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Intracranial Ancient Schwannoma Clinicopathological Update: Review of the Literature

Sunil Vitthalrao Jagtap*[1], Shubham S Jagtap[2], Abhilasha S. Jadhav[3], Riddhi S. Gaonkar[1], Bhumika M Siddhpara[1] and Ipsita Singh[1]

[1]Department of Pathology, KVV (Deemed to be University), Krishna Institute of Medical Sciences, India

[2]Department of Medicine, KVV (Deemed to be University), Krishna Institute of Medical Sciences, India

[3]Department of Pharmacology, KVV (Deemed to be University),Krishna Institute of Medical Sciences Deemed University, India

***Corresponding author:** Sunil Vitthalrao Jagtap, Department of Pathology, KVV (Deemed to be University), Krishna Institute of Medical Sciences, Karad-415110, India.

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Abstract

Schwannoma is a relatively uncommon, slow-growing, benign tumor that is derived apparently from the Schwann cells lining the nerve sheath. Ancient schwannoma is difficult to diagnose based on clinical and radiological features alone, hence definitive pathological diagnosis is necessary. A 50-year-old female patient presented with complaints of occipital headache, right sided loss of hearing, pain in ear, right hand weakness, unable to write, vertigo, and tinnitus, also deviation of angle of mouth to right side and difficulty in left eye closure since 2 weeks. No history of head trauma. No history of hypertention, diabetes. Pure tone audiometry showed down-sloping high frequency sensorineural hearing loss in the right ear. MRI: A large solid cystic spaceoccupying lesions (SOL), measuring 4.4x4.6x4.2cm at right cerebella-pontine angle extending to right vestibular cannal. The impression given was large solid cystic SOL suggestive of right vestibular schannoma. On histopathology tumor composed of spindle cells arranged in bundles and fascicles. Cellular areas show spindle cells arranged in palisading fashion and having organoid arrangement forming Verocay bodies (Antoni Type A areas). The cells in Antoni B areas have round condensed nuclei and indistinct cytoplasm. In other areas,tumor cells are loose, separated by abundant edematous stroma and numerous cysts are noted. The foci of increased cellularity, nuclear pleomorphism without mitosis were noted. Many irregular, multilobed hyperchromatic multinucleation containing intranuclear vacuoles were seen. Focal degenerative changes, hemosiderin deposition, inflammatory cell infiltration were noted.On histopatholical features reported as Ancient schwannoma from right cerebello-pontine angle.The immunohistochemistry showed SOX10, S100 – positivity and MIB1 (Ki 67) proliferation index was 1-2%. Herewith present clinical, radiological, histopatholical, immunohistochemical features and treatment of Ancient Schwannoma with review of literature.

Keywords: Intracranial Ancient Schwannoma; Cerebellopontine Angle Tumors; Pathology; Vestibular Schwannoma

Abbreviations

AS: Ancient Schwannoma; MRI: Magnetic Resonance Imaging; CT: Computed Tomography; SOL: Space-Occupying Lesion; CPA: Cerebellopontine Angle; IHC: Immunohistochemistry; WHO: World Health Organization; NF2: Neurofibromatosis Type 2; CNS: Central Nervous System; SOX10: SRY-Box Transcription Factor 10; S100: S100 Calcium-Binding Protein; Ki-67: Ki-67 Proliferation Index; MIB-1: Mindbomb Homolog-1 Labeling Index; H&E: Hematoxylin and Eosin; T1WI: T1-Weighted Imaging; T2WI: T2-Weighted Imaging; SWI: Susceptibility-Weighted Imaging.

Introduction

Schwannomas are benign peripheral nerve sheath tumors arising from Schwann cells [1]. The majority of schwannomas occur sporadically; however, a small proportion are associated with Neurofibromatosis Type 2 (NF2), an inherited autosomal dominant disorder caused by germline mutations in the NF2 gene located on chromosome 22q12 [2]. The NF2 gene encodes merlin (schwannomin), a tumor suppressor protein that plays a crucial role in regulating cell proliferation, adhesion, and cytoskeletal organization. Loss of merlin function predisposes affected individuals to the development of multiple schwannomas and other nervous system tumors.

Ancient schwannoma (AS) is now recognized as a rare histopathological variant, accounting for approximately 10% of all schwannomas [3]. It is characterized by a prolonged clinical course and slow growth, resulting in marked secondary degenerative changes within the tumor. The ancient schwannoma shows histological characteristics of degenerative changes that develops over the long term progression of the tumor, hence the name Ancient. Despite the pronounced degenerative alterations, ancient schwannomas remain benign lesions with an excellent prognosis following complete surgical excision.

The characteristic histopathological features of AS are primarily attributable to its long-standing nature. Grossly, these tumors are often larger than conventional schwannomas due to their prolonged period of growth. Microscopically, they demonstrate extensive degenerative changes, including hypocellular areas, stromal hyalinization, cystic degeneration, fibrosis, calcification, xanthomatous (fatty) change, hemorrhage, and thick-walled hyalinized blood vessels. Nuclear atypia, hyperchromasia, and pleomorphism may also be present; however, these changes represent degenerative phenomena rather than malignant transformation, as mitotic activity remains low or absent. The characteristic biphasic Antoni A and Antoni B architectural patterns may be preserved but are often partially obscured by these extensive degenerative changes [4,5].

AS can occur in any location containing peripheral nerves, although they have a predilection for deep-seated anatomical sites.6 The most affected locations include the flexor surfaces of the extremities, head and neck region, posterior spinal nerve roots, cerebellopontine angle, mediastinum, thorax, retroperitoneum, and pelvis. These tumors are more frequently encountered in middle-aged and elderly individuals, likely reflecting the prolonged duration required for the development of their characteristic degenerative changes. Because of their indolent growth and deep anatomical location, ancient schwannomas often remain asymptomatic until they attain a considerable size or produce symptoms secondary to compression of adjacent neurovascular structures [6].

Schwannomas are the primary lesion of cranial nerves involving trigeminal, facial, glossopharyngeal, vagus, and sometimes even accessory cranial nerve. Most commonly, schwannomas impact the central nervous system by involving the vestibular branch of cranial nerve VIII or the dorsal roots of the spinal cord. Intra-cranial schwannomas account for less than 8% of brain tumors, among which more than 80% arise from the vestibular nerve at cerebellopontine angle [7].

Case Scenarios with Review literature

Intracranial Ancient Schwannoma

Ancient schwannoma is a subtype of schwannoma with degenerative features, which often progresses slowly over a long period of time. A 50-year-old female patient presented with complaints of right sided loss of hearing and pain in ear of 6 months duration. Right hand weakness and unable to write. Associated with vertigo, tinnitus, swaying of body to the left side of 6 months duration. She also had occipital headache for 2 months back, and deviation of angle of mouth to right side and difficulty in left eye closure for 2 weeks. No history of head trauma. No history of hypertention, diabetes. Pure tone audiometry showed down-sloping high frequency sensorineural hearing loss in the right ear. On MRI showed a large solid cystic space-occupying lesions (SOL), measuring 4.4x4.6x4.2cm at right cerebellopontine angle extending to right vestibular cannal (Figure 1).

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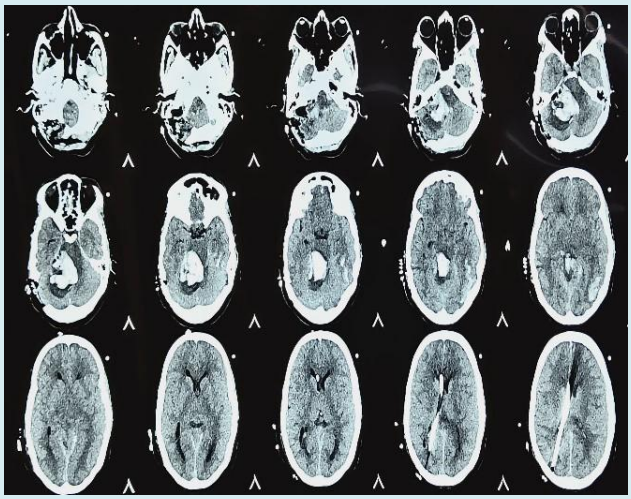


Figure 1: MRI Showed a Large Solid Cystic Space-Occupying Lesion at Right Cerebellopontine Angle.

Solid component of the SOL appears heterogeneously hyperintense on T2WI and heterogeneously on TIW images. Multiple tiny foci of blooming are noted within the SOL on SW images. No evidence of diffusion restriction. This lesion has caused moderate compression of pons and mild compression of right cerebellar hemisphere. It is causing mild compression and displacement of 4th ventricle. The impression given was large solid cystic space-occupying lesions suggestive of right vestibular schannoma. Retromastoid suboccipital craniotomy with excision of tumor was done. On gross we received two, irregular, yellow-brown, soft tissue pieces aggregating to 2x0.8x0.5 cm (Figure2).



Figure 2: Gross Irregular, Yellow-Brown Tumor.

Cut section reveals yellowish to brownish areas. Microscopic sections studied show a tumor composed of spindle cells arranged in bundles and fascicles (Figure 3). Cellular areas show spindle cells arranged in palisading fashion and having organoid arrangement forming Verocay bodies (Antoni Type A areas). The cells in Antoni B areas have round condensed nuclei & indistinct cytoplasm (Figure 4). In other areas, tumor cells are loose, separated by abundant edematous stroma and numerous cysts are note (Figure 4). The foci of increased cellularity, nuclear pleomorphism without mitosis were noted. Many irregular, multilobed hyperchromatic multinucleation containing intranuclear vacuoles were seen (Figure 5). The intervening stroma was fibro-collagenous and myxoid. Focal degenerative changes, hemosiderin deposition, inflammatory cell infiltration were noted. On histopatholical features reported as Ancient Schwannoma at right cerebello-pontine angle. The immunohistochemistry showed SOX10, S100 – positivity and MIB1 (Ki 67) proliferation index was 1-2%.

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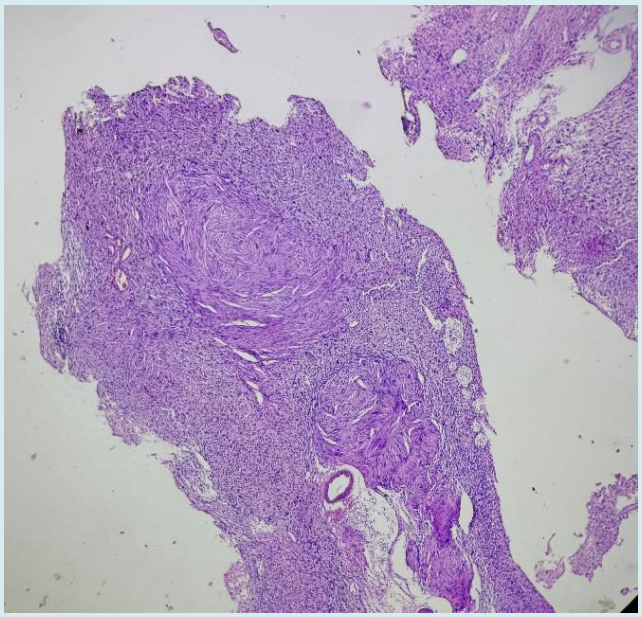


Figure 3 : Tumor Composed of Spindle Cells Arranged in Bundles And Fascicles (H& Estain ,40x).

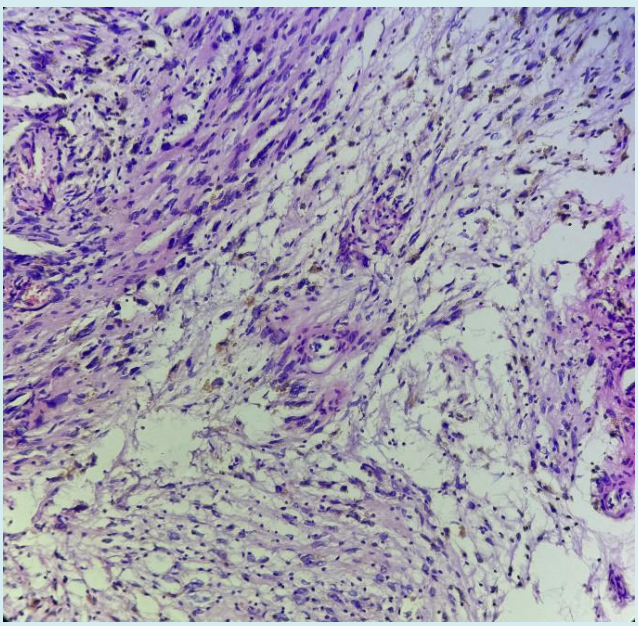


Figure 4 : Cellular Areas Shows Spindle Cells Arranged in Palisading Fashion and Having Organoid Arrangement Forming Verocay Bodies (Antoni Type A Areas). The Cells in Antoni B Areas (H& E Stain ,100x).

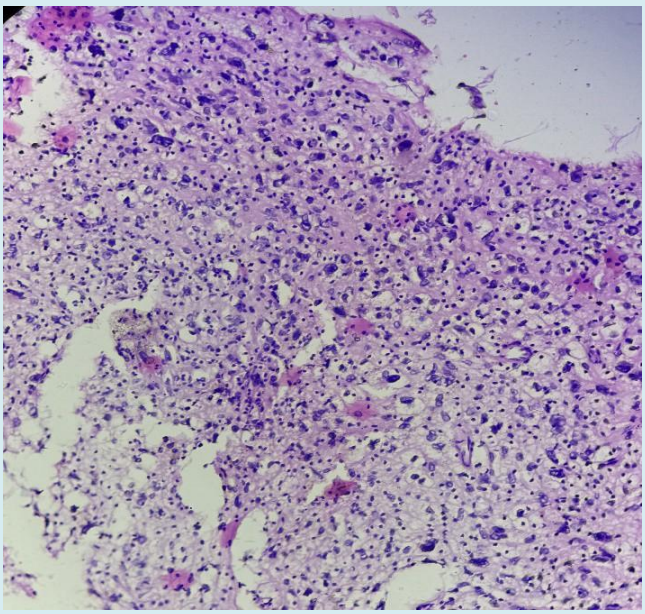


Figure 5: Foci of Increased Cellularity, Nuclear Pleomorphism, Multinucleation without Mitosis Were Noted (H& E Stain ,100x).

Discussion

Intracranial Ancient Schwannoma Overview

The term “ancient schwannoma” was first introduced by Ackerman and Taylor in 1951 during their clinicopathological evaluation of intrathoracic neurogenic tumors [8].

They observed schwannomas exhibiting extensive hypocellular areas and attributed these findings to longstanding degenerative changes rather than malignant transformation. Based on these distinctive histopathological features, they coined the term “ancient schwannoma” to describe this unique benign variant of schwannoma. AS is a pathological subtype of schwannoma. Tsuchiya, et al. reported first case of intracranial ancient schwannoma arising from the vestibular nerve [9].

Ugokwe K, et al. [5] reported the first case of intracranial AS and only three cases of intracranial AS have been reported upto 2005, all of which were trigeminal in origin [5]. A larger institutional study by Tsuchiya and Ikemura (2024) at the University of Tokyo analyzed 174 sporadic intracranial schwannomas and identified 13 cases (7.5%) of the ancient variant [10]. To our knowledge, AS of the intracranial region is an extremely rare histological variant, with fewer than 25 cases documented in English literature.

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Neuro Radiological Imaging of Intracranial Ancient Schwannoma

Recognizing Ancient Schwannoma (AS) can be challenging, particularly in asymptomatic patients or those presenting with only subtle symptoms, such as localized swelling, which often remains unnoticed until the tumor attains a considerable size. In our study, lesion sizes ranged from 1.5 to 11 cm in diameter, with 15 cases measuring more than 6 cm.

Radiologically AS are characterized by larger tumor size and a higher prevalence of cystic degeneration, intratumoral hemorrhage, and calcification compared with conventional schwannomas. Their substantial size and marked heterogeneity frequently mimic malignant neoplasms, particularly on MRI, where they typically appear as large, heterogeneous, and intensely enhancing soft-tissue masses. These imaging features may lead to diagnostic confusion with malignant peripheral nerve sheath tumors, synovial sarcomas, malignant fibrous histiocytomas, liposarcomas, and hemangiopericytomas, especially when prominent cystic components are present. Multivariable analysis revealed that cysts were a significant feature of patients with AS. Shultz propose considering AS in cases where MRI reveals a hypervascular soft-tissue mass with cystic regions, accompanied by amorphous calcifications on radiography. Isobe K imaging of ancient schwannoma.

Neuroimaging plays a pivotal role in the diagnosis of AS by delineating tumor extent, evaluating the involvement of adjacent neurovascular structures, and guiding surgical planning. Magnetic resonance imaging (MRI) is the imaging modality of choice. On MRI, trigeminal schwannomas typically demonstrate low signal intensity on T1-weighted images and high signal intensity on T2-weighted images, often with heterogeneous contrast enhancement reflecting cystic degeneration, hemorrhage, or other degenerative changes. On MRI or CT imaging, intracranial ancient schwannomas often exhibit radiological features that differ markedly from those of conventional schwannomas, frequently leading to preoperative misdiagnosis. As a result, they are commonly mistaken for other intracranial lesions, such as meningiomas, hemangiomas, or malignant sarcomas.

On computed tomography (CT), AS usually appear as well-circumscribed masses with enhancement of the capsule or pericystic regions, along with enhancement of adjacent degenerative components. Although these imaging characteristics may suggest the diagnosis, they are not specific, and histopathological examination remains the gold standard for definitive diagnosis [11].

Cystic schwannomas typically appear on brain MRI as large, heterogeneously enhancing masses because of the coexistence of solid tumor components and fluid-filled cystic spaces. On MRI, they usually demonstrate peripheral low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. In contrast AS are characterized by heterogeneous enhancement, with a significantly higher incidence of cystic degeneration reported in 72–92% of cases and calcification compared with conventional vestibular schwannomas. Their complex cystic architecture and variable enhancement patterns can closely mimic malignant tumors, making radiological diagnosis challenging [12].

Histopathological Diagnosis of Intracranial Ancient Schwannoma

AS is a rare histopathological variant of schwannoma that develops over a prolonged period and exhibits characteristic degenerative changes. Histologically, it is characterized by a relative reduction in Antoni A areas, along with prominent degenerative features including perivascular hyalinization, intratumoral hemorrhage, cystic degeneration, necrosis, calcification, and marked nuclear atypia with hyperchromasia. Despite the striking nuclear pleomorphism, mitotic activity is typically absent or minimal, helping to distinguish ancient schwannoma from malignant peripheral nerve sheath tumors. These pronounced degenerative and atypical features can pose significant diagnostic challenges and may lead to an erroneous diagnosis of malignancy.

Several histological variants of schwannoma have been described, including cellular, plexiform, epithelioid, ancient, and melanotic (melanocytic) schwannomas, each demonstrating distinct morphological characteristics while sharing a common Schwann cell origin [13,14].

Schwannoma exhibiting extensive degenerative changes is termed ancient schwannoma, a rare histological variant that accounts for approximately 0.8% of all soft-tissue tumors. It is typically a large, deeply situated, slow-growing lesion of long duration. Intracranial ancient schwannoma, particularly involving the vestibular nerve, is an uncommon benign neoplasm characterized by marked degenerative alterations, including cystic degeneration, hyalinized blood vessels, calcification, haemorrhage, hemosiderin deposition, and inflammatory cell infiltration [15].

Histologically, AS demonstrates prominent cellular and nuclear atypia with irregular, multilobulated, hyperchromatic nuclei, often containing intranuclear cytoplasmic vacuoles. Despite these striking cytological features, mitotic activity remains absent or minimal, supporting its benign nature and

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helping to distinguish it from malignant peripheral nerve sheath tumors.

AS is classified as a Grade 1 tumor as per the World Health Organization (WHO) tumors of the central nervous system, meaning it is definitively benign and extremely slowgrowing. AS is a benign tumor with a low Ki-67 index (2–3%) [16].

Histopathological Challenges and differential Diagnosis in Ancient schwannoma

AS is characterized by marked degenerative nuclear atypia, including pleomorphic, hyperchromatic, and enlarged nuclei. These histopathological features can mimic malignancy, frequently leading to diagnostic challenges and misdiagnosis as a malignant tumor. The degenerative changes are attributed to the long-standing, slow-growing nature of these tumors and are most commonly observed in elderly individuals. Degenerative alterations such as cystic change, calcification, hemorrhage, hyalinization, and, less commonly, ossification have been described. Ossification as a degenerative feature was also reported by Isobe et al. in 2004 during their evaluation of the imaging characteristics of ancient schwannomas. In vestibular schwannomas, the cystic variant is typically associated with larger tumor size, more rapid growth, and a shorter duration of symptoms than the solid variant, with matrix metalloproteinase-2 proposed as a potential contributor to cyst formation and poorer surgical outcomes [17-19].

Immunostaining of this tumor is positive for S-100, similar to that for other schwannoma subtypes [20,21]. AS show strong positivity for the S100 IHC marker in neural cells scattered in a loose degenerative stroma Table 1.

Year	Authors	Age/Gender	Ancient Schwannoma tumor location	Clinical presentations	Radiological features	Treatment
2005	Ugokwe K, et al. [5]	23year/male	Trigeminal Nerve	Headache, blurred vision, and ataxic gait	Rim-enhancing cerebellopontine angle (CPA) lesion	Gross-total macroscopic excision; uneventful recovery
2007	Mardi K, et al. [22]	42 year/ female	Right temporal lobe	Headache, Solid	Cystic mass lesion	Total resection
2010	Agrawal A, et al. [23]	70year/male	Left temporal region	Headache and one episode of generalized tonic-clonic seizures	Heterogeneous enhancing mass lesion left temporal region with perilesional oedema	Left frontotemporal craniotomy with near-totaldecompression of the lesion
2017	Micovic MV, et al. [4]	71year/ female	Olfactory Nerve	Generalized seizures	Intracranial aneurysm	Complete resection
2020	Al-Shudifat A, et al. [24]	35year/ female	Trigeminal Nerve	Seizures and left-sided weakness	Large cystic temporal lesion	Two-stage complete excision
2000 to 2021	Tsuchiya T, et al. [10] singleinstitution, retrospective study	14-76 year, male(46%) 13cases of AS out of174 intracranial schannomas	Vestibular , Trigeminal,other cranial nerves	General	MRI -tumoral cysts, bleeding, and calcification	Complete resection /Salvage treatment (surgery or radiosurgery)
2022	Otero-Fernández P, et al. [25]	61 year/ male	Accessory Nerve (XI) right cerebellomedullary cistern tumor	Headache and neck stiffness	Giant cystic lesion (45 mm); first reported case at the intracisternal nerve component	Near-total resection; cystic regrowth at 13 months; patient deceased after 2nd surgery

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2022	Tsuchiye T, et al. [9,26]	53 year/ female	Vestibular Nerve (CPA)	headache, hearing loss, dizziness, and tinnitus.	Multiple cystic lesions Rapid growth, High Ki-67 index (5%)	Near-total resection; early recurrence at 5 moths treated with Gamma knife
2022	Takeuchi Y, et al. [12]	61year/ male	Left hemisphere cerebellum	disorientation ,headache,	cystic lesion (6.5 cm)in left hemisphere cerebellum with a mural nodule , calcification	Total gross surgical excision
2024	Das P, et al. [27]	46 year/ male	Intramedullary	Headache,rightsided somatic and neuralgic shoulder pain and neck tightness	exophytic, lobulated, peripherally enhancing lesion at right hemimedulla and cervicomedullary junction	Surgery total excision of the tumor
2026	Jagtap SV, et al. present case	50 year / female	Right CP angle to vestibular nerve	vertigo, tinnitus, headache. right sided loss of hearing	large solid cystic SOL , measuring 4.4x4.6x4.2cm right cerebello-pontine angle.	Retromastoid suboccipital craniotomy with excision of tumor

Table 1: Intracranial ancient schwannoma review of the literature cases.

Treatment of Ancient Schwannoma

Clinically AS are characterized by slow progression and an indolent, long-standing clinical course. Despite their marked degenerative histological features, they are benign neoplasms with an excellent prognosis. Complete surgical excision remains the treatment of choice for ancient schwannomas and is generally curative, with preservation of the involved nerve whenever feasible [28,29]. Microscopic surgical excision is the preferred approach for symptomatic or large intracranial AS. Tumor enucleation is the technique of choice, as it enables meticulous removal of the tumor while preserving the structural integrity and functional continuity of the parent cranial nerve. Intracranial AS have been reported to be strongly associated with cyst formation while maintaining a benign clinical course, with low recurrence rates and infrequent need for salvage treatment. Accordingly, the primary goals of surgical management are complete tumor resection, preservation of neurological function, and minimization of postoperative morbidity and mortality. Once removed, overall prognosis is good, the recurrence rate is exceptionally low, and the long-term outlook is excellent. Malignant transformation is virtually non-existent.

Conclusion

Ancient schwannoma is typically benign, solitary, and slow-growing tumor . It is a subtype of schwannoma with degenerative features. Intracranial AS is a extremely rare benign tumor . Awareness of its characteristic secondary changes and detailed histomorphological spectrum aids in accurate diagnosis and ensures optimal management outcomes for patients. This review highlights the various cases and its importance in histomorphological evaluation to distinguishing these benign tumors from malignant counterparts, thereby guiding appropriate clinical management strategies.

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