Case Report

Hybrid peripheral nerve sheath tumor of parapharyngeal space having features of neurofibroma and schwannoma in an 8-year-old child – A rare entity

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Abstract

Tumors of the parapharyngeal space (PPS) are extremely rare in pediatric age group. Out of all head-and-neck neoplasms, PPS tumors comprise only 0.5%. Majority of neoplasms in poststyloid PPS are neurogenic tumors. Conventional benign peripheral nerve sheath tumor (PNST) includes neurofibromas, schwannomas and perineuriomas. Hybrid PNSTs are rare entities having combined features of more than one histologic type, and the World Health Organization Classification of Tumors of the Central Nervous System, in the latest 2016, 4th edition, has recently recognized and published it. The most common hybrid tumor is schwannoma/perineuroma followed by neurofibroma/schwannoma and neurofibroma/perineuroma. Here, we are reporting a hybrid PNST which was completely excised and having combined features of neurofibroma and schwannoma, confirmed by both histopathologically and immunohistochemically, in an 8-year-old child, in PPS.

Keywords: Neurofibroma, parapharyngeal space, peripheral nerve sheath tumor, schwannoma

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INTRODUCTION

Tumors of parapharyngeal space (PPS) being rare comprise only 0.5% of all head-and-neck neoplasms.[1] Most benign peripheral nerve sheath tumors (PNSTs) occur as pure lesions as neurofibroma, schwannoma and perineuroma.[2] Hybrid PNSTs are benign and may be containing areas of schwannoma, perineuroma and neurofibroma in varied combinations.[3,4] They have got recognition, a group of tumors rather than one distinct entity, and published in 4th edition of World Health Organization (WHO) classification of tumor of soft tissue and bone in 2013 and revised as classification of central nervous system (CNS) in 2016.[5,6]

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Hybrid neurofibroma and schwannoma present as a rare entity can be solitary or may be associated with syndromes such as neurofibromatosis (NF) and schwannomatosis.[4,7,8] Histologically, hybrid morphology is utmost important to acknowledge, to understand their association with NF and schwannomatosis, but scarceness of literature on PPS hybrid PNST embarks a diagnostic challenge and demands extreme vigilance and caution. Hybrid PNSTs of parapharyngeal space are extremely rare; to the best of our knowledge, this is the first case of solitary hybrid PNST of PPS in an 8-year-old child having feature of both

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neurofibroma and schwannoma which is unique and not associated with any syndrome.

CASE REPORT

An 8-year-old male child presented to a surgeon with 1-month history of painless lump on the left side of the neck with no history of weight loss, dysphagia, numbness or difficulty with mastication. The patient was not allergic to any drug and was not on any medication. Medical, family and personal history was not relevant. On examination, there was diffuse lump on the left-side upper neck, approximately 7.5 cm × 5 cm in size [Figure 1]. On palpation, the lesion was nontender, nonfluctuant, soft in consistency, partially mobile with normal overlying skin, without cervical lymphadenopathy. Fine-needle aspiration cytology was performed and gave impression of pleomorphic adenoma.

Computed tomography scan (CT scan) with contrast showed an enhancing mass, measuring about 5 cm × 3.6 cm × 2.5 cm, in the left posterior PPS (carotid space) and posterior cervical space displacing carotid arteries and jugular vein anterolaterally along with multiple small neck lymph nodes [Figure 2]. Laterally, the lesion was separated from the deep lobe of the parotid gland and inferiorly touched left submandibular gland and anterior margin of the sternocleidomastoid muscle. Axial short-tau inversion recovery image of magnetic resonance imaging (MRI) scan supported the CT scan findings, and the lesion extends laterally between the left submandibular gland and the anterior margin of the left sternocleidomastoid muscle. CT and MRI images were suggestive of benign neoplastic lesion and pleomorphic adenoma of salivary gland in PPS or benign nerve sheath tumor were included as differential diagnosis [Figure 3].

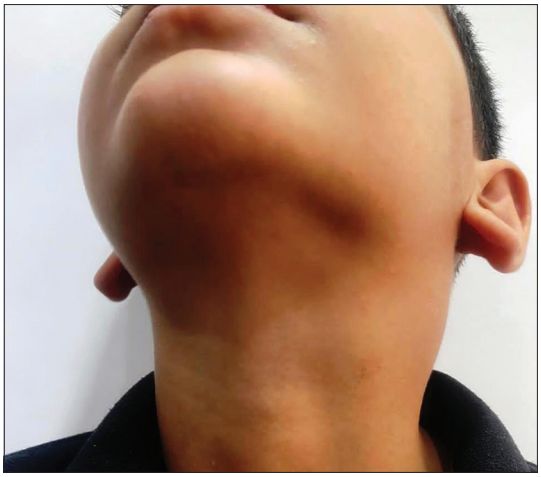

Figure 1: Preoperative clinical view

Cervical transparotid approach was taken with incision on the left upper part of the neck. After raising subplatysmal flap, the tail of the left parotid and submandibular gland dissected away from mass present posterior to the internal jugular vein and carotid artery. Meticulous care was taken in dissection at the carotid triangle, and the internal carotid artery, internal jugular vein and vagus nerve were cleared from the mass. Tumor mass was excised in toto and hemostasis ensured and closure done [Figures 4-6].

Macroscopically, the lesion is encapsulated and circumscribed, soft in consistency, measuring about 4.0 cm × 4.5 cm × 3 cm in size, along with few lymph nodes. Microscopically, two areas were evident, one with densely cellular and the other with diffuse spindle-shaped cells along with fibrillar and myxoid background consistent with schwannoma and neurofibroma, respectively [Figure 7]. In schwannomatous area, spindleshaped cells with plump nuclei were growing in fascicular pattern with hypercellular and hypocellular areas. Centrally, hypercellular area is present, showing vague palisading of cells along with haphazardly arranged hypocellular areas at periphery with few dilated vessels. Verocay bodies, typical of Antoni type A area, were absent, but palisading of cells is present [Figure 8]. Neurofibroma area shows cells with wavy nuclei, pointed at both ends, along with fibrillar and myxoid background [Figure 9].

Multiple immunohistochemical stains were used to confirm the diagnosis, including S100, glial fibrillary acidic protein (GFAP), CD34, epithelial membrane antigen (EMA), Ki-67 and smooth muscle actin (SMA). Neural origin of tumor was confirmed by intensely positive GFAP staining. [Figure 10]. S100 showed diffuse and intense

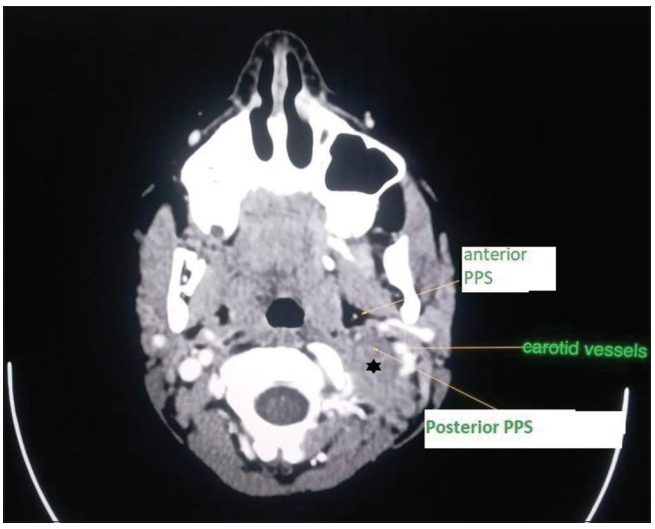

Figure 2: Axial view of computed tomography scan with contrast showing the tumor filling the left posterior parapharyngeal space

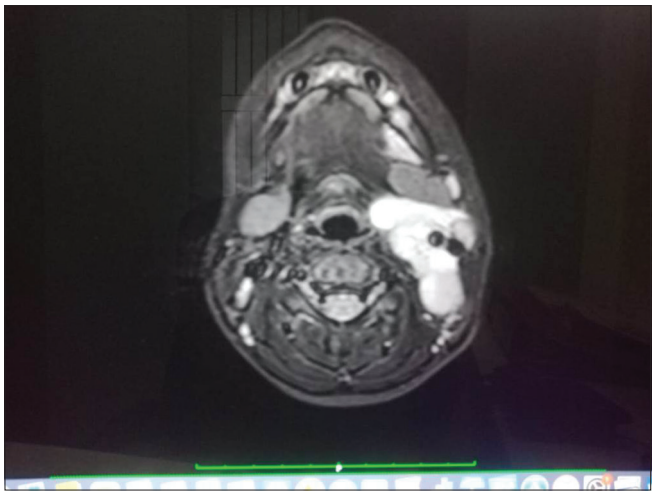

Figure 3: Axial short-tau inversion recovery image of magnetic resonance imaging showing tumor filling posterior pharyngeal space

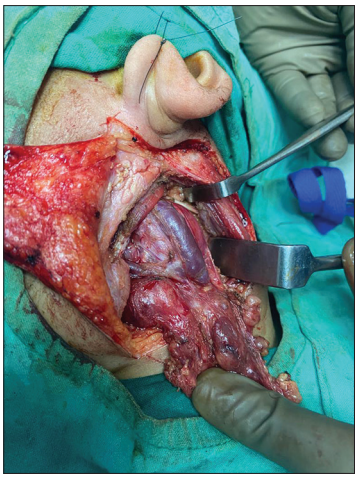

Figure 4: Peroperative clinical view after raising subplatysmal flap

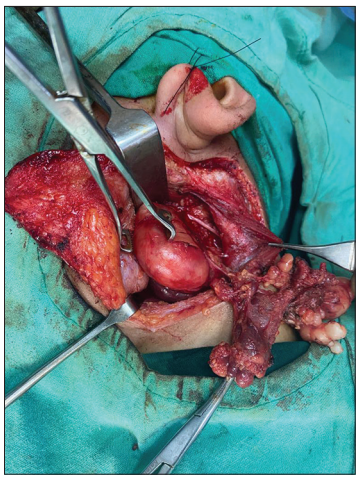

Figure 5: Separation of internal jugular vein, internal carotid artery and vagus nerve from tumor mass

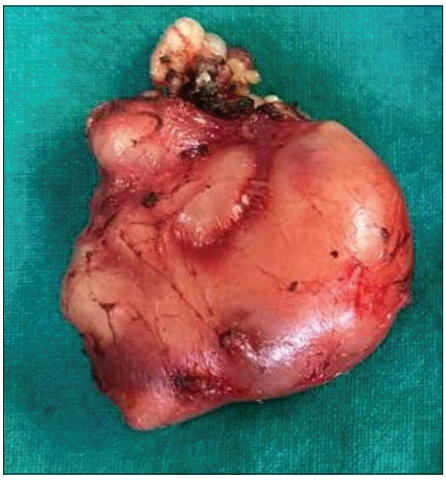

Figure 6: Excised gross specimen

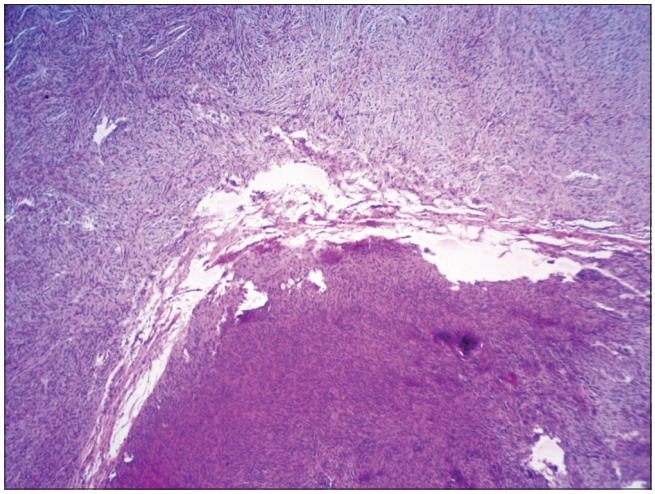

Figure 7: Lesion with hypercellular schwannoma area and loose myxoid neurofibroma area (H and E, ×4)

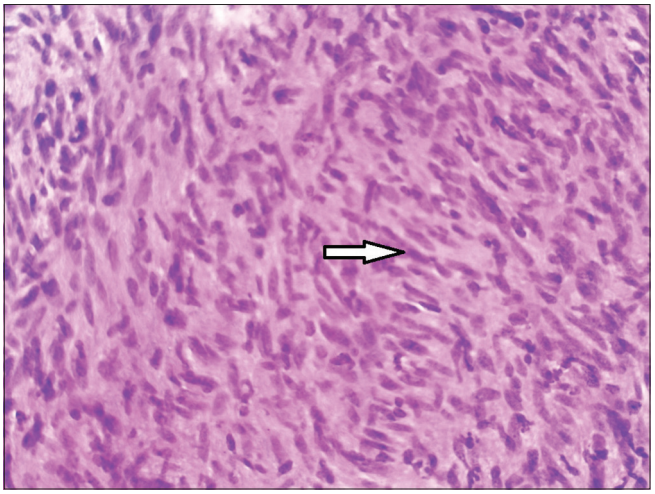

Figure 8: Nuclear palisading (arrow) of cells are seen in schwannoma area (H and E, ×40)

positivity in schwannoma part and variable positivity in neurofibroma component [Figure 11]. CD 34 was diffusely positive in whole tumor component but more intense in neurofibroma area [Figure 12]. Ki-67 index was lower and <2% [Figure 13]. EMA was negative [Figure 14]. SMA was negative which ruled out other spindle cell tumors of muscle origin like leiomyosarcoma [Figure 15].

Final diagnosis of hybrid PNST was made on the basis of histopathology and immunohistochemistry.

The most common differential diagnosis in our case was benign PNST that includes schwannoma, neurofibroma, perineuroma, fibrosarcoma and low-grade MPNST. MPNST was ruled out histopathologically by uniformity of cells and no pleomorphism. Immunohistochemically, Ki-67 index was <2% which also confirms the benign PNST. Perineuroma was distinguished by EMA which was negative in this case. Diffuse S100 positivity ruled out fibrosarcoma. Diffuse and strong positivity of S100 and variable positivity of CD34 in schwannomatous area and S100 and CD34 positivity in neurofibroma area confirms the diagnosis of hybrid PNST having combined features of neurofibroma and schwannoma.

Postoperative period was uneventful, and patients were discharged from hospital on the 3rd postoperative day.

He has been regularly followed up for 6 months and doing well except drooping of the upper eyelid of the same side which is progressively improving with physiotherapy.

DISCUSSION

PPS, in the suprahyoid region of the neck, is anatomically complex space of inverted pyramid shape, divided into two parts, the prestyloid and poststyloid. Anterior or

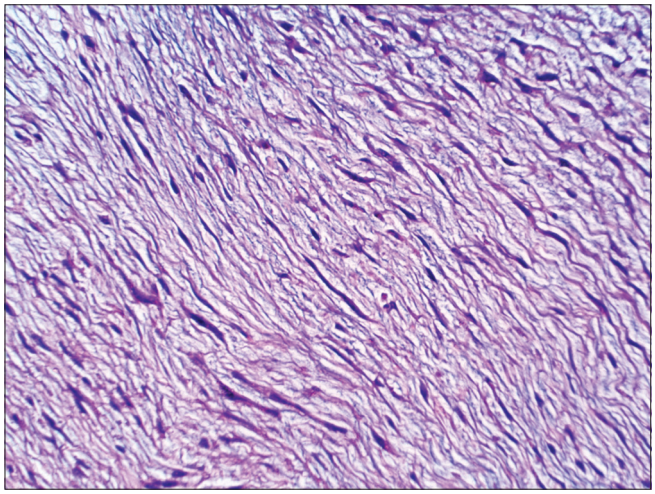

Figure 9: Loose, myxoid pattern with spindle-shaped cells in neurofibroma area (H and E, ×40)

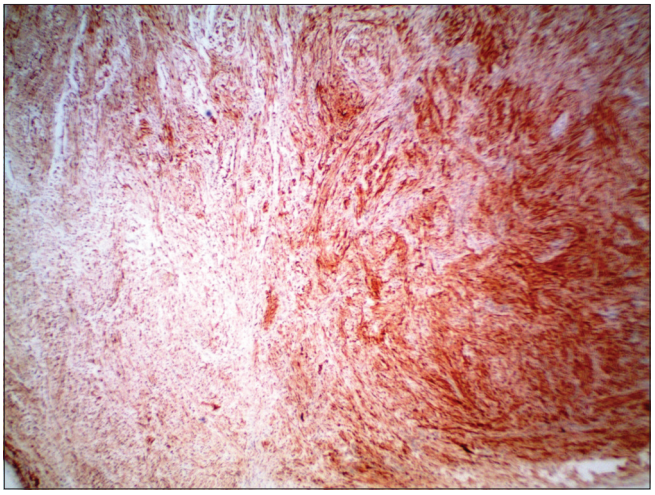

Figure 10: Glial fibro acidic protein positive in schwannoma and neurofibroma area

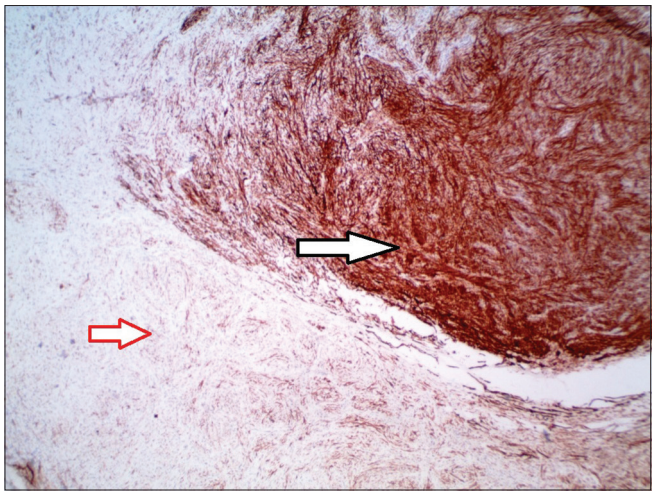

Figure 11: S100 reactivity in intense in schwannoma (black arrow) and variable in neurofibroma (red arrow) area

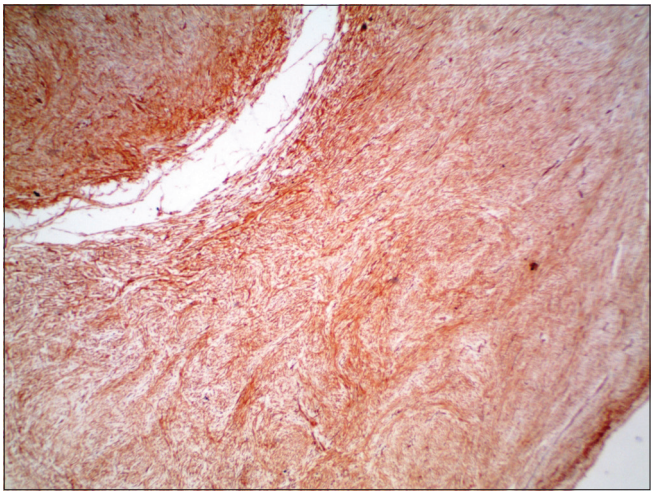

Figure 12: CD34 positivity in schwannoma and neurofibroma area

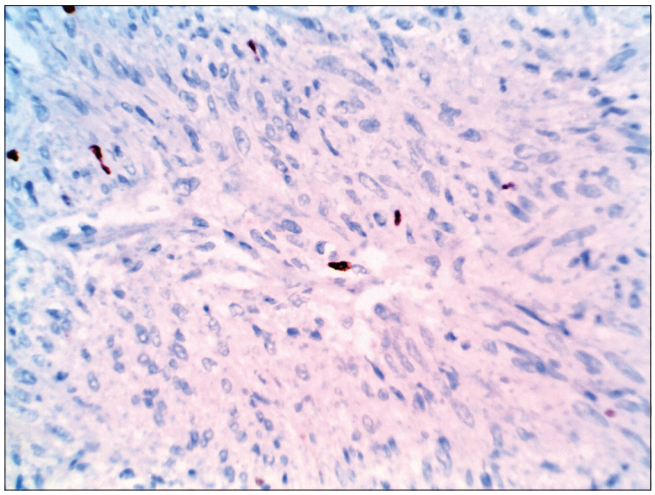

Figure 13: Ki-67 in schwannomatous area

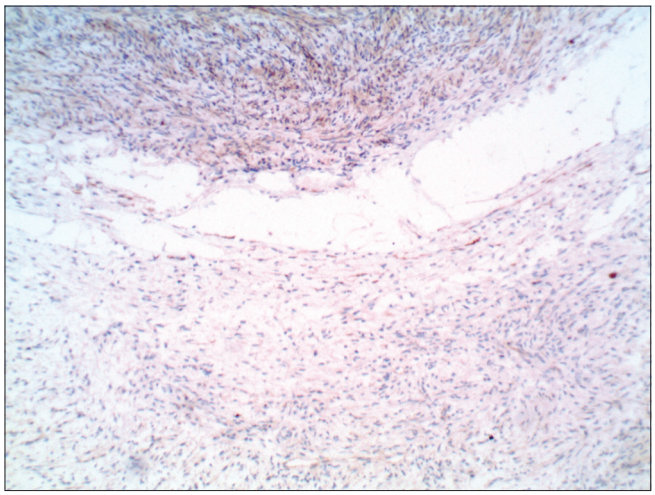

Figure 14: Epithelial membrane antigen negative in tumor area

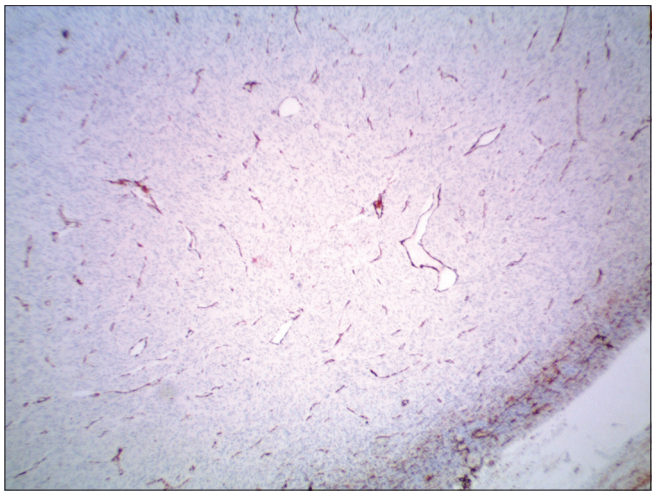

Figure 15: Smooth muscle actin negative in tumor area (only blood vessels are positive)

prestyloid compartment is mainly composed of minor or ectopic salivary gland, branches of mandibular nerve, internal maxillary artery, ascending pharyngeal artery and pharyngeal venous plexus, whereas posterior or retrostyloid compartment contains the internal carotid artery, internal jugular vein, cranial nerves IX, X, XI, XII, cervical sympathetic chain and lymph node.[1,9] Prestyloid compartment and poststyloid compartment mainly consist of salivary gland tumors and neurogenic tumors, respectively.[10] A review on PPS tumor, with average age approximately 46 years, showed a diverse group of varying histopathologies and more than 80% were benign.[10,11] A study of 23 primary parapharyngeal tumors reported that only three patients were under the age of 18 years and none of them were of neurogenic origin.[12] A study of 21 patients of primary PPS tumors showed, average age 41 years (20–70 years), that 57% of tumor were of neurogenic origin and among those 92% of cases were in poststyloid compartment.[13] Tumors of PPS are extremely rare in children, so special attention is required to achieve the diagnosis and surgical goal. The most common benign PNST includes schwannoma, neurofibroma and perineuroma. Schwannoma and perineuroma are mainly composed of pure population of Schwann cells and perineurial cells, respectively, but neurofibroma consists of mixture of endoneurial components, Schwann cells, axons, fibroblastic cells, perineurial cells and inflammatory cells also.[2] Most PNSTs are pure lesions while hybrid PNSTs are biphasic tumors having discrete areas of more than one histologic type of neurogenic tumor. Hybrid PNSTs have been included in the WHO classification, in the revised 4th edition 2016, of tumors of CNS published.[6] Hybrid neurofibroma – schwannoma being rare tumors – was first described by Feany *et al.* in series of nine cases, in which they conclude the presence of components of both neurofibroma and schwannoma in few nerve sheath tumors.[14] Hybrid PNST of PPS tumor are rare in children and this the first case, as best in our knowledge, we are reporting as it.

Usually, all age groups are affected by hybrid PNST, but young adults are affected more commonly. Lang *et al.* reported hybrid neurofibroma/schwannoma with multiple soft-tissue masses in a widespread distribution without any associated syndrome and quoted that hybrid PNST includes neurofibroma/perineuroma, schwannoma/perineuroma and neurofibroma/schwannoma and is mainly located on digits and extremities.[15] A retrospective study on 115 patients were reevaluated and 22 cases were found as hybrid PNST, which were formerly diagnosed as neurofibroma and schwannoma. Among those, 18 were confirmed as neurofibroma/schwannoma and 7 were in the head-and-neck area with an age range of 17–50 years.[16]

Solitary hybrid schwannoma/neurofibroma in children has been rarely reported in the literature. In a report of five cases of hybrid PNSTs, only one case, 5 years of age, was of neurofibroma/schwannoma on thigh.[4] Some hybrid PNSTs may be associated with certain tumor syndromes. Harder *et al.* have reported that hybrid neurofibroma/schwannoma is very frequently associated with NF1, NF2 or schwannomatosis, but more than 50% of such associations were multiple and majority of neurofibromas were of plexiform type which was not present in our case.[8]

The largest series of nine cases of hybrid neurofibroma/schwannoma, aged 12–66 years (median age: 37 years), arose mainly on the trunk, upper extremity and lower extremity. Out of nine patients, only one patient was confirmed with the definitive diagnosis of NF1. Hence, the authors conclude that hybrid tumors were not confined to the NF1.[14] By Alomair *et al.*, supraclavicular solitary hybrid neurofibroma/schwannoma was reported and reviewed multiple cases reported in the literature on solitary hybrid neurofibroma/schwannoma on different locations and was not associated with NF and schwannomatosis and none of them in PPS.[7] Our case, in an 8-year-old male child, is rare and unique and the first case of hybrid neurofibroma/schwannoma diagnosed in PPS and was not associated with NF1, NF2 and schwannomatosis which was confirmed by clinical examination. NF1 is clinically diagnosed by having two or more of the following seven diagnostic criteria: minimum 6 café au lait macules, 2 neurofibromas of any type or 1 plexiform type, axillary or inguinal freckling, optic nerve glioma, at least 2 Lisch nodules, distinctive osseous lesion and having first-degree relative with NF1. The pathognomic criteria for NF2 are bilateral vestibular schwannomas or first-degree relative with NF2 along with unilateral vestibular schwannomas or any two of the following: meningioma, glioma, schwannoma or juvenile posterior lenticular opacities. Possible clinical diagnostic criteria for schwannomatosis are at least 2 nondermal biopsies confirmed schwannomas with no radiographic evidence of bilateral vestibular schwannomas or one biopsy confirmed nondermal schwannoma or intracranial meningioma and a first-degree relative with schwannomatosis.[17] The present case was not consistent with NF1, NF2 and schwannomatosis syndrome.

The present case shows solitary swelling in PPS having features of both neurofibroma and schwannoma. FNAC diagnosis of pleomorphic adenoma was not in consistent with the final diagnosis in our case. Studies show variable results with FNAC of PPS tumors. All four preoperative fine-needle aspiration biopsies were inconclusive by Luna-Ortiz et al., but a study by Matsuki et al. showed 95.2% diagnostic rate of FNAC in PPS tumors, however among those neurogenic tumors of retrostyloid compartment had high diagnostic rate (33%)of inadequate samples.[13,18] The pathological finding is suggestive of hybrid PNST with mixed features of schwannoma and neurofibroma. IHC stain profile is consistent with the diagnosis of hybrid neurofibroma/schwannoma, S100 and GFAP positivity confirms a neural tumor and negative SMA excludes muscular tumor. Strong and diffuse S100 positivity in schwannomatous area and variable and diffuse staining of S100/CD34 in neurofibroma area confirms tumor have a feature of hybrid neurofibroma/schwannoma. Ki-67 index was low which was in favor of benign tumor. Pseudoptosis of the same side was noted after surgery which was relived after 1 week. Injury to the cervical sympathetic plexus may lead to Horner's syndrome which is usually recovered after few months of surgery.[19]

The pathogenesis of dual differentiation in hybrid neurofibroma and schwannoma remains unclear, but origin of this may be due to localized microenvironment change or from clonal genetic alteration.[14] No malignant change and recurrence has been reported in solitary hybrid schwannoma/neurofibroma in the literature.

CONCLUSION

PPS neck mass in children to be hybrid PNST is although quite rare, but possibility of diagnosis should always be kept in mind and should be correlated with collective clinical, radiological and pathological findings. Histopathology is hallmark in diagnosis of hybrid PNST but should always be confirmed by immunohistochemistry. Design of surgical approach depends on tumor location and size; in majority of PPS tumors, cervical transparotid approach is standard.

Although postoperative course is uncomplicated, possibility of cranial nerve deficit should be of prime importance in counseling during preoperative workup.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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