CASE REPORT

A radiological and histological comparison of two unusual adrenal incidentalomas

Shihleone LOONG1, Sathiyamoorthy SELVARAJAN1,2, Li Yan KHOR1,2

1Department of Anatomical Pathology, Singapore General Hospital. 2Duke-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, phaeochromocytomas and adrenocortical carcinomas. Other rare neoplasms arising in the adrenal gland include ganglioneuromas, paragangliomas, and neurofibromas.1–3 Some adrenal tumours such as adrenocortical adenomas or carcinomas and phaeochromocytomas can be associated with autonomous hormonal secretion, but it is usually not clinically detected in the settings of incidental adrenal tumours.2 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...
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, phaeochromocytomas, myelolipomas, haemangiomas, ganglioneuromas and metastatic tumours. 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...
ADRENAL INCIDENTALOMAS

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. It has a male predominance with the peak incidence in the fourth decades. The majority of reported adrenal adenomatoid tumours presented as incidentalomas identified on imaging studies performed for non-related conditions.

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. Preoperatively, adrenal tumours are often confused with other common adrenal gland tumours such as adrenocortical adenoma or carcinoma, myelolipoma, phaeochromocytoma and metastatic carcinoma, due to a lack of specific radiological features.

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. Four distinctive histologic patterns; adenoid, angiomatoid, solid and cystic have been described and most tumours contained a mixed patterns.

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

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.
characteristic. The epithelioid, flattened and signet-ring-like cells of these tumours all exhibit the same immunophenotype. The adrenal adenomatoid tumour may cause diagnostic difficulties as its histologic features may mimic other entities such as adrenocortical adenoma or carcinoma, phaeochromocytoma, myelolipoma, haemangioma, lymphangioma, angiosarcoma and metastases. 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. There has been no recurrence or metastatic disease reported thus far after complete excision.

Ganglioneuroma is a rare benign neoplasm that arises from neural crest cells of the sympatheticadrenal 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. It commonly arises in the posterior mediastinum, retroperitoneum and neck, with 20% occurring in the adrenal gland. Non-enhanced CT usually shows decreased attenuation measuring <40 Hounsfield units (HU) with punctate or discrete calcification. Contrast-enhanced CT features a homogeneously hypodense mass as compared with muscle, which surrounds vessels. MR imaging findings include decreased signal intensity on T1-weighted images and heterogeneously increased signal intensity on T2-weighted images, with gradual delayed enhancement. 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, phaeochromocytoma and adrenocortical carcinoma.

On gross examination, the adrenal ganglioneuroma is usually an encapsulated mass with a firm consistency and a homogeneous solid whitish cut surface. 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. The stroma is composed of fascicular Schwann cells and bundled with perineural 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. In the literature, a large (>6 cm) adrenal incidentaloma has a 25% probability of being an adrenal cortical carcinoma. 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. Complete excision is often associated with an excellent outcome and no recurrence.

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 adrenocarcinoma. 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. If the non-contrast CT is consistent with benign features (≤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. Some have proposed that surgical excision is recommended if the size of an adrenal incidentaloma is more than 4 cm, if the imaging is indeterminate, Surgical excision is indicated if an adrenal incidentaloma shows malignant features on imaging or evidence of hormone excess. 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