid, homogenous Fig 5(a)(b). Histopathological examination from the excised nodular lesions revealed infiltration of dermis by good number of foamy histiocytes along with giant cells, fibrosis and cholesterol clefts thus confirming the diagnosis as Normolipemic Tuberous xanthoma with giant cell reaction Fig 6 (a)(b)(c)(d).

Fig 1(a): Tuberous swellings on extensor surfaces near joints.

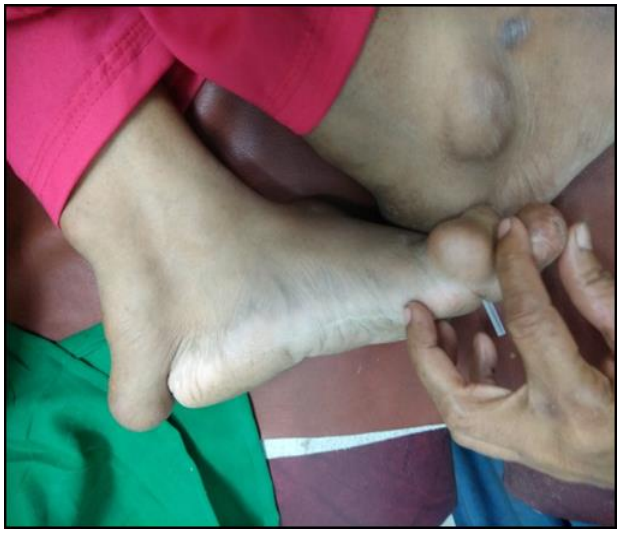

Fig 1(b): Swellings in the feet.

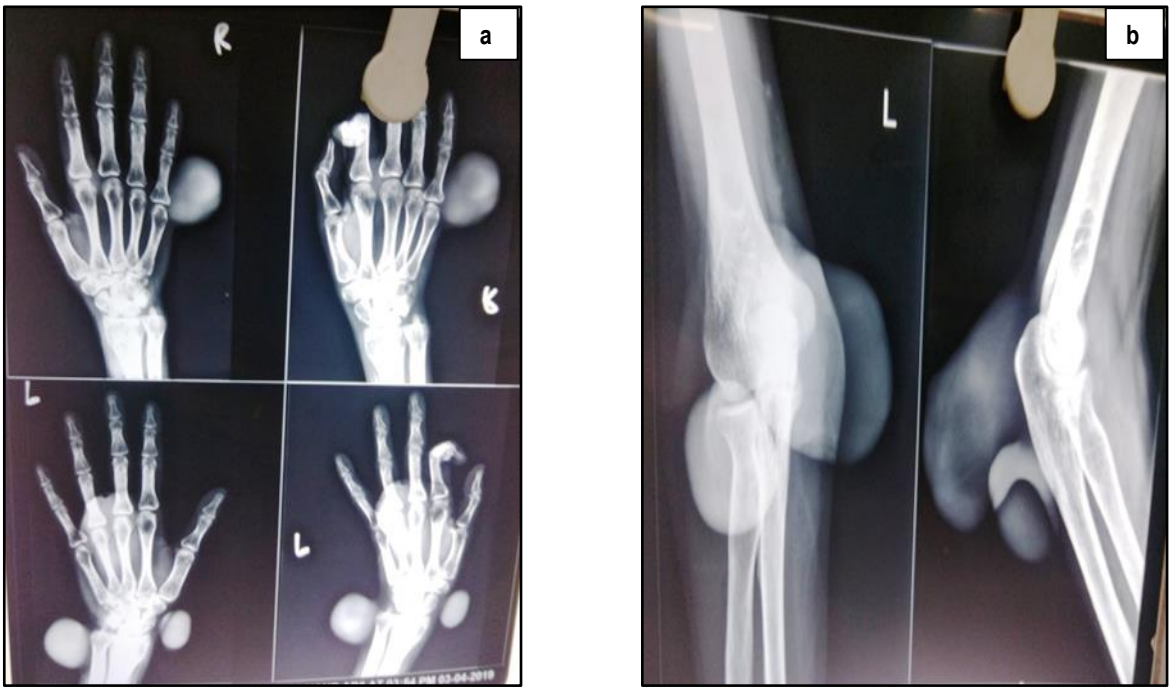

Fig 2(a)(b): Areas of dystrophic calcification like opacities around normal bony architecture.

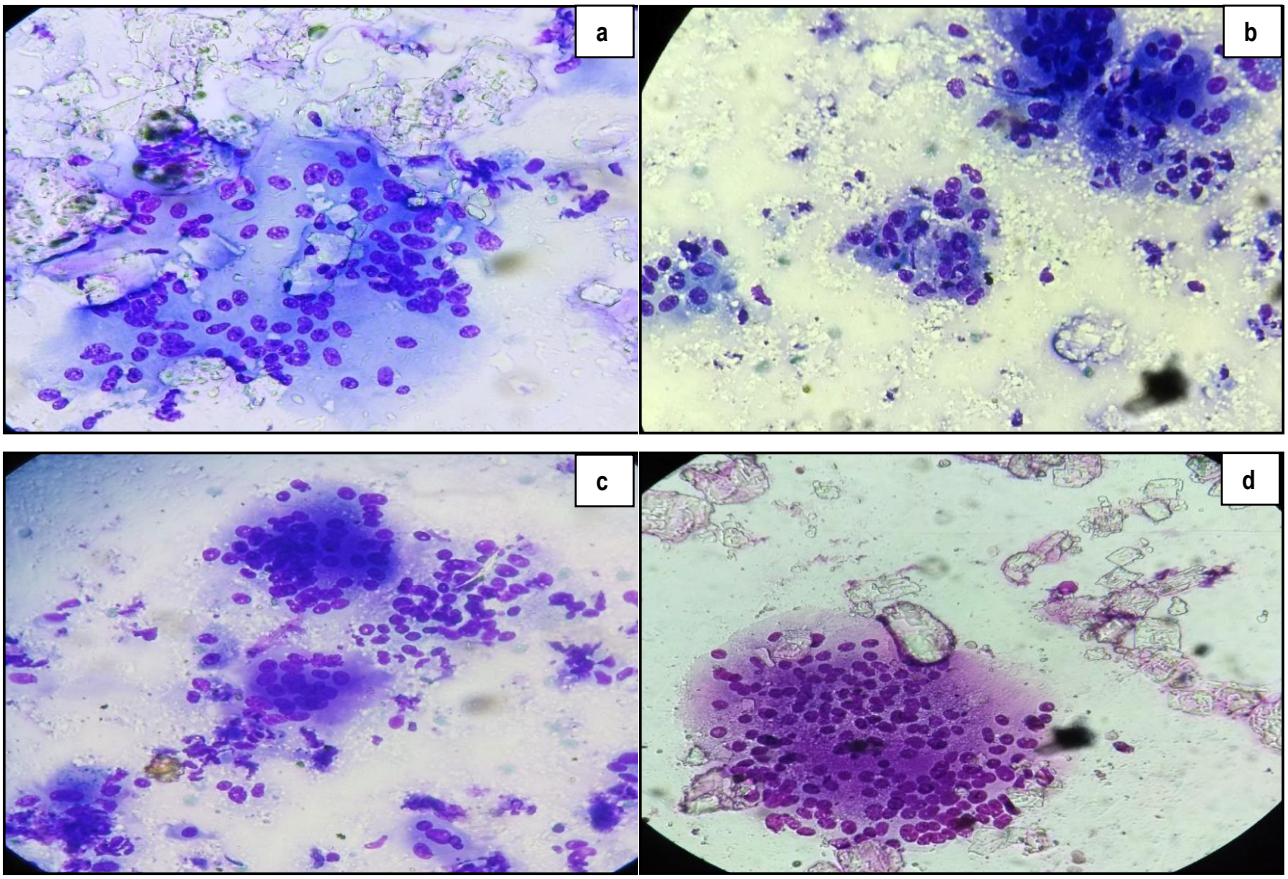

Fig 3 (a)(b): FNAC from tuberous swellings DQ stain –Showing clusters of foamy macrophages
Fig 3(c): showing good number of giant cells and Fig 3(d): showing cholesterol crystals and giant cells.

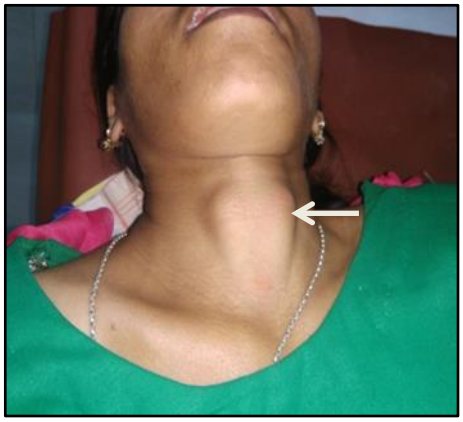

Fig 4(a): Incidental detected thyroid swelling

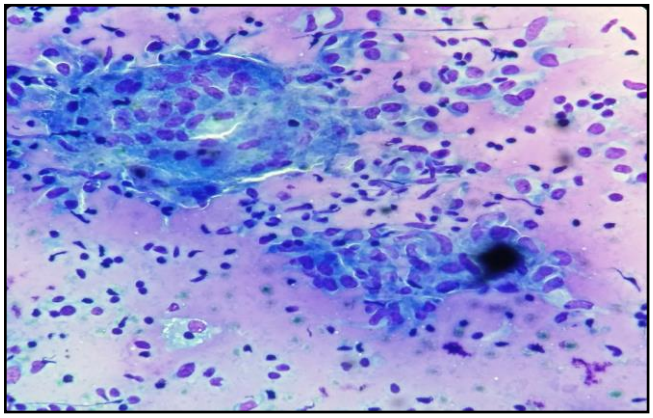

Fig 4(b): 100X-FNAC thyroid [DQ stain]: clusters of epithelioid cells.

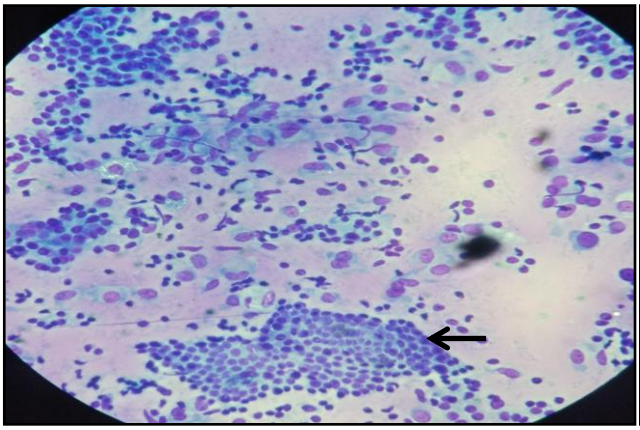

Fig 4(c): 100x-FNAC [DQ stain]: Thyroid follicular cells (arrow) in monolayered sheets admixed with dispersed epithelioid cells

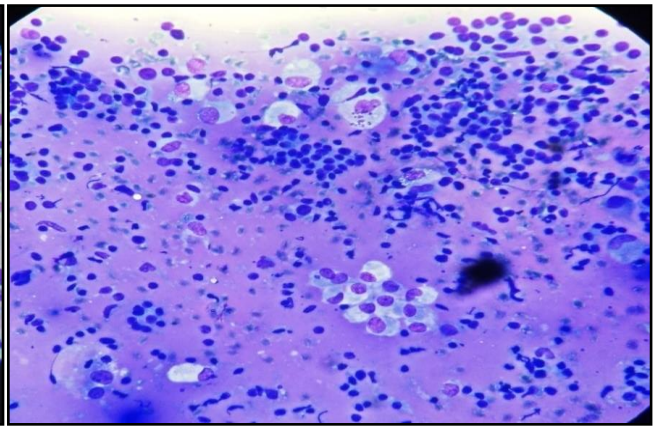

Fig 4(d): 100x –FNAC [DQ stain]: Thyroid follicular cells admixed with xanthoma cells.

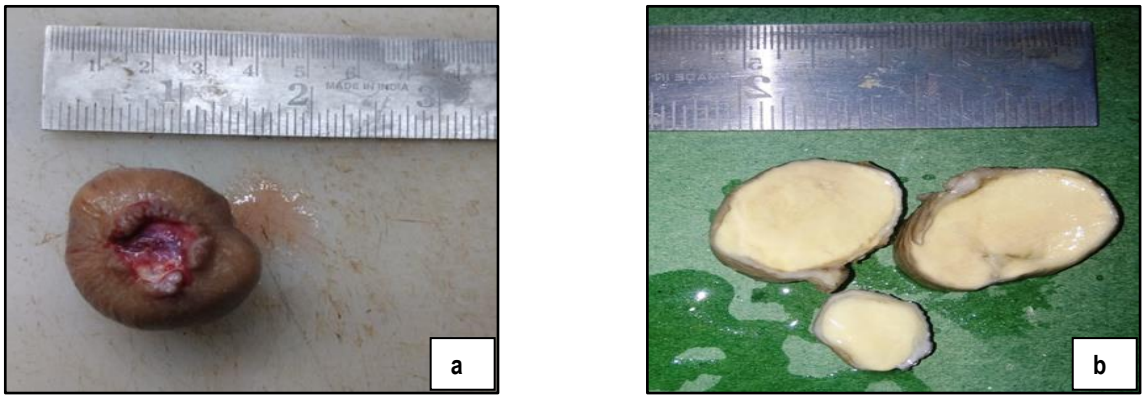

Fig 5(a): (unfixed, fresh) sample; (b) (post formalin fixation): Gross pic of a solitary excised nodule from a forearm measuring 4x3 cm.c/s solid homogenous.

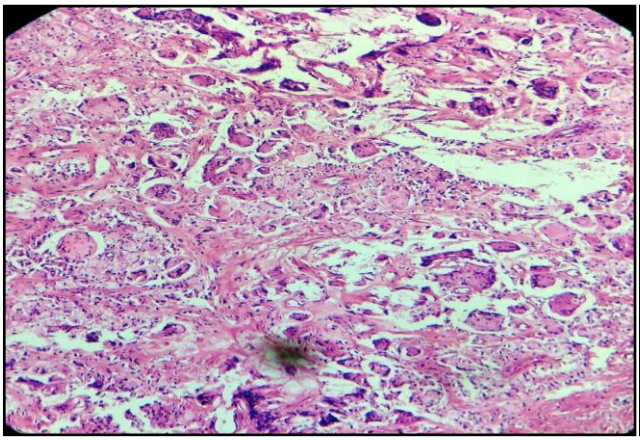

Fig 6(a): Histopathology of tuberous swellings LP 100X: Giant cells admixed with histiocytes.

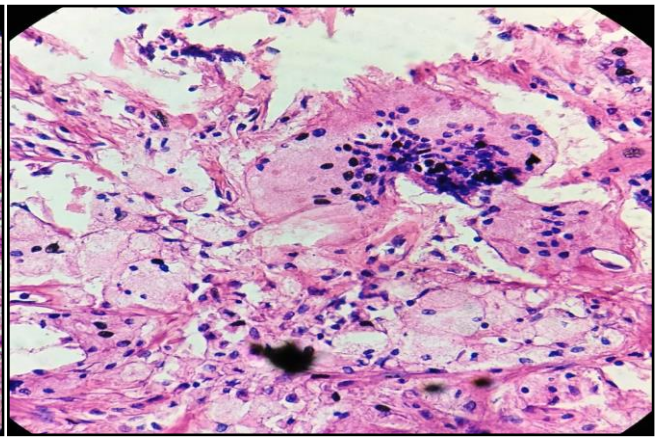

Fig 6(b): LP 100X: Good number of foamy histiocyes (xanthoma cells) with a giant cell.

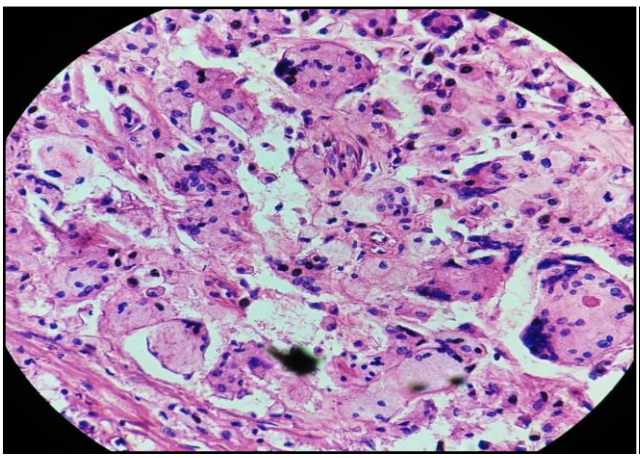

Fig 6(c): HP- 400X: Good number of giant cells.

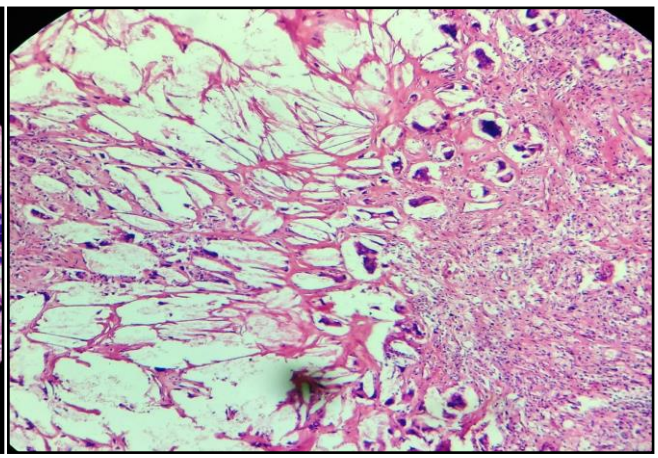

Fig 6(d): LP 100X: Areas of Cholesterol clefts with giant cell reaction.

DISCUSSION

Xanthomas are tumors or infiltrates of the skin varying from yellow to brown-red colour, which are due to lipid-containing cells in the dermis. Xanthomas may be the symptoms of a general metabolic disease[4], a generalized histiocytosis, or a local fat phagocytosing storage process.

Xanthomas consist of cholesterol, cholesterol esters, triglycerides, phospholipids and numerous lipid-laden foamy macrophages. Xanthomas may be broadly classified into several categories: Tendinous xanthoma, xanthoma tuberosum, eruptive xanthoma, xanthoma planum, and palmar xanthoma.[5] Tuberous xanthomas are firm, painless yellow nodules that coalese to form multilobulated tumours and usually develop in pressure areas such as extensor surfaces of knees, elbows, buttocks and are seen with type IIa or III hyperlipoproteinemia. In our case too xanthomas were present in these areas. Eruptive xanthomas are small, yellow papules developing in individuals with hyperlipoproteinemia types I, III, and V. Plane xanthomas occur in skinfolds, such as the palmar creases, and are characteristic of type III hyperlipoproteinemia. Occasionally they occur in normolipemic persons. Xanthelasmas are xanthomas of the eyelid and usually are observed in normolipemic persons, although they also occur in those with type IIa or III hyperlipoproteinemia. Xanthoma disseminatum and verruciform xanthoma are particular forms of xanthomas that occur in normolipemic patients.[6] Tuberous xanthomas are particularly associated with

hypercholesterolemia and increased level of LDL.[7] They can be associated with familial dysbetalipoproteinemia and familial hypercholesterolemia type (Frederickson IIa and III hyperlipoproteinemias), and they may be present in some of the secondary hyperlipidemias. However, our patient did not show any type of hyperlipidemia.

Several theories were earlier postulated regarding the pathology of xanthomas .Earlier, xanthomas were considered as a neoplastic lesion, but their association with hyperlipidemic states confirms that these are benign reactive lesions.[1] The pathogenesis suggested in such lesions are that the lipid in these lesions is derived from blood.[8] The serum lipoproteins leave the vascular compartment, traverse small vessels, and enter the macrophages of soft tissue. Once ingested by macrophages the lipoprotein is degraded to lipid, and the lipid is released to the extracellular space. The fibrosis characteristic of mature or longstanding xanthomas is believed to be related to the release of fibrogenic cytokines that are sensed by NOD like receptors of innate immunity. This series of events can be confirmed ultrastructurally by the sequential finding of lipoprotein between endothelium and basement membrane and finally in the pericytes. Although xanthomas can potentially occur at any soft tissue site, the localization stimulus seems directly related to the vascular permeability, as agents that increase permeability (e.g., histamine) can accelerate xanthoma formation at a given site. Likewise, minor trauma or injury that results in histamine release also accelerates xanthoma formation. This observation provides an explanation for the common occurrence of such lesions in the tendons of the hands and feet which would also be the probable cause in our case.

Histopathologically, xanthomas are characterized by the presence of vacuolated macrophages in dermis. These macrophages are lipid laden that gets dissolved and removed from tissue during histologic processing. They contain prominent fibrosis and occasional cholesterol clefts and plenty of giant cells

Review of literatures shows assosciations of multiple tuberous xanthomas with hyperlipidemic states. However diffuse normolipemic xanthomatosis have been reported in the literature, but this entity is uncommon[9-11] and are often associated with serious hepatic disease or hematological dyscrasias, especially multiple myeloma.[12] Unusual association of normolipemic cutaneous xanthomatosis with IgG gammopathy, hypernephroma, an unusual family cluster of leukemia have been reported by Hu et al.[13] Similarily Vail et al, reported a case of chronic myelomonocytic leukemia with cutaneous xanthomas.[14] Thus, normolipemic xanthomatosis has been found to be associated with either a systemic disease or malignancy. In our case it was associated with thyroid swelling (systemic manifestation) which was incidentally discovered on examination and was asymptomatic, whose FNAC findings was suggestive of granulomatous thyroiditis with xanthoma cell infiltration.

CONCLUSION

The patient was kept on follow up for 5 months and was asked to repeat lipid profile every month which yielded normal results. Cryotherapy with nitrous oxide was done for other larger tuberous lesions and was on oral antioxidants. She was put on thyroid medications to which she responded well. Our case is unique as tuberous xanthoma has occurred in a normolipemic subject, and its association with thyroid swelling as a systemic manifestation which is a rare occurrence. FNAC plays an indespinsable role in diagnosis as it helps to avoid the need of surgical biopsy in these multiple lesions and moreover xanthomas do respond to medical therapy alone and yields better results.

REFERENCES

1. Marcoval J, Moreno A, Bordas X, et al. Diffuse plane xanthoma: clinicopathologic study of 8 cases. J. Am Acad Dermatol. 1998;39:439.

2. Fahey JJ, Stark HH et al. Xanthoma of the Achilles tendon: seven cases with familial hyperbetalipoproteinemia. J Bone Joint Surg Am. 1973;55:1197.

3. Murphy GF, Sellheyer K, Mihm MC. The skin. In: Kumar V, Abbas AK, Fausto N, editors. Robbins and cotran pathologic basis of disease, 7th ed., Philadelphia: Elsevier; 2004. p. 1248.

4. Singh AJ, Sikarwar S, O P Jatav, and Saify K. Normolipemic tuberous xanthomas. Indian J Dermatol. 2009;54(2):176–9.

5. Zak A, Zeman M, Slaby A and Vecka M: Xanthomas: Clinical and pathophysiological relations. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2014; 158: 181-8.

6. Caputo R, Monti M, Berti E, Gasparini G. Normolipemic eruptive cutaneous xanthomatosis. Arch Dermatol 1986;122:1294-7.

7. Hata Y, Shigematsu H, Tsushima M, Oikawa T, Yamamoto M, Yamauchi Y, et al. Serum lipid and lipoprotein profiles in patients with xanthomas: A correlative study on xanthoma and atherosclerosis (I). Jpn Circ J 1981;45:1236-42.

8. Iton KW, Thomas C, Dunkerley DJ: The pathogenesis of xanthomata. J Pathol 1973;109:271.

9. Handa R, Gupta K, Wali JP. Normolipemic xanthomatosis. Postgrad Med J 1995;71:555-6.

10. Fleischmajer R, Tint GS, Bennett HD. Normolipemic tendon and tuberous xanthomas. J Am Acad Dermatol 1981;5:290-6.

11. Singla A. Normolipemic papular xanthoma with xanthelasma. Dermatol Online J 2006;12:19.

12. Rudolph RL. Diffuse “essential” normolipemic xanthomatosis. Int J Dermatol 1975;14:651-6.

13. Hu CH, Winkelmann RK. Unusual normolipidemic cutaneous xanthomatosis: A comparison of two cases illustrating the differential diagnosis. Acta Derm Venereol 1977;57:421-9.

14. Vail JT Jr, Adler KR, Rothenberg J. Cutaneous xanthoma associated with chronic myelomonocytic leukemia. Arch Dermatol 1985;121:1318-20.

Source of Support: Nil. **Conflict of Interest:** None Declared.

Cite this article as: Ashok Kumar Dash, Shushruta Mohanty, Sujit Manohar Swain, Biswajit Padhy, Milan Tripathy. Cytological Diagnosis of Multiple Normolipemic Tuberous Xanthoma: An Unusual Occurrence. Int J Med Res Prof. 2019 May; 5(3):189-93. DOI:10.21276/ijmrp.2019.5.3.041