

## CASE REPORT

### A radiological and histological comparison of two unusual adrenal incidentalomas

Shihleone LOONG<sup>1</sup>, Sathiyamoorthy SELVARAJAN<sup>1,2</sup>, Li Yan KHOR<sup>1,2</sup>

<sup>1</sup>Department of Anatomical Pathology, Singapore General Hospital. <sup>2</sup>Duke-NUS Medical School, Singapore

#### Abstract

**Introduction:** The increasing use of radiological imaging studies has given rise to ‘incidentalomas’. **Case Report:** We describe two unusual and diverse incidental adrenal gland lesions, an adenomatoid nodule and a mature ganglioneuroma. Both are deemed ‘indeterminate’ on radiological assessment. On histology, an adenomatoid nodule is composed of variably-dilated thin-walled cysts lined by bland flattened cells and solid areas of tubules lined by eosinophilic cells with plump nuclei and prominent nucleoli. The lining cells are immunoreactive for calretinin and WT1 while negative for CK5/6, ERG and CD31. Mature ganglioneuroma features fascicles of bland spindle cells with intermixed mature ganglion cells disposed within a background myxoid stroma with no immature neuroblastic component. These spindled Schwann cells are S100 positive. **Discussion:** Both adenomatoid nodule and mature ganglioneuroma are rare benign adrenal tumours that need to be differentiated from other, more common adrenal lesions. The management of adrenal incidentalomas is challenging. Surgical excision is indicated if an adrenal incidentaloma is more than 4 cm in size, shows malignant features on imaging or evidence of hormone excess.

**Keywords:** Adrenal incidentalomas, adenomatoid nodule, ganglioneuroma

#### INTRODUCTION

With the increased use of radiological imaging studies, adrenal incidentalomas are being detected more frequently. The most common adrenal tumours are adenomas, pheochromocytomas and adrenocortical carcinomas. Other rare neoplasms arising in the adrenal gland include ganglioneuromas, paragangliomas, and neurofibromas.<sup>1-3</sup> Some adrenal tumours such as adrenocortical adenomas or carcinomas and pheochromocytomas can be associated with autonomous hormonal secretion, but it is usually not clinically detected in the settings of incidental adrenal tumours.<sup>2</sup> In this case report, we highlight two very different benign adrenal incidentalomas, an adenomatoid tumour and a mature ganglioneuroma, which were classified as ‘indeterminate’ by imaging studies.

#### CASE PRESENTATION

The first case is a 58-year-old male who presented with abdominal pain. Computed

tomography (CT) scan of the thorax, abdomen and pelvis showed an incidental nodule in the left adrenal gland. Further imaging studies revealed an ovoid solid nodule within a well-defined thin-walled cystic lesion on the left adrenal gland measuring 4.6 x 4.2 x 3.4 cm (Fig. 1A). The nodules demonstrated attenuation characteristics of 19.2 on pre-contrast phase, 45.3 on venous phase and 46.1 on delayed phase. As the enhancement characteristics were not typical of an adenoma, the lesion was deemed ‘indeterminate’ on radiology. The patient subsequently underwent left adrenalectomy. On gross examination, the nodule appeared encapsulated with a predominantly solid whitish cut surface with focal myxoid area and cystic change. Microscopic examination showed a well-circumscribed solid cystic lesion encapsulated by a thin fibrous capsule and composed of variably dilated thin-walled cysts lined by bland flattened cells and solid areas of tubules lined by eosinophilic cells with plump nuclei and prominent nucleoli (Fig. 1B and 1C). The lining

Address for correspondence: Dr Khor Li Yan, MB BCH. Am. B. Pathology (AP/CP, Cytopathology), Department of Anatomical Pathology, Singapore General Hospital, 20 College Road, Academia, Diagnostic Tower, Level 10, 169856, Singapore. Tel: +65 63214911. Fax: +65 62276562  
Email: khor.li.yan@singhealth.com.sg

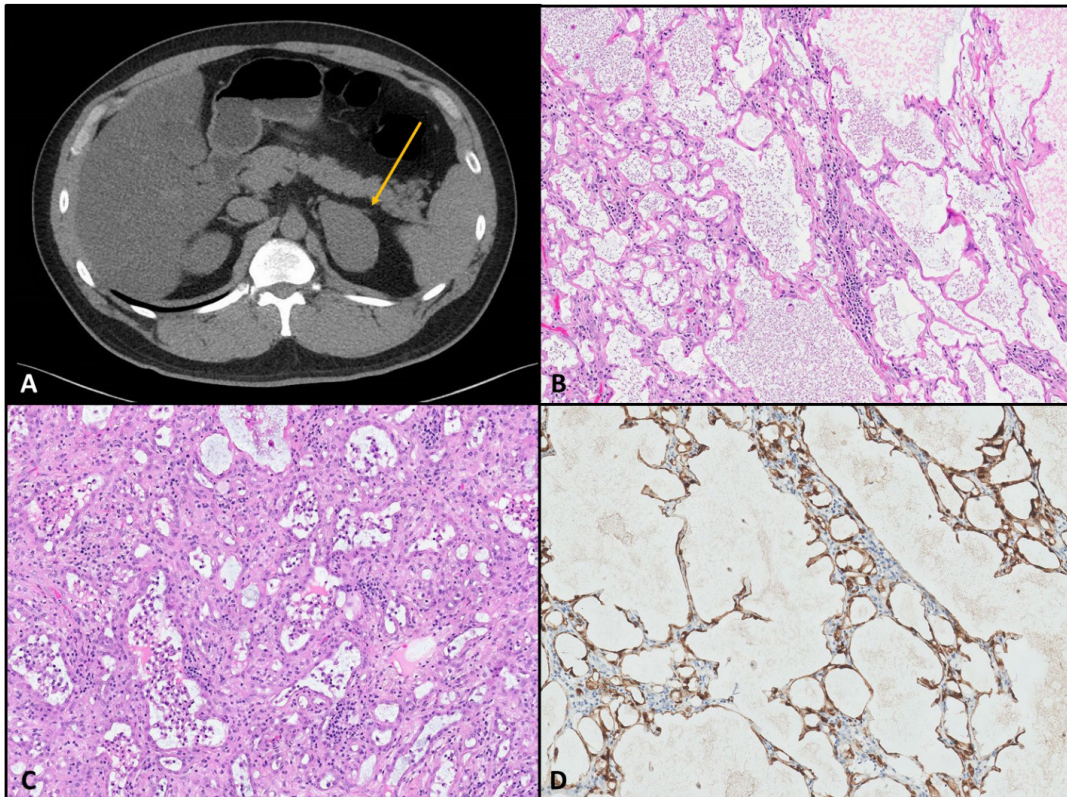


FIG. 1: (A) CT adrenal shows an ovoid nodule (orange arrow) arising from the left adrenal gland. (B) H&E stained section (magnification x100) showing variably dilated cysts lined by bland flattened cells. (C) H&E stained section (magnification x100) showing tubules lined by eosinophilic cells with plump nuclei. (D) Immunohistochemical stain for calretinin (magnification x100) showing cyst lining cells positive for calretinin.

cells were positive for calretinin (Fig. 1D) and WT1, while negative for CK5/6, ERG and CD31 by immunohistochemistry. A histologic diagnosis of a benign adenomatoid tumour was made.

The second case arose in a 41-year-old male who presented with non-specific abdominal discomfort and a left suprarenal mass identified on a CT scan of the abdomen and pelvis. A subsequent CT scan of the adrenal glands revealed a well-defined left suprarenal mass measuring 6.5 x 4cm arising from the medial limb and genu of the left adrenal gland (Fig. 2A). The mass was fairly homogeneous except for a small nodular area of enhancement in the medial and posterior aspects. It demonstrated a mild delayed enhancement and was thus, deemed 'indeterminate' on radiology. The patient subsequently underwent left adrenalectomy. Gross examination of the mass showed a firm and fibrotic appearance. Microscopic histological examination revealed a proliferation of slender bland spindle cells arranged in fascicles with

intermixed groups of matured ganglion cells within a background of fibromyxoid stroma (Fig. 2B and 2C). These spindle cells were confirmed to be Schwann cells by immunoreactivity for S100 (Fig. 2D). Scattered mast cells, chronic inflammatory cells and dystrophic calcifications were also seen. No residual immature neuroblasts were identified. Histological diagnosis of a mature ganglioneuroma was made.

## DISCUSSION

Adrenal masses in adult are most commonly accounted for by adrenocortical adenomas or carcinomas, pheochromocytomas, myelolipomas, haemangiomas, ganglioneuromas and metastatic tumours.<sup>3</sup> Adenomatoid tumour and ganglioneuroma represent rare entities that occur in the adrenal gland that often present as adrenal incidentalomas.

An adenomatoid tumour is a benign neoplasm of mesothelial origin that frequently occurs

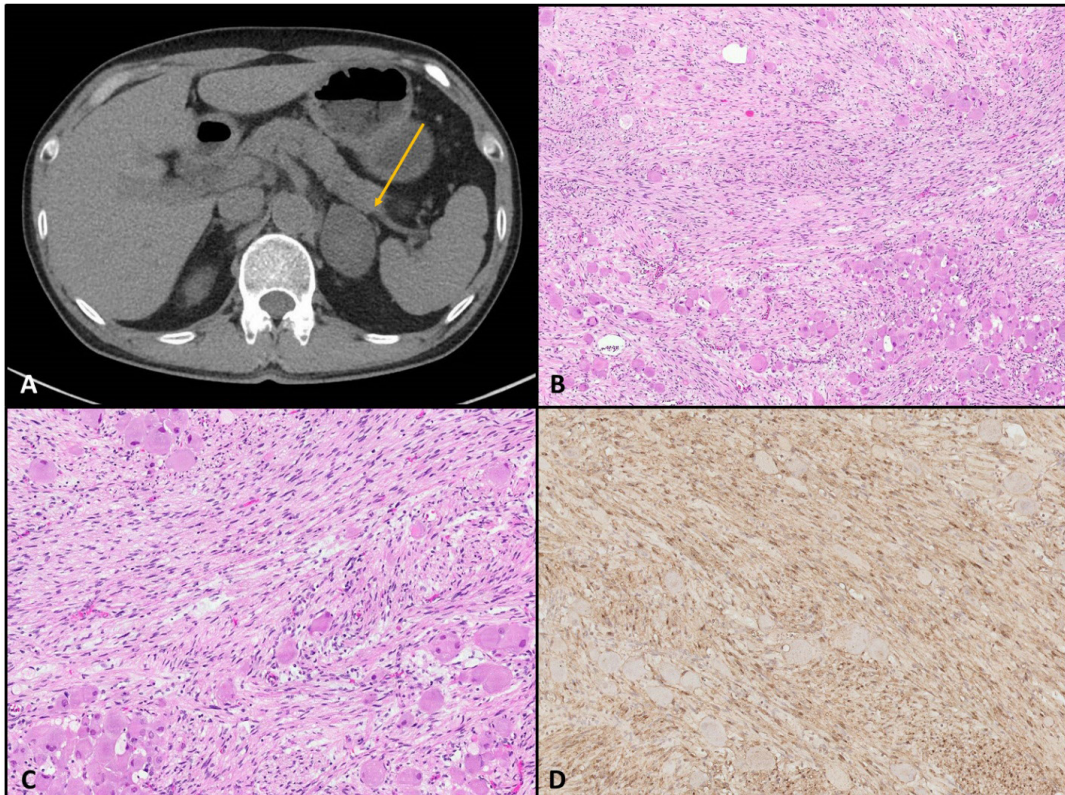


FIG. 2: (A) CT adrenal shows a homogeneous well-defined left suprarenal mass (orange arrow) arising from the medial limb and genu of the left adrenal gland. (B) H&E stained section (magnification x40) showing fascicles of bland spindle cells with intermixed ganglion cells. (C) H&E stained section (magnification x100) showing mature ganglion cells with no residual immature neuroblastic component. (D) Immunohistochemical stain for S100 (magnification x100) showing S100 positive spindle cells consistent with Schwann cells.

in the genital tracts of both male and female. Adenomatoid tumours occurring in the adrenal gland is rare. To the best of our knowledge, less than 40 cases of adenomatoid tumours occurring in the adrenal gland have been described thus far.<sup>4</sup> It has a male predominance with the peak incidence in the fourth decades<sup>5</sup>. The majority of reported adrenal adenomatoid tumours presented as incidentalomas identified on imaging studies performed for non-related conditions.<sup>5-7</sup>

Adenomatoid tumours can be solid and cystic on imaging studies. Contrast-enhanced CT usually shows a heterogeneously hypoattenuating mass with a well-circumscribed border and calcifications may be present. MR imaging findings are nonspecific and variable on T1-weighted, T2-weighted, and postcontrast images.<sup>8</sup> Preoperatively, adrenal tumours are often confused with other common adrenal gland tumours such as adrenocortical adenoma or carcinoma, myelolipoma, pheochromocytoma and metastatic carcinoma, due to a lack of specific

radiological features.<sup>9</sup>

Macroscopically, adenomatoid tumours are typically well-circumscribed or poorly defined with firm or soft consistency. The cut surfaces are usually smooth, greyish white to yellowish tan, with or without cystic areas. Histologically, adrenal gland adenomatoid tumours resemble their genital counterparts and comprise variably-sized tubules in a background of variably fibrous stroma. The tubules are lined by flattened cells to plump epithelioid cells with abundant eosinophilic cytoplasm. Signet-ring-like cells with apparent intracytoplasmic lumina are often present.<sup>7</sup> Four distinctive histologic patterns; adenoid, angiomatoid, solid and cystic have been described and most tumours contained a mixed patterns.<sup>7,10</sup>

The cells of the adenomatoid tumour often show strong immunoreactivity for calretinin, D2-40, S100, cytokeratins AE1/AE3, CAM 5.2, CK7 and vimentin.<sup>5-7</sup> Low MIB-1 proliferative activity, ranging from 0.2% to 2.7%, is

characteristic. The epithelioid, flattened and signet-ring-like cells of these tumours all exhibit the same immunophenotype.<sup>7</sup>

The adrenal adenomatoid tumour may cause diagnostic difficulties as its histologic features may mimic other entities such as adrenocortical adenoma or carcinoma, pheochromocytoma, myelolipoma, haemangioma, lymphangioma, angiosarcoma and metastases.<sup>6,7,11</sup> The presence of signet-ring-like cells may cause confusion with signet ring cell adenocarcinoma. However, the absence of nuclear atypia and the consistent reactivity to calretinin and WT1 support the diagnosis of an adenomatoid tumour. With indefinite radiological features, the treatment of choice is often surgical removal.<sup>5,11</sup> There has been no recurrence or metastatic disease reported thus far after complete excision.<sup>5,7</sup>

Ganglioneuroma is a rare benign neoplasm that arises from neural crest cells of the sympathoadrenal lineage. It represents the most well-differentiated tumour in the spectrum of neuroblastic tumours. It generally occurs more frequently in young adults but may also be observed in adults aged between 40 to 50 years.<sup>12-14</sup> It commonly arises in the posterior mediastinum, retroperitoneum and neck, with 20% occurring in the adrenal gland.<sup>12,15</sup>

Non-enhanced CT usually shows decreased attenuation measuring <40 Hounsfield units (HU) with punctate or discrete calcification.<sup>16</sup> Contrast-enhanced CT features a homogeneously hypoattenuating mass as compared with muscle, which surrounds vessels.<sup>17</sup> MR imaging findings include decreased signal intensity on T1-weighted images and heterogeneously increased signal intensity on T2-weighted images, with gradual delayed enhancement.<sup>16</sup> Although the imaging characteristics of adrenal ganglioneuroma have been well-described, the precise diagnosis using radiological evaluation is often difficult. As such, the differential diagnosis includes many benign and malignant tumours, including neuroblastoma and ganglioneuroblastoma in younger patients, as well as adrenocortical adenoma, pheochromocytoma and adrenocortical carcinoma.<sup>8</sup>

On gross examination, the adrenal ganglioneuroma is usually an encapsulated mass with a firm consistency and a homogeneous solid whitish cut surface.<sup>18</sup> Microscopically, it is characterised by the presence of ganglion cells individually distributed in the Schwannian stroma. There are two main subtypes, maturing and mature. The maturing ganglioneuroma

subtype has both maturing and mature ganglion cells, whereas the mature ganglioneuroma subtype has exclusively mature ganglion cells.<sup>19</sup> The stroma is composed of fascicular Schwann cells and bundled with perineurial cells. The mature Schwann cells are highlighted by S100 on immunohistochemistry.

Ganglioneuromas are slow-growing benign tumours that often remain clinically silent for a considerable time.<sup>20</sup> In the literature, a large (>6 cm) adrenal incidentaloma has a 25% probability of being an adrenal cortical carcinoma.<sup>21</sup> In our case, the size of the adrenal mass is 6.5 cm with indefinite radiological features. Therefore, surgical excision was done. Nevertheless, surgery still constitutes the gold standard for the treatment of primary adrenal ganglioneuroma.<sup>22,23</sup> Complete excision is often associated with an excellent outcome and no recurrence.<sup>20,24</sup>

In our institution, there are 18 cases of adrenal incidentalomas with no autonomous hormonal secretion reported in the past 5 years. These include 4 cases of mature ganglioneuroma, 1 case of adenomatoid nodule, 3 cases of myelolipoma, 4 cases of haemangioma/lymphangioma, 5 cases of benign cyst and 1 case of metastatic adenocarcinoma. The management of adrenal incidentalomas is challenging. Patients with adrenal incidentalomas on imaging studies should be screened for subclinical autonomous hormonal secretion such as catecholamine, cortisol or aldosterone excess.<sup>2</sup> If the non-contrast CT is consistent with benign features ( $\leq 10$  HU and homogenous) and the adrenal mass is smaller than 4 cm with no autonomous hormonal secretion, no further imaging and follow-up is required. However, if the adrenal mass is indeterminate in non-contrast CT, three options should be considered after a multidisciplinary team discussion taking into account the patient's clinical context: additional imaging with another modality, interval imaging in 6–12 months (non-contrast CT or MRI), or surgery.<sup>2,25</sup> Some have proposed that surgical excision is recommended if the size of an adrenal incidentaloma is more than 4 cm,<sup>26</sup> if the imaging is indeterminate. Surgical excision is indicated if an adrenal incidentaloma shows malignant features on imaging or evidence of hormone excess.<sup>25</sup> In both cases, the patients did not present with hormone excess. Both cases had masses of more than 4 cm with indeterminate imaging findings. Surgical excision was thus performed.

## CONCLUSION

Adenomatoid tumour and ganglioneuroma are rare tumours which may occur in the adrenal glands. Both tumours may present as incidental adrenal masses on imaging studies performed for other non-related conditions and they often have non-specific radiological findings resulting in surgical excision. Both tumours show benign histological features with a good prognosis after surgical excision. As they are both rare in the adrenal gland, an appropriate diagnosis should rely on the correlation of clinical, radiological and pathological findings. Non-contrast CT and evaluation of hormone excess are often necessary for investigating the nature of an adrenal incidentaloma and to guide the subsequent management.

## CONFLICT OF INTERESTS

The authors declared no conflict of interests

## REFERENCES

1. Hee YK, Sin GK, Kye WL, *et al.* Clinical study of adrenal incidentaloma in Korea. *Korean J Intern Med.* 2005; 20(4): 303-9.
2. Chatzelliis E, Kaltsas G. Adrenal Incidentalomas. [Updated 2016 Feb 5]. De Groot LJ, Chrousos G, Dungan K, *et al.*, editors. *Endotext* [Internet] South Dartmouth MDText.com, Inc. 2000.
3. Nieman LK. Approach to the Patient with an Adrenal Incidentaloma. *J Clin Endocrinol Metab.* 2010; 95(5): 4106-13.
4. Jiang G, Zhao Y, Fan C. An adenomatoid tumor of the right adrenal gland: a rare case report and review of the literature. *Int J Clin Exp Pathol.* 2018; 11(2): 1055-60.
5. Krstevska B, Mishevskaja SJ, Jovanovic R. Adenomatoid tumor of the adrenal gland in young woman: From clinical and radiological to pathological study. *Rare Tumors.* 2016; 8(4): 185-7.
6. Babinska A, Peksa R, Swiatkowska-Stodulska R, Sworczak K. The collection of five interesting cases of adrenal tumors from one medical center. *World J Surg Oncol.* 2014; 12(1): 1-8.
7. Isotalo PA, Keeney GL, Sebo TJ, Riehle DL, Cheville JC. Adenomatoid Tumor of the Adrenal Gland: A Clinicopathologic Study of Five Cases and Review of the Literature. *Am J Surg Pathol.* 2003; 27(7): 969-77.
8. Lattin GE, Sturgill ED, Tujo CA, *et al.* From the Radiologic Pathology Archives: Adrenal Tumors and Tumor-like Conditions in the Adult: Radiologic-Pathologic Correlation. *RadioGraphics.* 2014; 34(3): 805-29.
9. Rodrigo Gasque C, Martí-Bonmatí L, Dosdá R, Gonzalez Martínez A. MR imaging of a case of adenomatoid tumor of the adrenal gland. *Eur Radiol.* 1999; 9(3): 552-4.
10. Quigley J, Hart W. Adenomatoid tumors of the uterus. *Am J Clin Pathol.* 1981; 76: 627-35.
11. Wojewoda CM, Wasman JK, MacLennan GT. Adenomatoid tumor of the adrenal gland. *J Urol.* 2008; 180: 1123.
12. Tarantino R, Lacerda A, Cunha Neto S, Violante A, Vaisman M. Adrenal ganglioneuroma. *Arq Bras Endocrinol Metab.* 2012; 56(4): 270-4.
13. Yang Q, Xu B, Wang J, *et al.* Adrenal ganglioneuromas: a 10-year experience in a Chinese population. *Surgery.* 2010; 147: 854-60.
14. Rondeau G, Nolet S, Latour M, *et al.* Clinical and biochemical features of seven adult adrenal ganglioneuromas. *J Clin Endocrinol Metab.* 2010; 95(7): 3118-25.
15. Guo Y, Yang Z, Li Y, *et al.* Uncommon adrenal masses: CT and MRI features with histopathologic correlation. *Eur J Radiol.* 2007; 62(3): 359-70.
16. Maweja S, Materne R, Detrembleur N, *et al.* Adrenal ganglioneuroma. *Am J Surg.* 2007; 194(5): 683-4.
17. Radin R, David CL, Goldfarb H, Francis IR. Adrenal and extra-adrenal retroperitoneal ganglioneuroma: imaging findings in 13 adults. *Radiology.* 1997; 202(3): 703-7.
18. Adas M, Koc B, Adas G, Ozulker F, Aydin T. Ganglioneuroma presenting as an adrenal incidentaloma: a case report. *J Med Case Rep.* 2014; 8: 131.
19. Lloyd R *et al.* WHO Classification of Tumours of Endocrine Organs. 4th ed. International Agency for Research on Cancer; 2017.
20. Shetty P, Balaiah K, Gnana Prakash S, Shetty P. Ganglioneuroma Always A Histopathological Diagnosis. *Online J Heal Allied Sci.* 2010; 9(4): 19.
21. Mylonas KS, Schizas D, Economopoulos KP. Adrenal ganglioneuroma: What you need to know. *World J Clin Cases.* 2017; 5(10): 373-7.
22. Georger B, Hero B, Harms D, Grebe J, Scheidhauer K, Berthold F. Metabolic activity and clinical features of primary ganglioneuromas. *Cancer.* 2001; 91(10): 1905-13.
23. Economopoulos K, Mylonas K, Stamou A, *et al.* Laparoscopic versus robotic adrenalectomy: A comprehensive meta-analysis. *Int J Surg.* 2017; 38: 95-104.
24. Linos D, Tsirlis T, Kapralou A, Kiriakopoulos A, Tsakayannis D, Papaioannou D. Adrenal ganglioneuromas: incidentalomas with misleading clinical and imaging features. *Surgery.* 2011; 149(1): 99-105.
25. Fassnacht M, Wiebke A, Bancos I, Dralle H. Management of adrenal incidentalomas : European Society of Endocrinology Clinical Practice Guideline in collaboration with the European Network for the Study of Adrenal Tumors. *Eur J Endocrinol.* 2016; 175(2): G1-G34.
26. Mantero F, Arnaldi G. Management approaches to adrenal incidentalomas. A view from Ancona, Italy. *Endocrinol Metab Clin North Am.* 2000; 29: 107-25.