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Benign neural tumours: a clinico-pathologic study

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Abstract

Peripheral nerve sheath tumors include a spectrum of diseases ranging from benign to malignant entities. They include schwannoma, neurofibroma, malignant peripheral nerve sheath tumors, neurothekeoma, perineurioma, granular cell tumour, mucosal neuroma, and palisaded encapsulated neuroma. Schwannoma is a slow growing tumour derived from the neuroectoderm originating from the Schwann cells of the peripheral neural sheath, most commonly involving the VIII cranial nerve. Other sites in the body can also be affected. Neurofibroma is also a slow-growing tumour and can involve multiple sites. It can have a genetic predisposition. Definitive diagnosis requires histopathological confirmation. Immunohistochemical marker S-100 is confirms the diagnosis.

Keywords: Benign, Histopathology, Neurofibroma, Schwannoma.

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Introduction

Peripheral nerve sheath tumors include a spectrum of well defined clinicopathologic entities ranging from benign tumors, such as schwannoma and neurofibroma, to high grade malignant neoplasms including malignant peripheral nerve sheath tumors (MPNST).[(1)] Benign peripheral nerve sheath tumours generally include schwannoma and neurofibroma. The other rare benign tumours include neurothekeoma, perineurioma, granular cell tumour, mucosal neuroma, and palisaded encapsulated neuroma. Neurofibromas are benign tumours of non-myelinating schwann cells. In 90% of cases neurofibromas occur as isolated tumors, while only 10% occur in those with neurofibromatosis type I (NF1).[(2)] Schwannoma is a slow growing encapsulated benign rare tumor of neuroectodermal derivation originating from the Schwann cells of the peripheral neural sheath. Schwannomas arise from the spinal nerve roots and intracranial nerves, most commonly involving the VIII cranial nerve.[(3)]

Neurofibroma is a slow growing tumour which is usually asymptomatic and unlike schwannoma it is intimately attached to the nerve of origin and demonstrate autosomal dominant pattern of inheritance. Schwannoma is sporadically manifested as a solitary benign neoplasm. Occurrence of multiple Schwannoma usually indicates neurofibromatosis-2.

The present study was undertaken with the aim of ascertaining incidence, prevalence, distribution as well as the histomorphological features.

Material and Method

The present retrospective study included a detailed analysis of all patients with benign neural tumours in the Department of Pathology, Rohilkhand Medical College & Hospital, Bareilly, a tertiary care centre. The period of study was 3 years from July 2014 to June 2016. The age and sex of the patient, site of biopsy and other relevant clinical data were recorded. Patients of all ages, gender and sites were included in the study. A total of 28 cases were studied histopathologically. All cases proved to be benign and of neural origin were included. The tissue samples were fixed in 10% buffered formalin and processed routinely. Multiple sections were taken and one section was stained routinely using Haematoxylin & Eosin (H & E) stain, while the other section on a pre-coated slide was stained using Immunohistochemical marker S-100.

The results thus obtained were tabulated and analysed.

Results

A total of 28 cases of benign neural tumours were included in the present study. All cases were confirmed on histopathology. Of these 28 cases, 15 female and 13 males were included (Table 1). The age range was from 11 to 70 years with a mean of 32 years. The average age of patients with Schwannoma was 31.3 years, while for Neurofibroma was 32.9 years. There were 8 males and 7 females with Schwannoma and 5 males and 8 females with Neurifibroma. All the 28 cases presented as swelling. The duration of swelling varied from 1 month to 4 years.

Table 1: Showing distribution of Benign Neural Tumours

S. No.	Age	Sex	Site	Diagnosis
1	30	M	Left elbow	Schwannoma
2	45	F	Lt Axilla	Schwannoma
3	42	F	Rt arm	Schwannoma
4	11	F	Soft Palate	Schwannoma
5	50	M	Left Flank	Schwannoma
6	26	M	Scalp Swelling	Schwannoma
7	26	F	Rt Nostril	Schwannoma
8	43	M	Left supraclavicular region	Schwannoma
9	35	F	Left Axilla	Schwannoma
10	30	M	Left Thigh	Schwannoma
11	28	F	below the tongue	Schwannoma
12	35	M	Right Nasopharynx	Schwannoma
13	40	M	Right forearm.	Schwannoma
14	14	F	Right leg	Schwannoma
15	14	M	Hard palate	Schwannoma
16	18	M.	Rt lower limb	Neurofibroma
17	18	M.	Back	Neurofibroma
18	65	F.	Lower Leg	Neurofibroma
19	56	F.	Back	Neurofibroma
20	14	M.	Upper eyelid	Neurofibroma
21	14	M.	Upper eyelid	Neurofibroma
22	50	F.	Left Arm	Neurofibroma
23	70	M.	Left Side Neck	Neurofibroma
24	15	F.	Left Parotid swelling	Neurofibroma
25	15	F.	Mons Pubis	Neurofibroma
26	33	F.	Rt Buttock	Neurofibroma
27	23	F.	Rt Foot	Neurofibroma
28	36	F.	Lt Forearm	Neurofibroma

A case of giant Schwannoma was diagnosed in the left axilla of a 45 years old lady. The swelling was present for the past 8 months and was gradually increasing in size. She recently also started having pain and difficulty in movement of the left upper extremity. FNAC in this case showed cells with palisading arrangement of nuclei (Fig. 1a, 1b). The resected specimen was sent for histopathological examination. Grossly, it measured 6.5 x 4.5 x 3 cm in dimension (Fig. 1g). Histopathology and Immunohistochemical marker S-100 positivity confirmed it to be Schwannoma. A case of Schwannoma was diagnosed in the right nostril of a 26 years old female presenting as a pink fleshy mass with the complaints of nasal obstruction (Fig. 1c). It bled on touch. The duration of nasal obstruction and mass was one year as stated by the patient. The case was extensively worked-up with different immunohistochemical markers applied. S-100 and Vimentin were positive. CD-34 was focally positive while Desmin and Cytokeratin were negative.

The youngest patient was a 11 year old girl presenting with a globular swelling 1.5 cm in diameter in the soft palate. Histopathology proved it to be Schwannoma (Fig. 1d), which was S-100 positive on Immunohistochemistry (Fig. 2c).

The commonest site affected was Head & Neck in 8 (28.6%) cases followed closely by upper extremity involvement in 7(25%) cases. Oral cavity was involved in 3(10.7%) cases. In the oral cavity the sites affected were soft palate, hard palate and sub-lingual area. All these 3 cases were histopathologically proven to be Schwannoma (Fig 1e). Histologically there was predominantly compact cellular areas (Antoni type A) admixed with some loose, hypocellular myxoid areas (Antoni type B). Verocay bodies were noted (Fig. 1f).

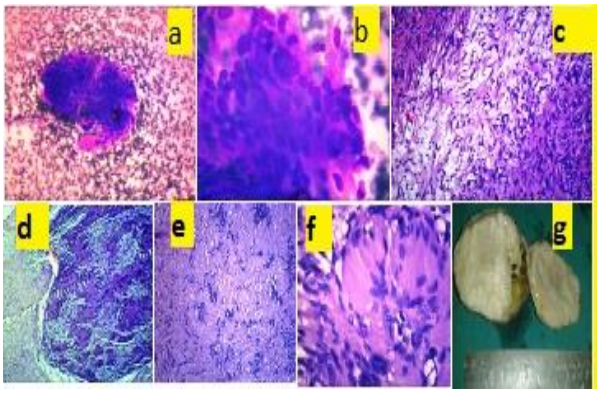

Fig. 1(a): Smear showing cytological picture of Schwannoma (LG x 100), (b). Smear showing cytological picture of Schwannoma with palisading nuclei (LG x 400), (c). Section showing alternating Antoni A and B areas in Schwannoma nose (H&E x 100), (d). Section showing predominance of Antoni A areas in Schwannoma hard palate (H&E x 400), (e). Section showing predominance of Antoni A areas in Intraoral Schwannoma (H&E x 100), (f). Section showing Verocay Body (H&E x 400), (g). Gross specimen showing giant Schwannoma Axilla

The maximum dimension of the swelling excised measured 5× 3.5 cm which was diagnosed as Neurofibroma involving the foot in a 23 year old female. 2 cases of Neurofibroma in teenage girls were observed at unusual sites-one in the left parotid region (Fig. 2a) and another over Mons pubis.

A case of swelling in the lower back in a 56 year old lady was excised surgically. Clinically it was labelled as lipoma. Sections showed Toluidine Blue positivity at most places highlighting the mast cells. The sections were S-100 and Vimentin positive and, negative for VEGF, Cytokeratin and CD-34. The final diagnosis was Cutaneous Neurofibroma (Fig. 2b, 2d).

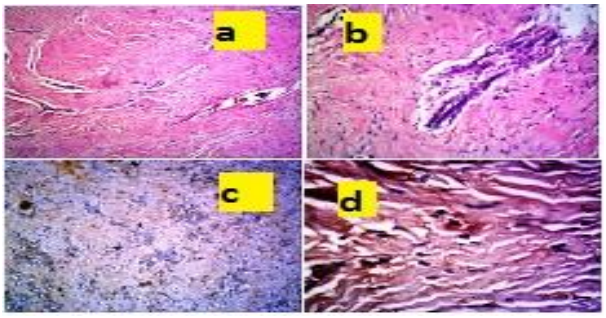

Fig. 2: (a).Section showing Neurofibroma Parotid (H&E x 100), (b). Section showing Cutaneous neurofibroma (H&E x 400), (c). Section showing S-100 positivity in Intraoral Schwannoma (IHC x 100), (d). Section showing S-100 positivity in Cutaneous Neurofibroma (IHC x 400)

Discussion

Approximately 25-40% of Schwannomas involve the head and neck, of which only 4% involve the nasal cavity and paranasal sinuses and 1% in the oral cavity. Only 29 cases of intraoral schwannoma have been reported so far.[4-7] The sites of occurrence are usually the tongue, palate, floor of mouth, buccal mucosa, and mandible in descending order of incidence.[8-9] Retroperitoneal schwannomas are rare and account for 0.7% to 2.7% of these tumors. Neurofibromas often involve the head and neck because of rich innervations in this area. In the oral cavity neurofibroma is reported to occur on tongue, lip, palate, gingiva, major salivary glands, and maxillary bones.[10] Schwannomas usually occur in the young and middle aged population with a slight female predilection[11] while no sex predilection was observed by Bansal R.[7]

Neurological symptoms in Schwannoma are rare.[12] The size and locations of lesions determine the presence and intensity of symptoms. Swelling is the most common symptom, followed by paresthesia. The reported duration of these tumors ranges from 3 months to 5 years.[8] Clinically, neurofibromas appear as soft, doughy mass and characterized by painless, slowly growing, superficial mass. Plexiform variety develops in deeper areas of the body near the nerve roots and accounts for 5% of cases. It is generally seen in the third decade of life; however, its occurrence between 10 months and 70 years of age has been reported.[13,14]

Spectrum of schwannoma includes-conventional, cellular, plexiform, and melanotic types. The psammomatous form is associated with Carney complex that includes cutaneous lentigines, myxomas of skin, subcutaneous tissue, and heart, and endocrinal neoplasms. Neurofibroma can be dermal or plexiform. Dermal neurofibromas involve a single peripheral nerve, while plexiform neurofibromas may involve multiple nerve bundles. Dermal neurofibromas do not undergo malignant transformation.[2] Plexiform neurofibromas occur earlier in life and can cause disfigurement, neurological and other clinical deficits. Plexiform neurofibromas are more difficult to treat and 10% cases can transform into malignancy. The diagnostic criteria for Neurofibromatosis 1(NF1) include any two of these features –positive family history, six or more café-au-lait macules, axillary freckling, multiple NFs, Lisch nodules (hamartomas of iris), optic nerve gliomas and skeletal abnormalities including sphenoid wing dysplasia or pseudarthrosis.[15]

Pre-operative diagnosis modalities; varying from ultrasound and CT to MRI may facilitate the diagnosis but no specific imaging exists. MRI allows better visualization of the tumor origin, vascular architecture and involvement of other organs.[12] Definite diagnosis can only be made by examination of biopsy specimens.

Schwannomas do not usually exceed a diameter of 5 to 6 cm, but tumours of 28 cm diameter have also been reported.[16] Intraoral schwannomas usually range from 1.0 to 5.0 cm in diameter. Histologically, schwannomas consist of compact cellular lesions (Antoni type A) and loose, hypocellular myxoid lesions with microcystic spaces (Antoni type B). The characteristic pattern is an alternation of these Antoni A and B areas. Verocay bodies and hyaline blood vessels are noted.[17] Schwannomas show positivity with S-100 protein and glial fibrillary acidic protein (GFAP) in many cases. The pericapsular region of a schwannoma may contain CD34-positive cells.[18] Variable CD68 positivity and Collagen IV staining is observed in benign neural tumours. Neurofibroma exhibits partial encapsulation. On gross examination neurofibromas have a tan-white appearance with a glistening cut surface. The connective tissue is highly cellular, interspersed with areas of nerve bundles. The cells are spindle shaped with wavy nuclei and separated by fine collagen fibers. Areas of myxomatous changes may be present. Mast cells, dilated blood vessels and entrapped adipocytes are usual. Positive immunoreactivity to S-100, Neuron-specific enolase, CD57, Vimentin, Podoplanin and Calretinin and, negative to Desmin and Pancytokeratin are observed.[14]

Malignant schwannomas are highly aggressive tumors that can infiltrate locally, and they have a high recurrence rate. Metastasis occurs commonly to the lungs and rarely to the regional lymph nodes. Death may occur by direct intracranial invasion or pulmonary metastasis. Enucleation with nerve preservation is preferred choice to offer better facial function.[19] An attempt to preserve continuity of nerve should be made. Prognosis of benign schwannomas is good. Recurrence especially in cases of incomplete excision has been reported in only 5-10% cases.[11,20-22] Histologically, a poor prognosis is indicated when the cells are fusiform, contain melanin granules, or if epithelioid cells are present.[23] Benign schwannomas can erode bone by pressure. The gold standard treatment of solitary neurofibroma is complete surgical excision.[13-14] Besides pain, plexiform neurofibromas are sometimes removed due to the possibility of malignant

transformation. Surgery in plexiform neurofibromas is usually difficult due to their large size and crossing over of tissue boundaries. Recurrence is seen in as many as 20% of the patients with a neurofibroma after complete resection and increases to 44% with subtotal resection. Radiotherapy may retard the growth and shrink the size of the tumour.[24] Neurofibrosarcomas can develop in about 5-16% of all patients with multiple neurofibromas associated with neurofibromatosis.[25]

Conclusion

Peripheral nerve sheath tumors include benign as well as malignant neoplasms. Benign tumours generally include schwannoma and neurofibroma. To arrive at a final diagnosis histopathology is mandatory. Surgical removal is the treatment of choice in both the benign entities. However, recurrence can occur if incomplete removal is made. So, a confirmatory diagnosis and careful and timely removal cures the patient with a good prognosis. Various sites can be affected in both the entities as highlighted in the present study.

In addition to the direct conclusion from the study it must be noted that prompt detailed histopathological analysis of all neural tumours will help in confirming the benign nature of the disease, which will decide the management and prognosis of the patient.

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