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Challenges in diagnosing schwannoma mimicking thyroid neoplasms on frozen section

Rahmi Ramadhani[1], Pamelia Mayorita[2], Aswiyanti Asri[3], Henny Mulyani[4], Hera Novianti[5]

[1,3,4]Departemen Patologi Anatomi, Fakultas Kedokteran, Universitas Andalas, Padang, Indonesia,
[2,5]Laboratorium Patologi Anatomi RSUP Dr. M. Djamil, Padang, Indonesia

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ABSTRACT

Schwannoma is a benign soft tissue tumor of the nerve sheath, composed of neoplastic cells with Schwann cell differentiation. It predominantly arises from peripheral nerves in the head, neck, and extremities, with a peak incidence in the fourth to sixth decades. Schwannoma is typically a solitary and sporadic lesion, affecting individuals of all ages, with an incidence rate of 4.4-5.23 cases per 100,000 people. The prevalence is around 7% of all primary nervous system tumors, often occurring in the head and neck (20-50%) and affecting cranial nerves such as N. Vagus and N. Sympathetic. This case report involves a 50-year-old female patient presenting with a right neck lump that had been present for 23 years, initially small but growing rapidly in the last 10 years with occasional pain. Initial imaging suggested a thyroid complex cyst, but further investigation, including a CT scan and intraoperative frozen section examination, raised suspicion for a malignant thyroid tumor. However, histopathological analysis confirmed the diagnosis of Schwannoma, distinguishing it from other potential malignant lesions, such as Anaplastic Thyroid Carcinoma (ATC). This case highlights the importance of intraoperative cytology and frozen section techniques for diagnosing Schwannoma. Although Schwannomas share morphological similarities with other tumors, particularly in the thyroid region, a multidisciplinary approach combining clinical, radiological, and histopathological findings is essential for an accurate diagnosis. This case also underscores the need for careful differential diagnosis in nerve sheath tumors located in the neck.

Corresponding Author:

Rahmi Ramadhani
Departemen Patologi Anatomi,
Fakultas Kedokteran,
Universitas Andalas,
Limau Manis, Kec. Pauh, Kota Padang, Sumatera Barat, 25175, Indonesia
Email: rahmiramadhani0204@gmail.com

INTRODUCTION

Schwannomais a benign soft tissue tumor of the nerve sheath consisting of neoplastic cells with Schwann cell differentiation that generally originate from peripheral nerves in the skin and subcutaneous tissue of the head and neck or along the flexor surface of the extremities.

Schwannoma is generally a solitary and sporadic lesion that can affect all ages but with a peak incidence in the fourth to sixth decade of life and no racial and gender predisposition. Schwannoma often appears as an asymptomatic mass or incidental finding with an incidence of 4.4 - 5.23 cases per 100,000 population. The prevalence of Schwannoma is around 7% of all primary tumors in the nervous system. The location predilection of Schwannoma is 20-50% in the head and neck region, 10-30% of Schwann cells in the vagus nerve, 10-20% of Schwann cells in the sympathetic nervous system (Chand et al., 2016)(Kobayashi et al., 2018).

Intraoperative frozen section pathological diagnosis can be used in determining further surgical management. Intraoperative pathological diagnosis with cytology and frozen section procedures plays an important role in the diagnosis of peripheral nerve specimens. The results of cytology and frozen section evaluation can be relied upon to guide surgeons in making intraoperative decisions. Pathologists provide the maximum information possible by linking clinical, radiological, macroscopic, cytopathological and histopathological information from frozen section procedures. Although the cytology and frozen section diagnostic approach has been carried out multidisciplinary, there are still limitations in the intraoperative diagnosis of peripheral nerve specimens. The limitations in this procedure can be overcome by understanding and analyzing possible errors and pitfalls during the procedure, thereby increasing the accuracy of the diagnosis (Lee & Tihan, 2015)(Borczuk et al., 2021).

The following is a case report of Schwannoma in the right coli region of a 50-year-old woman who was initially suspected of being a malignant right thyroid tumor. The patient underwent resection of the tumor suspected of being a thyroid tumor and underwent intraoperative frozen section examination and histopathological tissue examination.

The diagnostic limitations of frozen section procedures in differentiating between Schwannoma and Anaplastic Thyroid Carcinoma (ATC) primarily stem from the overlapping morphological and cytological features that both conditions can exhibit. Schwannomas, though typically characterized by spindle-shaped cells and a distinctive Antoni A and Antoni B pattern in their histology, can sometimes present in ways that mimic malignancies, especially in areas like the thyroid bed. On the other hand, ATC, a highly aggressive and poorly differentiated thyroid cancer, may also show spindle cell morphology, leading to diagnostic confusion during a frozen section analysis.

Frozen section techniques are useful for intraoperative decisions, but they have limitations in providing definitive diagnoses in cases where tumors display overlapping features. For instance, the nuclear pleomorphism and mitotic activity seen in ATC can sometimes be misinterpreted as features of schwannoma, particularly if the tumor is in a rare location like the thyroid bed, where schwannomas are not typically expected. Additionally, the lack of the typical peripheral nerve structures in a frozen section may make it difficult to distinguish schwannomas from other spindle cell lesions.

Thus, the main diagnostic limitation is the difficulty in distinguishing these two entities based solely on their morphology during the frozen section examination. To overcome this challenge, a comprehensive diagnostic approach involving intraoperative consultation with a pathologist, careful review of the clinical and radiological features, and potentially the use of additional markers or molecular techniques, is essential to make a more accurate diagnosis. A multidisciplinary approach and awareness of the differential diagnoses, including schwannoma and ATC, are crucial for clinicians to avoid misdiagnosis and guide appropriate surgical decision-making.

The theoretical framework often used to explain the importance of multidisciplinary collaboration in the diagnosis of atypical neck tumors is the biopsychosocial model combined with interdisciplinary team theory.

Biopsychosocial Model: This model emphasizes the holistic approach to patient care by integrating biological, psychological, and social factors in understanding a disease or condition. In

the context of atypical neck tumors, the biopsychosocial model supports the idea that a comprehensive diagnosis requires more than just a physical or pathological evaluation. Atypical neck tumors, which may present with non-specific or overlapping features, can benefit from the expertise of various specialists, including pathologists, radiologists, oncologists, surgeons, and other healthcare providers. The biopsychosocial model underlines that collaboration between these professionals is necessary to fully address the complexity of the tumor, considering both medical and psychosocial aspects of care.

Interdisciplinary Team Theory: This theory emphasizes the value of collaboration between professionals from different disciplines to achieve better outcomes. In the context of atypical neck tumors, interdisciplinary collaboration is critical because the diagnosis often requires input from several specialists who can provide complementary expertise. For example, radiologists can offer detailed imaging studies, pathologists can assess biopsy or frozen section results, and oncologists can evaluate potential cancerous etiologies. Surgeons also need to consider surgical options and potential risks. An interdisciplinary approach ensures that all aspects of the diagnosis, treatment options, and patient care are covered, leading to more accurate diagnoses and optimal treatment planning. Together, these frameworks underscore the necessity of multiple perspectives and areas of expertise when diagnosing complex or atypical conditions, such as neck tumors, which may not present in typical ways. Collaborative teamwork allows for more thorough evaluation, reduces the risk of misdiagnosis, and improves patient outcomes by ensuring that all relevant factors are considered in clinical decision-making.

RESEARCH METHOD

We report a case of a patient with a diagnosis of a right thyroid tumor suspected of being malignant which was later found from frozen section, histopathology, and immunohistochemistry examinations to be a Schwannoma in the neck region. Data were collected from the patient's medical records, supporting examination results and clinical follow-up.

RESULTS AND DISCUSSIONS

A 50-year-old female patient came for treatment to the surgical oncology polyclinic of Dr. M. Djamil Padang General Hospital on May 17, 2024 with a complaint of a lump in the right neck since 23 years ago. The lump was initially small, the size of a ping-pong ball, then the lump was felt to be getting bigger quickly over the past 10 years and was sometimes painful. The patient also complained of a hoarse voice but no difficulty swallowing and breathing. The patient had been advised surgery but no action had been taken. No other family members had similar complaints. The patient was diagnosed with a suspected malignant right thyroid tumor by the surgical oncology department.

Figure 1. Clinical photo of the patient

The general condition of the patient is that the patient appears moderately ill with cooperative compos mentis consciousness. The results of physical examination are blood pressure 140/80 mmHg, pulse rate 66x/minute, respiratory rate 20x/minute and body temperature 36.7oC. Eye examination is within normal limits. Thoracic region examination was within normal limits. Examinationheart within normal limits. Abdominal examination within normal limits. Left and right extremities within normal limits. Examination of the local status of the right coli region found that on inspection a skin-colored mass appeared, not ulcerated. On palpation, a mass measuring 10x9x8 cm was felt, solid, mobile, sometimes painful, and moved when swallowing (Figure 1). The results of routine blood laboratory tests on August 13, 2024 were leukocytosis (leukocytes 14,540/mm3). The results of clinical chemistry blood tests were within normal limits. The patient also underwent thyroid function tests (FT4 and TSH) with results within normal limits. On May 20, 2024, the patient underwent an ultrasound examination (USG) of the thyroid with the results of the right thyroid appearing very enlarged which pushed the trachea to the left. A cystic lesion with a clear boundary, regular edges, measuring 9.77 x 8.3 x 10.2 cm was seen. The lesion was accompanied by internal echo, multiseptation and calcification. The conclusion of the USG examination was a right thyroid complex cyst (Figure 2).

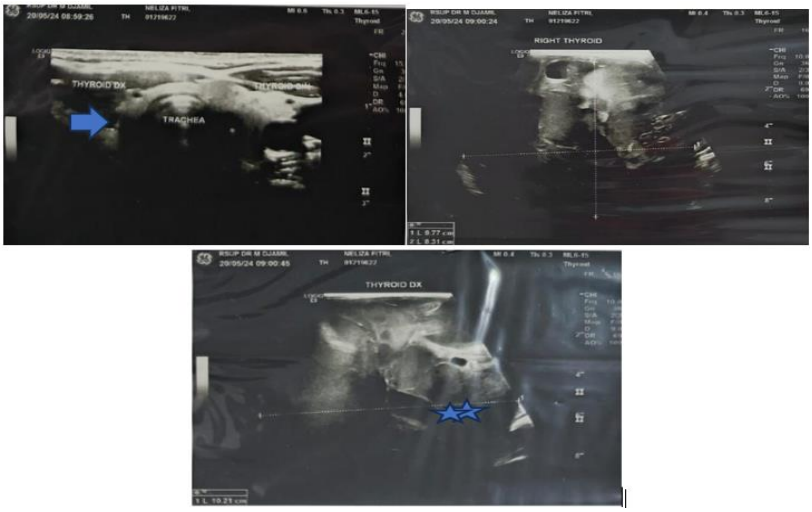

Figure 2. Thyroid USG examination. right thyroid pushing the trachea to the left (arrow); very large cystic lesion (asterisk)

The patient underwent an Anteroposterior (AP) chest X-ray examination with the results of trachea deviation to the left, pushed by a soft tissue mass in the right coli region. No other radiological abnormalities were seen on the chest radiograph (Figure 3).

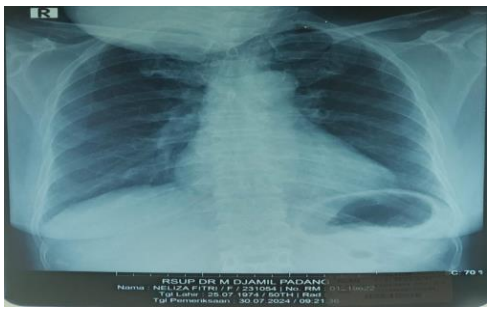

Figure 3. AP projection chest x-ray

CT scan of the neck showed a hypodense (cystic) mass in the right thyroid, round, indistinct borders, regular edges, septate, no calcification, measuring 10.7x12.7x12.7 cm. Post-contrast no enhancement was seen in the cystic component, but enhancement was seen in the cyst wall. The mass appeared to be pushing the trachea to the left, no nodules or cysts were seen. The conclusion is a cystic mixed solid tumor in the right thyroid.

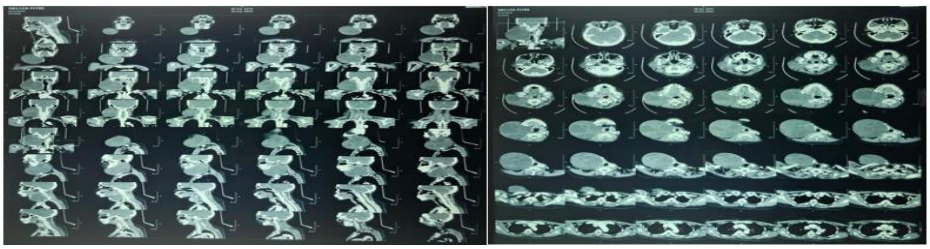

Figure 4. CT scan of the neck

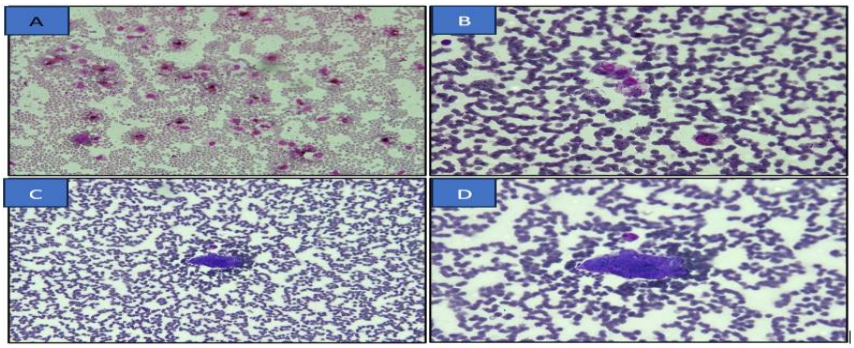

Figure 5. Microscopic BAJH. the distribution of macrophages (a,b) and follicular epithelial groups (c,d) are visible. he: a(100x), b(200x), giemsa: c(200x), d(400x)

The patient was advised to undergo a Fine Needle Aspiration Biopsy (FNA) examination to the Anatomical Pathology Laboratory. On microscopic examination of FNA, there was a distribution and cluster of macrophage cells, follicular epithelium with a background of colloid and erythrocytes. The interpretation of the FNA examination results was Benign (Bethesda II) with the impression: cystic lesions (Figure 2.3).

On August 30, 2024, the patient underwent total thyroidectomy and frozen section. The specimen was sent to the anatomical pathology laboratory with a clinical diagnosis of suspected malignant right thyroid tumor. Macroscopic examination found a piece of suspected thyroid tissue, 1 lobe, had been divided, yellowish brown, elastic, solid, measuring 14x9x7 cm, the cross section showed a solid white mass with lobes 14 cm in diameter with a hollow part containing fluid and brownish jelly 2-5 cm in diameter, 6 cassette prints, the rest were positive (Figure 6).

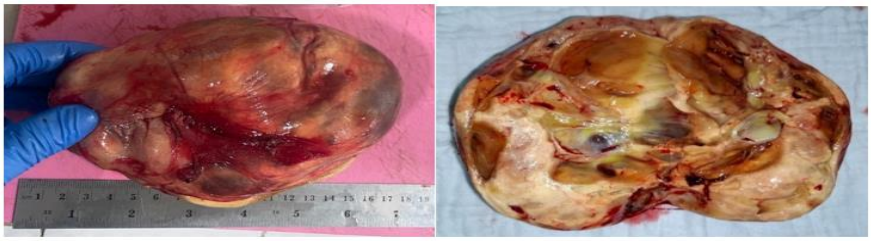

Figure 6. Macroscopic view: (A) intact, (B) cross-section

Examination of frozen section smears and microscopic imprints showed the distribution and clustering of spindle cells arranged in a sheet-like structure (Figure 7A,B).

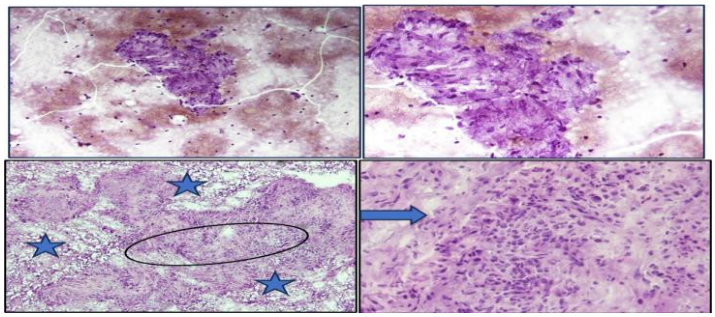

Figure 7. Microscopic image. Thyroid tissue section shows cavities (asterisks) and proliferation of spindle-shaped cells arranged in fascicular, storiform and solid sheet structures (black circles). These cells have round, oval to spindle-shaped nuclei (blue arrows). HE A: 100x, B: 200x, C: 400x.

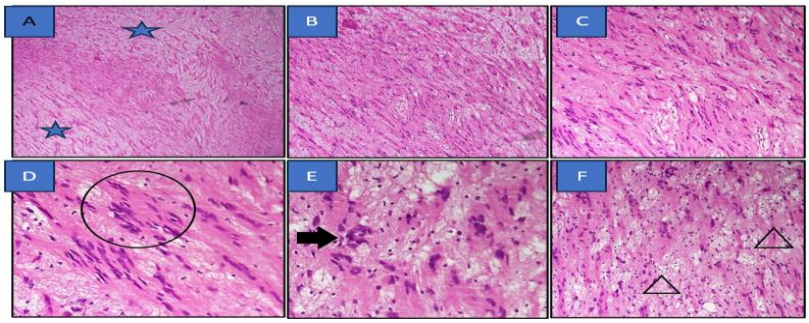

Figure 8. Frozen section paraffin block (BVC). The tissue section is seen consisting of a loose and hyalinized connective tissue stroma containing proliferation of spindle cells forming hypercellular and hypocellular areas (asterisks), some arranged in palisading to form "verocay bodies" structures (black circles). These cells have indented nuclei, some with an increased N/C ratio (black arrows). Groups of foamy macrophages are also seen in between (triangles). HE A: 40x, B&F: 100x, C: 200x, D&E: 400x,

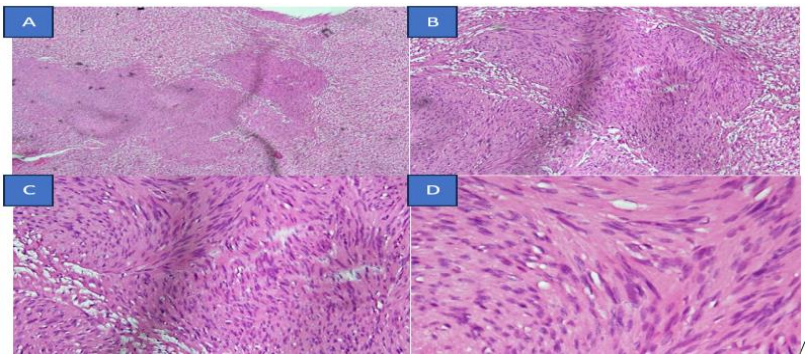

Figure 9. Microscopic picture of the follow-up wet open. tissue section showing a schwannoma. he staining, magnification a: 40x, b: 100x, c: 200x, d: 400x.

On microscopic examination of frozen section paraffin blocks (BVC), a loose and hyalinized connective tissue stroma containing proliferation of spindle cells forming hypercellular areas (Antoni A) and hypocellular areas (Antoni B), some arranged in palisading forming a "verocay bodies" structure. These cells have indented nuclei, some with increased N/C ratio. A collection of lymphocytes, plasma and foamy macrophages peritumoral and intrastromal are also

seen (Figure 8). Conclusion: Ancient Schwannoma dd/ Anaplastic Thyroid Carcinoma (ATC). Recommendation: add block and examination of IHK S100, Ki67, and PAX8. Additional preparations were performed through a follow-up wet open. On microscopic examination, the same examination results were still obtained, namely depicting a Schwannoma (Figure 9).

On the same date, other thyroid tissues were sent for histopathology. The specimens were received at the Anatomical Pathology Laboratory of Dr. M. Djamil Padang General Hospital in the form of 2 tissue bags: Bag I labeled thyroid, bag II labeled core biopsy. Macroscopic examination of label I showed a piece of thyroid tissue of 1 lobe with isthmus, brownish, dense and elastic, measuring 6x3x1.5 cm, the cross section showed a white part with a diameter of 0.5 cm printed with 4 cups in 4 cassettes. Macroscopic examination of label II core biopsy macroscopically showed pieces of brownish white tissue measuring 1x1x0.3 cm printed all in 1 cassette (Figure 10).

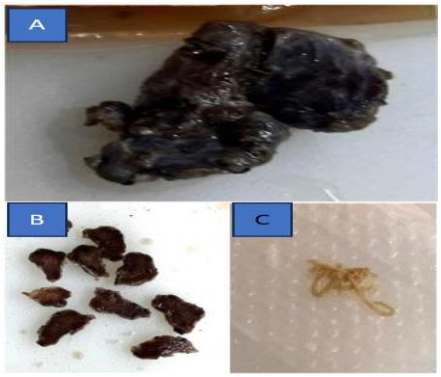

Figure 10. Macroscopic view of the thyroid. Label I (A) whole section; (B) cross-sectional photo; (C) Label II core biopsy

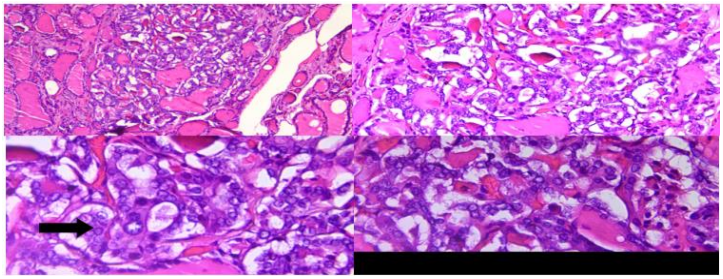

Figure 11. Microscopic image of label I. It shows a group of cells forming a follicular structure with an increased N/C ratio (arrow), thickened nuclear membrane (size <5mm). HE staining, A: 100x, B: 200x, C&D: 400x

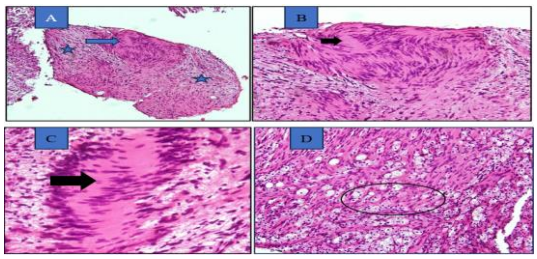

Figure 12. Label II core biopsy. Connective tissue stroma contains proliferation of spindle cells forming hypercellular areas (blue arrows) and hypocellular (asterisks) partly arranged in palisading (black arrows) forming the structure of "verocay bodies". Also visible are groups of foamy macrophages (black circles) HE staining, Magnification A: 100x, B&D: 200x, C: 400x

Microscopic examination of label I thyroid (Figure 11) microscopically shows a section of thyroid tissue consisting of thyroid follicles of varying sizes, lumens filled with colloid, lined with cuboidal epithelial cells, monomorphic nuclei. Hyperemic capillaries and areas of hemorrhage are also visible. In one place there is a group of cells forming a follicular structure with an increased N/C ratio, thickened nuclear membrane (size <5mm).

Microscopic examination of label II core biopsy (Figure 12) shows tissue sections consisting of connective tissue stroma containing proliferation of spindle cells with indented nuclei forming hypercellular areas (Antoni A) and hypocellular areas (Antoni B). These cells appear to be arranged in a palisading pattern forming a "verocay bodies" structure. Also seen are clusters and clusters of lymphocytes, plasma, and foamy macrophages. The conclusion is Total thyroidectomy, in frozen section results and histopathology tissue (paraffin block) Ancient Schwannoma, dd / Anaplastic Thyroid Carcinoma. Thyroid label: Papillary Thyroid Carcinoma (PTC) follicular variant (microcarcinoma). Label core biopsy with benign results, suggestive of soft tissue tumor. Recommended examination of IHK S100, Ki67, PAX8.

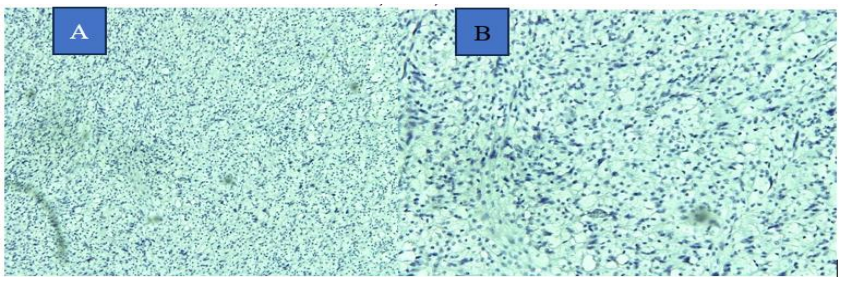

Figure 13. Negative IHK KI67 image. Magnification (A) 100x, (B) 200x

On October 1, 2024, the patient underwent a Ki-67 IHK examination. The results of the Ki-67 IHK examination were negative (Figure 13) so that the conclusion of the frozen section examination, histopathology (paraffin block) and IHK on the tissue that underwent frozen section of a Benign Soft Tissue Tumor is suitable for Ancient Schwannoma. In other thyroid lobes with a diagnosis of follicular variant PTC (microcarci noma) pT1NxMx.

A case of a 50-year-old woman who was clinically diagnosed with a right thyroid tumor suspected of being malignant has been reported. Physical examination showed a lump in the right neck since 23 years ago and felt increasingly enlarged over the past 10 years which was sometimes painful. The patient underwent a thyroid ultrasound examination with the result of a right thyroid complex cyst. The patient was advised to undergo a BAJH examination of the lump in the neck with the result of a cystic lesion. The patient underwent a CT-scan of the neck with the result of a cystic mixed solid tumor in the right thyroid. The patient underwent surgery to remove the thyroid tumor and a frozen section intraoperative consultation procedure for the lump suspected of being a right thyroid tumor suspected of being malignant. The results of the frozen section examination of the specimen suspected of being a right thyroid tumor suggested a malignant lesion, it was recommended to wait for a paraffin block to confirm the diagnosis. Paraffin block examination and subsequent wet opening showed Schwannoma results. Histopathological examination of 2 bags of specimens sent after the frozen section procedure showed a diagnosis of follicular variant PTC (microcarcinoma) on label I (thyroid) and benign soft tissue tumor on label II (core biopsy). The conclusion of the diagnosis in this patient was established Schwannoma dd/ ATC, IHK S100, Ki67, and PAX8 were recommended to confirm the diagnosis. The IHK Ki67 result was negative with the conclusion that it was appropriate for Schwannoma.

Intraoperative consultation for neurosurgical specimens can be challenging due to various factors. Most neuropathologists prefer smear preparation and frozen section to achieve the most

reliable diagnosis. Smear is more useful for background analysis and nuclear and cytoplasmic images.

The experience of Emel et al. in diagnosing schwannoma, not only smear is sufficient, but also with a combination of frozen section can be relied upon for accurate diagnosis (Pala et al., 2022). In this case, the cytomorphological features obtained from BAJH cytology, imprint cytology and frozen section were correlated with the microscopic findings from paraffin blocks, subsequent wet opens and histopathological examinations submitted to obtain a conclusion of the diagnosis of Schwannoma.

In this case, the tissue was initially suspected as a malignant right thyroid tumor. Frozen section was performed with the aim that if the results of malignant lesions were obtained, total thyroidectomy would be performed. Macroscopic examination found dense, elastic tissue, yellowish brown in color, with a yellowish white mass cross-section and a hollow part filled with fluid and brownish jelly with a diameter of 2-5 cm (Pala et al., 2022)(Chand et al., 2016).

In 2019, Ji Yun Kang et al also reported a case of schwannoma in the thyroid bed. A case was reported in a 33-year-old woman with a chief complaint of difficulty swallowing. The results of the USG showed a well-defined mass, oval in shape, with a hypoechoic image of a solid nodule with echogenic foci suggestive of macro and microcalcification in the left thyroid gland. The conclusion was suspicious of malignancy in the thyroid nodule. BAJH examination was performed twice with non-diagnostic results. Thyroidectomy on the left thyroid gland was performed, intraoperative frozen section results showed a spindle cell tumor. Macroscopic examination of the submitted tissue then showed a yellowish mass attached to the left thyroid lobe measuring 1.7x1.7x1.3 cm. The results of histopathological confirmation of the diagnosis showed schwannoma in the perithyroid tissue consisting of Antoni A and Antoni B areas, there was a small area of calcification, IHK S100 was positive for schwannoma (Saekhu et al., 2020).

In 2024 Serghei Convantsev et al also reported a case of schwannoma in the neck region "masking" as a thyroid tumor in a 32-year-old male patient with a complaint of a lump in the neck. The results of an ultrasound examination of the thyroid gland showed heterogeneous hypoechoic measuring 18x21x31 mm, clear boundaries and an area with abnormal blood flow in the left inferior parathyroid gland and the posterior surface of the left lobe of the thyroid gland. The results of the BAJH examination were performed twice with non-diagnostic results (Ansari et al., 2018)(Dosemane et al., 2022)(de Bakker et al., 2020). The patient was consulted with an endocrine surgeon to make a decision whether to perform hemithyroidectomy among the uncertainties, the patient underwent a "core needle biopsy" and the results of histopathological analysis showed a picture of Schwannoma. Then the surgical procedure was performed under general anesthesia in the neck region, a mass measuring 3 cm was seen, then the tumor was removed. Intraoperatively, the apex limit of this mass was at the level of the left thyroid gland lobe while the inferior part was at the jugular notch, the distal limit appeared to be in contact with the corpus vertebrae. The results of the postoperative histopathological examination were in accordance with the biopsy results, namely Schwannoma. IHK S100 examination showed positive results and Ki67 2% (Covantsev et al., 2024).

Schwannoma originating from the neck region can develop from the vagus nerve (11-20% of cases), can also originate from sympathetic branches (11-34% of cases), or from the cervical (3-50%) or brachial (17%) plexus (Hwang et al., 2023)(Moriya et al., 2012). Schwannoma is often asymptomatic, but depending on the location some can cause secondary symptoms such as swelling in the neck, dysphagia or hoarseness (Kumar, 2015)(Mohammad et al., 2020). The majority of patients are women aged 30-35 years who complain of a lump in the neck. Progressive difficulty swallowing complaints can indicate a malignancy. However, in some cases when it is difficult to distinguish between an extrathyroid mass and an intrathyroid lesion that will make further surgery unnecessary, then frozen section examination can be very useful in this situation which can be a guide for the surgeon to take further surgical action (Lenzi et al., 2017)(Prayson &

Napekoski, 2010). Ultimately a multidisciplinary approach including ultrasonographers, radiologists, pathologists and surgeons must work together, collaborate and coordinate to establish in order to determine further patient management (Kim et al., 2010)(Dey, 2018).

In this case, although the intraoperative frozen section procedure has been performed, due to the lack of clinical information and minimal information obtained, there is a possibility of "error" and "pitfall" during the diagnosis of frozen section examination results by pathologists in the anatomical pathology laboratory (Kerr & Laing, 2017). In the microscopic smear preparation, the distribution and grouping of spindle cells were found. The microscopic picture of the frozen section examination showed tissue consisting of connective tissue stroma containing spindle cells. Based on the examination of the smear and frozen section, it was concluded that the lesion was malignant. It is recommended to wait for the paraffin block to confirm the diagnosis. The microscopic picture of the paraffin block shows spindle cells arranged in a hypercellular area (Antoni A) and a hypocellular area (Antoni B). In the hypercellular area, these spindle cells are partially arranged in a palisading pattern forming "verocay bodies". This microscopic picture can be found in Schwannoma.

The classic picture of Schwannoma is “verocay bodies”. can help in the diagnosis of Schwannoma (Dean et al., n.d.)(Sarkar et al., 2017). However, in the diagnosis of Schwannoma in the neck region (thyroid bed), morphology alone is not enough because it often discrepancies with ATC spindle cell variants, especially in frozen section procedures. In frozen section procedures, the picture of “verocay bodies” can be unclear, so confirmation with paraffin blocks is needed and if necessary, it can be continued with IHC examination for certainty of diagnosis (KAPTAN et al., 2020)(Imen et al., 2021). The IHC test for Schwannoma shows strong positive S100 immunoreactivity in tumor cells which is a specific marker for Schwannoma (Mitra et al., 2010)(Jindal et al., 2017). In this case, the histopathological picture of the tumor tissue shows a picture of Schwannoma with characteristics of spindle cells that form hypercellular areas with “verocay bodies” and hypocellular areas (M. Kang et al., 2019)(Chang et al., 2019)(Kar et al., 2018).

In some cases, neck Schwannoma can be difficult to distinguish from thyroid lesions. 19,20 Schwannoma and ATC have spindle cells so it is often difficult to distinguish them using frozen section. To differentiate this, there must be good communication between the surgeon and the pathologist so that complete information is obtained regarding the clinical history, radiological findings, intraoperative findings and adequate tumor samples so that an accurate diagnosis can be made (Behuria et al., 2015)(J. Y. Kang et al., 2020)(Lester & Harrison, 2022).

CONCLUSION

What are the strategic suggestions for clinical practice regarding surgical decision-making (e.g., total thyroidectomy) when frozen section results still show uncertainty, and how should surgeons manage the risks and potential challenges associated with ambiguous results during intraoperative evaluation? In particular, intraoperative cytology and frozen section techniques are reliable methods for diagnosing schwannoma. However, schwannoma, despite its morphological characteristics, can sometimes be confused with spindle cell thyroid neoplasms, particularly anaplastic thyroid carcinoma (ATC), especially when located in the neck region or thyroid bed. Given these challenges, a comprehensive approach involving effective communication with the surgeon, a multidisciplinary team, and careful consideration of clinical, radiological findings, and other supporting tests can aid in establishing a more accurate diagnosis. This is particularly important in differentiating schwannoma from other nerve lesions, considering the many differential diagnoses that exhibit similar microscopic features. To strengthen the accuracy of intraoperative diagnosis in ambiguous neck tumors, hospitals and anatomic pathology laboratories can implement several operational recommendations. These recommendations focus on improving diagnostic accuracy, optimizing the use of available resources, and fostering effective

communication among the clinical and pathological teams. Enhance Communication Between Surgeons and Pathologists: Clear and direct communication between surgeons and pathologists is essential, especially when there is uncertainty in intraoperative diagnosis. Surgeons should provide detailed clinical information, including the patient's history, tumor location, and suspected diagnosis, while pathologists should relay their findings promptly and effectively. Regular case discussions, especially in complex or ambiguous cases, can help align surgical decisions with the pathology results. Utilize a Multidisciplinary Team (MDT) Approach: Incorporating a multidisciplinary approach that includes surgeons, pathologists, radiologists, oncologists, and other relevant specialists can improve diagnostic accuracy. Regular tumor board meetings where complex cases are reviewed can offer diverse perspectives and insights, allowing for a more comprehensive evaluation of the case, especially when frozen section results are ambiguous. Implement Advanced Diagnostic Techniques: In addition to frozen section analysis, incorporating advanced molecular diagnostics or immunohistochemistry (IHC) during the intraoperative period can provide additional clues. For example, using markers like S100 and SOX10 for Schwannomas or PAX8 and TTF-1 for thyroid malignancies can help distinguish between different pathologies. Incorporating these techniques during intraoperative consultation can reduce the risk of misdiagnosis. Invest in High-Quality Frozen Section Equipment and Training: Ensuring that frozen section techniques are performed with high-quality equipment and by trained personnel is essential for improving diagnostic reliability. Laboratories should invest in maintaining the equipment and provide ongoing training for staff to keep up with advances in pathology techniques. Pathologists should be encouraged to utilize well-defined protocols for the evaluation of ambiguous cases. Develop Clear Diagnostic Protocols for Ambiguous Cases: Hospitals should establish clear protocols for handling cases where there is uncertainty in diagnosis. This may include steps for further evaluation, such as extending intraoperative consultation with an expert pathologist, or using additional tests such as intraoperative cytology or imaging modalities like ultrasound or CT scans. Establishing clear guidelines helps ensure consistency in handling complex cases and reduces the likelihood of misdiagnosis. Incorporate Second Opinion Services: When faced with ambiguous frozen section results, hospitals should consider implementing a policy where second opinions from experienced pathologists or consultation with outside specialists are readily available. This can provide additional reassurance and help guide the surgical team in making more informed decisions. Implement Continuous Education and Training: Ongoing education for both surgeons and pathologists on the latest advancements in diagnostic techniques, the potential for tumor overlap (such as Schwannomas and Anaplastic Thyroid Carcinoma), and emerging research on atypical neck tumors is essential. Regular workshops or case study reviews can help practitioners stay current with best practices and avoid common diagnostic pitfalls. Invest in Post-Operative Follow-up and Reevaluation: In cases of uncertainty, hospitals should have a robust post-operative follow-up plan that includes reevaluating biopsy or intraoperative findings after further histological analysis. This ensures that any discrepancies in intraoperative diagnosis are caught early, reducing the risk of incorrect treatment plans being implemented. By adopting these operational strategies, hospitals and pathology laboratories can improve the accuracy and reliability of intraoperative diagnoses in ambiguous neck tumors, leading to more precise surgical decision-making, better patient outcomes, and reduced risks of misdiagnosis.

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