

Squamous cell carcinoma developing in a long-standing case of tuberous xanthoma: An incident unreported hitherto

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ABSTRACT

Cutaneous squamous cell carcinoma, characterized by malignant transformation of normal epidermal keratinocyte is the second most common nonmelanoma skin cancer that has many predisposing factors. Tuberous xanthomas have not yet been reported as a predisposing factor. We report here the case of long-standing tuberous xanthoma in a middle-aged gentleman complicated by cutaneous squamous cell carcinoma, probably the first such report in the Indian literature.

Key words: Complication, cutaneous squamous cell carcinoma, tuberous xanthoma

INTRODUCTION

Cutaneous squamous cell carcinoma (SCC), occurring as a result of malignant transformation of the epidermal keratinocytes, has a plethora of risk factors implicated in different populations. Xanthomas commonly occur due to disturbance in lipoprotein metabolism.^[1,2] Tuberous xanthomas are firm, painless, red-yellow nodules, which can coalesce to form multilobulated tumors commonly affecting the pressure areas, such as the extensor surface of the knees, the elbows, and the buttocks.^[3,4] Herein we present the first report of long-standing tuberous xanthoma as a risk factor for cutaneous SCC, reaffirming the fact that search for newer risk factors for cancer must continue in the future.

CASE REPORT

A middle-aged gentleman presented to us with multiple asymptomatic, large, firm, multilobulated masses over the knees, heels, and interphalangeal joints, which were present for the preceding 20 years. Besides, there was a noduloulcerative lesion over the back of the lower part of the right leg. To start with, a few small swellings developed over the right heel, followed by left heel, knees, and interphalangeal joints. Gradually, these swellings increased in size to attain the present

status. There was a similar mass in the right lower leg above the heel, prior to the development of the ulcerative lesion. His past medical and surgical history, including drug history were unremarkable. Family history was noncontributory. He had not received any treatment for this condition. On cutaneous examination, there were multiple firm yellowish-orange nodules distributed over the interphalangeal joints, knees, and heels [Figures 1 and 2]. The lesions were nontender, firm to hard on palpation, ranging from 4 to 8 cm in diameter. There was also a noduloulcerative lesion over the right heel [Figure 3]. No lymph node was palpable. Systemic examination was within normal limits. Routine biochemical investigations were within normal limits. Lipid profile revealed a total cholesterol of 430 mg/dL, low-density lipoprotein cholesterol 320 mg/dL, triglycerides 380 mg/dL, and high-density lipoprotein cholesterol 44 mg/dL. Hepatitis B virus, VDRL (Venereal Disease

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Figure 1: Multiple firm multilobulated masses over the interphalangeal joints of right hand



Figure 2: Firm skin-colored mobile masses over the right knee



Figure 3: Multiple firm yellowish-orange nodules over the heels. Note the noduloulcerative lesion above the right heel

Research Laboratory) Test, and HIV serology were nonreactive. Chest radiography, and ultrasonographic scan of the abdomen and pelvis were normal. Histopathological examination from a representative nodular lesion over the interphalangeal joint showed collections of foam cells and lipid-laden macrophages with areas of fibrosis and cholesterol clefts indicative of tuberous xanthoma [Figure 4]. However, histology of the ulcerative lesion showed irregular nests, cords, or sheets of neoplastic keratinocytes invading the dermis to various depths. There were horn pearls as well [Figure 5]. This confirmed the diagnosis of cutaneous squamous cell carcinoma (CSCC). The patient was started on atorvastatin and referred to the surgeon for appropriate management.

DISCUSSION

CSCC is a malignant tumor arising from the epidermal keratinocytes. CSCC classically presents as a shallow ulcer with heaped up edges often covered by a plaque, in sun-exposed areas. Typical surface changes include scaling,

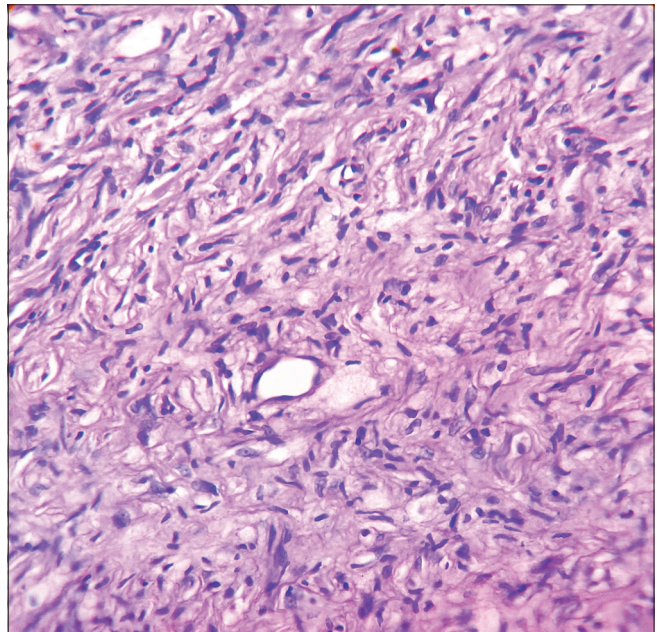


Figure 4: Photomicrograph showing collections of foam cells, lipid laden macrophages, areas of fibrosis, cholesterol clefts, fibroblasts, and histiocytes (H and E, $\times 40$)

crusting, ulceration, or even a cutaneous horn. A biopsy should be performed from any such suspicious lesion to confirm the diagnosis. CT scan or MRI may be helpful in delineating the extent of the disease. Low-risk CSCC on the trunk and extremities can be treated with electrodesiccation and curettage. For invasive cases, surgical excision and Mohs micrographic surgery are the primary treatment modalities.^[5] Radiation therapy is typically used as an adjuvant to surgery. Systemic chemotherapy may be considered for metastatic

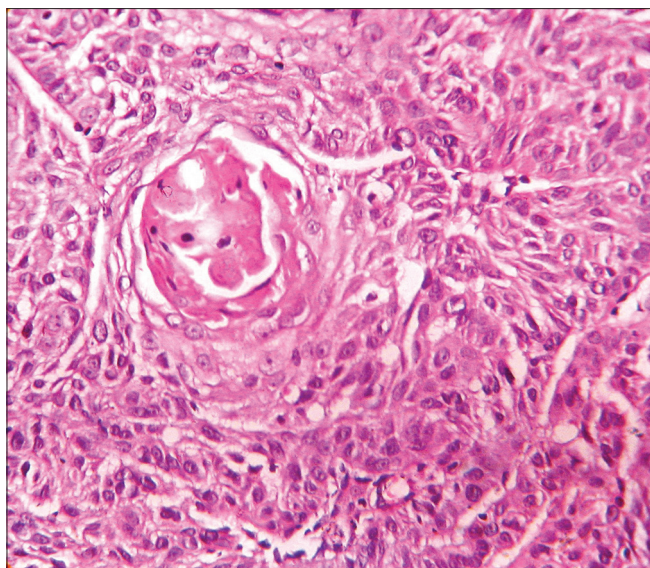


Figure 5: Photomicrograph showing keratin pearls and malignant squamous cells. (H and E, $\times 40$)

CSCC.

Well known risk factors for development of CSCC include UV exposure, immunosuppression, exposure to ionizing radiation or chemical carcinogens, human papillomavirus infection.^[6] Other conditions reported to have been associated with cutaneous SCC include acne conglobata, hidradenitis suppurativa,^[7] dissecting folliculitis of the scalp, lupus vulgaris,^[8] chronic deep fungal infection, xeroderma pigmentosum,^[9] dystrophic epidermolysis bullosa,^[10] epidermodysplasia verruciformis, dyskeratosis congenita, porokeratosis of Mibelli,^[11] Marjolin's ulcer, burn or thermal injury,^[12] venous ulcers, lymphedemas, discoid lupus erythematosus,^[13] erosive oral lichen planus, lichen sclerosis et atrophicus, mutilating keratoderma, and necrobiotic lipoidica.

Tuberous xanthomas start as small xanthomas, usually over the extensor aspects of the elbow and knees, occasionally these can be of large size when they are called giant tuberous xanthomas.^[14] They develop over pressure areas such as heels and plantar surface of feet, and rarely in the bone marrow. However, atypical locations of tuberous xanthoma such as upper eyelids^[15] have also been reported. They can be associated with familial hypercholesterolemia^[16] and familial dysbetalipoproteinemia,^[17] sitosterolemia.^[18] They may be present in some of the secondary hyperlipidemias (eg, nephrotic syndrome, hypothyroidism). Complications of tuberous xanthoma is mainly due to hyperlipidemia, which may cause atherosclerosis (e.g., coronary artery disease) and pancreatitis.^[19]

Although CSCC has not yet been reported as a complication of tuberous xanthoma, verruciform xanthoma (VX) has been reported to be associated with SCC in a couple of cases.^[20,21] It was hypothesized that the SCC arose co-incidentally

in the epidermis overlying the xanthoma or adjacent to it; and later these two conditions joined each other. Takiwaki *et al.*^[21] proposed that VX occurred as a reactive process on an overlying verrucous carcinoma or carcinoma *in situ*. In our case too, it may be assumed that CSCC and tuberous xanthoma are related in a similar fashion; but most likely the two are coincidental. We must however keep in mind the possibility of tuberous xanthomas being a premalignant condition, and thus subject such cases to careful periodic histologic scrutiny and closer clinical follow-up to detect any malignancy at the earliest.

To the best of our knowledge, this is the first report of CSCC developing as a complication of long-standing tuberous xanthoma. While newer risk factors for CSCC are yet to be elucidated, we must be aware of its occurrence over long-standing xanthomas.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Diepgen TL, Mahler V. The epidemiology of skin cancer. *Br J Dermatol* 2002;146:1-6.
2. Parker F. Xanthomas and hyperlipidemias. *J Am Acad Dermatol* 1985;13:1-30.
3. Mohan KK, Kumar KD, Ramachandra BV. Tuberous xanthomas in type IIA hyperlipoproteinemia. *Indian J Dermatol Venereol Leprol* 2002;68:105-6.
4. Bhagwat PV, Tophakhane RS, Kudligi C, Noronha TM, Thirunavukkarasu A. Familial combined hypercholesterolemia type II b presenting with tuberous xanthoma, tendinous xanthoma and pityriasis rubra pilaris-like lesions. *Indian J Dermatol Venereol Leprol*. 2010;76:293-6.
5. Brodland DG, Zitelli JA. Surgical margins for excision of primary cutaneous squamous cell carcinoma. *J Am Acad Dermatol* 1992;27:241-8.
6. Cutaneous squamous cell carcinoma and human papilloma virus. *Actas Dermosifiliogr* 2007;98:583-93.
7. Constantinou C, Widom K, Desantis J, Obmann M. Hidradenitis suppurativa complicated by squamous cell carcinoma. *Am Surg* 2008;74:1177-81.
8. Kiedrowicz M, Królicki A, Stanisława BG, Maleszka R. Squamous cell carcinoma arising from radiation-treated lupus vulgaris scar. *Indian J Dermatol Venereol Leprol* 2011;77:253.
9. Baisakh MR, Khalkho J, Khan MA. Multiple squamous cell carcinoma of face in a child with xeroderma pigmentosa-A case report. *Austral-Asian J Cancer* 2009;8:133-5.
10. Weschler HL, Krugh FJ, Domonkos AN, Scheen SR, Davidson CL Jr. Polydysplastic epidermolysis bullosa and development of epidermal neoplasms. *Arch Dermatol* 1970;102:374-80.
11. Oberste-Lehn H, Moll B. Porokeratosis Mibelli und Stachelzellcarcinom. *Hau Tarzt* 1968;19:399-403.
12. Habif TP. Premalignant and malignant nonmelanoma skin tumors. In: Habif TP, editor(s). *Clinical Dermatology*. 4th ed. Vol. 4. Mosby, Edinburgh. Elsevier Publications; 2007. p. 744-7.

13. Halder RM, Bridgeman-Shah S. Skin cancer in African Americans. *Cancer* 1995;75(Suppl):667-73.
14. Babu R, Venkataram A, Santhosh S, Shivaswamy S. Giant tuberous xanthomas in a case of type IIA hypercholesterolemia. *J Cutan Aesthet Surg* 2012;5:204-6.
15. Shukla Y, Ratnawat PS. Tuberous xanthoma of upper eye lids (a case report). *Indian J Ophthalmol* 1982;30:161-2.
16. Maher-Wiese VL, Marmer EL, Grant-Kels JM. Xanthomas and inherited hyperlipoproteinemias in children and adolescents. *Pediatr Dermatol* 1990;7:166-73.
17. Royer M, Bulai Livideanu C, Periquet B, Maybon P, Lamant L, Mazereeuw-Hautier J, *et al.* Orange skin and xanthomas associated with lycopenaemia in a setting of type III dyslipoproteinemia. *Ann Dermatol Venereol* 2009;136:42-5.
18. Merkens LS, Myrie SB, Steiner RD, Mymin D. Sitosterolemia. In: Pagon RA, Adam MP, Ardinger HH, Bird TD, Dolan CR, Fong CT, *et al.*, editors. *GeneReviews®*. 1993-2014. Seattle, WA: University of Washington; 2005.
19. Austin MA, Hutter CM, Zimmern RL, Humphries SE. Familial hypercholesterolemia and coronary heart disease: A HuGE association review. *Am J Epidemiol* 2004;160:421-9.
20. Mannes KD, Dekle CL, Requena L, Sanguenza OP. Verruciform xanthoma associated with squamous cell carcinoma. *Am J Dermatopathol* 1999;21:66-9.
21. Takiwaki H, Yokota M, Ahsan K, Yokota K, Kurokawa Y, Ogawa I. Squamous cell carcinoma associated with verruciform xanthoma of the penis. *Am J Dermatopathol* 1996;18:551-4.