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Microcystic/Reticular Schwannoma: Morphological Features Causing Diagnostic Dilemma on Fine-Needle Aspiration Cytology

Authors' Contribution:
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Data Collection B
Statistical Analysis C
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Manuscript Preparation E
Literature Search F
Funds Collection G

ABCEF Shunyou Gong
ABD Said Hafez-Khayyata
ABDFG Wei Xin

Department of Pathology, University Hospitals of Cleveland and Case Western Reserve University School of Medicine, Cleveland, OH, U.S.A.

Corresponding Author: Wei Xin, e-mail: wei.xin@uhhospitals.org
Conflict of interest: None declared

Patient: Male, 28
Final Diagnosis: Microcystic/reticular Schwannoma
Symptoms: Neck fullness • finger tingling and numbness
Medication: —
Clinical Procedure: Surgical resection
Specialty: Anatomic Pathology

Objective: Rare disease

Background: Schwannoma is a common, benign, peripheral nerve sheath tumor. Fine-needle aspiration (FNA) has been very useful for diagnosing classic Schwannoma. Recently, a new morphological variant, the so-called microcystic/reticular Schwannoma, has been recognized. Although histological features of microcystic/reticular Schwannoma have been described, there are no available reports on its FNA cytological appearance.

Case Report: A 28-year-old male presented with right arm and finger tingling and numbness. Physical examination found a right lower neck mass. He underwent FNA, followed by needle core biopsy. A diagnosis of microcystic/reticular schwannoma was made. In this case report, we focused on the FNA diagnostic features, thoroughly searched the literature, and discussed relevant information for differential diagnosis.

Conclusions: Unlike classic Schwannoma, microcystic/reticular variant has unique cytological features which can mimic those of several morphologically similar mass lesions, making the FNA interpretation more challenging. Cytopathologists should be aware of this new variant of Schwannoma when evaluating FNA cytology of mass lesions showing low-grade, paucicellular, and myxoid features.

MeSH Keywords: Biopsy, Fine-Needle • Diagnosis • Neurilemmoma

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Background

Schwannoma arises from the Schwann cells that encompass the peripheral nerve bundles. The classic anatomic locations of Schwannoma include the distal extremities and head and neck regions. Schwannoma cases are seen predominantly in adults and have no significant sex predilection [1–4]. Schwannoma often presents as a painless, circumscribed, usually encapsulated mass, with a bland-looking spindle cell morphology with mixed Antoni A (hypercellular, often containing Verocay bodies) and Antoni B areas, and strongly positive for S-100 protein by means of immunohistochemistry (IHC) [5]. Most Schwannomas are benign and usually cured by surgical resection, although the so-called "malignant Schwannoma" does rarely occur.

Although a minor component of a reticular growth pattern has been described in some cases of conventional Schwannomas [6,7], Liegl et al. reported a series of Schwannomas showing a predominantly/exclusively microcystic/reticular growth pattern. These Schwannomas, termed "microcystic/reticular schwannomas", were considered as a distinct clinico-pathological variant for their predilection for visceral organs and unique morphological features. Apart from the characteristic microcystic and reticular growth patterns, this tumor variant lacks Antoni A, Antoni B areas, and Verocay bodies, which are, in contrast, commonly seen in conventional Schwannomas. Additionally, Schwann cells exhibited abundant eosinophilic cytoplasm and were variably set in a myxoid or collagenous stroma [8]. Here, we report the FNA features of a case of microcystic/reticular Schwannoma arising in the lower neck/thoracic region and involving fibrofatty tissue and skeletal muscle. To the best of our knowledge, the present case is the first report of FNA cytological features of this rare variant of Schwannoma.

Case Report

A 28-year-old male presented to his primary care physician with right lower neck fullness for the past 5–6 years, and a 1-month history of right arm and finger tingling and numbness. He did not have decreased sensation in the tingling areas. Physical examination revealed a palpable mass in the right lower neck, extending to the upper back, with the brachial plexus and subclavian blood vessels right on the anterior surface of the mass. A neurogenic tumor was highly suspected.

MRI showed a 14-cm multi-lobulated mass in the right neck extending to the retroclavicular region and the superior portion of the thorax. The mass appeared to be infiltrating into the posterior scalene muscle and supraspinatus muscle on the right side, with extension into the plane of brachial plexus and anterior displacement of the axillary artery and vein,

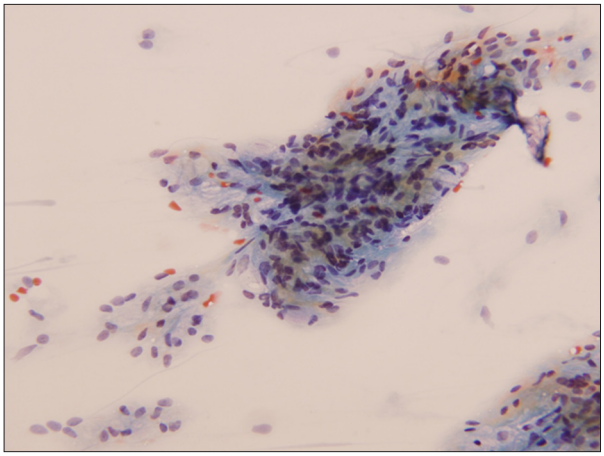

Figure 1. Fine-needle aspiration smear of tumor (Pap stain, ×100) showed monotonous population of bland spindle cells set in a myxoid background.

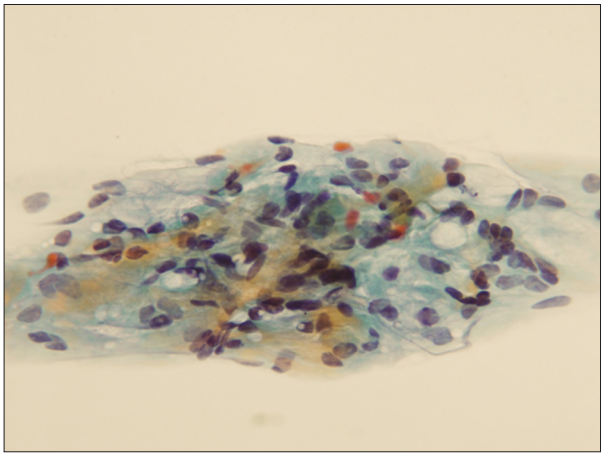

Figure 2. Fine-needle aspiration smear of tumor (Pap stain, ×400) demonstrated clusters of cells forming microcystic structures. The cells had bland nuclei with inconspicuous nucleoli, and exhibited abundant eosinophilic cytoplasm without distinct cell borders. Neither mitotic figures nor necrosis were seen.

but without definite evidence of encasement of brachial plexus structures, arterial encasement, or venous thrombosis. There was no evidence of bony remodeling, or extension to the cervical spine or beyond the pleura. The radiologic findings were suggestive of a neurofibroma, peripheral nerve sheath tumor, or vascular tumor.

CT-guided FNA was performed for cytological diagnosis. Several passes with a 20-gauge needle were performed. On Papanicolaou-stained slides, the specimen was cellular and consisted of a monotonous population of uniform, bland spindle cells set in a myxoid background (Figure 1). Clusters of cells forming microcystic structures were evident. Neither mitotic figures nor necrosis were seen. The cells had bland nuclei

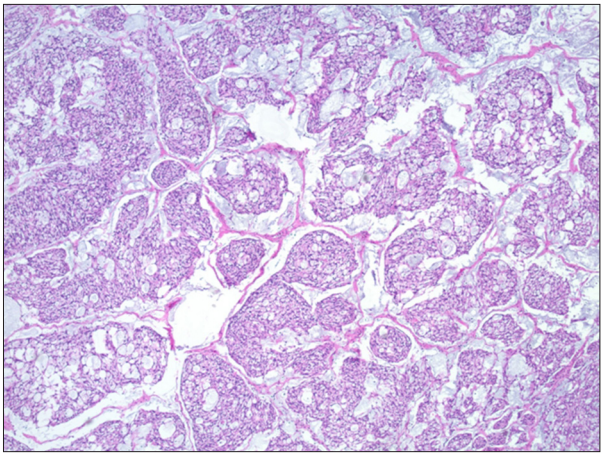

Figure 3. H&E stained sections of surgically resected tumor (×40) showed numerous microcystic structures formed by spindle cells, architecturally demonstrating a plexiform growth pattern.

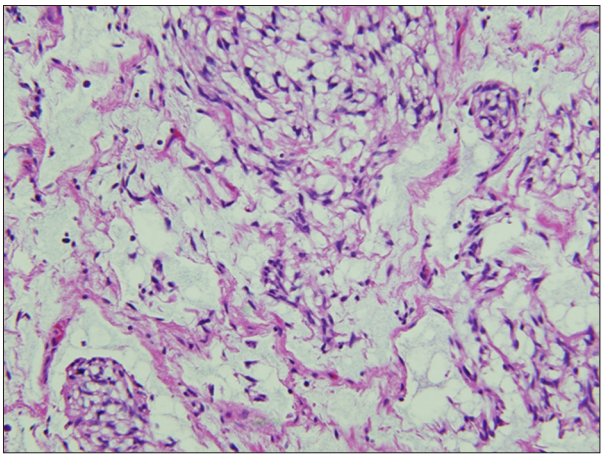

Figure 4. H&E stained sections of surgically resected tumor (×200) revealed that the tumor cells had abundant eosinophilic cytoplasm and bland-looking nuclei with no mitotic activity. A myxoid background was prominent. No Antoni A or Antoni B areas were present. No Verocay bodies could be identified.

with inconspicuous nucleoli, and they exhibited abundant eosinophilic cytoplasm without distinct cell borders (Figure 2). Based on the morphology, the differential diagnoses included benign peripheral nerve sheath tumor (schwannoma, neurofibroma), low-grade sarcoma or carcinoma, and infection diseases. AFB, GMS, and Gram stains were negative for organisms. The spindle cells were uniformly and strongly positive for S-100 and were negative for GFAP, AE1/AE3, CD117, desmin, CD34, and CD68. Although cytological and IHC findings strongly suggested the diagnosis of Schwannoma, no features of classic Schwannoma, such as Antoni A and Antoni B areas and Verocay bodies, were seen. A tissue biopsy for a definitive histopathological diagnosis was suggested.

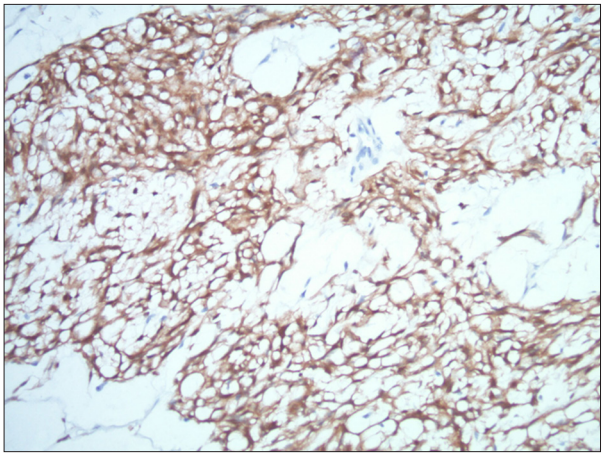

Figure 5. S100 immunohistochemical stain of surgically resected tumor (×200) showed that the tumor cells were strongly positive for S-100 protein.

Accordingly, the patient underwent needle core biopsy. The lesion was composed of bland-looking spindle cells connected by complex weblike maximal eosinophilic cytoplasmic extensions. Myxoid substance was present intracellularly and extracellularly. The tumor cells had unremarkable and inconspicuous nucleoli, with no mitotic activity identified. IHC stains showed that the tumor cells were positive for S-100 protein and negative for AE1/AE3, CAM 5.2, SMA, CD34, and p63. The morphological and IHC findings supported the diagnosis of reticular/microcystic schwannoma, and complete surgical excision was suggested.

The tumor was resected completely and sent for pathological examination. Grossly, a tan-brown, homogeneous, fleshy, multilobulated, soft tissue mass, involving the skeletal muscle and fibrofatty tissue, was observed. The tumor measured 13 cm in its greatest dimension, had an irregular shape, and it was encapsulated, with no areas of necrosis, hemorrhage, or cystic degeneration. All resection margins were tumor-free. Histological examination showed bland-looking spindle cells forming microcystic structures and architecturally demonstrating a plexiform growth pattern (Figure 3). A myxoid background was prominent. No Antoni A or Antoni B areas were present. No Verocay bodies could be identified. The tumor cells had abundant eosinophilic cytoplasm and bland-looking nuclei with no mitotic activity (Figure 4). The neoplastic cells were strongly positive for S-100 protein (Figure 5), and negative for synaptophysin and chromogranin. The final diagnosis was reticular/microcystic Schwannoma. The patient recovered well and was discharged 2 days after the surgery. No recurrence was reported after 4 years and 3 months.

Discussion

Schwannoma is a common peripheral nerve sheath tumor which rarely recurs. Most Schwannomas develop in the subcutaneous

soft tissue of the head and neck, and distal extremities. Classic schwannoma usually presents as an encapsulated mass that histologically demonstrates intermixed Antoni A, Antoni B areas, and Verocay bodies. The bland-looking spindle tumor cells are strongly positive for S-100 protein, and EMA highlights the capsule [5]. Several morphological variants of Schwannoma have been reported, including ancient Schwannoma, cellular Schwannoma, plexiform Schwannoma, melanotic Schwannoma, epithelioid Schwannoma, hybrid Schwannoma/perineurioma, hybrid Schwannoma/neurofibroma, and glandular Schwannoma [9]. Recently, a new variant of Schwannoma, reticular/microcystic Schwannoma, was reported [8]. This new variant of Schwannoma has a predilection for the GI tract and demonstrates characteristic strands of bland spindle cells in a myxoid background, with various proportions of microcystic structures. In contrast to the classic Schwannoma, microcystic/reticular Schwannoma does not show alternating Antoni A, Antoni B areas, and Verocay bodies. Since the introduction of this new variant, several case studies have been published. Most cases arose from the GI tract and other visceral organs [8,10–12]. Only rare cases occurred in subcutaneous soft tissue [13].

Our case was a 28-year-old male who presented with a slowly growing, 13-cm, lobulated, encapsulated mass in the lower neck/upper back location. The tumor involved the fibrofatty tissue and skeletal muscle, raising concern of malignancy. However, the tumor was grossly encapsulated and cytologically bland. Neither mitotic activity nor necrosis was present. Microscopically, the tumor was composed of characteristic strands of spindle cells with extensions of eosinophilic cytoplasm, in a background of myxoid and fibrillary collagen. The tumor cells were uniformly and strongly positive for S-100 protein, and negative for cytokeratin and CD34. All the above features supported the diagnosis of microcystic/reticular Schwannoma. The tumor was resected successfully and no recurrence has been reported to date.

Differential diagnosis for this case includes several morphologically similar soft tissue tumors, including neurofibroma [14], reticular perineurioma [15], myoepithelioma [5], and nerve sheath myxoma [16]. Neurofibroma, which generally demonstrates patchy S-100 protein positivity, was ruled out because the spindle cells were strongly and uniformly positive for S-100 in our case. Reticular perineurioma can have overlapping morphology with microcystic/reticular Schwannoma, but the tumor cells are negative for S-100 protein and positive for EMA. Myoepithelioma demonstrates reticular distribution of spindle cells and myxoid background; however, a certain degree of pleomorphism on histology is usually seen and a proportion of tumor cells are stained epithelial markers, such as EMA. Unlike our case, nerve sheath myxoma is S-100 protein-negative.

FNA is extremely valuable in diagnosing soft tissue tumors, including Schwannoma. The procedure is only minimally invasive and can be carried out at a physician's office. Moreover, FNA is very cost-effective and has fairly high sensitivity and specificity. For example, a study found that the sensitivity, specificity and positive predictive value of FNA in diagnosis of soft tissue tumors were 91.5%, 92.5%, and 95.5%, respectively [17]. For classical Schwannoma cases, FNA usually shows clusters of spindle cells and remnants of Verocay bodies. S-100 protein is uniformly positive. Schwannoma can be reliably diagnosed at FNA if all of the above features are seen [18]. In our case, FNA did not show Verocay bodies, but instead showed strands of bland-looking spindle cells with indistinct cell borders and delicate eosinophilic cytoplasm, some forming microcystic structures, in a myxoid background. The tumor cells were strongly positive for S-100 and negative for EMA and other epithelial markers. A diagnosis of microcystic/reticular schwannoma was suggested and confirmed by thorough examination of a surgical specimen. To the best of our knowledge, this is the first report of FNA features of microcystic/reticular Schwannoma.

Conclusions

We reported a case of microcystic/reticular variant of Schwannoma, a rare entity with FNA features very distinct from those of classic Schwannoma, making the FNA interpretation more challenging. Cytopathologists should be alert for this new variant of Schwannoma when they are dealing with an FNA of soft tissue mass, demonstrating bland-looking spindle cells with reticular/microcystic structures in a myxoid background.

References:

1. Veliovits D, Fiska A, Zorbas G, Tentes AA: Retroperitoneal schwannomas. Am J Case Rep, 2012; 13: 244–46
2. Guastini L, Mora R, Dellepiane M, Salami A: Excision of a tongue schwannoma with the Harmonic Scalpel®: Bloodless and harmless. Am J Case Rep, 2010; 11: 119–22
3. Zhao Y-B, Zhang L-C, Den Z-X, Hu W-L: Schwannoma of the adrenal gland. Am J Case Rep, 2009; 10: 209–12
4. Magro G, Torrisi A, Amico P et al: Ancient schwannoma of the thyroid: report of a case and comprehensive review of the literature. Am J Case Rep, 2008; 9: 182–87
5. Weiss SW, Goldblum JR: Enzinger and Weiss's soft tissue tumors. 5th ed. 2007, St. Louis: Mosby. xiv, 1268 p
6. Kazakov DV, Magro G, Yu Orlov A et al: Benign schwannoma with perineurioma-like areas: A clinicopathologic study of 11 cases. Int J Surg Pathol, 2006; 14(4): 320–25
7. Scheithauer BW, Woodruff J, Erlandson RA: Atlas of Tumor Pathology: Tumors of the Peripheral Nervous System, 3rd series. 1999, Washington, DC: AFIP
8. Liegl B, Bennett MW, Fletcher CD: Microcystic/reticular schwannoma: a distinct variant with predilection for visceral locations. Am J Surg Pathol, 2008; 32(7): 1080–87

9. Phan DC, Gleason BC: Recent developments in benign peripheral nerve sheath tumors. J Cutan Pathol, 2008; 35(12): 1165–69
10. Li S, Ai SZ, Owens C, Kulesza P: Intrapancreatic schwannoma diagnosed by endoscopic ultrasound-guided fine-needle aspiration cytology. Diagn Cytopathol, 2009; 37(2): 132–35
11. Liegl B, Bodo K, Martin D et al: Microcystic/reticular schwannoma of the pancreas: a potential diagnostic pitfall. Pathol Int, 2011; 61(2): 88–92
12. Pang JM, Mahar A, Shannon K et al: Reticular and microcystic schwannoma of the parotid gland. Pathology, 2013; 45(1): 96–98
13. Lau PP, Yau DT, Lau WH et al: Multinodular reticular schwannoma in the head and neck region: a potential diagnostic pitfall. Int J Surg Pathol, 2013; 21(1): 54–58
14. Saito M1, Tominaga S, Suzuki R et al: Unusual rapidly growing gastric myxoid neurofibroma: a case report. Gastroenterol Jpn, 1992; 27(2): 240–45
15. Graadt van Roggen JF, McMenamin ME, Belchis DA et al: Reticular perineurioma: a distinctive variant of soft tissue perineurioma. Am J Surg Pathol, 2001; 25(4): 485–93
16. Fetsch JF, Laskin WB, Miettinen M: Nerve sheath myxoma: a clinicopathologic and immunohistochemical analysis of 57 morphologically distinctive, S-100 protein- and GFAP-positive, myxoid peripheral nerve sheath tumors with a predilection for the extremities and a high local recurrence rate. Am J Surg Pathol, 2005; 29(12): 1615–24
17. Dey P, Mallik MK, Gupta SK, Vasishta RK: Role of fine needle aspiration cytology in the diagnosis of soft tissue tumours and tumour-like lesions. Cytopathology, 2004; 15(1): 32–37
18. Domanski HA, Akerman M, Engellau J et al: Fine-needle aspiration of neurilemoma (schwannoma). A clinicocytopathologic study of 116 patients. Diagn Cytopathol, 2006; 34(6): 403–12