

Pigmented Neurofibroma : A Case Report with Immunohistochemical and Ultrastructural Study

Shubhangi Vinayak Agale*, Arun R Chitale**

Abstract

Pigmented neurofibroma is a rare variant of neurofibroma showing melanin production. The clinical diagnosis is difficult to establish requiring the histopathological examination to differentiate between the melanotic neurofibroma and other pigmented tumours.

We report an unusual case of a huge, recurrent, pigmented neurofibroma with extended, macroscopically striking pigmentation in a 45 year old patient without stigmata of neurofibromatosis 1.

The histochemical, immunohistochemical and ultrastructural findings support a melanotic line of differentiation besides Schwann cell differentiation.

Introduction

Pigmented neurofibroma (PNF) is a unique subtype of neurofibroma which is rare and contains melanin producing cells.¹⁻¹⁰ Most occur in patients with neurofibromatosis¹ and are of diffuse type, although some have features of both diffuse and plexiform types.¹

The pigment is not usually appreciated on gross examination and requires histologic examination. The pigmented cells which are dendritic or epithelioid in shape are dispersed throughout the tumour and express both S100 protein and melanin markers.^{2,3} The presence of melanin producing cells in PNF can be explained on the basis of origin of both, the melanocytes and Schwann cells from multipotent neural crest cells.

Although melanogenic potential of Schwann cells is suggested and proved in the literature,^{4,5} few reports provide

ultrastructural confirmation.⁶⁻⁸

We document the clinicopathological and ultrastructural findings of pigmented neurofibroma and discuss the differential diagnosis.

Case Report

A 45 Yr/M first presented in January 2006 with a long history of a left gluteal mass. He had noticed a small, slightly elevated nodule in childhood and the tumour had gradually increased in size. There was no history of fever, loss of weight or pain, but history of recurrence of tumour after excision was present.

Physical examination revealed an elevated, nonulcerated, soft to rubbery mass measuring 35x17x11 cms, involving the left gluteal region but sparing the anal orifice. The stigmata of neurofibromatosis 1 were absent.

Pathological Findings

Gross examination : The resected, large mass measured 35x17x11 cms. and was covered with thick, hyperpigmented, skin. The cut surface revealed an ill-demarcated, solid, grayish white to tan, glistening, soft to rubbery tumour involving the dermis and subcutis. The striking feature was the presence of macroscopic pigmentation in the form of dark brown to blackish streaks. There was haemorrhage but no evidence of necrosis (Fig. 1).

Microscopic examination : The tumour had

*Associate Professor, Department of Pathology, Grant Medical College, Mumbai 400008.**Chief of Department of Surgical Pathology and Electron Microscopy, Jaslok Hospital and Research Centre, Mumbai.

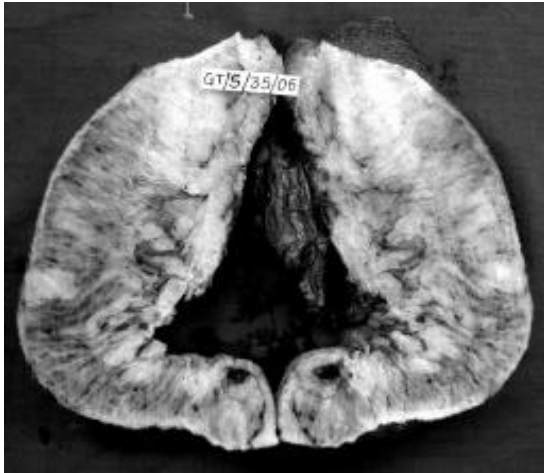


Fig. 1 : A large tumour involving the dermis and subcutis, measuring 35x17x11; cut surface solid, grayish white to tan, rubbery, with brownish streaks.

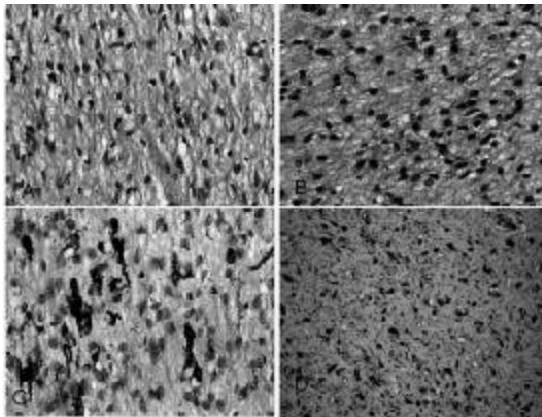


Fig. 2 : Diffuse neurofibroma with fine fibrillary matrix and fusiform Schwann cells embedded in it (A and B; H and E X100, X40). Masson-Fontana showing presence of jet black pigment in cells (C, X 100). S-100 positive Schwann cells (D, X 100).

characteristic appearance of diffuse neurofibroma with uniform matrix of fine fibrillary collagen and short fusiform to rounded Schwann cells embedded in it. Focal areas of conventional neurofibroma in the form of short fascicles of spindle cells with wavy nuclei and myxocollagenous matrix was present along with Wagner - Meissner - like bodies (Fig. 2).

The peculiar feature was the presence of spindle,

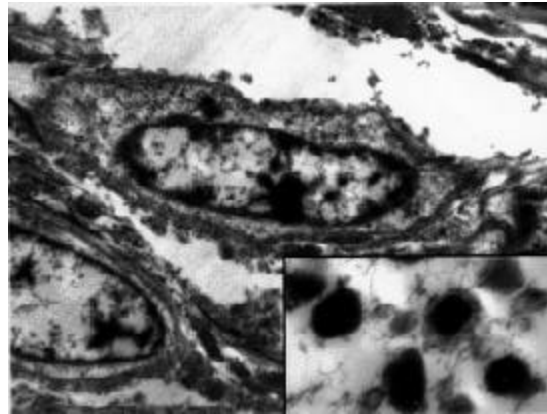


Fig. 3 : Electron microscopy showing Schwann cell with fuzzy basal lamina (x 8000), and melanosomes (inset, x 60,000).

dendritic, tadpole-shaped and epithelioid pigmented cells in clusters throughout the tumour; but had a tendency to locate in deep dermis and subcutis. The pigment was granular and brownish black.

The mitotic figures were absent but tumour infiltration into the subcutaneous fat and muscle was observed. There was no evidence of junctional melanocytic activity or naevus cell clusters in the superficial dermis.

Histochemistry : The pigment containing cells were positive (Jet Black) with Fontana-Masson silver nitrate reduction and were depigmented by a melanin bleach method. Prussian blue staining was negative.

Immunohistochemistry : There was proliferation of S-100 protein positive Schwann cells with sparse and focal immunoreactivity for CD34 indicating fibroblastic proliferation.

Electron Microscopy : On electron microscopy tumour cells appeared spindle shaped arranged in broad bands with intervening collagen. The cell surface was covered with illdefined, fuzzy basal lamina. The melanosomes were present in few cells (Fig. 3).

Discussion

Neurofibromas are the familiar benign tumours of peripheral nerve sheath and are composed of perineurial cells, Schwann cells, fibroblasts, neuritis and mucopoly-saccharide matrix.¹ In the spectrum of neurofibromas the pigmented tumours are rare^{5,7} variants

usually showing only faint macroscopically obvious pigmentation⁶ and accounting for 1% of all neurofibromas.^{1,2} These tumours can occur on their own or be associated with neurofibromatosis 1.^{1,3} The rarity of the entity is evident from the small number of lesions published in the medical literature, especially Indian literature.

Pigmented neurofibromas are more frequent in dark skinned populations with an age range of 2-71 years and usually involve head and neck, buttock, lower leg and thigh.¹⁻³ Because of the diffuse pattern of growth these lesions may recur, but malignant transformation or metastasis has not been known.^{1,2,3} Our patient was a 45 year old, Indian male with a recurrent tumour of the buttock. The tumour was present since childhood without stigmata of neurofibromatosis 1.

Macroscopically tumour involves dermis and subcutis and measures 1 to 50 cm with a glistening, gray tan cut surface, ill-defined margins and rubbery consistency.^{2,3,7} Pigmentation within the tumour varies from absent to striking blackish flecks.^{2,6,7}

The received resected tumour had above features with macroscopic pigmentation in the form of brownish black streaks, prominent in the deep dermis and subcutis. Microscopically it is characterized by diffuse neurofibroma having fine fibrillary collagenous matrix in which the Schwann cells are embedded, small abnormal nerve segments and scattered Wagner - Meissner-like bodies. Some have features of diffuse and plexiform types. Melanin - producing cells tend to be located in the deep dermis and subcutis, accompanying neurofibroma components in the more superficial dermis.³ According to Motoi³ *et al* this unique distribution pattern of melanin-producing cells in PNF can be a major useful tool for

distinguishing this tumour from other "pigmented tumours."

The "pigmented tumours" which have to be differentiated from PNF are melanotic schwannoma, pigmented dermatofibrosarcoma protuberans, cellular blue nevus, congenital neuronevus and neurocristic hamartoma.

Melanotic schwannoma (MS) is a rare form of pigmented neural tumour linked to Carney's complex, characterized by the presence of myxomas, spotty pigmentation, endocrine overactivity and other abnormalities. It is better "marginated" and deep seated than pigmented neurofibroma and exhibits gross pigmentation and cystic change more commonly. The histomorphological features which distinguish MS from PNF are, presence of cellular areas alternating with hypocellular areas, cells with peculiar syncytial quality, presence of psammoma bodies, large and epithelioid pigmented cells and uniformly intense immunostaining for S-100 protein.^{1,8}

Pigmented dermatofibrosarcoma protuberans is an uncommon tumour with a predilection for the truncal region which is not usual for pigmented neurofibroma.¹ It has prominent storiform pattern with random distribution of dendritic pigment cells^{1,3,9} which differs from unique distribution pattern of melanin producing cells in PNF. The uniform fibroblastic cells, repetitive storiform pattern, strong positivity for CD 34 and lack of S-100 protein immunoreactivity usually make this distinction apparent.^{1,2,3,9}

Cellular blue nevus presents typically in young adults in the lumbosacral and buttock region. The tumour has dumbbell-like configuration and exhibits a more solid, organoid or nested growth than pigmented neurofibroma. It typically lacks prominent proliferation of Schwann cells, abnormal

nerve trunks, fibrillary collagenous matrix and Wagner-Meissner-like bodies.

The distinction between congenital neuronevus and pigmented neurofibroma is less clear-cut. The presence of junctional activity and or superficial nevoid component with typical clinical features support the diagnosis of a congenital neuronevus over that of a pigmented neurofibroma.^{1,2,10}

The neurocristic hamartoma presents as an isolated cutaneous mass of small to moderate size with normal skin tone or bluish discolouration, preferentially involving the face or scalp and associated with a complex proliferation of nevomelanocytes, Schwann cells and pigmented dendritic and spindle cells.

The histomorphological features of diffuse neurofibroma with unique pattern of melanogenesis, immunoreactivity with CD34 and S-100 protein and ultrastructural findings enabled us to diagnose present case as pigmented neurofibroma and differentiate it from the "pigmented tumours". The follow-up of three months is too short to predict the outcome in this case but none of the pigmented neurofibromas in previous studies are known to have undergone malignant transformation.^{1,2,3}

References

1. Weiss SW, Goldburn JR. Soft tissue tumors. St. Louis (MO) : Mosby ; 2001: 1123 -37.
2. Fetsch JF, Michal M, Miettinen M. Pigmented (melanotic) neurofibroma : a clinico pathologic and immunohistochemical analysis of 19 lesions from 17 patients. *Am J Surg Pathol* 2000; 24:331-

43.

3. Motoi T, Ischida T, Kawato A, Motoi N, Fukayama M. Pigmented neurofibroma : review of Japanese patients with an analysis of melanogenesis demonstrating coexpression of C-met proto oncogene and microphthalmia associated transcription factor. *Hum Pathol* 2005; 36 : 871 - 77.
4. Spence AM, Rubinstein LJ, Conley FK, Herman MM. Studies on experimental malignant nerve sheath tumor maintained in tissue and organ culture system. Melanin pigment and melanogenesis in experimental neurogenic tumors; a reappraisal of the histogenesis of pigmented nerve sheath tumors. *Acta Neuropathol* 1976; 35 : 27-45.
5. Bird CC, Willis RA. The histogenesis of pigmented neurofibromas. *J Pathol* 1969; 97 : 631-637.
6. Deshpande RB, Chitale AR. Melanotic neurofibromas : A report of two cases. *Indian J Cancer* 1987; 24 : 53-61.
7. Kuhnen C, Herter P, Soimaru C, Homann HH, Johnen G. Pigmented (Melanotic) neurofibroma. Report of an unusual case with immunohistochemical, ultrastructural analyses. *Pathol Res Pract* 2002 ; 198 : 125-31.
8. Carney JA. Psammomatous melanotic schwannoma : a distinctive heritable tumor with special association including cardiac myxoma and the Cushing syndrome. *Am J Surg Pathol* 1990 ; 14 : 206-22.
9. Fleteher CD, Theaker JM, Flanagan A, *et al.* Pigmented dermatofibrosarcoma protuberans (Bednar tumour).; melanocytic colonization or neuroectodermal differentiation? A clinicopathological and immunohistochemical study. *Histopathology* 1988; 13 : 631-43.
10. Kim EJ, Lee KH, Kim J, Park CJ. A case of a pigmented neurofibroma resembling a giant congenital melanotic nevus. *Korean J Dermatol* 2008; 46 : 800-4.