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Primary adrenal anastomosing haemangioma

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Anastomosing haemangioma (AH), a recently recognized, rare, benign vascular tumour, first discovered in the genitourinary tract, frequently affects the kidney and can be associated with end-stage renal disease [1]. It rarely occurs in the adrenal glands [2–3] and has been officially identified as a unique renal haemangioma subtype in the World Health Organization's (2016) classification of tumours of the urinary system and male genital organs. Considering associated imaging and pathological findings, it is similar to other malignant tumours such as angiosarcoma. Herein, we report a case of adrenal AH with the aim of improving the understanding of this rare tumour and promoting its accurate diagnosis and optimal management.

A 46-year-old man visited the hospital for a physical examination, which revealed a right adrenal mass. Computed tomography of the abdomen revealed a 2.0-cm mass in the right adrenal gland, which was diagnosed as a pheochromocytoma (Fig. 1). The patient had a 10-year history of hypertension and started medication after diagnosis. The patient took antihypertensive drugs (irbesartan and hydrochlorothiazide tablets) once per day, and his hypertension was well controlled.

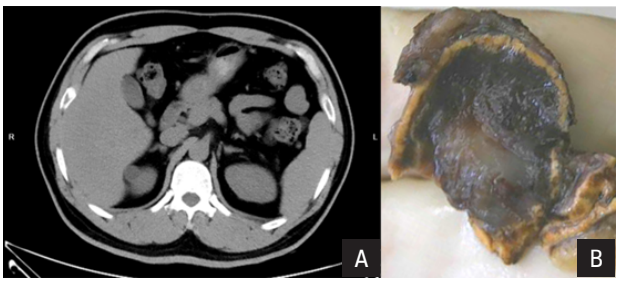

Figure 1. A. *Computed tomography scans showing a round mass in the right adrenal gland.* **B.** *Resected specimen showed a red, soft, well-defined mass in the adrenal gland*

Laboratory tests showed metanephrines at 33.1 pg/mL (normal reference range, 0–62 pg/mL), aldosterone at 111.52 ng/L (normal reference range, 50–313 ng/L), renin at 2.06 μg/L/h (normal range reference range, 1.45–5.00 μg/L/h), and an aldosterone/renin ratio of 5.41 (normal reference range, 0–30) in blood serum. The patient underwent right adrenalectomy and was followed up for 19 months. No recurrence or metastasis was detected.

A red, soft, well-defined mass 2.0 cm in diameter was observed in the excised right adrenal gland specimen. Histopathological examination revealed that the main tumour was composed of a splenic sinus-like vascular cavity, consisting of fissure and grid-like spaces of different sizes anastomosing with each other. The vascular cavity was lined with a single layer of flat, hobnail-like endothelial cells, and showed bleeding and fibrinous thrombus deposition (Fig. 2). The cytological characteristics of tumour cells were mild, the nuclear chromatin was uniform, the nucleolus was inconspicuous, mitosis was not observed, and there was no necrosis. Immunohistochemical staining of tumour cells was positive for CD31, CD34, EGR, and factor VIII, whereas cytokeratin, D2-40, and CD8 were negative (Fig. 3).

AH is a recently reported vascular tumour found mainly in the elderly population. Initially considered unique to the genitourinary system, it was later reported in the liver, gastrointestinal tract, ovary, adrenal gland, and paravertebral soft tissue [2]. AH has unique histopathological characteristics, comprising capillary-sized vascular channels, rare-to-absent mitosis, and mild-to-no nuclear atypia. Moreover, AH can appear as small fibrin thrombi, intracytoplasmic eosinophil globules, extramedullary haematopoiesis, or interstitial sclerosis [2]. Immunohistochemical analysis revealed diffuse endothelial marker staining, including ETS-related gene (ERG), friend leukaemia integration-1 (FLI1), CD31, CD34, and factor VIII. Immu-

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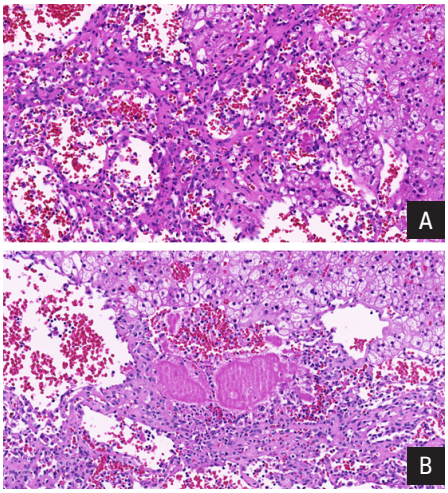

Figure 2. A. *The tumour was composed of anastomosing blood vessels with the adrenal cortex at the edges.* **B.** *The tumour cells had mild nuclear atypia, an inconspicuous nucleolus, and absent mitosis. Fibrin thrombotic deposition in the vascular cavity could also be seen*

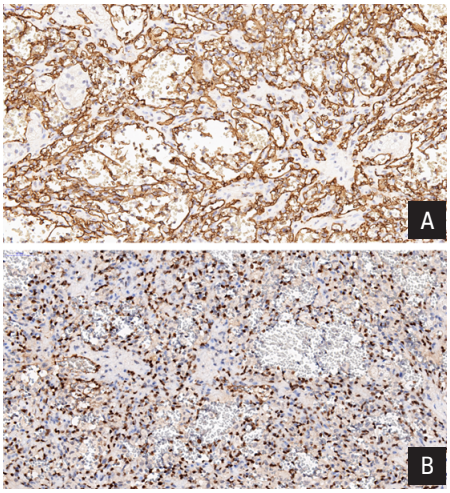

Figure 3. A. *CD34 (+) immunohistochemistry;* **B.** *ERG (+) immunohistochemistry. Endothelial cell differentiation was confirmed by immunohistochemical staining for CD34 and ERG*

nohistochemical staining of smooth muscle actin showed supporting pericytes at endothelial cell edges. Immunohistochemical staining for Ki-67 showed that endothelial cell proliferative activity was low. Immunostaining for CD8, D2-40, and glucose transporter 1 (GLUT-1) was negative, indicating that the tumour was not associated with splenic sinusoids, lymphangiogenic tumours, or juvenile haemangioma [4]. Sanger sequencing and mass array analysis revealed mutations in codon 209 of *GNAQ* and *GNA11* and in codon 205 of *GNA14* in AH. The overall mutation rate was 91% [5].

Although the diffuse, irregular vascular channels and mild cellular atypia of AH can mimic angiosarcoma, AH lacks hyperchromatic cells, an abundance of mitotically active endothelial cells, and significant necrosis. Moreover, the presence of mature adipose tissue, fibrin thrombi, and extramedullary haematopoiesis also suggests the possibility of AH. Although AH can grow irregularly in some soft tissues, these benign tumours lack the typical diffuse, invasive growth of angiosarcoma [6]. Differential diagnoses of AH also involve spleen tissue, manifesting as an accessory spleen or splenosis. Significant normal capsules, red pulp, white pulp, and arterioles of the accessory spleen can help to clearly distinguish it from AH. Although the AH vascular structure is similar to that of splenosis to some extent, splenosis only involves the red splenic pulp. Occasionally, CD8 immunohistochemical staining is positive, whereas for AH, it is negative [6].

The patient's prognosis was good. Much evidence shows that AH exhibits benign biological behaviour. There was no evidence of metastasis or recurrence after complete resection of the lesion. In some cases, after an accurate-core biopsy diagnosis and no further treatment, follow-up results show a lack of tumour progression [4].

In conclusion, we described the clinicopathological features of a rare AH case in the adrenal gland. Its similar anastomotic appearance could lead to the differential diagnosis of angiosarcoma. Recognizing this rare tumour can reduce angiosarcoma overdiagnosis and avoid unnecessary treatment.

Conflict of interests

The authors have no conflicts of interest to disclose.

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Competing interests

None declared.

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