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ORIGINAL ARTICLE

Degenerated (Ancient) Schwannomas: Unraveling Unusual Locations and Treatment Management

Dejenere (Eski) Schwannomlar: Olağandışı Yerleşimlerin Çözülmesi ve Tedavi Yönetimi

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ABSTRACT

Introduction: Schwannomas, originating from Schwann cells in peripheral nerve sheaths, exhibit diverse clinical manifestations and unpredictable behavior. Among them, ancient schwannomas, with distinctive degenerative features, present in atypical locations and pose diagnostic challenges. This study explores their unique characteristics and implications for diagnosis and management.
Material and Methods: The study was designed as a retrospective analysis of 7 adult patients aged ≥18 years diagnosed with paraspinal, presacral, sacral, or para-aortic tumors, and all histologically confirmed as ancient schwannomas. Data for analysis were collected from patients treated and followed up at Ankara City Hospital between April 2017 and December 2022. Ethical approval and informed consent were obtained before inclusion in the study.
Results: The most common symptoms included the presence of a local lump (71,4%) and localized or radiating pain (57,1%). Notably, one patient (14,2%) was incidentally diagnosed during the evaluation process. Surgical intervention played a crucial role in the management of these tumors, with 71,4% of patients underwent complete resection while 28,5% underwent subtotal resection. Tumor recurrence occurred in 42,8% of cases, prompting the administration of radiotherapy as part of the treatment strategy. Imaging findings, particularly on MRI, played a crucial role in the accurate identification of ancient schwannomas. These tumors displayed isointensity on T1-weighted images and heterogeneous hyperintensity on T2-weighted images, along with distinctive heterogeneous contrast enhancement.
Conclusion: Ancient schwannomas exhibit unique histological features and distinctive MRI characteristics, differentiating them from other nerve sheath tumors. Early diagnosis and complete surgical resection offer favorable outcomes. Awareness of this entity is essential for managing peripheral nerve sheath tumors effectively.

Keywords: Schwannoma, Ancient, Benign tumor, neural tumors, Schwann cells.

ÖZ

Giriş: Periferik sinir kılıflarındaki Schwann hücrelerinden kaynaklanan Schwannomlar, çeşitli klinik belirtiler ve öngörülemeyen davranışlar sergilerler. Bunlar arasında, belirgin dejeneratif özelliklere sahip olan eski schwannomlar atipik lokasyonlarda bulunur ve tanısal zorluklar oluşturur. Bu çalışma, bunların benzersiz özelliklerini ve tanı ve yönetim için etkilerini araştırmaktadır.
Gereç ve Yöntemler: Çalışma, paraspinal, presakral, sakral veya para-aortik tümör tanısı konan ve histolojik olarak antik schwannom olduğu doğrulanan ≥18 yaşındaki 7 yetişkin hastanın retrospektif analizi olarak tasarlanmıştır. Analiz için veriler, Nisan 2017 ile Aralık 2022 tarihleri arasında Ankara Şehir Hastanesinde tedavi ve takip edilen hastalardan toplanmıştır. Çalışmaya dahil edilmeden önce etik onay ve bilgilendirilmiş onam alınmıştır.
Bulgular: En sık görülen semptomlar lokal bir kitlenin varlığı (%71,4) ve lokalize veya yayılan ağrı (%57,1) idi. Özellikle, 1 hastaya (%14,2) değerlendirme sürecinde tesadüfen tanı konuldu. Cerrahi müdahale bu tümörlerin yönetiminde önemli bir rol oynamış, hastaların %71,4'üne tam rezeksiyon, %28,5'ine ise subtotal rezeksiyon uygulanmıştır. Vakaların %42,8'inde tümör nüksü meydana gelmiş ve bu da tedavi stratejisinin bir parçası olarak radyoterapi uygulanmasını gerektirmiştir. Görüntüleme bulguları, özellikle de MRG, eski schwannomların doğru tanımlanmasında çok önemli bir rol oynamıştır. Bu tümörler T1 ağırlıklı görüntülerde izointensite ve T2 ağırlıklı görüntülerde heterojen hiperintensite ve belirgin heterojen kontrast artışı göstermiştir.
Sonuç: Antik schwannomlar benzersiz histolojik özellikler ve ayırt edici MRG özellikleri sergileyerek diğer sinir kılıfı tümörlerinden ayrılırlar. Erken tanı ve tam cerrahi rezeksiyon olumlu sonuçlar sağlamaktadır. Bu antitenin farkında olmak, periferik sinir kılıfı tümörlerini etkili bir şekilde yönetmek için gereklidir.

Anahtar Kelimeler: Schwannoma, Antik, Benign tümör, nöral tümörler, Schwann hücreleri.

Introduction

Schwannomas, benign nerve sheath tumors arising from Schwann cells, have long intrigued medical researchers and clinicians with their diverse clinical manifestations and unpredictable behavior (1). Among the intriguing subsets of these tumors are the degenerated (ancient) Schwannomas, which exhibit distinctive histopathological characteristics, and they are found in atypical locations within the body (2). This article delves into the enigmatic world of degenerated Schwannomas, shedding light on their unique features, unusual occurrences, and the implications these atypical presentations hold for diagnosis, treatment and patient

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care. Conventional Schwannomas, though generally benign, can still cause significant morbidity due to their location and compressive effects on surrounding structures (3). However, degenerated Schwannomas present an additional layer of complexity, as their histological alterations give rise to a fascinating set of challenges for clinicians and pathologists alike (4). While much research has been conducted on typical Schwannomas, there remains a knowledge gap concerning the less common degenerated variants.

Typically, these tumors are most commonly observed between the ages of 20 and 50 and present with clinical features that include the presence of a palpable mass, reduced nerve function, and localized pain (5). While Schwannomas can develop from any central or peripheral nerve within the body, they are notably absent in the olfactory and optic nerves (5). Among the regions with the highest prevalence of Schwannomas are the head, neck, mediastinum, retroperitoneum and the inner surface of the extremities. Interestingly, the vestibulocochlear nerve (CN VIII) stands out as the most frequent cranial nerve from which these tumors originate.

In clinical practice, both computed tomography (CT) and magnetic resonance imaging (MRI) have demonstrated their value by providing information about potential malignant attributes, the existence of local or distant metastases and any neural entanglement. However, there is no distinctive imaging trait specific to Schwannomas, making it essential to rely on histopathological analysis for an unequivocal diagnosis. On a macroscopic level, Schwannomas are identifiable by their flesh-colored appearance and well-defined masses or large cysts enclosed by a collagenous capsule (4). Prominent histopathological characteristics encompass the presence of Verocay bodies, hyalinized vessels, and variable zones exhibiting Antoni A (densely packed spindle fibers) and Antoni B (less dense, microcystic, hypocellular regions containing macrophages and collagen) (1). Immunohistochemical analysis usually demonstrates widespread, robust expression of pericellular type IV collagen and S-100 protein (1,4).

As the understanding of Schwannomas continues to evolve, their association with neurocutaneous syndromes and the role of NF2 tumor suppressor gene suppression are subjects of ongoing research. Moreover, the intricate interplay between clinical features, imaging findings and histopathological insights holds paramount importance in facilitating accurate diagnosis and guiding optimal treatment strategies.

Throughout this article, we will explore the distinct morphological changes seen in degenerated Schwannomas, which set them apart from their conventional counterparts. Ancient schwannoma, a rare subtype of schwannoma, displays a distinctive histological profile featuring hemorrhage, nuclear hyperchromatism, calcification, cystic degeneration pleomorphism and myxoid stroma (2). The presence of these atypical characteristics can create diagnostic challenges, potentially leading to misdiagnosis as a malignant tumor. Understanding the unique attributes of ancient schwannomas is crucial for accurate identification and appropriate management of this benign but diagnostically deceptive neoplasm. Additionally, we will investigate the intriguing phenomenon of degenerated Schwannomas occurring in atypical locations within the body. This unusual propensity for localization raises important questions about the underlying pathogenesis and may have crucial implications for their clinical management.

In the following pages, we will explore the intricacies of degenerated Schwannomas, presenting a comprehensive analysis of their histopathological features, clinical manifestations, diagnostic challenges and therapeutic options. It is expected that this article will not only pique the interest of researchers and clinicians but also offer valuable insights that will shape the future management of these captivating tumors.

Materıal and Methods

Study Design and Patient Selection:

This retrospective study was conducted at tertiary education and research hospitals to investigate prognostic factors, patient characteristics and outcomes of ancient schwannomas in adult patients aged ≥18 years. The study focused on 7 individuals diagnosed with paraspinal, presacral, sacral or para-aortic tumors. All cases were histologically proven to be ancient schwannomas. The data for analysis were collected from patients treated and followed up at Ankara City Hospital and Erol Olçok Training and Research Hospital between April 2017 and December 2022. Ethical approval was obtained from the Institutional Review Board, and written informed consent was obtained from each patient before inclusion in the study.

Data Collection and Preoperative Assessment:

All patients underwent computed tomography (CT) and/or magnetic resonance imaging (MRI) with contrast enhancement scans both prior to and following their surgical procedures. Individuals under the age of 18 and those with a diagnosis of conventional Schwannomas were not included in the study. Prior to surgery, comprehensive preoperative blood tests, extensive neurological assessments, and cranial imaging were routinely conducted to identify any preoperative symptoms. The primary symptoms evaluated included visual abnormalities, cranial nerve dysfunction, instability in gait, motor deficiencies, cognitive impairments, sensory disruptions, and the most commonly reported symptom, localized pain.

Treatment Approach:

Every patient underwent a maximal safe extended surgical resection, and radiotherapy was integrated into the treatment protocol. A minimally invasive approach was employed as an operative technique

to achieve maximal tumor removal. The primary focus was on preserving root function during the resection of intraspinal tumor extensions, with emphasis on utilizing intraoperative neurophysiologic monitoring. For intraspinal extensions spanning up to 3 spinal levels, a unilateral hemilaminectomy technique was utilized. This involved retaining paravertebral muscles on the tumor side to access the hemilaminae, which were then removed using a high-speed pneumatic drill to expose the dural sac.

In cases of paraspinal tumors, often dorsolaterally positioned due to their origin from the dorsal root, a posterior or posterolateral approach was employed. Resection of dumbbell tumors presented additional challenges, necessitating a combination of techniques such as multilevel laminectomy, costotransversectomy and anterior exposure involving neck dissection, thoracotomy, or retroperitoneal exposure.

Ensuring a watertight closure, the dura mater was sutured with 4–0 wire, and additional reinforcement was provided using fibrin glue and epidurally applied fat. In instances requiring laminectomy, a bilateral muscle dissection was performed, followed by removal of laminae to expose and open the dural sac for tumor removal under the operating microscope. Notably, spinal instability did not necessitate instrumentation in any of the cases.

The surgical procedures were categorized into four groups as follows: 1) complete resection, involving the removal of over 95% of the tumor; 2) subtotal resection, characterized by the removal of tumor mass ranging from >50% to <95%; 3) partial resection, indicating the surgical extraction of less than 50% of the tumor; and 4) biopsy. The date of the surgery was regarded as the point of diagnosis.

Statistical Analysis:

Data analysis was performed using IBM SPSS 25.0 (Armonk, NY: IBM Corp.) and MedCalc 15.8 (MedCalc Software bvba, Ostend, Belgium) statistical package programs. Descriptive statistical methods including frequency, percentage, mean, standard deviation, median, and min-max values were utilized to compare qualitative data.

Results

Between 2017 and 2022, a total of 7 adult patients underwent surgical intervention for tumors located in different regions: 2 patients had lumbar paraspinal tumors, 1 had cervical paraspinal tumor, 1 had thoracic paraspinal tumor, 1 had presacral tumor, 1 had sacral tumor, and 1 had para-aortic tumor. The mean age at the time of surgery was 50,1±9 years, and 3 of the patients (42,8%) were male. Among the presenting symptoms, 5 patients (71,4%) experienced a local lump, 4 patients (57,1%) reported localized or radiating pain, 2 patients (28,5%) presented with urinary disturbances, and 3 patients (42,8%) reported tingling sensations. Notably, 1 patient (14,2%) was incidentally diagnosed during the evaluation process (Table 1).

The average maximum diameter of the tumors was measured at 7,4 ± 2,2 cm. In fact, intramuscular schwannomas were frequently associated with the presence of entering and exiting nerves, whereas such nerve involvement was not observed in cases of ancient schwannomas.

Among the patients, 5 (71,4%) underwent complete resection while 2 patients (28,5%) underwent subtotal resection. Following the initial surgeries, 3 patients (42,8%) experienced tumor recurrence, prompting the administration of radiotherapy as part of the treatment strategy (Table 1).

Table 1: Patient characteristics, radiologic findings and pathologic anomalies

Patients	Age	Sex	Localisation	Preop Symptoms	Surgical Resection	MRI Findings	Diameter (cm)	Pathologic findings	Outcome	Complications
1	55	F	Lumbal Paraspinal	Lump, Pain, Tingling sensation	Complete	Split Fat sign, denervation change	11,2	cystic degeneration, fibrosis, lobulation	Cure	None
2	44	F	Lumbal Paraspinal	Lump, Tingling sensation	Complete	Split Fat sign, denervation change	6,5	fibrosis, stromal edema, pleomorphism	Cure	None
3	34	F	Sacral	Lump, urinary disturbances	Complete	Split Fat sign, denervation change	5,4	xanthomatous change, perivascular hyalinization, hyperchromasia	Recurrence, RX	None
4	48	M	Cervical paraspinal	Pain, lump, Tingling sensation	Complete	Split Fat sign, denervation change	8,7	cystic degeneration, fibrosis, perivascular hyalinization, hyperchromasia	Cure	None
5	56	M	Thoracal Paraspinal	Pain, Lump	Complete	Split Fat sign, denervation change	9,1	xanthomatous change, stromal edema, pleomorphism	Cure	None
6	61	M	Pre-sacral	Pain, urinary retention	Subtotal	Split Fat sign, denervation change	6,7	cystic degeneration, fibrosis, lobulation, pleomorphism	Recurrence, RX	None
7	53	F	Para-aortic	Incidentally	Subtotal	Split Fat sign, denervation change	4,7	cystic degeneration, fibrosis, lobulation, pleomorphism	Recurrence, RX	None

M:Male, F:Female, MRI: Magnetic Resonance Imaging, Rx: radiotherapy

Upon examination of MRI findings, all patients exhibited the split fat sign and denervation changes. Ancient schwannomas appeared isointense on T1-weighted images and displayed heterogeneous hyperintensity on T2-weighted images (Figure 1). Furthermore, these tumors exhibited distinctive heterogeneous contrast enhancement, which aided in their differentiation from other lesions (Figure 2). The "split fat sign" refers to the characteristic appearance of an area of fatty tissue being split or displaced by an adjacent mass or tumor (6,7). This sign is often seen in certain soft tissue masses, particularly nerve sheath tumors like schwannomas, where the mass disrupts the normal distribution of fat, resulting in a visible separation or splitting of the fatty tissue. The split fat sign can be helpful in distinguishing certain benign tumors, like schwannomas, from other soft tissue lesions during radiological evaluation (6).

Ancient schwannomas are recognized for their unique degenerative traits, which encompass cystic alterations, fibrosis, stromal edema, xanthomatous transformations and perivascular hyalinization (6) (Figure 3). These modifications are ascribed to the extended growth of the tumor, resulting in vascular insufficiency, that is why they are referred to as "ancient." Despite these changes, ancient schwannomas demonstrate a behavior akin to typical schwannomas. Under microscopic examination, they display regions of cellular density intertwined with a myxoid matrix. However, these cellular areas tend to become sclerotic or fibrotic and may experience degenerative transformations over time, potentially leading to the formation of hematomas and cysts (6,7). The absence of mitoses, cohesive clusters of spindle-shaped cells, and positive immunostaining with S100 help differentiate ancient schwannomas from malignancies (8). Surgical excision is essential for establishing a definitive diagnosis and achieving cure, with complete resection preserving surrounding structures whenever possible. Symptoms of compression such as pain and numbness are common presentations necessitating surgical intervention for these benign tumors.

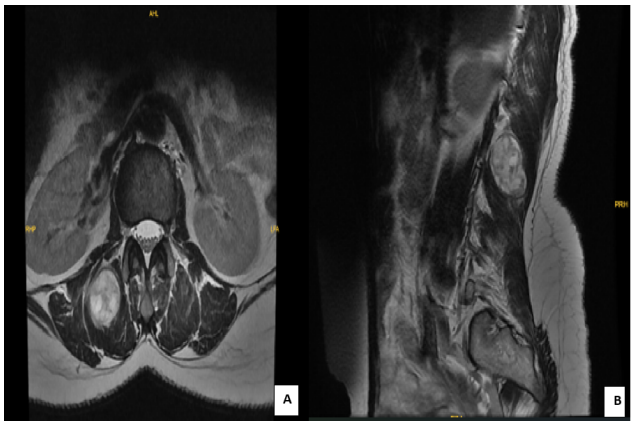

Figure 1: 55-year-old female patient who presented with axial lumbalgia and lump, tingling sensation diagnosed with paraspinal intramuscular mass, non-contrast lumbar MRI was performed. T2 weight MRI showed an encapsulated mass in the right paravertebral muscle. A) axial section, B) sagittal section.

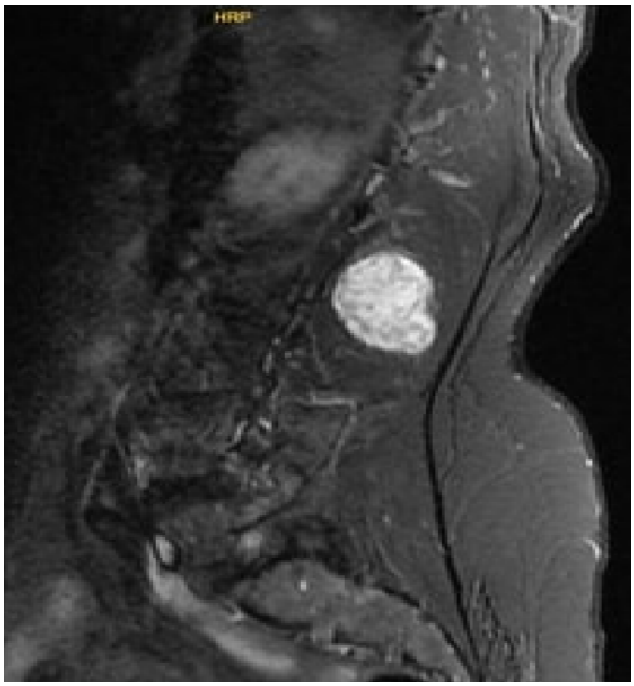

Figure 2: Contrast lumbar MRI was performed on the same patient. It showed well-circumscribed spherical tumor with homogeneous contrast enhancement.

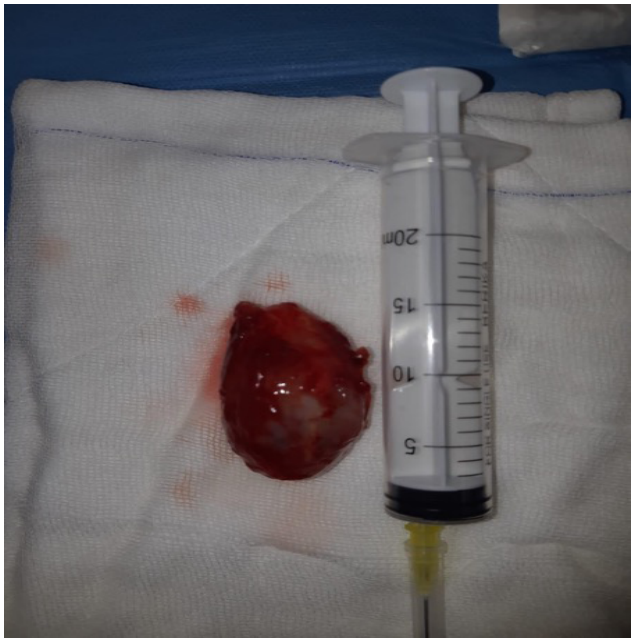

Figure 3: Gross pathological examination of thoracal paraspinal tumour, the 9,1 cm mass revealed a cystic, flesh-tan, focal hemorrhagic and mottled solid mass with yellow, viscous fluid compatible with schwannoma.

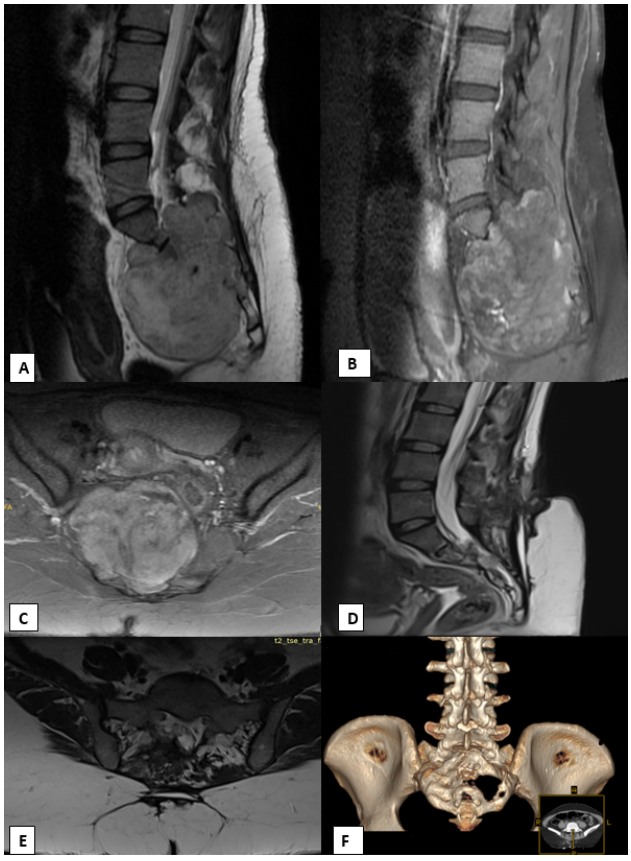

Figure 4: A)Sagittal MRI scan displaying a giant sacral mass in a 34-year-old female patient. The mass appears with heterogeneous intensity on T2-weighted imaging (T2WI). B) Sagittal contrast-enhanced MRI scan revealing the sacral mass. C) Axial contrast-enhanced MRI scan providing an additional view of the sacral mass. D) Postoperative sagittal T2-weighted MRI scan showing the outcome after the excision of the sacral mass. E) Postoperative axial T2-weighted MRI scan displaying the result of the surgical removal of the sacral mass. F) Postoperative 3D computed tomography images of the sacral region, offering a comprehensive visualization of the surgical outcome.

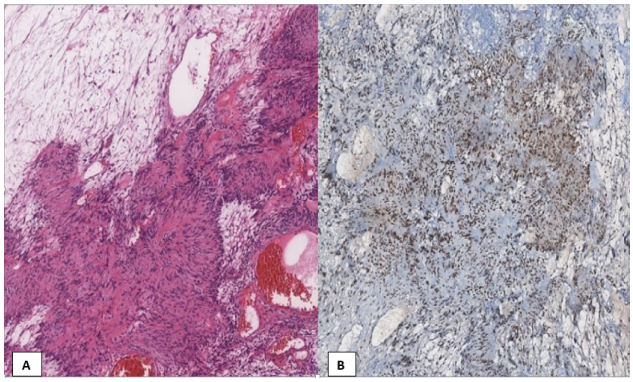

Figure 5: Monotonous spindle cells that form a palisade-like structure in a few focal areas around the vessels that are intact. A) Hematoxylin and Eosin-stained tumor, widespread bleeding, hyalinization and degeneration are observed within the tumor (×10). B) Immunohistochemical staining showed diffuse S-100 positivity and activity with SOX10. Staining with CD34 was negative.

Discussion

Schwannomas, alternatively termed neurilemmomas, are benign tumors that arise from Schwann cells found in the peripheral nerve sheaths, specifically within soft tissues (1). Typically originating from sensory nerves, they may occasionally have a motor nerve origin. The head and neck as well as the extremities are the most common sites of origin. Because of the ample areolar space available, these tumors frequently manifest later, causing compression effects and degenerative alterations. Typically, the clinical progression is gradual and prolonged, with rare occurrences of malignant transformation. Histologically, schwannomas exhibit distinctive features with Antoni A areas, featured by highly cellular spindle-shaped cells, and Antoni B areas, showing a myxoid stroma (5).

Schwannomas, rare encapsulated tumors, are typically found in peripheral nerves of the limbs, head and neck. Extraspinal locations of ancient schwannomas are not very common. Their occurrence in the para-aortic localisation is infrequent, constituting 0,7% to 2.7% of all primary schwannomas, and 0.5% to 1.2% of all para-aortic tumors (9). Retroperitoneal locations are also rarely described in the literature (10). This retroperitoneal localization predominantly affects individuals in their mid-50s, with a slightly higher prevalence in females (2:3 ratio) (11). Various types of schwannomas, including cellular, glandular, epithelioid, melanotic and ancient variants have been identified. Despite their rarity and diverse presentations, the understanding of these tumor types is crucial for accurate diagnosis and appropriate management.

One of the infrequent variations of schwannomas is the ancient schwannoma, which was initially documented by Ackerman and Taylor in 1951 (12). These tumors account for just 0.8% of all soft tissue neoplasms (13). Ancient schwannomas display distinctive degenerative features, including cystic changes, fibrosis, stromal edema, xanthomatous alterations and perivascular hyalinization. Additionally, degenerative nuclear modifications such as pleomorphism, lobulation, and hyperchromasia may be evident. These alterations are attributed to the extended growth or "aging" of the tumor, resulting in vascular insufficiency, that is why they are termed "ancient schwannomas." Despite these degenerative changes, ancient schwannomas exhibit behavior similar to typical schwannomas. Under microscopic examination, they exhibit areas of cellularity interspersed with a myxoid matrix although the cellular regions tend to become sclerotic or fibrotic, potentially leading to the development of hematomas and cysts over time. In particular, the nuclear palisades commonly seen in classic schwannomas are absent in ancient schwannomas. Although nuclear atypia and hyperchromasia are frequent in these tumors, differentiating them from malignancy can be established by the absence of mitotic activity and the preservation of cohesive clusters of spindle-shaped cells. Additional diagnostic confirmation can be achieved through flow cytometry, which assesses DNA ploidy, and immunostaining with S100 protein, further supporting their benign neural origin (6,7,13) (Figure 5).

Ancient schwannomas typically manifest with symptoms related to compression, such as pain

and numbness, necessitating surgical removal for a conclusive diagnosis. A complete surgical excision of the tumor, whenever possible while safeguarding adjacent structures, serves as a curative approach. In this discussion, we have presented two instances of the uncommon pathological condition of ancient schwannomas originating in the retroperitoneum. These tumors are characterized by slow growth and a benign course, often causing pressure-related symptoms. Surgical resection remains the primary treatment, and if there is suspicion of the diagnosis prior to surgery, since recurrences are rare, it is vital that all surrounding structures be protected.

Ancient schwannomas exhibit distinct MRI characteristics that set them apart from other nerve sheath tumors, particularly neurofibromas and malignant lesions. On T1-weighted images, ancient schwannomas appear isointense while on T2-weighted images, they display heterogeneous hyperintensity. Additionally, these tumors exhibit heterogeneous contrast enhancement. Interestingly, these imaging features can sometimes evoke concerns of malignancy during the initial evaluation due to their resemblance to certain malignant tumors.

In contrast, neurofibromas typically present with slightly hyperintense or isointense signals on T1-weighted images while on T2-weighted images, they show heterogeneous hyperintensity with homogeneous contrast enhancement. Understanding these distinctive MRI patterns is essential in accurately differentiating ancient schwannomas from other nerve sheath tumors and preventing misdiagnoses.

When confronted with MRI findings resembling malignancy, clinicians should be aware of the unique radiological features associated with ancient schwannomas, enabling prompt and precise diagnosis, and guiding appropriate management strategies.

Conclusion

In conclusion, ancient schwannomas represent a rare and intriguing subset of soft-tissue tumors. While their degenerative changes can mimic malignancy, meticulous histological examination and immunostaining help confirm their benign nature. Early diagnosis and complete surgical resection with preservation of surrounding structures offer excellent prognosis, making awareness of this entity crucial for clinicians managing patients with peripheral nerve sheath tumors.

Author Contributions

Conceptualization: GG, EÇ, SG, Investigation:GG, EÇ, YŞ, ZD, Project administration: GG, AD, SG, Resources: EÇ, YŞ, ZD, EI, BT, Surgery: GG, AD,EI,BT, Writing – original draft: EÇ, YŞ, ZD, Writing – review & editing: GG, AD

Disclosure Statement

All authors declare that they have no conflict of interest to disclose.

Ethics Statement

This study was approved by the Institutional Review Board (TUEK E1-23-3858), and written informed consent was obtained from each patient.

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