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Clinicopathological, Cytological, and Immunocytochemical Characteristics of 17 Schwannoma Cases Diagnosed by Fine-Needle Aspiration Cytology

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ABSTRACT

Objective: Schwannomas are benign tumors that originate from Schwann cells of the nerve sheath. Fine-needle aspiration cytology (FNAC) is a valuable tool for the pre-operative diagnosis of schwannomas, especially in locations where surgical resection is associated with significant morbidity. In this study, we aimed to identify the clinical, cytological, and immunohistochemical features of 17 schwannoma cases diagnosed by FNAC and to compare our findings with previously published case series in the literature.

Materials and Methods: We retrospectively reviewed 17 cytological specimens from patients with a cytological diagnosis of schwannoma between 2019 and 2024. The clinical data of the patients were retrieved from the hospital information management system. The cases were re-evaluated based on their cytological features.

Results: Of these patients, 10 were female and 7 were male. The patients' ages ranged from 36 to 78 years (mean 54 years). Four cases were hypercellular, seven showed moderate cellularity, and six were hypocellular. In all the cases, the cells formed cohesive fragments. All nuclei exhibited tapering ends and appeared wavy, hook-like, or comma-shaped. All cases displayed filamentous cytoplasmic extensions and syncytium-like clusters. Immunocytochemical evaluation was performed in all but two cases. S100 staining was strong in 14 cases and moderate in one. Sox10 was positive in five cases.

Conclusion: The diagnostic assessment of schwannomas integrates clinical evaluation, imaging, and cyto-histological analysis. FNAC facilitates preoperative planning by characterizing the lesion. Characteristic cytological findings include spindle cell clusters, nuclear palisading, Verocay bodies, and a fibrillary background.

Keywords: Cytological features, Fine-needle aspiration cytology, Schwannoma

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INTRODUCTION

Schwannomas, also known as neurilemmomas, are benign, typically slow-growing tumors that originate from Schwann cells of the nerve sheath.[1,2] These tumors are typically benign, solitary, slow-growing, and well-encapsulated.[2-5] Schwannomas can occur throughout the body but are commonly found in the head-and-neck region.[1] They may arise from cranial nerves, spinal nerve roots, or peripheral nerves.[2,3,6,7] The pre-

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cise etiology of schwannomas remains unclear, although some cases are associated with genetic syndromes such as neurofibromatosis type 2 (NF2).[6] In the early phase, schwannomas generally lack pathognomonic symptoms, with the majority of cases presenting as painless, palpable, solitary masses. In advanced stages, clinical manifestations may include neurological deficits and symptoms related to compression or obstruction.[5]

Fine-needle aspiration cytology (FNAC) is a valuable tool for the preoperative assessment of schwannomas,[5,8] especially in locations where surgical resection is associated with significant morbidity.[9,10] FNAC can help differentiate schwannomas from other lesions, guiding clinical management and surgical planning.[8,9] However, it is essential to recognize the limitations of FNAC, as the cytomorphological features of schwannomas can overlap with those of other spindle cell tumors, potentially leading to diagnostic challenges.[11] In some instances, FNAC may be inconclusive, necessitating further investigation, such as trucut biopsy or imaging studies.[12]

Histologically, schwannomas exhibit two distinct patterns. Antoni A areas consist of compact, elongated cells with cytoplasmic extensions arranged in interlacing fascicles and contain Verocay bodies, typically found in regions of high cellularity with a minimal stromal matrix. The Antoni B areas, on the other hand, are hypocellular, featuring loosely distributed nuclei. Cystic degeneration and localized necrosis may also be encountered.[13]

The cytological features of schwannomas typically reflect their histological architecture, which is characterized by alternating areas of high and low cellularity known as Antoni A and Antoni B areas, respectively.[14] In cytological smears, these areas manifest as fragments of tightly cohesive fascicles with variable cellularity, corresponding to Antoni A areas, and scattered spindle cells against a myxoid background, representing Antoni B areas.[14,15] The presence of fibrillary stroma, consisting of delicate, wispy strands of collagen, is also a common finding,[11,16] contributing to the overall cytomorphological picture. Tumor cells usually have fusiform nuclei, fine chromatin, and an indistinct cytoplasm.[17] Nuclear palisading, a characteristic arrangement of nuclei in parallel rows, can be observed in some cases.[16,17] Verocay bodies, which are acellular areas surrounded by palisaded nuclei, are considered a hallmark of schwannomas but are not always present in cytological specimens. The absence of Verocay bodies does not exclude the diagnosis of schwannoma, especially in certain variants, such as ancient schwannomas.[16]

However, the cytological diagnosis of schwannoma is not always straightforward.[11] Several factors can contribute to diagnostic challenges, including cystic degeneration, hyaline changes, and degenerative atypia.[4,18] Cystic degeneration can result in poor cellularity of the aspirate, making it difficult to identify the characteristic cytomorphological features,[4] whereas degenerative atypia, seen in ancient schwannomas, can mimic malignancy.[18]

To improve the accuracy of cytological diagnosis, ancillary techniques such as immunohistochemistry can be employed. Schwannomas typically show strong and diffuse positivity for the S100 protein, a marker of neural crest origin.[6,19] This immunohistochemical feature can help differentiate schwannomas from other spindle cell lesions that are negative for the S100 protein.[20]

In this study, we aimed to identify the clinical, cytological, and immunohistochemical features of 17 schwannoma cases diagnosed by FNAC and to compare our findings with previously published case series in the literature.

MATERIALS AND METHODS

A retrospective search of the pathology report information system using the keywords "spindle cell" between 2019 and 2025 identified 59 cases diagnosed with "spindle cell proliferation," "proliferating spindle cells," "spindle cell tumorous lesion," and "spindle cell mesenchymal tumor" based on FNAC results. Cases those with other spindle cell tumors, and where slides were unavailable in the archive, were excluded, resulting in a series of 17 cases (28%). Sixteen of these cases were reported as spindle cell mesenchymal neoplasms, with a note that the lesion could be a schwannoma. One case was reported as "spindle cells on a fibrinous background" due to cell scarcity, with schwannoma being the primary differential diagnosis.

All samples were obtained by FNAC performed by a radiologist using 23–25-gauge needles. The clinical and demographic data of the cases were obtained from pathology reports. Each patient had conventional smear preparations, liquid-based cytology slides, and cell blocks in available materials. Air-dried smears were stained with May-Grünwald-Giemsa, whereas alcohol-fixed smears were stained using Papanicolaou staining. Immunohistochemical analysis was performed for diagnostic purposes and was not repeated in the present study. All slides of cases retrieved from archives and re-evaluated for cytomorphological characteristics. Each case was assessed for cellularity, presence of large cohesive tissue fragments, nuclear shape, nuclear palisading, and presence of filamentous cytoplasm.

The cases were re-evaluated based on their cytological features (cellularity, architecture, nuclear shape, pleomorphism, and cytoplasmic features). The histopathological follow-up was noted in available cases.

Statistical Analysis

Data analysis performed using the Statistical Package for the Social Sciences 25.0 program. Descriptive statistics for the evaluation of results were shown in the form of mean, and the nominal variables were shown as the number of cases and (%).

Ethical Approval

This study was approved by the İstanbul Training and Research Hospital Clinical Research Ethics Committee (Number: 107, Date: May 02, 2025) and was conducted under the principles of the Helsinki Declaration.

RESULTS

Of these patients, 10 were female and 7 were male. The patients' ages ranged from 36 to 78 years (mean 54 years). The clinical features of the patients are summarized in (Table 1). In the cytological evaluation, each case was assessed for cellularity, presence of large cohesive tissue fragments, nuclear shape, nuclear palisading, and presence of filamentous cytoplasm.

The cytologic features of the patients are summarized in (Table 2). Four cases were hypercellular (23.5%), seven showed moderate cellularity (41.2%), and six were hypocellular (35.3%). In all the cases, the cells formed cohesive fragments (100%) (Figs 1–4). In 12 cases (70.5%), the tumor cells were also observed to be singly dispersed in the background. All nuclei exhibited tapering ends and appeared wavy, hook-like, or comma-shaped (Figs 1–5).

In one case (5.8%), cells with relatively larger nuclei were present; however, the nuclei still showed tapered ends and fine chromatin structures, similar to the other cases. Nuclear palisading, cellular Antoni A, and hypocellular Antoni B areas were prominent in only two cases (11.7%). No prominent nucleoli were observed in any of the cases.

All cases displayed filamentous cytoplasmic extensions and syncytium-like clusters, with indistinct cytoplasmic borders (Figs 2–4). Mitosis was not observed in any of the cases. Immunocytochemical evaluation was performed in all but two cases. The cell blocks in the two cases did not contain sufficient material for further analysis. In these cases, immunohistochemical analysis was performed on the excised specimens.

S100 staining was strong in 14 cases (82%) and moderate in one (Fig. 6). Sox10 was positive in five cases (29%). No desmin, SMA, or CD34 staining was observed.

The excision materials of seven cases were also examined to confirm the diagnosis of schwannoma. One case was followed up clinically, as the patient did not consent to surgery. Clinical follow-up information was not available for the remaining nine cases.

Table 1. Clinicopathological and ımmunohistochemical characteristics of 17 schwannoma cases

Case number	Age	Sex	Localization	Tumor size (cm)	Immunhistochemistry
1	77	Female	Neck	1.8	S100 + Desmin - CD34 - Ki67 <%1
2	56	Female	Neck	2.8	None
3	49	Female	Axilla	3	S100 + Desmin - SMA - CD34 - Ki67 %1
4	36	Male	Neck	3.9	S100 + CD34 -
5	44	Female	Neck	4.5	S100 + SMA - Desmin - Ki67 %2–3
6	61	Male	Neck	1.6	S100 + SMA - CD34 - Desmin -
7	36	Female	Preauricular	4.5	S100 + Desmin -
8	70	Female	Trunk	4.5	S100 + Sox10 + Desmin - CD117 - SMA - CD34 - Ki67 %1
9	59	Female	Trunk	3	S100 + Sox10 + SMA - Desmin - CD117 - DOG1 - CD34 - Ki67 %2–3
10	46	Female	Neck	2.5	S100 + Sox10 + SMA - Desmin - CD34 -Ki67: %2–3
11	47	Male	Leg	2	S100 + SMA - CD34 - Ki67 %1
12	55	Female	Trunk	4	S100 + SMA - CD34 - Ki67 %1
13	52	Male	Neck	2.7	S100 + SMA - Desmin - CD34 - Ki67 %1
14	50	Male	Axilla	1.4	Sox10 + S100 + CD34 - SMA - Desmin - Ki67%1
15	78	Female	Neck	2.1	S100 + CD68 - SMA -
16	49	Male	Neck	5.5	S100 + Sox10 + SMA - CD34 - Ki67 %1–2
17	56	Male	Neck	2	None

Cases indicated as "None" did not undergo immunohistochemical analysis.

Table 2. Cytological features of fine-needle aspiration samples in 17 schwannoma cases

Case number	Cellularity	Cohesive fragments	Wavy, hook-like nuclei	Palisading cells	Filamentous cytoplasm
1	Hypercellular	Yes	Yes	No	Yes
2	Moderate	Yes	Yes	No	Yes
3	Moderate	Yes	Yes	No	Yes
4	Hypercellular	Yes	Yes	Yes	Yes
5	Hypocellular	Yes	Yes	No	Yes
6	Moderate	Yes	Yes	No	Yes
7	Hypocellular	Yes	Yes	No	Yes
8	Hypocellular	Yes	Yes	No	Yes
9	Hypocellular	Yes	Yes	No	Yes
10	Hypercellular	Yes	Yes	Yes	Yes
11	Hypercellular	Yes	Yes	No	Yes
12	Moderate	Yes	Yes	No	Yes
13	Hypocellular	Yes	Yes	No	Yes
14	Moderate	Yes	Yes	No	Yes
15	Hypocellular	Yes	Yes	No	Yes
16	Moderate	Yes	Yes	No	Yes
17	Moderate	Yes	Yes	No	Yes

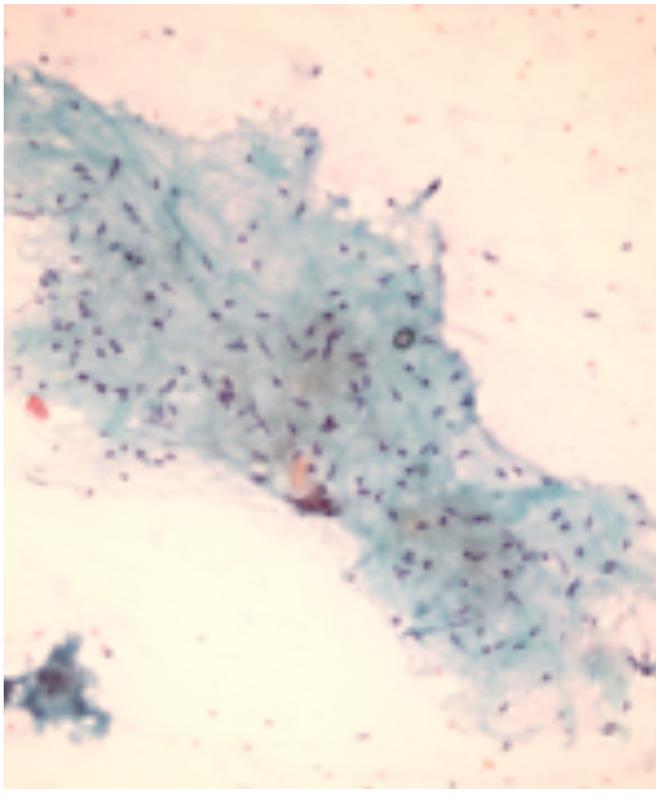

Figure 1. Spindle-like tumoral cells forming a cohesive fragment (Papanicolaou ×200).

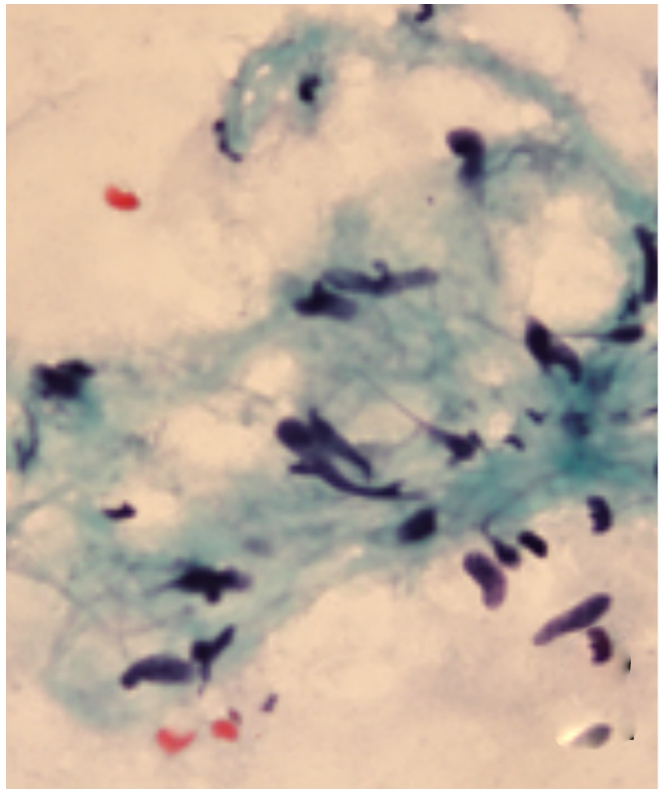

Figure 2. Fibrillar cytoplasmic extensions (Papanicolaou ×1000).

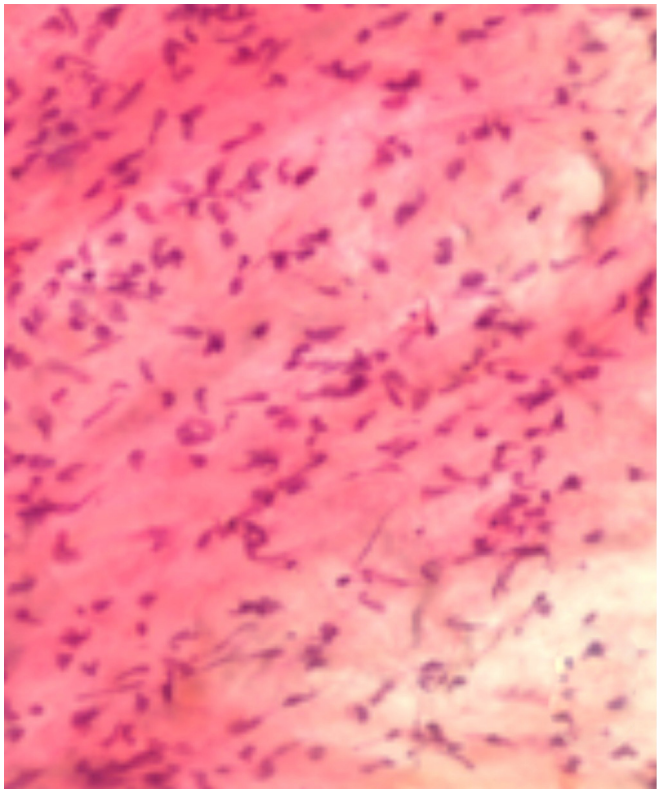

Figure 3. Cells with spindle-like nuclei in cohesive fragments (Papanicolaou ×400).

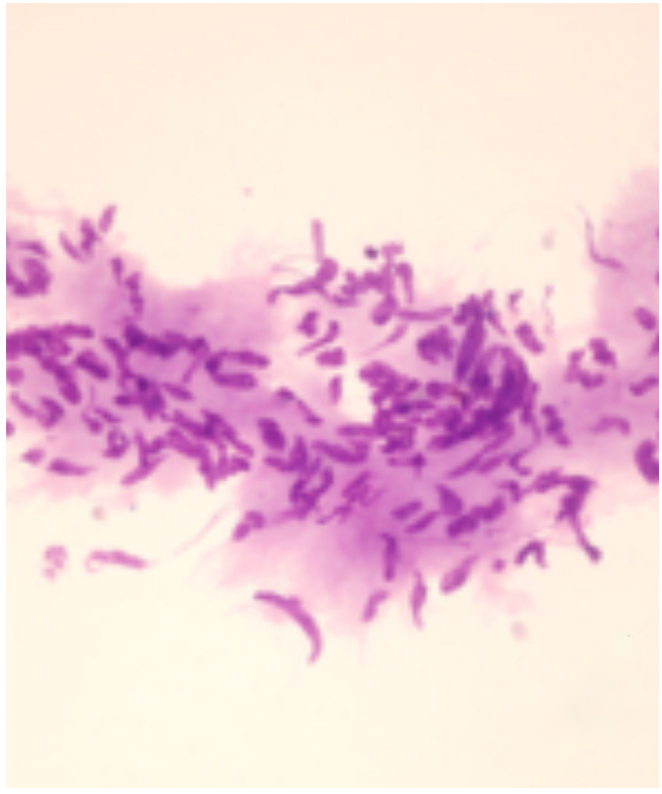

Figure 4. Wave and comma-shaped pointed nuclei (May-Grünwald-Giemsa ×400).

DISCUSSION

Schwannomas are benign, typically slow-growing tumors that originate from Schwann cells, which are specialized cells that form myelin sheaths around nerve fibers in the peripheral nervous system.[21,22] Schwannomas are more frequently seen in adults, with the highest incidence occurring between the ages of 25 and 55.[1] There is no preference for sex.[1,3] In our study, the patients' age ranged from 36 to 78 years, with a mean age of 54. Although the difference was not significant, the majority of the patients were female (10 out of 17).

These tumors are generally solitary masses that can occur anywhere in the body where nerve tissue is present, although they are more commonly found in the head, neck, and extremities.[3] Most of our cases (11/17) were located in the head-and-neck region, similar to previous reports. Three cases involved the extremities (two in the axilla and one in the thigh), while the remaining three involved the trunk.

The encapsulation of these tumors often contributes to their slow growth and can make early detection challenging, as they may not cause noticeable symptoms until they become large enough to compress the surrounding tissues or nerves.[3,23] In our cases, lesion sizes ranged from 1.4 cm to 5.5 cm, with a mean diameter of 3.04 cm.

The etiology of schwannomas is not fully understood, but they are generally considered to be sporadic occurrences, meaning that they arise without a clear hereditary pattern. However, they can be associated with certain genetic conditions such as NF2.[24] None of our patients had an NF2 mutation.

Schwannomas typically exhibit a cellular composition dominated by spindle-shaped cells, which are elongated with tapered ends and oval nuclei. These cells are derived from Schwann cells, which are myelin-producing cells in the peripheral nervous system. Spindle cells are arranged in cohesive fascicles and clusters, forming a characteristic pattern that is helpful in distinguishing schwannomas from other spindle cell lesions.[16,23] In our case series, four cases were hypercellular, seven exhibited moderate cellularity, and six were hypocellular. In all cases, the cells formed cohesive fragments. In addition to the features described in the literature, singly dispersed tumor cells in the background were observed in 12 cases.

Nuclear palisading, a distinctive feature of schwannomas, is observed in some cases in addition to their diagnostic

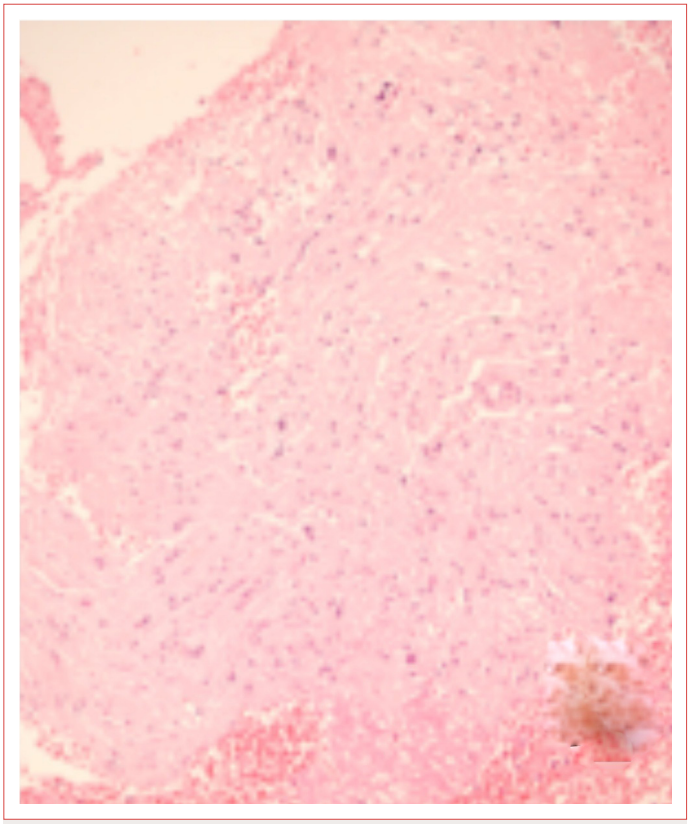

Figure 5. Fragment of spindle-like cells in cell block section (HE ×200).

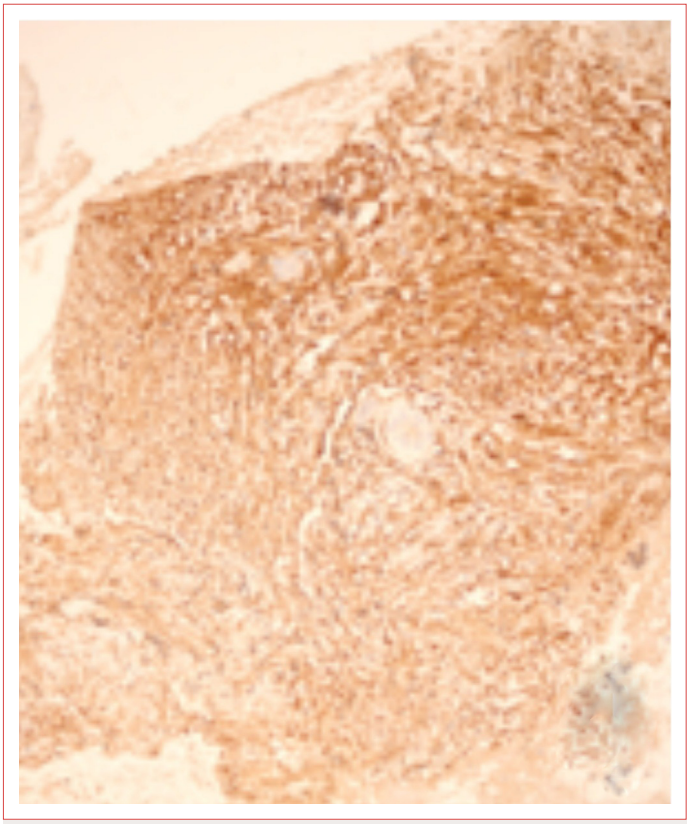

Figure 6. Tumoral cells stained with S100 (×200).

uniqueness. Nuclear palisading refers to the alignment of nuclei in parallel rows, which creates a pick fence-like appearance. This feature is particularly prominent in areas of high cellularity and is thought to be due to the tendency of Schwann cells to align along the nerve fibers. Although nuclear palisading is not entirely specific to schwannomas, its presence can be a helpful clue in the diagnosis, especially when combined with other cytological features.[23,25] Alternating cellular (Antoni A) and hypocellular (Antoni B) areas are the characteristic histological features of schwannomas, reflecting the variable density of cells and stromal components within the tumor. Antoni A areas are characterized by high cellularity with densely packed spindle cells arranged in fascicles and clusters. Nuclear palisading and Verocay bodies were often prominent in these areas. Antoni B areas, on the other hand, are characterized by low cellularity with loosely arranged spindle cells embedded in a myxoid or edematous stroma. These areas may contain scattered lymphocytes, histiocytes, or mast cells. The presence of both Antoni A and Antoni B areas is a hallmark of schwannomas and is helpful in distinguishing them from other spindle cell lesions that may exhibit more uniform cellularity.[5,17]

Unlike previous studies, nuclear palisading and Antoni A and B areas, which would suggest schwannoma, were observed in only two of our cases (2/17). This was thought to be related to the fact that the majority of cases had medium or hypocellular smears, and the sampling did not reflect these areas of the tumor.

Schwannoma cells are characterized by oval or elongated nuclei with pointed ends and indistinct cytoplasmic borders. The nuclei were typically uniform in size and shape, with finely granular chromatin and inconspicuous nucleoli. The nuclear contours may be smooth or slightly irregular, but marked pleomorphism or atypia is usually absent, except in certain variants, such as ancient schwannomas. The indistinct cell borders reflect the syncytial nature of Schwann cells, which are closely apposed to each other without clear cytoplasmic boundaries.[15,16] In our cases, all the nuclei exhibited tapering tips and appeared wavy, hook-like, or comma-shaped. In one case, cells with relatively larger nuclei were present; however, the nuclei still showed tapered tips and fine chromatin structures, similar to other cases. Syncytium-like clusters with filamentous cytoplasmic extensions and indistinct cytoplasmic borders were observed in all the cases.

Nuclear enlargement and pleomorphism can be observed, especially in ancient schwannomas, potentially leading to misdiagnosis. In ancient schwannomas, degenerative changes resulted in nuclear enlargement, hyperchromasia (increased staining intensity), and irregular nuclear contours, mimicking the features of malignant tumors. However, the presence of other degenerative features, such as cystic degeneration, hyalinization, and hemorrhage, should raise suspicion of an ancient schwannoma rather than a malignant tumor.[17,18]

A myxoid background may be observed, particularly in areas of cystic degeneration, in addition to the complexity of schwannoma stromal characteristics.[16,26] A myxoid background was not observed in any of the cases.

Verocay bodies, representing areas of nuclear palisading with associated acellular zones, are a diagnostic clue for schwannomas.[23,27] Verocay bodies are distinctive structures consisting of parallel rows of nuclei (nuclear palisading) alternating with zones of eosinophilic and acellular material. These are thought to represent areas of basement membrane deposition and collagen accumulation. Verocay bodies are not always present in schwannoma aspirates, but when they are observed, they are highly suggestive of the diagnosis. Verocay bodies were not observed in any case.

Schwannomas typically exhibit strong and diffuse immunoreactivity for S100 protein, a marker of neural crest origin.[17,19,28] This immunohistochemical feature can help differentiate schwannomas from other spindle cell lesions that are S100 negative.[17,20] Sox10 is a reliable marker of neural crest differentiation that is consistently expressed in schwannian and melanocytic tumors.[29] Immunocytochemical evaluation was performed in all but two of our cases. S100 staining was strong in 14 cases and moderate in 1 case. Sox10 was positive in five cases. No staining was observed with Desmin, SMA, or CD34. The cell blocks of two cases did not contain sufficient material for further analysis; in these cases, immunohistochemical studies were performed on excision specimens.

The cytological features of schwannomas can overlap with those of other spindle cell lesions, such as neurofibromas, leiomyomas, gastrointestinal stromal tumors (GISTs), and fibromatosis.[11,30,31] Neurofibromas such as schwannomas are peripheral nerve sheath tumors that can exhibit spindle-shaped cells and fibrillary stroma. However, neurofibromas typically lack encapsulation and Verocay bodies, which are often present in schwannomas.[31]

Leiomyomas and GISTs, which are smooth muscle tumors, can also exhibit spindle-shaped cells, potentially leading to diagnostic confusion. These tumors may exhibit overlapping cytological features with schwannomas, such as elongated nuclei and indistinct cytoplasm.[30,31] However, leiomyomas and GISTs typically lack the characteristic Antoni A and B areas seen in schwannomas.[30] Leiomyomas are actin, desmin, and H-caldesmon positive and negative for CD34, S100, sox10, CD117, and DOG1.[32] GISTs, particularly in extra-gastrointestinal locations, can resemble schwannomas, posing a diagnostic challenge when they occur outside of their typical location.[33] Immunohistochemical staining for CD117 and CD34 is crucial for differentiating GISTs from schwannomas, providing key markers for distinguishing these tumors. CD117 (KIT) is a receptor tyrosine kinase that is expressed in most GISTs, whereas CD34 is a hematopoietic progenitor cell antigen that is also expressed in a significant proportion of GISTs. In contrast, schwannomas are typically negative for both CD117 and CD34.[33] The absence of S100 protein expression in GISTs further aids in distinguishing them from schwannomas, providing an additional marker for differentiating these lesions. While schwannomas are typically strongly positive for the S100 protein, GISTs are typically negative.[33,34]

Fibromatosis, a benign fibrous proliferation, can mimic schwannomas owing to its spindle cell morphology and fibrous stroma.[11,31] However, fibromatosis typically lacks encapsulation and Verocay bodies. In addition, fibromatosis may exhibit a more infiltrative growth pattern compared to the circumscribed appearance of schwannomas.[11] In the parotid gland, myoepitheliomas can mimic schwannomas owing to their spindle cell morphology, creating a diagnostic challenge in this specific location.[9,11] Myoepitheliomas typically exhibit a more disorganized cellular arrangement than schwannomas, with cells arranged in cords, nests, or sheets.[17,27] Immunohistochemistry can help distinguish between these tumors and provide additional information to aid accurate diagnosis. Myoepitheliomas are typically positive for epithelial markers, such as cytokeratin and epithelial membrane antigen, as well as myoepithelial markers, such as SMA, calponin, and p63. In contrast, schwannomas are typically positive for S100 protein and negative for epithelial markers.[25]

The differential diagnosis of schwannoma also includes malignant peripheral nerve sheath tumor (MPNST), a rare but aggressive sarcoma that arises from peripheral nerves.[20,35,36] MPNSTs can exhibit overlapping cytological features with schwannomas, particularly in well-differentiated cases.[20] However, MPNSTs typically exhibit more pronounced nuclear atypia, higher mitotic activity, and necrosis.[20] Immunohistochemistry can also be helpful in distinguishing MPNSTs from schwannomas.[20,36] While both schwannomas and MPNSTs may express the S100 protein, MPNSTs often exhibit loss of S100 expression in poorly differentiated areas.[20] In addition, MPNSTs may express other markers such as p53, Ki-67, and nerve growth factor receptor.[36]

However, it is important to note that S100 protein is not entirely specific for schwannomas and can be expressed in other tumors, such as melanomas, myoepitheliomas, and some soft tissue sarcomas.[20,37] Therefore, S100 immunostaining should be interpreted in conjunction with cytomorphological findings and other clinical and radiological data.[5,12]

In some cases, the cytological and immunohistochemical features of schwannomas may be ambiguous, making definitive diagnosis difficult. In these cases, molecular analysis can provide additional information to support diagnosis. Identification of an NF2 mutation can confirm the diagnosis of schwannoma, even in the absence of classic cytological or immunohistochemical features.[6]

The presence of cystic degeneration and hypocellularity can lead to insufficient or inaccurate specimens, further complicating the cytological diagnosis of schwannoma. Cystic degeneration, which is a common feature of schwannomas, can result in aspiration of fluid with few or no diagnostic cells. Hypocellularity, or a low number of cells in the aspirate, can also make it difficult to evaluate the cytological features and arrive at a definitive diagnosis.[11,16,38]

CONCLUSION

The diagnostic workup for schwannomas typically involves a combination of clinical examination, imaging studies, and cytological or histological analysis. FNAC can guide surgical planning and prevent unnecessary, extensive procedures by providing valuable information regarding the nature of the lesion before surgery. The cytological features of schwannomas include cohesive clusters of spindle-shaped cells, nuclear palisading, Verocay bodies, and a fibrillary stroma. However, the diagnosis can be challenging owing to cystic degeneration, degenerative changes, and overlapping features with other spindle cell lesions. Palisading, Antoni A and B areas, and Verocay bodies, which are cytological features expected to be seen in schwannomas, may or may not be seen rarely, as in our case series. This was not surprising for specimens with low cellularity. The presence of typical pointed nuclei and fibrillar cytoplasm with unclear boundaries are important diagnostic clues. However, these features, which are not specific to schwannomas, need to be confirmed by immunohistochemical techniques, especially by S100 immunhistochemistry. A comprehensive approach that integrates the clinical, radiological, and cytological findings is essential for the correct diagnosis and management of schwannomas.

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DECLARATIONS

Ethics Committee Approval: The study was approved by İstanbul Training and Research Hospital Clinical Research Ethics Committee (No: 107, Date: 02/05/2025).

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