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rare tumors

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Comprehensive study of ancient schwannoma: Exploring histomorphological diversity and diagnostic challenges

Chaithra Gowthuvalli Venkataramana[1], Soumya Gupta[2], Rakshatha Nayak[1], Sinchana KM[1], Sharada Rai[1] and Ranjitha Rao[1]

Abstract

Background: Ancient schwannoma is a rare subtype of schwannoma characterized by an extended duration of development and distinctive degenerative changes. These changes encompass relative loss of Antoni type A areas, perivascular hyalinization, hemorrhage, cystic necrosis, calcification, and the presence of atypical nuclei that can mimic sarcomatous pleomorphism. These histologic features often lead to diagnostic challenges, with ancient schwannomas frequently being misdiagnosed as malignant tumors. **Objectives:** This study aims to provide a comprehensive evaluation of the histomorphological spectrum observed in ancient schwannoma. **Methods:** A retrospective analysis was conducted on 248 schwannoma cases received at our tertiary health centre, spanning the years 2017 to 2023. Among these cases, 25 were identified as ancient schwannoma. Extensive examination of degenerative changes was performed using hematoxylin and eosin-stained paraffin-embedded tissue sections under light microscopy. **Results:** Patient ages ranged from 22 to 82 years, with a nearly equal distribution between genders (12 females and 13 males). Tumors were located in various anatomical sites including the forearm, brain, abdomen, retroperitoneum, intradural space, lumbar region, and pelvis. Tumor dimensions varied from 1.5 to 11 cm. Histologically, most cases exhibited nuclear atypia, cystic changes, hemorrhage, and siderophages, along with perivascular hyalinization, myxoid change, calcification, and xanthomatous change. Immunohistochemistry confirmed the neural origin of these tumors. **Conclusion:** Recognition of the diverse spectrum of secondary changes, coupled with the presence of focal areas showing paucicellular and cellular spindle cell arrangements, is crucial for the accurate diagnosis of ancient schwannoma. This study underscores the importance of histomorphological evaluation in distinguishing these benign tumors from malignant counterparts, thereby guiding appropriate clinical management strategies.

Keywords

Ancient schwannoma, peripheral nerve, histomorphology, degeneration, neurilemmoma

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[1]Department of Pathology, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, Karnataka, Manipal, India
[2]Department of Pathology, Pimpri Chinchwad Municipal Corporation's Post Graduate Institute, Yashwantrao Chavan Memorial Hospital, Pune, India

Corresponding author:
Rakshatha Nayak, Department of Pathology, Central Laboratory, Kasturba Medical College, Attavar, Mangalore-576104, India.
Email: rakshatha.nayak@manipal.edu

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Introduction

Schwannomas are common benign tumors originating from the peripheral nerve sheath, capable of developing anywhere in the body, with the head and neck being the most frequent locations, followed by the extremities. Occasionally, some of these tumors can grow to unusually large sizes and exhibit a high incidence of degenerative changes. This variant of schwannoma, known as "ancient schwannoma," was first identified by Ackerman and Taylor in 1951. They recognized the necessity for a distinct term to describe a subset of larger schwannomas showing microscopic evidence indicative of prolonged growth and coined the term "ancient" for such tumors.[1] These rare tumors often present over a long duration, exhibit significant degenerative alterations, and frequently display nuclear atypia. Ancient schwannomas typically grow slowly and attain considerable size, affecting predominantly elderly individuals, particularly those in their fifth and sixth decades.[1–6]

Histologically, ancient schwannomas manifest a spectrum of features including hemorrhage, cystic changes, calcification, myxoid changes, and nuclear atypia. Mild to moderate nuclear atypia, a common finding, can resemble sarcomatous pleomorphism and contribute to diagnostic challenges. The hypothesis that these changes are degenerative in nature is supported by the presence of fibrous nodules within these tumors. The developmental course involves initial diffuse overgrowth and vascularization, followed by reduced vascularity with thickening of vessel walls and decreased connective tissue cellularity, eventually leading to the appearance of hyalinized areas.[7–11] Despite these histologic alterations, ancient schwannomas typically maintain benign behavior, with rare instances of malignant transformation.[3] The presence of degenerative changes and pleomorphism often leads to erroneous diagnoses of malignancy due to their similarities in radiological and histological features.

In this study, we present 25 cases of ancient schwannoma that were extensively evaluated for all degenerative histomorphological features, including nuclear atypia. This comprehensive analysis aims to enhance understanding of the histopathological spectrum of ancient schwannoma and facilitate accurate diagnosis and management.

Materials and methods

A retrospective cross-sectional observational study was conducted on 248 cases of schwannomas received at our Tertiary Health Centre's Department of Pathology between 2017 and 2023. Among these cases, 25 were diagnosed as ancient schwannoma. Clinical details such as age, gender, lesion site, size, and symptom duration were extracted from the laboratory information system. Hematoxylin and eosin (H&E) stained slides were examined under light microscopy. Immunohistochemistry with S100 protein was performed to confirm the neural origin of the tumors. The study focused on evaluating the spectrum of histomorphological features present in each case of ancient schwannoma. This included analyzing degenerative changes such as hemorrhage, cystic changes, calcification, perivascular hyalinization, the presence of siderophages or macrophages, myxoid changes, xanthomatous changes, and features of nuclear atypia. Each feature's presence or absence was systematically recorded in a data sheet for comparative and statistical analysis.

The aim of the study was to comprehensively characterize the histopathological profile of ancient schwannomas, providing insights into their morphological diversity and enhancing diagnostic accuracy in clinical practice.

Results

The study revealed a diverse profile of ancient schwannomas across various demographic and clinical parameters. The age at presentation ranged widely from 22 to 82 years, with nearly equal distribution between the age groups: 20–40 years and 41–60 years each accounting for eleven cases, and three cases in the 61–80 age group. In terms of gender, there was a slight female predominance with 13 cases (52%) compared to 12 cases (48%) in males.

Regarding tumor localization, the pelvis and lumbar region were the most common sites, observed in a majority of patients, followed by the head and neck region including the brain. Tumors were also noted in the abdomen, retroperitoneum, vertebrae, adrenal gland, pelvic region, and foot. Specifically, 7 cases (28%) were located in the pelvis and lumbar region, 5 cases (20%) each in the abdomen and head and neck region, and 4 cases (16%) in the upper limbs. Lesions in the lower limbs were observed in 2 cases (8%), while the exact location was unspecified in 2 other cases.

The size of the lesions varied significantly, with the largest dimension ranging from 1.5 to 11 cm. The majority of cases (42%) had lesions in the 3–6 cm range, whereas 8 cases had lesions smaller than 3 cm and 6 cases had lesions larger than 6 cm. Grossly, these lesions showed areas of hemorrhage, mucoid degeneration, and cystic degeneration in the majority of the cases (Figure 1).

Symptom duration varied widely from 4 months to 30 years, with presenting symptoms typically including pain and swelling.

Histologically, the study focused on various features (Figures 2–6) including hemorrhage, cystic changes, nuclear atypia, presence of siderophages or macrophages, perivascular hyalinization, calcification, myxoid changes, xanthomatous changes, and ossification. One case even exhibited metaplastic bone formation. Nuclear atypia was characterized by irregular nuclear membranes, nuclear smudging, and hyperchromasia. Some cases showed

Figure 1. The gross image of ancient schwannoma showing areas of haemorrhage, myxoid and cystic changes.

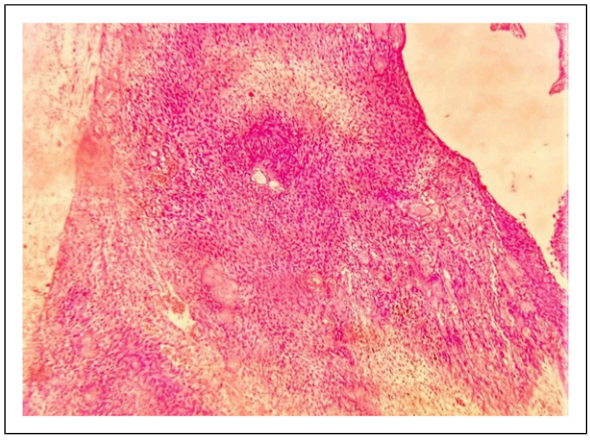

Figure 2. Microscopic appearance of ancient schwannoma showing spindle cells with myxoid changes (H&E, 10x).

macrophages without hemosiderin. These secondary changes often dominated the tumor area, interspersed with focal areas displaying the classical Antoni A (hypercellular) and Antoni B (hypocellular) patterns typical of schwannomas.

The distribution and prevalence of these histological features were systematically analyzed and are illustrated in Figure 7, providing a comprehensive understanding of the morphological spectrum of ancient schwannomas in this study cohort.

Discussion

Ancient schwannoma, a variant typically observed in elderly individuals, predominantly affects those in their fifth and sixth decades of life.[10–12] However, our study exhibited a broader age distribution, with patients ranging from 22 to over 60 years old, and a significant proportion falling

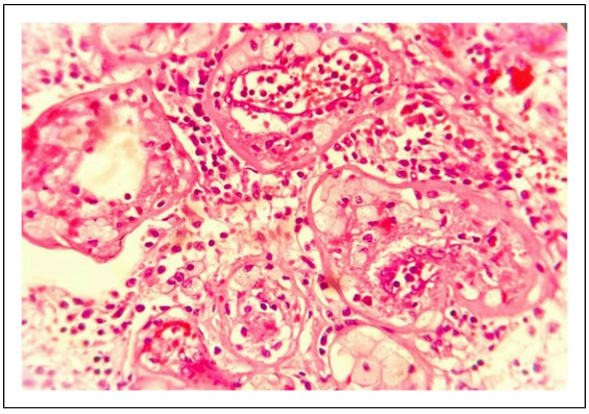

Figure 3. Microscopic appearance of ancient schwannoma showing perivascular hyalinisation (H&E, 40x).

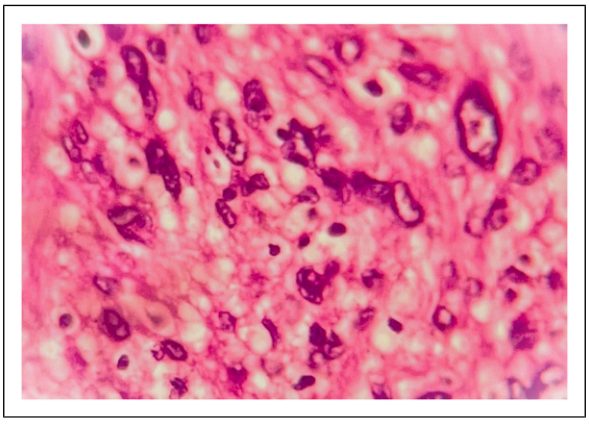

Figure 4. Microscopic appearance of ancient schwannoma showing nuclear atypia (H&E, 100x).

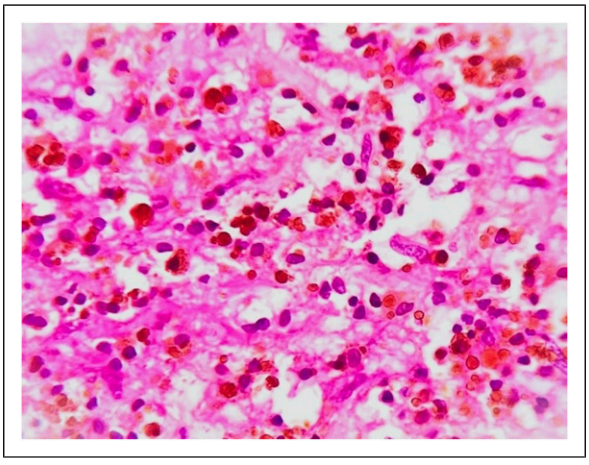

Figure 5. Microscopic appearance of ancient schwannoma showing siderophages and haemorrhage (H&E, 40x).

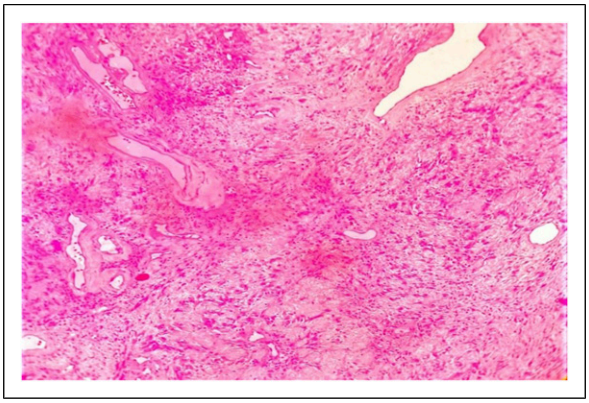

Figure 6. Microscopic appearance of ancient schwannoma showing areas of haemorrhage, perivascular hyalinization and cystic changes (H&E, 10x).

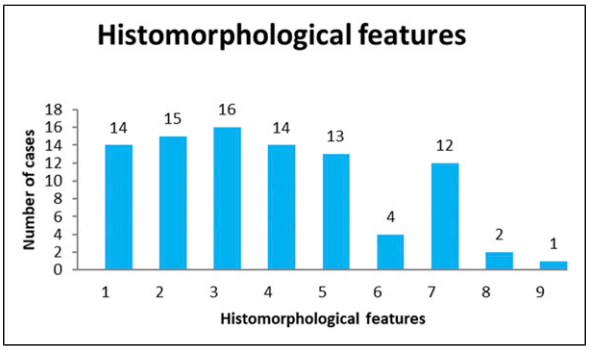

Figure 7. Distribution of the histomorphological features. 1: hemorrhage, 2: cystic change, 3: nuclear atypia, 4: siderophages/ macrophages, 5: hyalinisation, 6: calcification, 7: myxoid change, 8: xanthomatous change, 9: ossification.

between 30 and 60 years. This age diversity underscores the variability in presentation compared to the typical demographic pattern described in the literature.

Regarding gender distribution, while general schwannomas tend to show a slight female predilection, specific data on the ancient variant's gender association are sparse.[12–14] In our study cohort, females accounted for 52% of the cases, suggesting a slight female preponderance compared to what is traditionally reported for schwannomas in general.

Recognizing ancient schwannoma poses challenges, particularly in asymptomatic patients or those with only minor symptoms like local swelling, which often go unnoticed until the tumor reaches a considerable size. In our study, lesions ranged from 1.5 to 11 cm in diameter, with 15 cases exceeding 6 cm. This substantial size can mimic malignant tumors, especially on MRI, where a large, heterogeneous, and well-enhanced soft-tissue mass in an extremity might suggest malignancy. Radiologically, this similarity can lead to confusion with various tumors such as malignant peripheral nerve sheath tumors, synovial sarcomas, malignant fibrous histiocytomas, liposarcomas, or hemangiopericytomas, particularly due to the presence of cystic areas.[10]

Histologically, ancient schwannoma is underexplored due to its rarity, with few articles detailing its characteristics. While calcification isn't always evident on radiographs, Shultz et al. propose considering ancient schwannoma in cases where MRI reveals a hypervascular soft-tissue mass with cystic regions, accompanied by amorphous calcifications on radiography.[10] Despite these radiological hints, histology remains the definitive gold standard for diagnosis.[12]

Schwannomas can be classified into several subtypes based on their histological features, including ancient, microcystic-reticular, epithelioid, cellular, psammomatous, and melanotic types. Ackermann and Taylor were the first to describe this rare variant of schwannoma known as ancient schwannoma in 1951.[1] They gave the term ancient schwannoma to the schwannomas with increased cellularity and cellular atypia. Additional findings include diffuse fibrosis, hyalinization, nuclear pleomorphism, nuclear kinking, and hyperchromasia. Verocay bodies with nuclear palisading may also be seen but hypocellular (Antoni B) areas are more common than hypercellular (Antoni A) areas.[4] It is believed that the long duration of tumor growth and ageing perpetrates these degenerative changes. These histomorphological characteristics are confusing and make a precise diagnosis challenging. Increased cellularity and atypia are features of malignancy and account for the overdiagnosis of these tumors as malignant. However, these lesions have low or rare mitosis counts. Careful histological examination is required to rule out other similar or malignant tumors.[9] Immunohistochemistry (IHC) is a useful ancillary test that helps in the final diagnosis. Ancient schwannomas show strong positivity for the S100 IHC marker in neural cells scattered in a loose degenerative stroma. Meanwhile, malignant peripheral nerve sheath tumors show infiltrative borders, geographic necrosis, increased pleomorphism, and mitosis with either patchy or negative staining of S100.[15] Other differentials include leiomyosarcomas with hyaline degeneration which show spindle cells with cigar-shaped nuclei and rarely pleomorphic hyalinising angiectatic tumors which show pleomorphic spindle cells with intranuclear pseudo-inclusions, hyalinisation, and ectatic blood vessels. However, both these tumors are negative for S100 and are positive for SMA (smooth muscle actin) and CD34, respectively on IHC.[16]

In the present study, degenerative changes comprising of hemorrhage, cystic change, calcification, perivascular hyalinisation, presence of siderophages or macrophages, myxoid change, and xanthomatous change along with the features of nuclear atypia were noted in the cases. The

nuclear atypia comprised of nuclear membrane irregularity, smudging of the nucleus, and nuclear hyperchromasia. Some cases exhibited macroscopic cystic changes, while the majority showed microcystic changes appreciated under microscopy. Haemorrhage and congested blood vessels were a common finding. Siderophages were seen in increased number in most of the cases along with few cases showing macrophages without hemosiderin. Perls staining was done in those cases to confirm the presence of siderophages. In our study, calcification was observed in less than half of the cases. Ossification, as a degenerative change, was also noted by Isobe et al. in 2004 during their evaluation of imaging findings in cases of ancient schwannoma, although it was not detected radiographically.[10] Similarly, in our study, a case involving a large mass measuring 10 cm in its greatest diameter, located in the lumbar region, exhibited ossification as a histomorphological feature, among others. Understanding the full spectrum of histomorphological characteristics seen in ancient schwannoma can provide valuable insights for distinguishing these cases from malignant tumors.

Ancient schwannoma is typically benign, solitary, and slow-growing. Originating from Schwann cells of the nerve sheath, it often closely abuts major nerves. The standard treatment for any benign lesion is excision without additional medical intervention. However, subtotal excision increases the risk of local recurrence, although such recurrences are rare and have been infrequently reported in the literature.[13,14]

Conclusion

In conclusion, ancient schwannoma presents as a rare neurogenic tumor with distinctive histological features and a propensity for slow growth. Awareness of its characteristic secondary changes and detailed histomorphological spectrum aids in accurate diagnosis and ensures optimal management outcomes for patients. Continued research and clinical vigilance are necessary to further elucidate its pathogenesis and refine diagnostic and therapeutic strategies.

Author contributions

1. Study design, data collection, data analysis, data interpretation, literature search, generation of figures: Dr Chaithra GV, Dr Soumya Gupta, Dr Rakshatha Nayak 2. Writing of the manuscript drafting the article or revising it critically for important intellectual content, and final approval of the version to be published: All authors.

Declaration of conflicting interest

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Ethical statement

Ethical approval

The Institutional Ethics Committee (Kasturba Medical College, Mangalore), Reg. No. ECR/541/Inst/KA/2014/RR-20, DHR Reg. No. EC/NEW/INST/2020/742 waived the need for ethics approval and patient consent for the collection, analysis and publication of the retrospectively obtained and anonymised data for this non-interventional study.

ORCID iD

Rakshatha Nayak https://orcid.org/0000-0002-7257-1465

Data availability statement

All data generated or analyzed during this study are included in this published article.

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