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Peripheral nerve sheath tumors – case series in tertiary health care center in the central India

Sarika More[1], Madhubala Swarnakar[2], Rajendra Kumar Chandrakar[3], Sujata Singh[4]

[1]Professor, Department of Pathology, RKDF Medical College, Hospital and Research Centre Bhopal, Madhya Pradesh, India, [2]Assistant Professor, [3]Professor, Department of Pathology, Shri Shankaracharya Institute of Medical Sciences, Bhilai, Chhattisgarh, India, [4]Senior Resident, Department of Pathology, CIMS, Bilaspur, Chhattisgarh, India

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ABSTRACT

Peripheral nerve sheath tumors (PNST) are one of the most common neoplasms, with classical morphology and histopathological features, but they can be diagnostically challenging at times. Albeit well defined subtypes of PNST have been described in literature, but controversies regarding reporting and typing of these tumors persists. Malignant PNSTs represent a diagnostically challenging group. Although the diagnosis and classification of most PNST are relatively straightforward, borderline grey zone neoplasms continue to be a diagnostic difficulty. In our case series, we attempt in providing some useful information for the oncopathologist to help navigate these persistent and challenging problems. In the present study, we found 26 cases of PNST, out of which the most common was schwannoma (n = 18), followed by neurofibroma (n = 7) and one case of malignant type, that is, malignant PNST. The cases involving all age from 12 to 65 years, showing slight male preponderance.

Key words: Malignant peripheral nerve sheath tumors; Neurofibroma; Schwannoma; Neurofibromatosis type

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INTRODUCTION

Peripheral nerve sheath tumors (PNST) encompass a spectrum of well-defined clinicopathologic entities,[1] ranging from benign neural tumors to high-grade malignant PNST (MPNST), which are often resistant to conventional treatments.[2] A subset of peripheral nerve tumors is difficult to classify, demonstrating hybrid morphologic features overlapping with previously discrete diagnostic categories, such as schwannoma and perineurioma.[3-7]

Neurofibromas are benign tumors, they are mixture of non-neoplastic peripheral nerve components perineurial cells, axons, fibroblasts, and variable inflammation, grossly neurofibromas are tan white, glistening on cut section and growth pattern is either well defined intraneural or diffuse infiltration of soft tissue at extraneural site.

Neurilemmomas are benign neoplasm of schwann cell origin, grossly it is well circumscribed masses with degenerative changes and variable admixture of compact spindled Antoni A areas and hypocellular myxoid. Schwannoma variants include cellular schwannoma and plexiform schwannoma.

MPNST arising from a peripheral nerve or in extraneural soft tissue and showing nerve sheath differentiation.[8]

CASE PRESENTATION

We identified 26 cases of PNST including a rare site of parapharyngeal region and as a mesenteric mass. The age ranged from 12 to 65 years with most patients being in the 4th and 5th decade. M: F ratio is 1.3:1.

Address for Correspondence:
Dr. Madhubala Swarnakar, Assistant Professor, Department of Pathology, Shri Shankaracharya Institute of Medical Sciences, Junwani, Bhilai - 490 020, Chhattisgarh, India. **Mobile:** +91-9229456892. **E-mail:** mulkalwarmadhu@gmail.com

Case 1–10

Out of total 26 cases, 18 were found to be of Schwannoma, among 18 cases of schwannoma, 10 case were of classical type schwannoma, showing typical antoni A and antoni B type cells and alternate hypo and hypercellular areas.

Case 11–13

Out of 18 schwannoma cases, three being morphologically found as ancient schwannoma, because cells exhibiting marked pleomorphism, myxoid degeneration, hemorrhage, and cystic changes (Figure 1a-c).

Case 14–16

Out of 18 schwannoma cases, three being morphologically found as cystic schwannoma, the tumors grossly presented as cystic mass with thin septations, filled with serous fluid inside, cyst wall showing changes of neural tumor of schwannomatous origin, two cases were involving extremities (Figure 2a-c).

We found one of the cystic schwannomas at very rare site, presented as mesenteric mass, of aged 43 years female, present in out patient department with palpable lump lower abdomen (left side), on guided aspiration only mucinous fluid mixed with blood was aspirated, then she was advised for histopathological examination (HPE) for confirmation and typing of lesion. Post-operative specimen received in our histopathology section. Grossly, an encapsulated mass received measuring 10.5×8.5×6 cm, which on cut section cystic-solid to variegated in appearance, multiple sections taken and processed. On microscopic examination, there were many large cystic areas filled with mucinous fluid and at places hemorrhagic areas seen. Cyst wall showing a sheet of spindle shaped tumor cells with wavy nuclei, arranged in herring-bone pattern showing alternate hypocellular and hypercellular (antoni A and B) areas with myxoid stroma and presence of verocay bodies at places (Figure 3a-e).

Case 17

Among all schwannoma cases, one was diagnosed as cellular schwannoma, present at unusual location of parapharyngeal region, showing high cellularity but having minimal pleomorphism.

Case 18

Among all schwannoma cases, one was of plexiform type schwannoma, located at popliteal fossa of young child,

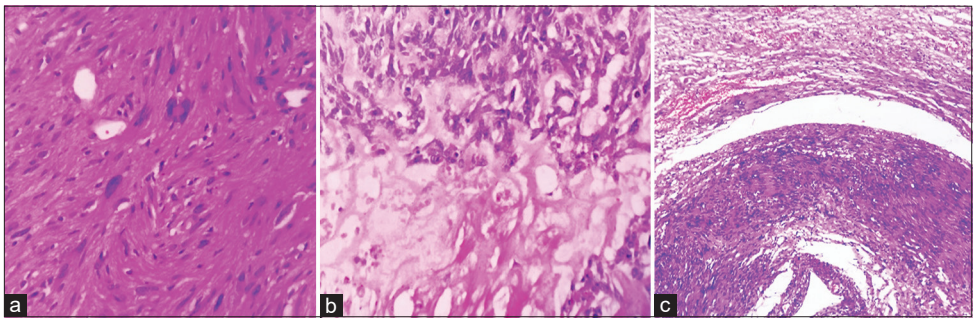

Figure 1: (a-c) Ancient schwannoma. (a) Marked pleomorphism H and E stain (×400). (b) Myxoid degeneration H and E stain (×400). (c) Cystic change H and E stain (×100)

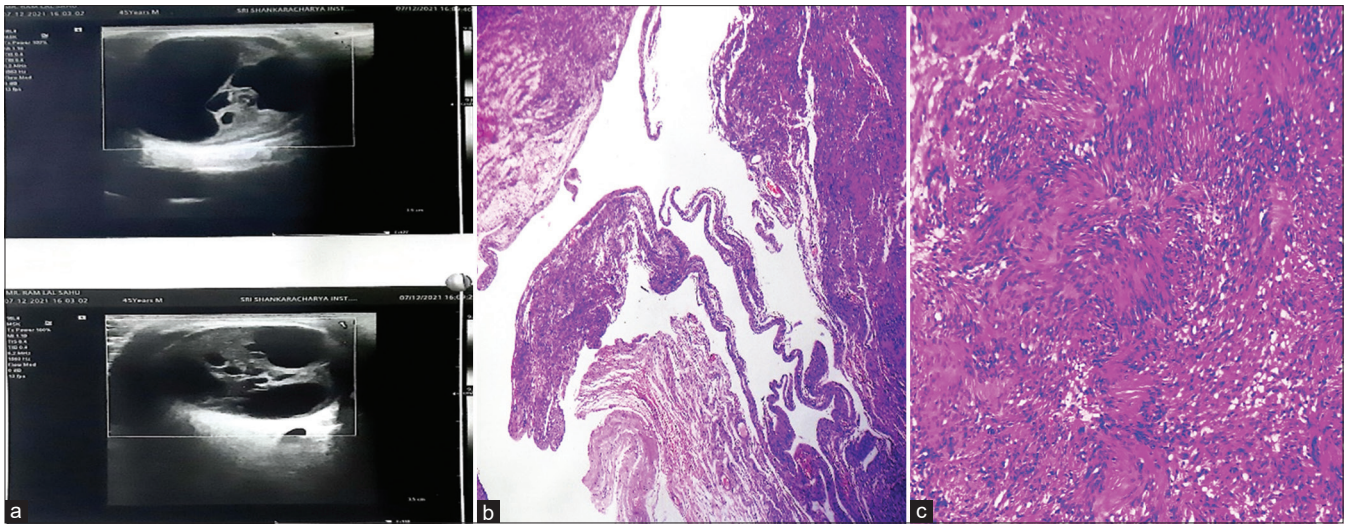

Figure 2: (a-c) Cystic schwannoma. (a) Cystic change on ultrasonography. (b) Cyst formation H and E stain (×400). (c) Biphasic tumor H and E stain (×100)

mimicking plexiform neurofibroma, but showing nodular configurations with alternate hypo and hypercellular areas (antoni A and B areas) (Figure 4a-c).

Distribution of tumors (schwannoma)

Tumor was distributed all over the body involving central nervous system (CNS) to the nerves located at the periphery. Among these, three were presented as intradural-extramedullary space occupying lesions (SOL), two were presented extradurally located at L3-L4 region, one located at CP angle, one case located at parapharyngeal region, which is highly uncommon site for this tumor (Table 1).

On HPE, it was diagnosed as cellular type schwannoma which was again a rare variant (Figure 5a-f).

Remaining cases include one at supraclavicular region, one-one cases at right vestibule and acoustic region also, remaining cases were from the upper and lower extremities. The case of plexiform schwannoma is also an uncommon variant which was located at popliteal fossa of a young child.

Case 19–23

The second most common type was of neurofibroma, out of seven cases of NF, five cases were being of classical type.

Case 24–25

Remaining two cases were identified as plexiform type neurofibroma. Two cases of plexiform neurofibroma were involving peripheral region (Figure 6a and b).

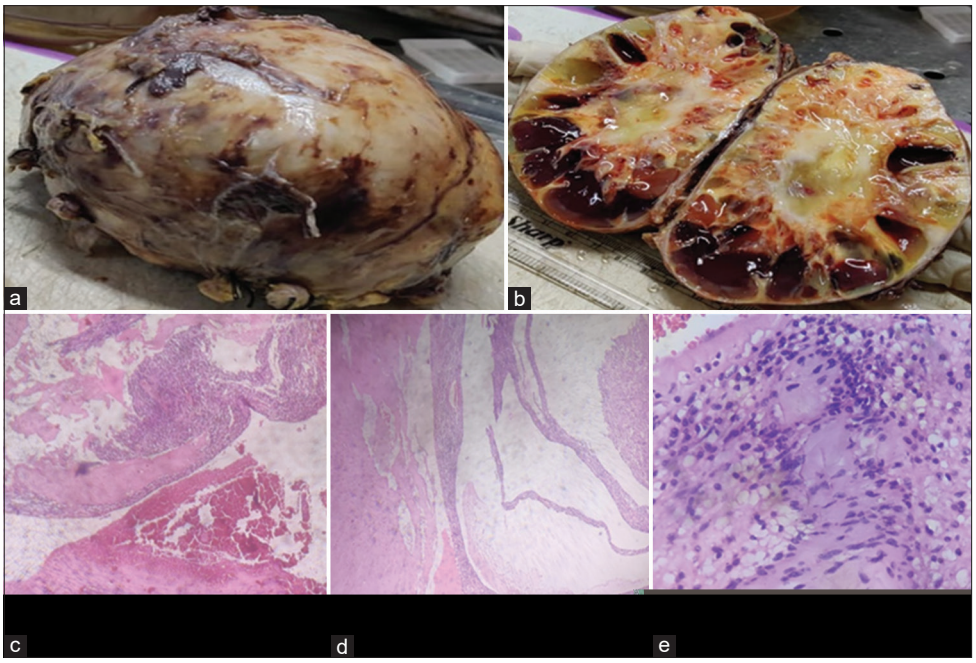

Figure 3: (a-e) Cystic schwannoma-mesenteric mass. (a) Gross-encapsulated intact mass. (b) Cut section-cystic-solid to variegated in appearance, cyst filled with mucinous fluid and blood clots. (c) Microscopic examination showing cystic and hemorrhagic areas (H and E stain, ×400). (d) Cystic spaces filled with mucinous material and cyst wall formed by solid sheet of tumor cells (H and E stain, ×400). (e) Tumor cells forming verocay bodies with palisaded nuclei (H and E stain, ×1000)

Figure 4: (a-c) Plexiform schwannoma. (a) Plexiform pattern H and E stain (×100). (b) Biphasic areas H and E stain (×100). (c) Spindled cells with indistinct cytoplasm and elongated nuclei H and E stain (×400)

Table 1: Demographic distribution of cases of schwannoma (n=18)

S. No.	Age	Sex	Site	Diagnosis
1	44	M	Superficial retroperitoneal nerve	Schwannoma
2	42	M	C3-C4	Schwannoma
3	54	M	Extradural L3-L4	Schwannoma
4	35	F	Intradural-extramedullary SOL	Schwannoma
5	55	F	Right vestibule	Schwannoma
6	15	F	Supraclavicular	Schwannoma
7	43	M	Intradural-extramedullary SOL (C1-C4)	Schwannoma
8	30	F	Extradural L3-L4	Schwannoma
9	36	M	Cerebellopontine angle	Schwannoma
10	48	M	Medial aspect of left calf	Schwannoma
11	55	F	Right acoustic region	Ancient Schwannoma
12	49	F	Limb	Ancient Schwannoma
13	45	F	Limb	Ancient Schwannoma
14	40	M	Limb	Cystic Schwannoma
15	28	M	Thigh	Cystic Schwannoma
16	43	F	Mesenteric mass	Cystic Schwannoma
17	27	F	Parapharyngeal mass	Cellular schwannoma
18	21	M	Popliteal fossa	Plexiform Schwannoma

M: Male, F: Female, SOL: Space occupying lesions

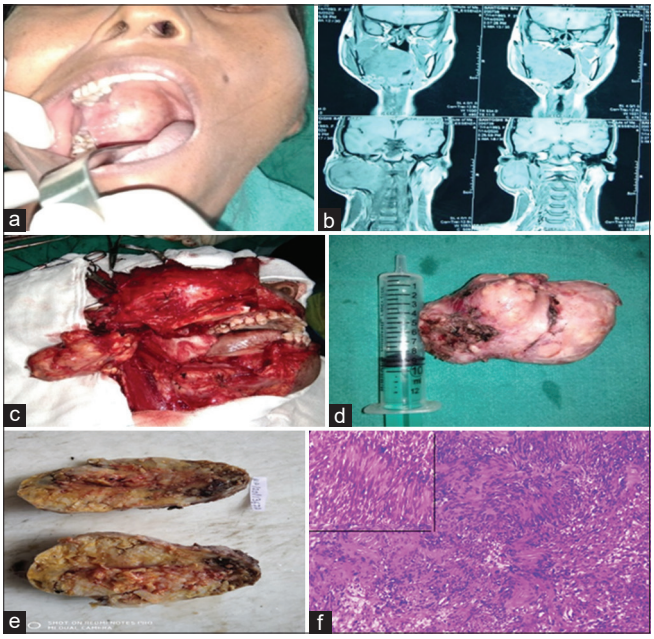

Figure 5: (a-f) Parapharyngeal schwannoma. (a) Clinical presentation. (b) Radiological findings. (c) Intraoperative parapharyngeal mass. (d) Post-operative lump. (e) Gross-well circumscribed. (f) Antoni A and B areas H and E stain (×100), inset (×400)

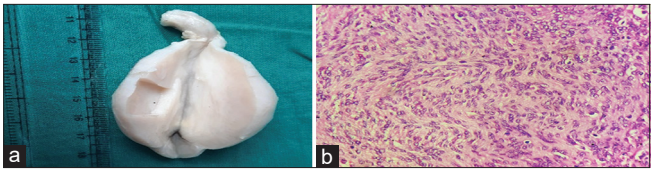

Figure 6: (a and b) Neurofibroma (a) Gross image-glistening grey white surface. (b) Wavy serpentine nuclei H and E stain (×400).

Distribution of tumors of neurofibroma

This tumor was also distributed from CNS to the nerves located at the periphery. Among these, three were presented as intradural-extramedullary SOL, one was intradural in location, one case of neurofibroma presented as axillary mass, which was incidentally diagnosed in case of infiltrating ductal carcinoma of breast in female of age only 31 years. (Table 2)

Case 26

We found only one case of malignancy, which was diagnosed as MPNST, the case was presented as retroperitoneal mass located near appendix, which was uncommon site for neural tumors (Table 3).

The tumor exhibits high pleomorphism and mitosis as well necrosis but morphologically neural origin was maintained focally (Figure 7a-e).

DISCUSSION

The PNST is characterized by neoplastic proliferations with Schwann cell differentiation, represents the primary neoplastic cell component of neurofibroma,[9] characterized cytologically by wavy nuclear contours and S-100 protein expression.[10,11]

Schwannomas occur at all ages but most common found in between the ages of 20 and 50 years[12] with equal distribution. Schwannomas are usually solitary sporadic lesions found in head, neck, and flexor surfaces of the upper and lower extremities.[13] Consequently, the spinal roots and the cervical, sympathetic, vagus, peroneal, and ulnar nerves are most commonly affected. In a population-based study of schwannomas, about 90% were sporadic, 3% occurred in patients with neurofibromatosis type (NF)2, 2% in those with schwannomatosis, and 5% in

Table 2: Demographic distribution of cases of neurofibroma (n=7)

S. No.	Age	Sex	Site	Diagnosis
19	32	M	Intradural tumor	Neurofibroma
20	27	M	Intradural-extramedullary SOL	Neurofibroma
21	38	M	Intradural-extramedullary SOL	Neurofibroma
22	31	F	Axillary mass	Neurofibroma
23	50	M	Intradural-extramedullary SOL	Neurofibroma
24	65	F	Left hand	Plexiform neurofibroma
25	12	M	Painful swelling right wrist	Plexiform neurofibroma

M: Male, F: Female, SOL: Space occupying lesions

Table 3: Demographic distribution of cases of MPNST (n=1)

S. No	Age	Sex	Site	Diagnosis
26	51	F	Retroperitoneal mass, appendix	MPNST

F: Female, MPNST: Malignant peripheral nerve sheath tumors

association with multiple meningiomas in patients with or without NF2.[14] In our case series, we found incidence of schwannomas in all ages but most common being between 4th and 5th decade with equal distribution. The most commonly affected site is extremities followed by spinal cord and parapharyngeal space being the rarest site of occurrence of schwannoma. A 42-year-old female patient of parapharyngeal schwannoma presented with asymptomatic growth measuring 5×4×3 cm, noted 3 months earlier with negative history of change in voice quality, difficulty in swallowing or lock jaw, no lymph nodes were palpable in the neck region. On radiology, a well-defined heterogenous lesion was noted on the right parapharyngeal region. The tumor was excised and sent for HPE. Grossly, the tumor was solitary, well circumscribed, and solid grey-white mass. The cut surface showed grey-white tan with focal hemorrhagic area. On microscopy, the tumor showed classical hypercellular and hypocellular areas.

Ancient schwannomas are those displaying marked nuclear atypia of a degenerative type.[15,16] Moreover, a significant number are located in deep structures such as the retroperitoneum.[16] We found three cases of ancient schwannoma, site being acoustic region and limb. The tumor exhibited marked nuclear pleomorphism, central cyst formation, and focal areas of myxoid degeneration.

There is a rare variant called cystic schwannoma first described in 2008[17] median age 63 years, range 11–93 years. Often arises in gastrointestinal tract submucosa;[18] also other sites. Not associated with NF1 or 2. In our study, we found three cases of cystic schwannoma in a 45-year-old male, with an unlikely site for cystic schwannoma being distal forearm and another cystic schwannoma being present on thigh in a 28-year-old male,ultrasonography was performed in the distal forearm and it showed multiple cysts formation with clear margins. Third case was 43 years female presented with palpable abdominal lump, later on it comes to be rare site for cystic schwannoma. On microscopy, tumor showed cyst formation and classical biphasic pattern. It was treated with local excision and there was no history of recurrence.

The growth pattern of neurofibromas is localized, diffuse, or plexiform, localized form is seen most commonly as a superficial and solitary tumor. Diffuse and plexiform neurofibromas are associated with NF1, sporadic neurofibromas occurring in NF1. In the series by Geschickter,[12] about 90% of neurofibromas were of the solitary or sporadic type, and the remainder was found in the setting of NF1. In our study, seven cases of neurofibroma, five being localized variants, sporadic in origin and two being plexiform variant associated with NF1 were found. An unusual case of 31-year-old female presented in surgical outpatient department with a right breast lump in the lower outer quadrant measuring 9×7×3 cm and palpable axillary mass measuring 6×3.5×3 cm for the past 8 months. On microscopy, the breast lump was diagnosed as invasive duct carcinoma (mucinous type) and the axillary mass turned out to be localized variant of neurofibroma. On gross examination of axillary mass was a solid grey-white nodule with glistening tan white cut surface. HPE showed presence of Schwann cells with wavy serpentine nuclei intermixed with collagen. This is a very rare presentation of neurofibroma with invasive duct carcinoma of breast.

MPNST is mostly found in patients 20–50 years of age.[19-25] The most common locations are the trunk and extremities, followed by the head-and-neck area.[26,27] Most frequently affect the sciatic nerve. The presenting symptoms are an enlarging painful or painless mass. In our study, the incidence being in 4th decade appearing as rapidly growing retropritoneal mass with metastasis to lung, liver, and bone. The patient presented with abdominal pain, lower back pain, and loss of appetite. On microscopy, a striking herringbone pattern of spindle cells with brisk mitotic activity, necrosis, and focal myxoid areas was seen. Fibrosarcoma was considered a differential diagnosis. Tumor cells showed positivity for S-100 and was diagnosed as MPNST.

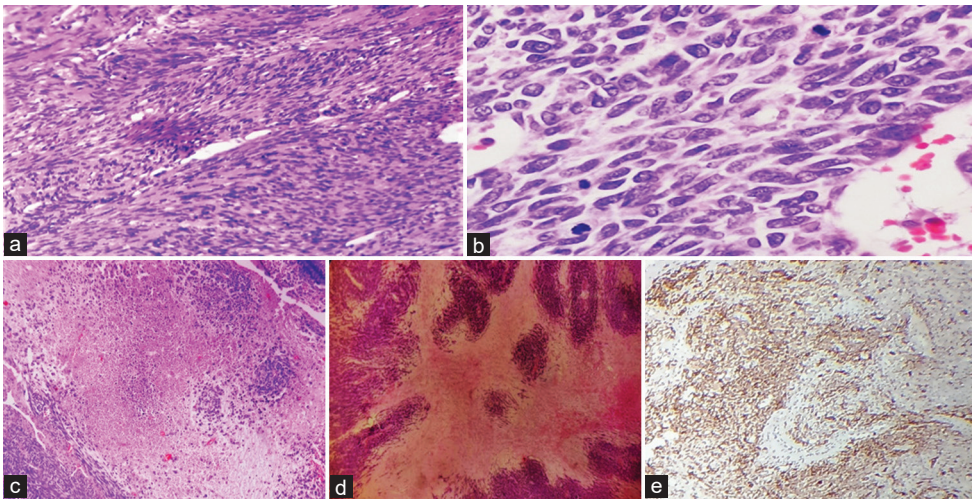

Figure 7: (a-e) Malignant peripheral nerve sheath tumors. (a) Herring bone pattern H and E stain (×10). (b) Brisk mitosis H and E stain (×400). (c) Necrosis H and E stain (×400). (d) Myxoid changes H and E stain (×400). (e) IHC-S100 positivity (×400)

CONCLUSION

Cellular schwannoma of parapharyngeal space is very rare and is associated with overall excellent prognosis. Neurofibroma can rarely present with invasive duct carcinoma of breast. Surgical excision and histopathological examination is mandatory for all the cystic, solid-cystic, or solid masses whether they are involving extremities, retroperitoneal, or presented as intra-abdominally. Another important site is CNS presenting as SOL. This emphasizes the importance of thorough examination of specimen for any incidental neural tumors. Excision followed by adjuvant radiotherapy is the mainstay of treatment in cases of malignant peripheral nerve sheath tumors. Difficulty in accessibility of cranial MPNST explains the subtotal resection and hence poor prognosis in such cases, metastasis to the spinal cord is the most often site followed by lung and bone. A close post-operative follow-up is highly recommended to prevent further recurrence and complication.

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REFERENCES

1. Louis DN, Ohgaki H, Wiestler OD and Cavenee WK. WHO Classification of Tumours of the Central Nervous System. 4th ed. Lyon: International Agency for Research on Cancer; 2016. p. 214-228.
2. Slomiany MG, Dai L, Bomar PA, Knackstedt TJ, Kranc DA, Tolliver L, Maria BL, et al. Abrogating drug resistance in malignant peripheral nerve sheath tumors by disrupting hyaluronan-CD44 interactions with small hyaluronan oligosaccharides. Cancer Res. 2009;69(12):4992-4998. https://doi.org/10.1158/0008-5472.CAN-09-0143
3. Hornick JL, Bundock EA and Fletcher CD. Hybrid schwannoma/perineurioma: Clinicopathologic analysis of 42 distinctive benign nerve sheath tumors. Am J Surg Pathol. 2009;33(10):1554-1561. https://doi.org/10.1097/PAS.0b013e3181accc6c
4. Kazakov DV, Pitha J, Sima R, Vanecek T, Shelekhova K, Mukensnabl P, et al. Hybrid peripheral nerve sheathtumors: Schwannoma-perineurioma and neurofibroma-perineurioma. A report of three cases in extradigital locations. Ann Diagn Pathol. 2005;9(1):16-23. https://doi.org/10.1016/j.anndiagpath.2004.12.001
5. Michal M, Kazakov DV, Belousova I, Bisceglia M, Zamecnik M and Mukensnabl P. A benign neoplasm with histopathological features of both schwannoma and retiform perineurioma (benign schwannoma-perineurioma): A report of six cases of adistinctive soft tissue tumor with a predilection for the fingers. Virchows Arch. 2004; 445(4):347-353. https://doi.org/10.1007/s00428-004-1102-5
6. Shelekhova KV, Danilova AB, Michal M and Kazakov DV. Hybrid neurofibroma-perineurioma: An additional example of anextradigital tumor. Ann Diagn Pathol. 2008;12(3):233-234. https://doi.org/10.1016/j.anndiagpath.2008.02.012
7. Spinner RJ, Scheithauer BW, Perry A, Amrami KK, Emnett R and Gutmann DH. Colocalized cellular schwannoma and plexiform neurofibroma in the absence of neurofibromatosis. Case report. J Neurosurg. 2007;107(2):435-439. https://doi.org/10.3171/JNS-07/08/0435
8. Louis DN, Ohgaki H, Wiestler OD and Cavenee WK. WHO Classification of Tumours of the Central Nervous System. 2nd ed. Lyon: International Agency for Research on Cancer; 2007. p. 114-547.
9. Perry A, Roth KA, Banerjee R, Fuller CE and Gutmann DH. NF1 deletions in S-100 protein-positive and negative cells of sporadic and neurofibromatosis 1 (NF1)-associated plexiform neurofibromas and malignant peripheral nerve sheath tumors. Am J Pathol. 2001;159(1):57-61. https://doi.org/10.1016/S0002-9440(10)61673-2
10. Chaubal A, Paetau A, Zoltick P and Miettinen M. CD34 immunoreactivity in nervous system tumors. Acta Neuropathol. 1994;88(5):454-458. https://doi.org/10.1007/BF00389498
11. Weiss SW, Langloss JM and Enzinger FM. Value of S-100protein

in the diagnosis of soft tissue tumors with particular reference to benign and malignant schwann cell tumors. Lab Invest. 1983;49(3):299-308.

12. Geschickter CF. Tumors of the peripheral nerves. Am J Cancer. 1935;25:377-410.
13. Stout AP. The peripheral manifestations of specific nerve sheath tumor (neurilemoma). Am J Cancer. 1935;24(4):751-1780.
    https://doi.org/10.1158/ajc.1935.751
14. Antiheimo J, Sankila R, Carpen O, Pukkala E, Sainio M and Jääskeläinen M. Population based analysis of sporadic and Type 2 neurofibromatosis-associated meningiomas and schwannomas. Neurology. 2000;54(1):71-76.
    https://doi.org/10.1212/wnl.54.1.71
15. Ackerman LV and Taylor FH. Neurogenous tumors within the thorax. Cancer. 1951;4(4):669-691.
    https://doi.org/10.1002/1097-0142(195107)4:4<669:aid-cncr2820040405>3.0.co;2-b
16. Dahl I. Ancient neurilemoma (schwannoma). Acta Pathol Microbiol Scand A. 1977;85(6):812-818.
    https://doi.org/10.1111/j.1699-0463.1977.tb03896.x
17. Liegl B, Bennett MW and Fletcher CD. Microcystic/reticular schwannoma: A distinct variant with predilection for visceral locations Am J Surg Pathol. 2008;;32(7):1080-1087.
    https://doi.org/10.1097/PAS.0b013e318160cfda
18. Chetty R. Reticular and microcystic schwannoma: A distinctive tumor of the gastrointestinal tract. Ann Diagn Pathol. 2011;15(3):198-201.
    https://doi.org/10.1016/j.anndiagpath.2010.02.011
19. Bunge MB, Wood PM, Tynan LB, Bates ML and Sanes JR. Perineurium originates from fibroblasts: Demonstration *in vitro* with a retroviral marker. Science. 1989;243(4888):229-231.
    https://doi.org/10.1126/science.2492115
20. Huber CC and Lewis LD. Amputation neuroma- their development and prevention. Arch Surg. 1920;1(1):85-113.
    https://doi.org/10.1001/archsurg.1920.01110010098007
21. Fraitag S, Sherardi R and Wechsler J. Hyperplastic pacinian corpuscles: An uncommonly encountered lesion of the hand. J Cutan Pathol. 1994;21(5):457-460.
    https://doi.org/10.1111/j.1600-0560.1994.tb00289.x
22. Hart WR, Thompson NW, Hildreth DH and Abell MR. Hyperplastic pacinian corpuscles: A cause of digital pain. Surgery. 1971;70(5):730-735.
23. Rhode CM, Jennings WD Jr. Pacinian corpuscle neuroma of digital nerves. South Med J. 1975;68(1):86-89.
    https://doi.org/10.1097/00007611-197501000-00023
24. Reed RJ, Fine RM and Meltzer HD. Palisaded encapsulated neuromas of the skin. Arch Dermatol. 1972;106(6):865.
25. Albrecht S, Kahn HJ and From L. Palisaded encapsulated neuroma: An immunohistochemical study. Mod Pathol. 1989;2(4):403-406.
26. Le Guellec S, Decouvelaere AV, Filleron T, Valo I, Charon-Barra C, Robin YM, et al. Malignant peripheral nerve sheath tumor is a challenging diagnosis: A systematic pathology review, immunohistochemistry, and molecular analysis in 160 patients from the French Sarcoma Group database. Am J Surg Pathol. 2016;40(7):896-908.
    https://doi.org/10.1097/PAS.0000000000000655
27. Ducatman BS, Scheithauer BW, Piepgras DG, Reiman HM and Ilstrup DM. Malignant peripheral nerve sheath tumors. A clinicopathologic study of 120 cases. Cancer. 1986;57(10):2006-2021.
    https://doi.org/10.1002/1097-0142(19860515)57:10<2006:aid-cncr2820571022>3.0.co;2-6

Authors Contribution:
SM- Concept and design of the study, interpreted the results, reviewed the literature, and manuscript preparation; **MS**- Concept and design of the study, interpreted the results, reviewed the literature, and manuscript preparation and revision of the manuscript; **RKC**- Interpreted the results, reviewed the literature, statistically analyzed and interpreted, and preparation of manuscript; and **SS**- Interpreted the results, concept, coordination, review of literature, and manuscript preparation.

Work attributed to:
Shri Shankaracharya Institute of Medical Sciences, Junwani, Bhilai, Chhattisgarh, India.

ORCID ID:
Dr. Sarika More - https://orcid.org/0000-0002-4937-5941
Dr. Madhubala Swarnakar - https://orcid.org/0000-0002-3477-6689
Dr. Rajendra Kumar Chandrakar - https://orcid.org/0000-0003-0696-3492
Dr. Sujata Singh - https://orcid.org/0000-0001-5128-7679

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