

Hybrid Neurofibroma Turning to Malignant in Type I Neurofibromatosis Patient

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Abstract: Peripheral Nerve Sheath Tumors include Neurofibroma, Schwannoma and Perineurinoma. Schwann cell is the cell of origin for the development of both neurofibroma and schwannoma. These tumors are referred to as Benign Peripheral Nerve Sheath Tumors (BPNST). Neurofibromatosis is an autosomal dominant hereditary disease of the nervous system. Histologically, two unrelated types have been reported i.e. Neurofibromatosis type 1 and type 2. Recently, an extremely rare entity of hybrid neurofibroma-schwannoma has been reported, where tumor will represent the features of both neurofibroma and schwannoma.

A 30-year-old woman presented with multiple neurofibromatosis of type I with single separate swelling on the right arm for three years. She also had multiple café-au-lait spots. The swelling over the right arm was globular in shape, which was progressively enlarging in size for the last six months. Patient's mother also had similar multiple swellings all over the body. Neurofibroma was our provisional diagnosis. Tumor was excised and sent for Histopathological examination, it was reported as hybrid neurofibroma-schwannoma with features suggestive of malignant transformation.

We wish to report this case since most of the subcutaneous peripheral nerve sheath tumors are benign and rarely can turn in to malignant. In our case also the tumor was turning to malignant which is a rare entity.

Keywords: Hybrid Neurofibroma/ Schwannoma, Neurofibromatosis (Nf), Peripheral nerve sheath tumor- PNST, Schwannomatosis.

I. Introduction

Neurofibroma and schwannoma are the most common peripheral nerve sheath tumors and both arise from Schwann cells. They arise from spinal nerves; can rarely arise from cranial nerves. These are all slow growing, oval shaped benign tumors with definite capsule located in the subcutaneous plane [1]. Pain and parasthesia is a feature in large tumors where the tumour exerts extrinsic pressure over nerve fibres. These tumors commonly present in the 3rd and 4th decade of life, men and women are equally effected [2]. Neurofibromatosis (Nf) is an autosomal dominant hereditary disease. Neurofibromatosis is of two types, neurofibromatosis (Nf) type 1 and type 2. Type 1 Nf is most common, associated with gene mutation on chromosome 17. It is said to be type I when two of the seven findings are present i.e. multiple subcutaneous neurofibromas, café-au-lait spots, freckles on unusual places such as arms pit and groin, Lisch nodules, optic nerve glioma, skeletal dysplasia, and affecting the first-degree relatives [3]. Type 2 NF is less common than NF1. Type 2 Nf is associated with the development of multiple schwannomas, meningiomas and ependymomas. Type 2 Nf is linked to mutation of NF2 gene which is located on chromosome 22. [4]. However, hybrid lesion does not fit into this system, has been reported separately. Hybrid tumors will have histological features of both neurofibroma and schwannoma [5]

II. Case Report

A 30 year old female presented with a discrete swelling on antero-medial aspect of right arm for 3 years along with multiple neurofibromatosis. The swelling was 12 X 10 cm in size, ovoid in shape with well defined borders and restricted vertical mobility. The swelling was located in the subcutaneous plane. The swelling was progressively increasing in size, had become painful for past 6 months and tender on palpation (Fig. 1). There were engorged veins in the skin over the swelling. The patient also had multiple tumours of varying sizes distributed all over the body. Patient's mother also had similar swellings all over the body.



Fig.1: Picture showing the tumour in Antero-Medial aspect of Right upper arm. Evidence of engorged veins seen over skin.

The MRI revealed a well-defined ovoid shaped, encapsulated hyper dense lesion with hypo to isointense areas, suggestive of peripheral nerve sheath tumour (PNST) - probably a neurofibroma (Fig.2)



Fig.2: MRI - Ovoid mass, showing Heterogeneously Iso to Hyperintense lesion 11x7.9x8.3cm.s/o PNST

Our provisional diagnosis was isolated neurofibroma in a neurofibromatosis type I patient and likely to be malignant. The tumour was approached by vertical incision, it was found to be arising from the perineural sheath of musculo-cutaneous nerve. Subcapsular excision of the tumour was carried out to prevent nerve injury (fig. 3). No nerve palsy was noticed post operatively. The excised specimen was sent for histological examination.

Gross: cut section showed grey white to yellow spaces with myxoid, multiple cystic areas of varying sizes.

Microscopic: Tumour is composed of spindled cell elements of varying cellularity. Marked hypocellular and hypercellular areas observed. Spindle cells arranged in fascicular pattern, criss cross pattern reminiscent of herring bone and vague whorls. Nucleus is ovoid to spindle shaped with buckling in few. Few large nuclei with prominent nucleoli are seen. Numerous hyperchromatic nuclei with abnormal stellate mitotic figures are observed.

Impression: Hybrid Schwannoma-Neurofibroma with features suggestive of early malignancy transformation. (Fig.3,4,5)

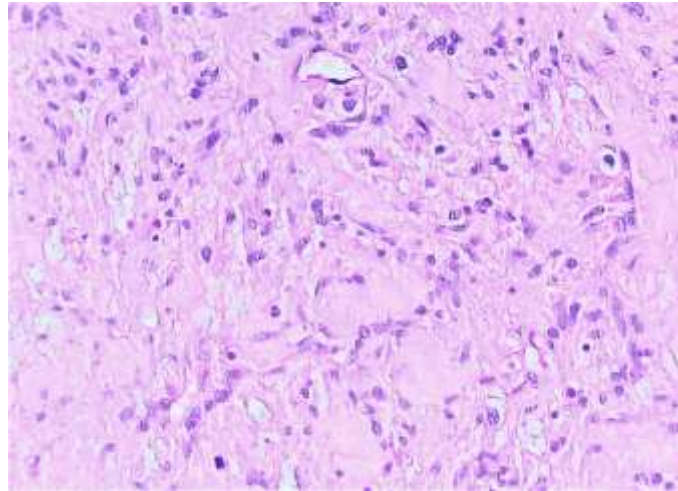


Fig.3: Nuclear palisading around fibrillary process-Verocay bodies, are seen in cellular areas suggestive of Schwannoma

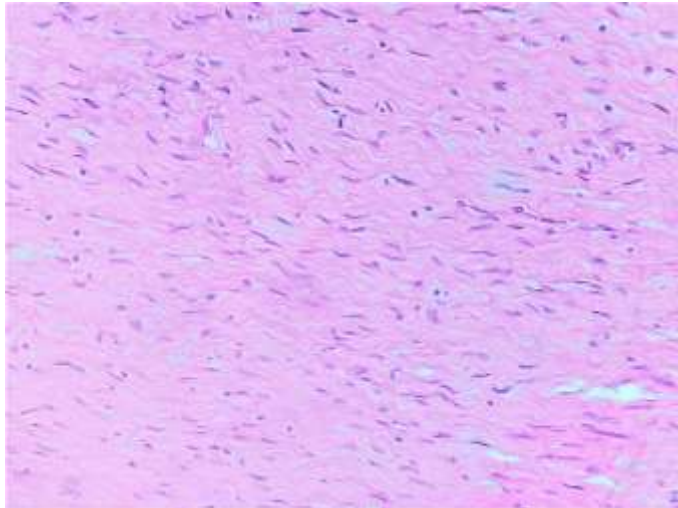


Fig.4: Schwann cells with wire like collagen fibrils, wavy serpentine nuclei with pointed ends suggestive of Neurofibroma

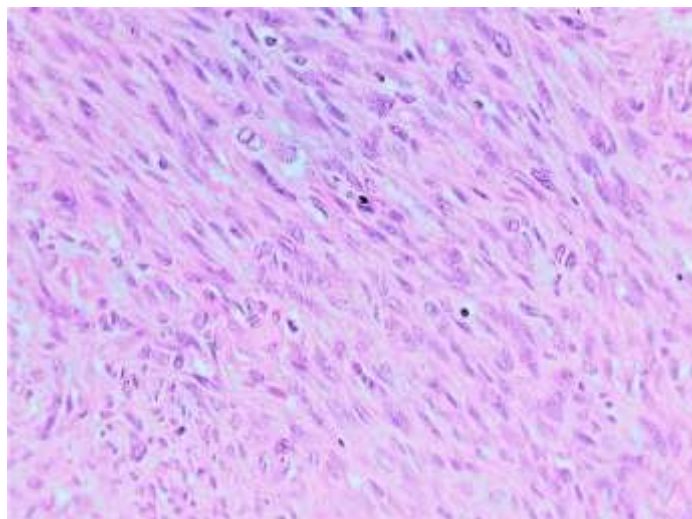


Fig.5: Cellular pleomorphism and mitotic figures, suggestive of: Malignancy

III. Discussion

Peripheral nerve sheath tumours which include neurofibromas, schwannomas, and perineuriomas, arise from Schwann cells. They commonly arise from peripheral spinal nerves, can rarely arise from cranial nerves. Tumor can commonly present in the 3rd and 4th decade of life. Men and women are equally affected. Our patient is also in the same age group. PNST present as slow growing oval shaped soft tissue masses in the subcutaneous plane [1]. Large tumors are painful and there can be pain and parasthesia as the tumour exerts extrinsic pressure over nerve fibres [2]. Most of them are benign; however malignant transformation can take place rarely, as we noticed in our case. The most common location is extremities and digits; however atypical sites like colon also have been reported. [6]

Neurofibromatosis Type 1, an inherited genetic disorder, gives rise to multiple subcutaneous tumours distributed all over the body. It is otherwise called von Recklinghausen disease, named after a German pathologist and professor in Strasburg. It is due to a germline mutation in the NF1 gene located on chromosome 17(17q11.2), encoding for the protein Neurofibromin. Clinically it is diagnosed by presence of 2 of the 7 diagnostic criteria, multiple subcutaneous neurofibromas, café-au-lait spots, axillary freckling, optic nerve glioma, Lisch nodules, skeletal dysplasia, and affecting the first-degree relatives. In our case patient was having multiple neurofibromas, café-au-lait spots and her mother had history of similar swellings.

Neurofibromatosis Type 2 occurs less frequently than NF1, associated with a variety of tumors, especially schwannomas, meningiomas, and ependymomas. The responsible gene is located on the long arm of chromosome 22, responsible for the protein Merlin which is tumor suppressor gene. The hallmark of NF2 is the development of multiple schwannomatosis.

However, hybrid lesion does not fit into this system, has been reported separately. These tumors will have histological features of both neurofibroma and schwannoma [7,8]. Neurofibroma/schwannoma hybrid tumors are rare and are usually present in association with schwannomatosis and neurofibromatosis however can present as an isolated form. Before excision, there is need to confirm the diagnosis by FNAC. Smaller lesions need excision biopsy. MRI helps in assessing the site of the tumor its relation to surrounding structures. Surgical excision is the treatment of the choice. Sub-capsular excision of the tumor is the treatment of the choice if the tumor adherent to major nerve.

IV. Conclusion

Hybrid neurofibroma/ schwannoma is a part of peripheral nerve sheath tumors. Commonly associated with Nf type I or type 2 syndrome. However they can present in isolated form. Hybrid variety can represent microscopic features of both neurofibroma and schwannoma. Almost all are benign, however malignant transformation can occur. The common site is peripheral nerve sheath in subcutaneous plane particularly arises from extremities. Surgical excision is the treatment of the choice. Sub capsular excision of the tumor is the treatment of the choice if the tumor adherent to major nerve.

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