

## Case Report

# Primary adrenal microcystic/reticular schwannoma: clinicopathological and immunohistochemical studies of an extremely rare case

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**Abstract:** A case of primary adrenal microcystic/reticular schwannoma affecting the right adrenal gland in a 31-year-old female was reported. Histologically, the tumor significantly consisted of strikingly anastomosing strands of spindle cells imparting a microcystic and reticular pattern with a focal transition to epithelioid nests. Immunohistochemically, S-100 and CD56 protein showed a uniform and strong positivity, GFAP and EMA weakly and focally expressed, but AE1/AE3, CK5/6, CD31, CD34, calretinin, D2-40, WT1, CgA, Melan-A and Neu-N were negative. The patient lived through a calm period for 4 months after the whole right paranephros was removed with no evidence of relapse. This interesting case showed primary adrenal microcystic/reticular schwannoma is characteristic of a distinctive and infrequent morphology compared to another subtype of schwannoma involved in the paranephros. To be familiar with its significant histological features would prompt us to take it into consideration when facing the mimickers.

**Keywords:** Microcystic/reticular schwannoma, adrenal gland, pathology, immunohistochemistry, differential diagnosis

## Introduction

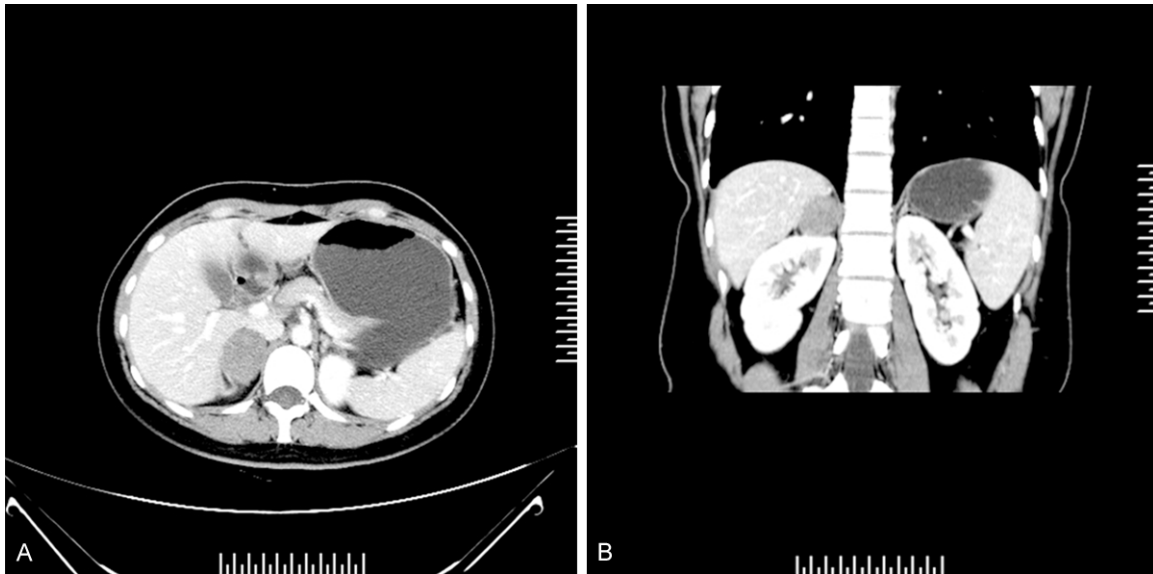
Schwannomas, as a benign peripheral nerve sheath tumors (BPNSTs), generally affect subcutaneous tissue of the head or neck region or the distal extremities [1]. Other than the classical schwannoma known as Antoni A and B areas in various proportions, Verocay bodies, and hyalinized vessels, varying morphologies had been appreciated, including ancient, cellular, melanotic, plexiform, glandular and epithelioid subtypes [1, 2]. Primary adrenal nerve sheath tumors are extraordinarily uncommon. Identical to those of schwannoma at other automatic sites, the neoplasm in adrenal glands shares an abundant morphologic spectrum [3]. Recently, Rliegl et al reported a rare series of schwannomas bearing a distinctly microcystic and reticular architecture designated as “microcystic/reticular schwannoma”, one of which affected in adrenal gland was demonstrated [4]. Herein, we added a second case to describe the distinctive characteristics and discuss the relevant differential diagnosis.

## Clinical history

A 31-year-old female was admitted for discovering a lump involved the right adrenal gland by the ultrasonography when performed a routine health examination. Computed tomography (CT) scan showed the tumor presented with a well-defined demarcation with 42 mm×29 mm in maximum cross-section with a uniform density, reminiscent of adrenocortical adenoma (Figure 1A, 1B). No evidence of hormonal hypersecretion by the laboratory study. The right adrenal gland with the lump was totally resected, and the patient lived through a calm period without any evidence of relapse or metastasis for 4 months.

## Materials and methods

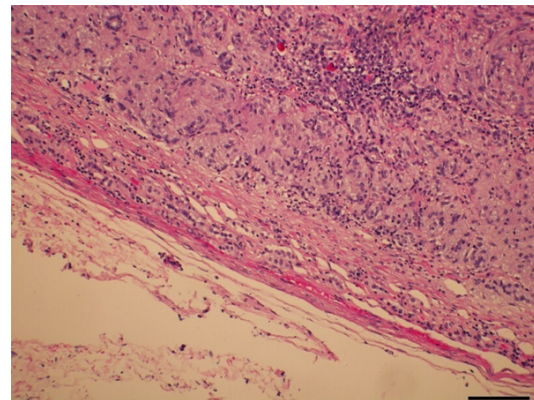
The surgical specimen were fixed in 4% formalin, embedded routinely in paraffin and then stained with hematoxylin and eosin. Immunohistochemical studies were performed using commercial antibodies in the Ventana Bench



**Figure 1.** Axial and coronal CT showed a tumor with a well-defined demarcation and a uniform low density involved in the right adrenal gland.



**Figure 2.** The tumor showed demarcated and round-like appearance with a grayish yellow color and a subtle firm cut surface.



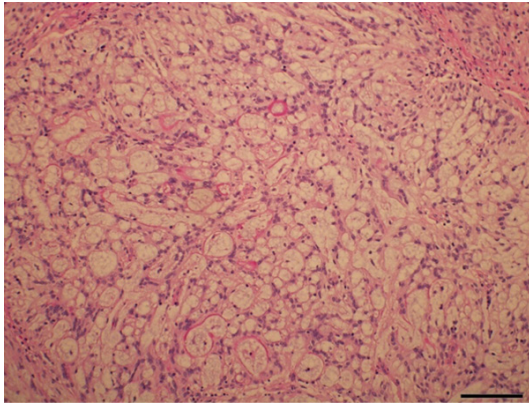
**Figure 3.** The tumor with well encapsulated pushing the normal adrenal tissues; Note the top right of this image showing the tumor's epithelioid region.

Mark XT instrument (Ventana System, Tucson AZ). The antibodies included S-100, CD56, CgA, EMA, AE1/AE3, CK5/6, CD31, CD34, calretinin, D2-40, WT1, Melan-A, Neu-N and Ki-67 (all above from Ventana, prediluted).

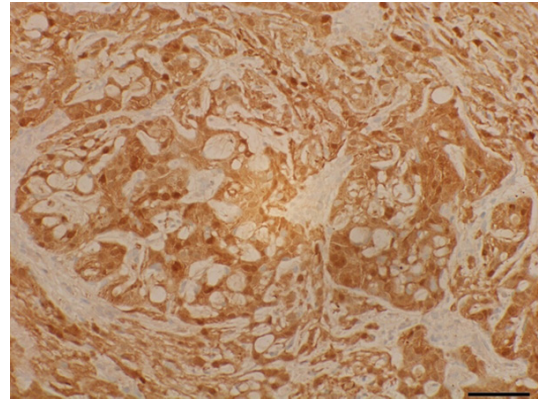
## Results

In gross, the tumor revealed a demarcated and round-like appearance measuring 4 cm in diameter and weighing 30 g with a grayish yellow color and a subtle firm cut surface (**Figure 2**). Microscopically, the tumor was well encapsulated and pushed the normal adrenal tissues

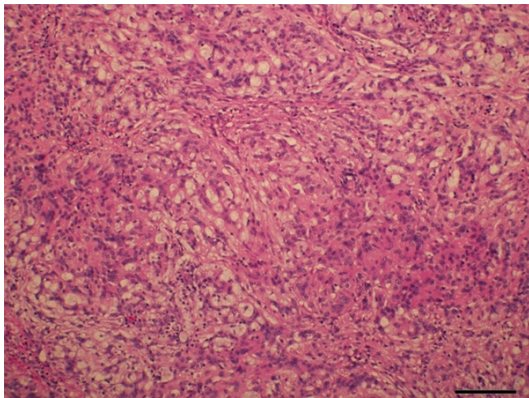
(**Figure 3**). The spindle cells organized in a significantly intersecting and anastomosing cords or strands pattern with eosinophilic cytoplasm and oval nuclei, superficially resembling a signet-ring or cribriform appearance (**Figure 4**). Focally, epithelioid cells arranged in nests gradually transformed into the classical microcystic structure (**Figure 5**). Obvious lymphocytes infiltrated and necrosis and mitotic image were not observed. Immunohistochemically, S-100 (**Figure 6**) and CD56 protein were diffusely positive throughout the lesion and GFAP and EMA focally expressed, but AE1/AE3, CK5/6, CD31, CD34, calretinin, D2-40, WT1, CgA, Melan-A



**Figure 4.** Tumor cells arranged in a significantly intersecting and anastomosing cords or strands pattern.



**Figure 6.** Tumor cells strongly and diffusely expressed S-100 protein.



**Figure 5.** Transition zone between the microcystic/reticular and epithelioid region.

and Neu-N were negative. Proliferative index Ki-67 was approximately 5%.

### Discussion

Analogous to the primary adrenal gland schwannoma, as one of extremely rare adrenal incidentaloma, there are no prominent clinical presentation and established guidelines to discover the adrenal microcystic/reticular schwannoma in time [5]. Only one same case was reported by RLiegl et al, so data were deficient to elaborate the epidemiologic features and gender and age predilection. Grossly, the neoplasm tends to be fully encapsulated pushing the adrenal tissues with a grayish yellow appearance. Histologically, the proliferating spindle tumor cells are circumscribed in the fibrous capsule and arrange in intersecting strands forming a distinctive and striking microcystic and reticular architecture with or without focal infiltration.

Focally but not dominated, epithelioid cells forming the nests or pocketing pattern, mimicking the epithelioid schwannoma, can be encountered and, alike the situation of our case, the evident transformation between these two components could easily appreciated [4]. Tumor cells share the similar immunophenotype like other morphologic variants, which are diffusely positive for S-100 protein, but negative for cytokeratins, Desmin, SMA, synaptophysin, chromogranin, CD56, and HMB45.

Several entities in adrenal gland with gland-like or microcystic architecture should be ruled out. The most important differential diagnostic consideration is adrenal cortical adenoma/hyperplasia, particularly with a pseudoglandular pattern [6]. However, a typical presentation of Cushing's syndrome or hyperaldosteronism in clinic, "organoid" configuration in focal areas, and usually positive stains for Melan-A, inhibin, calretinin can easily tell apart [7]. Adrenal adenomatoid tumor is another rare benign incidentaloma with a typically sieve-like architecture and infiltrates the normal adrenal tissues. Whereas, differing from schwannoma, adrenal adenomatoid tumors lack of sharp demarcation and are immunoreactive for mesothelium markers such as calretinin, C5/6, WT1, and D2-40, but negative for S-100 and GFAP [8]. Occasionally, gastrointestinal poorly differentiated adenocarcinoma involved the adrenal gland bearing ring-like appearance may seem to be a deceptive masquerader, but the infiltrative nature and positive immunostain for cytokeratin contribute to avoid falling into diagnos-



tic trap [4]. Sometimes, microcystic pattern may be confused with the well-differentiated liposarcoma or myxoid liposarcoma. However, existence of the evidence of nerve sheath-differentiated morphologic and immunostaining features, and deficiency in amplification of *MDM2*, *CDK4* as well as overexpression of the proteins, abundant myxoid matrix and prominent branching or plexiform capillary network, and the juxtaposition of *DDT3* and *TLS*, can aid us rule out these adipocytic tumors [9, 10]. In addition, the focal compact nests composed of epithelioid tumor cells can mimic pheochromocytoma. Existence of the clinical manifestation of hypertension or/and tachycardia, prominent “organoid” or neuroendocrine growth pattern in histology and CgA immunoreactivity support the diagnosis of pheochromocytoma. The mainstay of treatment is surgically excision; the sick reported in most literature were performed by tumor-removed operation and have an excellent favorable prognosis [4, 11].

In conclusion, primary adrenal microcystic/reticular schwannoma is an extremely rare incidentaloma with distinctive and misleading morphologic characteristics. An accurate diagnosis tends to be based on the recognition of this benign neoplasm to exclude otherwise mimickers by virtue of clinical presentation, image information, histological and immunohistochemical features.

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## Disclosure of conflict of interest

None.

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## References

[1] Kurtkaya-Yapici O, Scheithauer B and Woodruff JM. The pathobiologic spectrum of Schwannomas. *Histol Histopathol* 2003; 18: 925-934.

[2] Laskin WB, Fetsch JF, Lasota J and Miettinen M. Benign epithelioid peripheral nerve sheath tumors of the soft tissues: clinicopathologic spectrum of 33 cases. *Am J Surg Pathol* 2005; 29: 39-51.

[3] Lau SK, Spagnolo DV and Weiss LM. Schwannoma of the adrenal gland: report of two cases. *Am J Surg Pathol* 2006; 30: 630-634.

[4] Liegl B, Bennett MW and Fletcher CD. Microcystic/reticular schwannoma: a distinct variant with predilection for visceral locations. *Am J Surg Pathol* 2008; 32: 1080-1087.

[5] Jakowski JD, Wakely PE Jr and Jimenez RE. An uncommon type of adrenal incidentaloma: a case report of a schwannoma of the adrenal medulla with cytological, histological, and ultrastructural correlation. *Ann Diagn Pathol* 2008; 12: 356-361.

[6] Bollito ER, Papotti M, Porpiglia F, Terzolo M, Cracco CM, Cappia S, Gubetta L and Mikuz G. Myxoid adrenocortical adenoma with a pseudoglandular pattern. *Virchows Arch* 2004; 445: 414-418.

[7] Zhang PJ, Genega EM, Tomaszewski JE, Pasha TL and LiVolsi VA. The role of calretinin, inhibin, melan-A, BCL-2, and C-kit in differentiating adrenal cortical and medullary tumors: an immunohistochemical study. *Mod Pathol* 2003; 16: 591-597.

[8] Hamamatsu A, Arai T, Iwamoto M, Kato T and Sawabe M. Adenomatoid tumor of the adrenal gland: case report with immunohistochemical study. *Pathol Int* 2005; 55: 665-669.

[9] Hostein I, Pelmus M, Aurias A, Pedetour F, Mathoulin-Pelissier S and Coindre JM. Evaluation of *MDM2* and *CDK4* amplification by real-time PCR on paraffin wax-embedded material: a potential tool for the diagnosis of atypical lipomatous tumours/well-differentiated liposarcomas. *J Pathol* 2004; 202: 95-102.

[10] Knight JC, Renwick PJ, Dal Cin P, Van den Berghe H and Fletcher CD. Translocation t(12;16)(q13;p11) in myxoid liposarcoma and round cell liposarcoma: molecular and cytogenetic analysis. *Cancer Res* 1995; 55: 24-27.

[11] Mohiuddin Y and Gilliland MG. Adrenal schwannoma: a rare type of adrenal incidentaloma. *Arch Pathol Lab Med* 2013; 137: 1009-1014.