

CASE REPORT

Non psammomatous melanocytic schwannoma presenting as a subcutaneous nodule: A rare presentation of a rare lesion

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ABSTRACT

Melanocytic schwannoma (MS) is an extremely rare soft tissue tumor accounting for less than 1% of all primitive nerve sheath tumors, with a predilection for spinal nerve involvement. To date, only 20 cases of cutaneous/subcutaneous MS have been described in literature. Here, we describe a case of MS presenting as a subcutaneous nodule in a 22-year-old male in right thigh. On examination, the nodule measured 2.5 x 2.0 x 1.5 cm with overlying skin showing a bluish hue and an ulcer. With a preoperative diagnosis of hemangioma, the patient was taken up for wide local excision and was diagnosed as a case of non psammomatous melanocytic schwannoma based on clinical, histological, and immunohistochemical studies. Immunohistochemistry revealed positivity with S-100, HMB-45, and Melan A with pericellular Laminin positivity. Carney's syndrome was ruled out. MS needs to be differentiated from other pigmented lesions like pigmented neurofibroma, Bednar tumor, cellular blue nevus, and especially malignant melanoma, which has an obvious ominous prognosis. Since MS can show unpredictable behavior especially in absence of overt malignant features, a long term follow up with or without radiotherapy is recommended.

Key words: Carney's syndrome, laminin, malignant melanoma, melanotic schwannoma

Introduction

Melanocytic schwannoma (MS) is an extremely rare soft tissue neoplasm with approximately 100 cases reported so far in various locations, especially in cervical and thoracic spinal nerve roots.^[1,2] It is composed of pigment producing cells of neural crest origin with ultra structural evidence of schwann cell differentiation along with presence of melanosomes in varying stages of development.^[3] MS occurring in cutaneous/subcutaneous location is an extremely rare occurrence with only 20 cases reported till date.^[4] We reviewed two case series on MS and found that the occurrence of cutaneous MS was three out of thirteen

cases in one and two out of twenty five cases in the other series with involvement of lumbar, shoulder, abdominal wall, arm and lower leg regions.^[1,3] Since most of these lesions have a benign clinical course, it needs to be differentiated from other pigmented lesions like malignant melanoma, especially in cutaneous and subcutaneous locations which has an obvious ominous prognosis. Extreme rarity of the lesion coupled with the problems faced at differential diagnosis especially at this location has prompted us to report this case.

Case Report

A 22-year-old male presented with a subcutaneous nodule in his right thigh of one and a half years duration which was gradually increasing in size and was noticed after a history of minor trauma. One week back, the nodule had ulcerated with associated pain. There was no other associated significant present or past history. On examination, a subcutaneous nodule was seen over the posterior aspect of mid portion of thigh measuring 2.5 x 2.0 x 1.5 cm. The swelling was firm and freely mobile over the underlying tissue. The overlying skin showed an ulcer measuring 1.0 x 0.8 cm with the rest of the skin showing a bluish hue. Rest of the skin examination showed no evidence of other subcutaneous nodules or any pigmented lesion. Examination of regional lymph nodes was unremarkable.

Access this article online

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DOI:

10.4103/1793-5482.148789

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Routine hematological and biochemical investigations done including a peripheral blood smear were within normal limits. With a preoperative diagnosis of hemangioma, the patient was taken up for wide local excision of the lesion. We received a wide local excision specimen measuring 3.0 x 2.5 x 1.5 cm with an overlying skin cover measuring 3.0 x 2.5 cm. The skin showed a bluish hue and an ulcer measuring 1.0 x 0.8 cm [Figure 1a]. On cut surface, a jet black unencapsulated tumor was seen with small tongue like projections in the surrounding tissue [Figure 1b]. Microscopic examination revealed a tumor, over lined by epidermis, showing focal ulceration along with native adnexal structures [Figure 2a]. The deeper dermis showed a tumor arising from the nerve [Figure 2b]. The tumor was heavily pigmented and was composed of hypercellular and hypocellular areas [Figure 3a]. The hypercellular areas showed spindle shaped cells arranged variably in long and short fascicles and theques with pallisading of nuclei [Figure 3b and c]. These cells had spindle shaped nuclei with evenly dispersed chromatin and indistinct nucleoli along with little amount of fibrillary cytoplasm. Also seen were large ganglion cells with abundant pigment laden cytoplasm with single to multiple nuclei showing vesicular nuclear chromatin and prominent nucleoli. Hypocellular areas were myxoid with few hyalinized blood vessels. Deeper part showed small foci of invasion into the

surrounding soft tissues. No Verocay bodies were noted. There was no evidence of junctional activity or progressive dermal maturation. There was no evidence of atypia, mitoses or necrosis in the tumor. No psammoma bodies or sheets of mature adipose tissue were seen. The sections from the tumor were reviewed after depigmentation with 0.5% potassium permanganate (KMnO₄) and the findings were confirmed. Positivity with Masson's Fontana (MF) stain and negativity with Periodic Acid Schiff (PAS) and iron stains confirmed the melanin nature of the pigment. Immunohistochemical marker study was done after depigmentation of the section which revealed positivity with S-100, HMB-45, and Melan A, and negativity with cytokeratin (CK) and Epithelial Membrane Antigen (EMA) [Figure 4a,b]. Reticulin stain and Laminin immunostain revealed a biphasic staining pattern with prominent areas of pericellular staining. Proliferattion markers including Ki67 and p53 were done which revealed positivity in <1% of cells. With the above findings, diagnosis of non psammomatous melanocytic schwannoma was offered. Since some cases of MS are associated with Carney's syndrome, a detailed mucocutaneous examination was performed to rule out lentiginos, an echocardiogram was performed to rule out myxomas and biochemical evaluations were done to rule out endocrine hyperactivity. All these investigations were negative and hence Carney's syndrome was ruled out. Since our patient showed ulceration of overlying skin and focal invasion in deeper portions of the tumor, he was advised for close follow-up and adjuvant radiotherapy. However, our patient did not show any evidence of recurrence or metastasis after a period of 10 months.

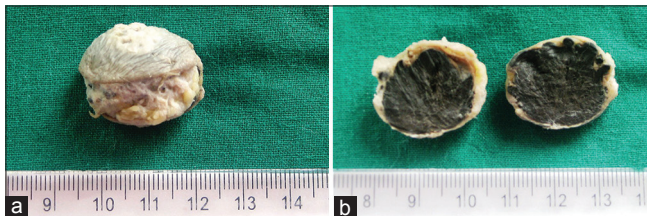


Figure 1: Photomicrograph showing (a) External surface of a wide local excision specimen with an overlying skin cover showing a bluish hue and an ulcer measuring 1.0x0.8cm; (b) Cut surface showing a jet black unencapsulated tumor with small tongue like projections in the surrounding tissue

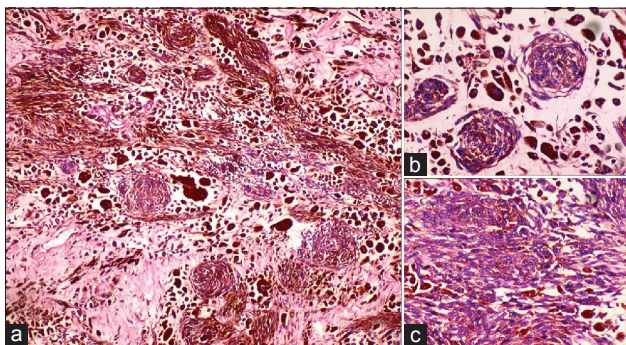


Figure 3: Photomicrographs showing (a) Heavily pigmented tumor composed of hypercellular and hypocellular myxoid areas (H and E, x100). The hypercellular areas showed; (b) Theques with pallisading of nuclei along with ganglion cells; (c) Spindle shaped cells arranged variably in long and short fascicles (H and E, x400)

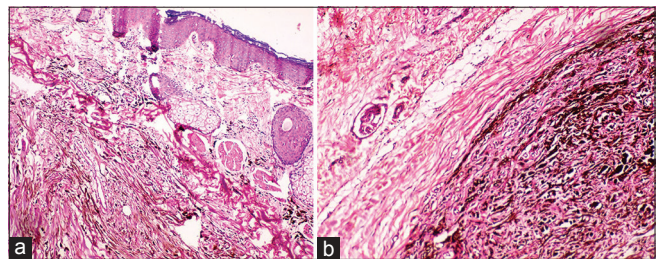


Figure 2: Photomicrograph showing (a) Pigmented tumor over lined by epidermis along with native adnexal structures (H and E, x100). (b) The deeper part showing the tumor arising from the nerve bundle on the left of photomicrograph (HandE, x100)

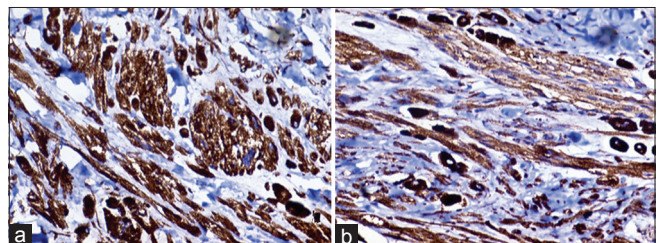


Figure 4: Photomicrograph showing (a) S-100 and (S-100, x400); (b) HMB-45 (HMB-45, x400) cytoplasmic immunopositivity

Discussion

MS was first described by Millar in 1932 as malignant melanotic tumor of ganglion cells and was subsequently termed as melanocytic schwannoma by Fu *et al.* in 1975.^[5,6] MS is known to occur in two forms - psammomatous and non-psammomatous and, in 1990s, there was a renewed interest as Carney noticed the association of the psammomatous subtype of MS with Carney's syndrome.^[2,3,7] MS is a tumor of the young (mean age, 38 years) with no sex predilection occurring predominantly in the cervical and thoracic spinal nerve roots and sympathetic ganglia.^[1,2] Rarer sites include cerebellum, orbit, soft tissue, heart, alimentary tract, trachea, cervix, temporozygomatic region, fibula, skin and subcutaneous tissue.^[1,2,4] Depending on the site and rate of growth, most cases present with a local mass with associated pain and neurological symptoms.^[1] Grossly, MS is usually a well circumscribed tumor with majority being over 5 cm in diameter and is seen to arise in relation to a nerve.^[1] Microscopically, it is characterized by spindle to polygonal cells with abundant intracytoplasmic melanin pigment and bland nuclear features.^[1,2,8] Unlike conventional schwannomas, Verocay bodies, and microcyst formations are rare in MS.^[1,3,8] However, features like alternating hypercellular and hypocellular areas, formation of neuronal theques/palisades, presence of hyalinized blood vessels and ganglion cells and origin from a nerve bundle along with diffuse S-100 positivity allowed us to make the diagnosis of MS. MS associated with Carneys syndrome shows psammoma bodies and sheets of mature adipocytes which were not found in our case.^[1-3,8] Ganglion cells have been described in only a few cases before our including the original case described by Millar.^[5] Some conventional schwannomas also show intracytoplasmic grayish pigment but it is chemically lipofuscin and is PAS and iron positive and Masson's Fontanna (MF) negative.^[1,3] Also these cells are negative for HMB45 and Melan-A.^[1,3] The presence of intracellular melanin coupled with absence of classical features of schwannoma may lead to an erroneous diagnosis of other pigmented lesions like pigmented neurofibroma, Bednar tumor, cellular blue nevus, and malignant melanoma.^[1,3] Pigmented neurofibromas are diffuse and show only microscopic pigment within relatively scant cytoplasm. Moreover, the nuclei are small and elongated as compared to ovoid nuclei with delicate chromatin and distinct nucleolus in MS.^[1,3] Bednar tumor has less amount of pigment and is S-100, HMB-45, and melan-A negative and is CD 34 positive.^[1] The distinction from malignant melanoma is particularly difficult and, in fact, about 45% cases MS were misdiagnosed as malignant melanoma in one of the series.^[1,3,8] Moreover, immunostains like S100, Melan A, and HMB-45 are diffusely positive in both.^[1,8] However, absence of nuclear atypia/mitoses, presence of fascicles, cellular whorls and ganglion like cells, and origin from a nerve should alert to an alternative diagnosis on microscopy. Since the distinction between the two is clinically significant, recently,

these have been distinguished by the use of reticulin stain and immunostaining with laminin and collagen IV.^[1,3] These stains show predominantly pericellular staining pattern in MS while in malignant melanoma staining is seen around group of cells. These stains also help to differentiate cellular blue nevus from MS. Recently, GNAQ gene (present on chromosome 9q21) mutations have been found to be useful in such lesions with positivity indicating melanocytic nevi/ melanomas (positive in 75% and 25% cases, respectively). Moreover, none of the nine cases of MS showed positivity for GNAQ mutations.^[3] Ultra structural examination in MS reveals features of Schwann cells with presence of intracytoplasmic melanosomes in varying stages of development.^[1,3] Other differentials like meningeal melanocytoma and pigmented meningioma were not considered as our case was in subcutaneous location.

Although, recurrence and malignant transformation in conventional schwannomas is exceptionally rare, the prognosis of MS is unpredictable and metastasis is known to occur in absence of overt malignant features.^[1,8] A recent report by Hong-ying *et al.* has reported a recurrence rate of 18.2% and a metastatic rate of 9.1% after a mean follow-up period of 5.9 years. Furthermore, Decouvelaere *et al.* have emphasized the importance of long term follow up as only 53% of the 77 patients he reviewed were disease free after a follow-up period of more than five years.^[9] Although local recurrence rate at the subcutaneous location is similar to that seen in other locations, a single case developed wide spread metastasis out of a total of 20 cases analyzed. Management of the patients is mostly done by wide local excision; however, due to paucity of cases, post-surgical management is controversial and adjuvant radiotherapy has been suggested as a means to improve outcomes.^[1] The utility of adjuvant radiotherapy is highlighted by a recent report in which the surgical exploration did not include adequate surgical margins and hence was given 60 gray adjuvant radiotherapy. The patient did not show any signs of recurrence/ metastasis after 24 months follow-up. The tumor in our patient showed aggressive features and hence was advised radiotherapy and close follow-up.

To conclude, MS is a rare tumor and should not be confused histologically with other pigmented lesions especially malignant melanoma as this distinction is very important in planning the management of the patient. Immunohistochemical staining with laminin and collagen IV can be of immense value in this distinction. Moreover, in view of its unpredictable behavior, especially in the absence of overt malignant features, long terms follow-up with or without radiotherapy is recommended. Further studies with larger number of cases will be required to better delineate the management of such cases.

Acknowledgement

We wish to thank Ms. Ashwini Shivaji Suryawanshi, working as lab technician, for her technical support in preparation of the manuscript.

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How to cite this article: Gulati HK, Joshi AR, Anand M, Deshmukh SD. Non psammomatous melanocytic schwannoma presenting as a subcutaneous nodule: A rare presentation of a rare lesion. *Asian J Neurosurg* 2016;11:317-8.

Source of Support: Nil, **Conflict of Interest:** None declared.