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Giant Cell Tumor of Soft Tissue on the Forearm Skin: Case Report and Literature Review

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Abstract

BACKGROUND: Giant cell tumor of the soft tissue (GCTST) is a very rare neoplasm that occurs predominantly in in the fifth decade of life presented as a benign looking painless mass and is associated with a local recurrence rate of 12% and very rare metastasis.

CASE REPORT: Here, we report a case of a 6-year-old boy with 14-month history of a growing painful hyperpigmented nodule in the right forearm without any antecedent of infection or trauma which was diagnosed by histopathological examination and immunohistochemistry as a GCTST after complete excision.

CONCLUSION: This case raises the awareness of diagnosis and management of GCTST that should be considered at any age group and should be differentiated from the melanocytic tumors on the skin.

Introduction

Giant cell tumor of the soft tissue (GCTST) is a very rare entity with a slow-growing course revealing a high similarity to conventional giant cell tumor of bone (GCTB) [1], [2]. It occurs predominantly in in the fifth decade of life and has no sex predilection, presented as a benign looking painless mass mainly located in the lower limb, upper limb, followed by the trunk then the head-and-neck region [3]. According to the literature, GCTST exhibits a benign behavior in the majority of cases with high recurrence rate if inadequately excised and extremely low metastatic possibility especially to the lungs [4]. Given its rarity, very little can be seen in the literature regarding its diagnostic challenge [2]. We report a case of a GCTST in a young boy located in his forearm with ulceration, hyperpigmentation, and rapid growing making a clinical suspicion of melanoma, after excision with surgical margins, the histological and immunohistochemical features were consistent with GCTST showing no recurrence for 20-month follow-up.

Case Report

A 6-year-old boy came to the clinic giving a history of a growing painful hyperpigmented nodule in the right forearm for 14 months without any antecedent of infection or trauma. The lesion began as a hyperpigmented papule that grew rapidly. Physical examination revealed a soft, smooth, well-demarcated, ulcerated, and mildly tender nodule measuring 4 cm in maximal diameter (Figure 1). The dermatologist asked for surgical consultation.

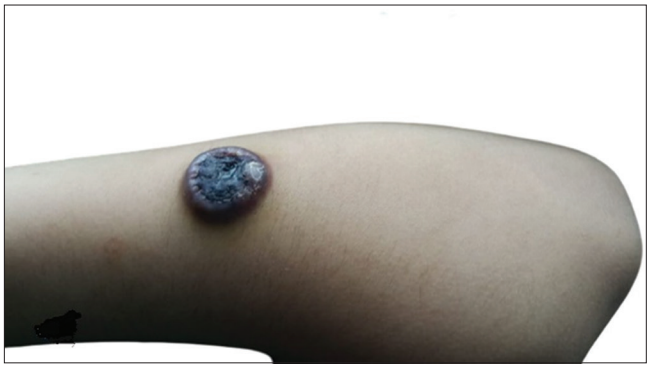

Figure 1: The clinical picture of the forearm hyperpigmented mass

The surgeon completely excised the lesion with grossly free margins and sent it for histopathological examination with fear of melanoma.

Histological examination revealed an ulcerated and well circumscribed dermal and subcutaneous tumor composed of dilated blood vessels, RBCs, mononuclear epithelioid cells, and multinucleated giant cells admixed with lymphocytes, eosinophils, and scattered spindle shape cells showing occasional mitosis (Figure 2). Immunohistochemistry study was performed showing positive staining of CD68 (histiocyte marker) and negative staining for S100 (neural and melanocytic marker). The morphological features supported by the immunohistochemical results are those of a giant cell tumor of soft tissue confirmed after consultation and cooperation between different pathologists excluding the overlapping giant cell lesion such as plexiform or aneurysmal fibrohistiocytic tumor, dermatofibroma, giant cell type malignant fibrous histocytoma (MFH), and nodular fasciitis. The patient has been remained recurrence-free for 20 months after excision.

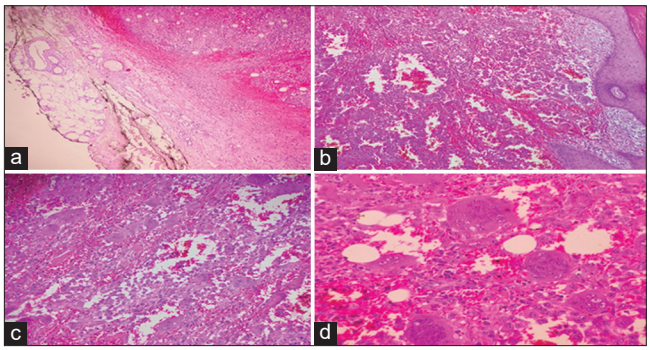

Figure 2: H&E stained histopathology picture, (a) Circumscription and painted free surgical margin (×40). (b) The lesion appears in dermal tissue (×100). (c) Vascular proliferation, hemorrhage and histiocytes (×200). (d) Giant cells appear (×400)

Discussion

The first introduction of GCTST was in 1972 in two separate papers, one described it as a benign lesion that shares similarities with giant GCTB [5], while the other described it as a malignant giant cell type [6]. Later, Folpe *et al*. [7] was the first to introduce the term giant cell tumor of soft tissue in 1999, detailing some of its histological characters and pathological behaviors and reclassifying it as a tumor of low malignant potential. However, the last classification from the World Health Organization in 2020 categorized GCTST as a subtype of a group named fibrohistiocytic tumors and described it as a neoplasm of uncertain behavior, with a recommendation to no longer use the description of “low malignant potential” [8].

Histopathology is the gold standard for such challenging skin related tumors [9]. On histopathological examination, GCTST consists of multinucleated osteoclast-like cells presented with mononuclear cells. Despite the morphological similarities with GCTB, there is distinction at the genetic level [8].

GCTST occurs in superficial and deep structures of soft tissues [2]. Almost, two-thirds of cases are reported to be located in the upper and lower extremities and rarely found in the head, neck, and trunk [1], [3], [7], with no etiology detected to the moment [8].

While it is scarce for the skin to be affected [10], [11], our case presented with painful hyperpigmented and ulcerated nodule in the right forearm making a clinical suspicion of the most malignant melanocytic tumor of the skin, melanoma. However, most reported cases were presented as painless growing mass with a size that ranges from <1 cm to 10 cm [1], [3]. Some cases showed invasion of surrounding structures, rendering it harder for complete surgical excision and increasing the possibility for recurrence [12], [13], [14] metastasis was reported predominantly to the lung in very rare cases in the literature [15], [16], [17], [18].

GCTST shows no incidence difference with regard to the age or sex; however, it is usually seen in patients aged 40–60 [3].

In our study, no radiological investigation was obtained since the lesion was cutaneous. Although radiological imaging might not establish the diagnosis, it helps to recognize the nature of the lesion in terms of consistency and heterogeneity and to define its anatomical borders especially in cases of invasion of surrounding tissues [12], [13], [16]. CT scan and MRI mostly reveal an image of solid mass, heterogeneous, and usually hemorrhagic [3].

For most of the published cases, GCTST is histologically characterized by the presence of multinodular architecture with fibrous septa in between cellular nodules that contain hemosiderin-laden macrophages [1]. The nodules are aggregates of multinuclear cells, which are round to oval, added to osteoclast multinucleated giant cells; together are immersed in a highly vascularized stroma. Mitotic activity occurs and ranges from 1 to 30/high power field.

Table 1: Previously reported cases of skin GCTST

Year	Study	Type	Tumor site	Patient age/sex	IHC	Treatment
2021	Hogeboom *et al*.[24]	Case report	Periocular	3 Y/F	SMA +, CD68 +, S100 -, Melan-A - , HMB-45 -, P16 -Desmin -, myo-D1 -, NKIC3 -	Excision (as mentioned by the authors)
2017	Hafiz *et al*.[25]	Case report	Ear	28 Y/F	No	Local excision
2014	Righi *et al*.[26]	Case report	Lip	36 Y/F	Vimentin +, CD68 +, S100 -	Excision
2010	Nguyen *et al*.[27]	Case report	Thigh	40 Y/F	No	Excision
2010	Lentini *et al*.[19]	Case report	Face (right paranasal region)	79 Y/F	NA	Local excision
2009	Boneschi *et al*.[13]	Case report	Groin	73Y/M	CD68+and SMA+	Excision
2008	Tejera-Vaquerizo *et al*.[28]	Case report	Finger	54 Y/M	CD68+, S100-, CD45-ve	Excision
2007	Mardi and Sharma[29]	Case report	Finger	30 Y/M	No	Excision
2002	Hoang *et al*.[11]	Case series (5 cases)	1- Foot 2- Elbow 3- Plamar 4- Shoulder 5- Forehead	1–75Y/M 2–76 Y/M 3–6 Y/F 4–43 Y/F 5–73 Y/M	CD68 +, Alpha1 antichyomotrypsin +, CK -, S100 -	Local excision
2001	Holst and Elenitsas[23]	Case report	Thigh	55 Y F	No	Excision
2000	Oliveira *et al*.[3]	Retrospective	extremities	(mean 35Y)	CD68 +	Local excision
1990	Maheswaran and Addis[30]	Case report	Face	92 Y/M	NA	Excision
1981	Angervall *et al*.[18]	Retrospective	Thigh	64Y/M	NA	Excision

No: No immunohistochemistry done, NA: Not available, SMA: Smooth muscle actin, CK: Cytokeratin, GCTST: Giant cell tumor of the soft tissue, IHC: Immunohistochemistry, HMB: Human Melanoma Black.

There is absence of atypia, pleomorphism, and tumoral giant cells; necrosis is rarely reported [15], [19]. Nearly third of GCTST cases demonstrated vascular invasion and half of them have metaplastic bone formation that may undergo aneurysmal bone-like cyst changes. Additional findings include stromal hemorrhage and possible regressive changes such as stromal fibrosis and clusters of foamy macrophages [3], [7].

Our case was in accordance with previously reported cases regarding the immunohistochemistry; they stained negative for S100 and positive for CD68-diffusely in the multinucleated cells and focally in mononuclear cells [11], [13], [19], [20], [21] excluding malignant lesions such as melanoma and MFH and the other differential benign and low malignant lesions. Surgical excision is the first choice for treatment of this lesion [3], [21]. Post-surgical recurrence rate is 12% [8]; however, the rate increases in cases of invasion or involvement of deep delicate structures due to the difficulty of complete surgical resection [12], [14], [22], [23]. To the best of our knowledge, all previously reported cases of GCTST in skin were treated with excision where we searched and reviewed the literature for skin GCTST cases (Table 1). Around two-thirds (11/17) of skin cases were seen in extremities, where the majority of cases were adults or old age.

Consequently, this urges the need for an additional treatment line such as radiotherapy, which is reported to be used on few occasions [31], [32]. In 2013, FDA approved Denosumab as a new therapeutic option for GCT of bone; it is a human monoclonal antibody that is thought to work by inhibiting the activity of osteoclast-like giant cells through the pathway of RANK-RANKL [33] In one recent study, denosumab was used for GCTST in thyroid after recurrence due to incomplete removal; this novel use relieved the symptoms and reduced the tumor size [14]; hence, more studies are needed to evaluate the role of denosumab as a potential line of treatment for GCTST.

Conclusion

GCTST tumor should be considered in any age group and should be differentiated from the melanocytic tumors of the skin. Complete excision is largely curable and histopathology confirmed by immunohistochemistry is essential for differentiation and accurate diagnosis.

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Consent

Informed consent was provided from the patient's father.

Authors Contribution

AH, KN, MA, SKAH, and HAS: conceived and designed the case study. AH, MA, AA, MSA, HAH, AS, and MAA: conducted research, provided research materials, and collected and organized data. AH, KN, AA, MSA, AS, MAA, HAS. and SKAH analyzed and interpreted data. AH, AA, and MA wrote initial draft of article. All authors prepared the final draft of article. All

authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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