Section: Pathology

Case Series

HISTOPATHOLOGICAL SPECTRUM OF SCHWANNOMA VARIANTS: A CASE SERIES OF DIVERSE PRESENTATIONS

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Received *: 10/04/2026*
Received in revised form *: 03/06/2026*
Accepted *: 20/06/2026*

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DOI: 10.70034/ijmedph.2026.2.612

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (2); 3719-3723

ABSTRACT

Background: Schwannomas are usually benign, encapsulated peripheral nerve sheath tumours of Schwann cell origin. Although conventional schwannoma is most common, several uncommon histological variants (ancient, plexiform, cellular and cystic) have distinct morphological features that can pose a diagnostic challenge owing to their similarity to other benign and malignant spindle cell lesions. The aim is to study the clinicopathological characteristics and histopathological spectrum of schwannoma variants encountered in routine surgical pathology practice.

Materials and Methods: In this retrospective case series, 11 patients with histologically confirmed schwannoma variants diagnosed between January 2023 and October 2025 were included. Clinical information, gross and microscopic findings, and immunohistochemistry, where available, were reviewed and analysed.

Results: There were five cystic, two ancient, two plexiform and two cellular schwannomas, in patients aged 30 to 70 years with a male predominance. The tumours were located in the neck, supraclavicular, axillary, and extremity, facial, retroperitoneal and lower-back regions. Lesions were well circumscribed, 2.7–7.5 cm in size, and histologically showed Antoni A and B areas with Verocay bodies. Ancient schwannomas showed degenerative changes and plexiform schwannomas showed multinodular growth. Cellular schwannomas were hypercellular and S100-positive. Cystic schwannomas showed marked cystic change, haemorrhage and haemosiderinisation, without significant mitotic activity or necrosis.

Conclusion: Schwannoma variants display a broad spectrum of histomorphological features and may mimic other spindle cell or cystic lesions. Histopathological evaluation, supported where appropriate by immunohistochemistry, is a crucial tool for accurate diagnosis and proper management.

Keywords: Schwannoma, schwannoma variants, cystic schwannoma, cellular schwannoma, histopathology.

INTRODUCTION

Schwannomas, also called neurilemmomas, are benign, slow-growing tumours that arise in the peripheral nerve sheaths, which are made up of Schwann cells. They may occur in isolation or in association with genetic conditions such as neurofibromatosis type 2 and schwannomatosis, and are generally solitary, located on the flexor surfaces of the extremities, head or neck.[1,2] Histologically,

they are comprised of hypercellular Antoni A zones with spindle cells and Verocay bodies, alternating with hypocellular Antoni B zones.[3]

Schwannomas can have several different histopathological variants, such as cellular, ancient, plexiform, epithelioid, microcystic and melanotic, with varying growth patterns and cellular morphology. Cellular schwannomas consist of dense Antoni A regions, occasional mitoses, no Verocay bodies, and may resemble sarcomas. In ancient schwannomas, there are many degenerative features (hyalinisation, nuclear atypia) that are not malignant but rather the result of a prolonged state of metabolic stress.[4,5]

It can be difficult to make a correct and accurate diagnosis of a soft tissue tumour because such lesions may resemble aggressive malignancies. Hypercellularity and nuclear pleomorphism can lead to misdiagnosis, for example as malignant peripheral nerve sheath tumours or leiomyosarcomas. Clinicopathological assessment and immunophenotypic confirmation, particularly by the presence of S100 protein, are extremely important for differentiation.[5,6]

It is important to recognise schwannoma variants, both for planning surgery and for counselling the patient. Misdiagnosis of benign variants as malignant can result in unnecessary surgery and generate neurological problems, while underdiagnosis of recurrence may result in poor management. The case series presented here highlights the diversity in clinical and radiological presentation of schwannomas and the importance of using immunohistochemical staining to correctly diagnose the condition and avoid unnecessary over-treatment.

MATERIALS AND METHODS

This study examined 11 schwannoma cases diagnosed in the Department of Pathology at Chettinad Hospital and Research Institute, Chennai, India, from January 2023 to October 2025. This included both hospital admissions and specimens received from affiliated peripheral centres. Patient details, clinical findings and imaging reports were collected. For the retrospective cases (January 2023 – December 2024), stored slides, blocks and records were retrieved from departmental archives. From January 2025 to October 2025, new diagnoses were confirmed prospectively.

All specimens underwent fixation in 10% neutral buffered formalin for 24–48 hours, followed by appropriate sampling. Tissues were processed routinely, sectioned and stained with haematoxylin and eosin for microscopic review. Key histological features such as cellular patterns, architecture, degeneration and variant-specific features were recorded using a standard checklist. S100 immunohistochemistry confirmed neural origin. Results were summarised with case counts and percentages.

RESULTS

Table 1: Distribution of schwannoma variants

Variant	Number of Cases (n = 11)
Cystic schwannoma	5 (45.5%)
Ancient schwannoma	2 (18.2%)
Plexiform schwannoma	2 (18.2%)
Cellular schwannoma	2 (18.2%)

Table 2: Clinical data of schwannoma variants

Sl. No.	Variant	Sex	Age (years)	Location	Clinical Diagnosis
1	Ancient	M	55	Axilla	Lipoma
2	Ancient	M	70	Supraclavicular region	Soft tissue tumour
3	Plexiform	M	34	Neck	Nerve sheath tumour
4	Plexiform	M	37	Upper neck	Benign soft tissue tumour
5	Cellular	M	42	Face	Schwannoma
6	Cellular	F	36	Retroperitoneum	Leiomyoma
7	Cystic	M	68	Neck	Cystic neck swelling
8	Cystic	F	45	Axilla	Lipoma
9	Cystic	M	52	Upper extremity	Soft tissue tumour
10	Cystic	M	30	Thigh	Benign cystic lesion
11	Cystic	M	40	Lower back	Nerve sheath tumour

The age of the patients ranged from 30 to 70 years, with a male predominance (male:female ratio = 9:2). The duration of symptoms varied from 6 months to 4 years. Tumours were encountered in diverse anatomical locations, including the neck, supraclavicular region, axilla, upper extremity, lower back, thigh, face, and retroperitoneum. Clinically, most patients presented with a slowly enlarging painless mass. None had a history suggestive of neurofibromatosis.

Table 3: Histopathological features of schwannoma variants

Histopathological Feature	Ancient (n=2)	Plexiform (n=2)	Cellular (n=2)	Cystic (n=5)
Encapsulation	2	2	2	5
Antoni A areas	2	2	2	5
Antoni B areas	2	2	1	5
Verocay bodies	2	2	2	5
Cystic degeneration	2	0	0	5
Hyalinisation	2	0	1	3
Nuclear atypia	2	0	0	0
Haemorrhage	1	0	0	2
Haemosiderin-laden macrophages	1	0	1	2
Myxoid degeneration	1	0	0	2
Necrosis	0	0	0	0
Significant mitosis	0	0	0	0

Clinical Diagnosis

Preoperative diagnoses varied depending on the location and radiological appearance of the lesion. The provisional diagnoses included lipoma, benign soft tissue tumour, cystic hygroma, leiomyoma, lymphadenitis, fibrolipoma, nerve sheath tumour, and non-specific cystic lesions. Histopathological examination was required for definitive diagnosis in all cases.

Gross Findings

Tumour size ranged from 2.7 cm to 7.5 cm in greatest dimension. All lesions were well circumscribed and predominantly encapsulated. Cut surfaces were typically grey-white to tan-white and glistening. The ancient schwannomas showed cystic degeneration and focal brown discolouration. Plexiform schwannomas exhibited multinodular architecture. Cellular schwannomas were predominantly solid and fleshy. The cystic schwannomas demonstrated multiloculated cystic spaces containing serous or haemorrhagic fluid with residual grey-white solid areas.

Microscopic Findings

Ancient Schwannoma (n = 2)

Both tumours were encapsulated and exhibited characteristic Antoni A and Antoni B areas with Verocay bodies. Prominent degenerative changes including cystic degeneration, hyalinisation, haemorrhage, and nuclear atypia were identified. Haemosiderin-laden macrophages were present in one case. No mitotic activity or necrosis was observed.

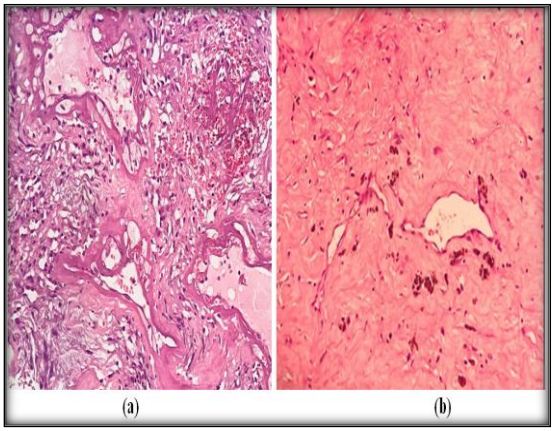


Figure 1 (a, b): Ancient schwannoma (H&E). (a) Cystic degeneration; (b) hyalinisation with haemosiderin-laden macrophages

Plexiform Schwannoma (n = 2)

The lesions showed a multinodular plexiform growth pattern with spindle cells arranged in Antoni A and Antoni B areas. Verocay bodies and nuclear palisading were readily identified. The tumours were well circumscribed and demonstrated a lobulated architecture without atypical features.

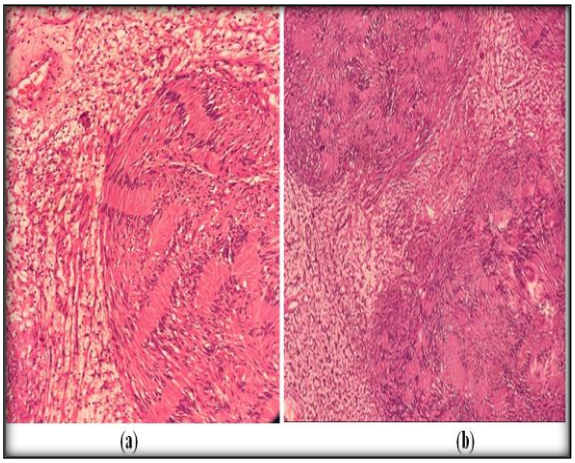
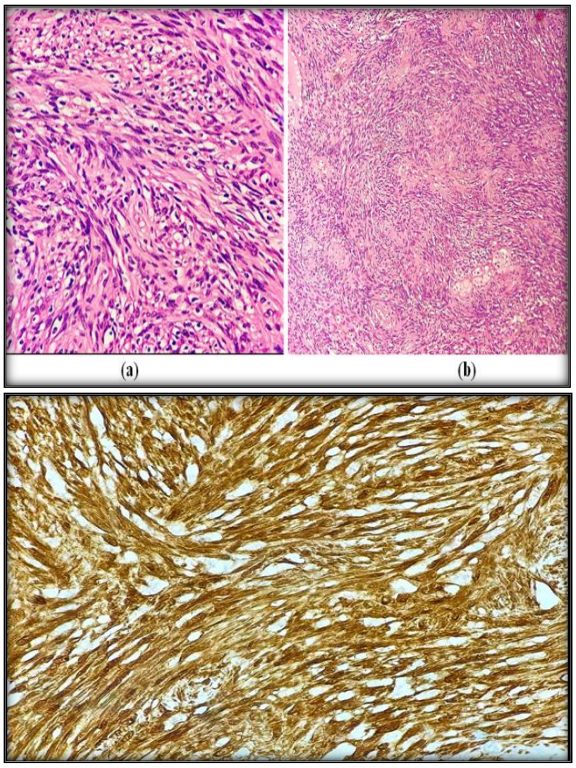


Figure 2 (a, b): Plexiform schwannoma (H&E). (a) Characteristic plexiform pattern; (b) Verocay bodies with Antoni A and B areas

Cellular Schwannoma (n = 2)

Both tumours were predominantly composed of densely cellular Antoni A areas with only focal Antoni B regions. Tumour cells were spindle-shaped with elongated wavy nuclei. Hyalinised blood vessels and occasional macrophages were noted. Mitotic activity was inconspicuous and necrosis was absent. Immunohistochemistry showed diffuse strong S100 positivity.



(c)

Figure 3 (a–c): Cellular schwannoma. (a) Predominantly Antoni A areas (H&E); (b) high cellularity (H&E); (c) diffuse strong S100 positivity (IHC – S100).

Cystic Schwannoma (n = 5)

All five tumours demonstrated extensive cystic spaces within an otherwise typical schwannoma. Histologically, encapsulated spindle cell proliferations arranged in Antoni A and Antoni B patterns with Verocay bodies were identified. Additional findings included hyalinisation, haemorrhage, myxoid degeneration, haemosiderin-laden macrophages, and focal calcification in selected cases. No significant mitotic activity or necrosis was observed.

DISCUSSION

Eleven schwannoma variants were evaluated in the present study: five cystic schwannomas, two ancient schwannomas, two plexiform schwannomas, and two cellular schwannomas. The tumours were found at various ages and in a variety of anatomical sites, consistent with the known tendency of schwannomas to develop anywhere in the peripheral and autonomic nervous system where Schwann cells are present.[7,8]

Ancient Schwannoma

Ancient schwannoma is a rare degenerative Schwann cell tumour in which the tumour has been present for a long time, leading to cystic degeneration, haemorrhage, hyalinisation, calcification, and marked nuclear atypia. Although these tumours show pleomorphism and hyperchromatism, they are benign and show little mitotic activity or necrosis. In both ancient schwannomas in our series, classical Antoni A and Antoni B areas were found with Verocay bodies, along with cystic alteration and stromal hyalinisation. In slowly growing tumours, chronic ischaemic alterations are well documented and are secondary to these changes, similar to those reported here.[7,8]

Plexiform Schwannoma

Plexiform schwannoma is a rare variant with a multinodular or plexiform growth pattern, accounting for about 5% of schwannomas. The histology is essentially that of a schwannoma, in which the characteristic Antoni A areas, nuclear palisading and Verocay bodies are present, but with a peculiar plexiform arrangement. In both plexiform schwannomas in the present study, multinodular encapsulated nodules were seen, consisting of Antoni A and Antoni B areas of spindle cells. Recognition of this variant is important as it can be mistaken for plexiform neurofibroma, which occurs in NF-1 and can undergo malignant transformation.[9,10]

Cellular Schwannoma

Cellular schwannoma is a well-recognised benign variant, first described by Woodruff et al. It features significant hypercellularity, predominance of Antoni A areas, few Antoni B areas, and diffuse S100 immunoreactivity. It can be confused with malignant peripheral nerve sheath tumour (MPNST) owing to its increased cellularity, occasional nuclear atypia and fascicular growth pattern. Both cellular schwannomas in the present study showed dense cellular proliferation of spindle cells, hyalinised blood vessels and diffuse S100 immunoreactivity. No significant tumour necrosis or mitotic activity was seen. These findings are shared by Casadei et al., who stressed that diffuse S100 positivity and lack of geographic necrosis are helpful features for differentiating a cellular schwannoma from MPNST.[11,12]

Cystic Schwannoma

Cystic schwannoma is a degenerative schwannoma involving widespread cystic transformation, which may occur due to vascular insufficiency, haemorrhage or prolonged growth of the tumour. Macroscopically they may be primarily cystic and could be confused clinically and radiologically with a benign cystic tumour. All five cystic schwannomas in our series had large areas of cyst formation, mixed Antoni A and Antoni B areas, and Verocay bodies. The associated findings were haemorrhage, haemosiderin-laden macrophages, hyalinisation and myxoid degeneration. These findings have been noted in previous reports, and residual conventional schwannoma architecture is crucial to make a diagnosis.[7,8]

The Role of Histopathology and Immunohistochemistry

Histopathological examination is the gold standard for the diagnosis of schwannoma variants. Antoni A and Antoni B areas, Verocay bodies, encapsulation and variant-specific features must all be recognised to classify them correctly. Immunohistochemistry is useful for confirmation, and diffuse, intense S100

positivity is a common feature in schwannomas. The Schwann cell differentiation of the cellular schwannoma and some cystic schwannomas was confirmed by the diffuse expression of S100 in our study.[11,12]

This series focuses on the wide range of histomorphological features of schwannomas, including the uncommon variants. Ancient schwannomas may mimic malignancy, cellular schwannomas may resemble malignant peripheral nerve sheath tumours (MPNST), plexiform schwannomas require differentiation from plexiform neurofibromas, and cystic schwannomas may be confused with benign cystic lesions. Careful histopathological examination and the use of immunohistochemistry can lead to accurate diagnosis and patient management.

CONCLUSION

There are various histopathological variants of schwannoma that can simulate benign and malignant lesions. The morphological characteristics of schwannomas were distinct in this series, and the tumours all had the typical architecture of schwannoma but with cystic, ancient, plexiform and cellular features. Recognition of these variant-specific patterns, together with careful histopathological evaluation and supporting immunohistochemistry, is crucial for a correct diagnosis and proper patient management.

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