



Case Report

Ectopic adrenal adenoma causing gross hematuria: Steroidogenic enzyme profiling and literature review

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Abbreviations & Acronyms

3 β HSD = 3 β -hydroxysteroid dehydrogenase
CA19-9 = carbohydrate antigen 19-9
CEA = carcinoembryonic antigen
CT = computed tomography
IgG4 = immunoglobulin G4
NSE = neuron-specific enolase
PCA = positive cell area
SCC = squamous cell carcinoma antigen
sIL-2R = soluble interleukin-2 receptor
TA = total area

Introduction: Aberrant cortical adrenal tissues are not generally identified in adults. Herein, we present a very rare case of an ectopic adrenal tumor located in the renal hilum that caused gross hematuria.

Case presentation: A 33-year-old man suddenly presented with asymptomatic gross hematuria. Abdominal computed tomography revealed a 35-mm mass in the left renal hilum encroaching the renal vein. Following the surgical removal with frozen section of the mass, his gross hematuria immediately improved. Pathological analysis of the specimen revealed the features adrenal adenoma. Immunohistochemical staining for key steroidogenic enzymes confirmed the adrenocortical origin without excessive hormone production.

Conclusion: This is the first case of an ectopic adrenocortical adenoma in the renal hilum that caused gross hematuria without hormonal symptoms.

Key words: ectopic adrenal adenoma, gross hematuria, renal hilum tumor, steroidogenic enzyme.

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Keynote message

This is the first case of an ectopic adrenocortical adenoma in the renal hilum that caused gross hematuria without excessive hormone production. To further investigate the etiology and hormonal function of the mass, we performed immunohistochemical analysis of key steroidogenic enzymes with literature review.

Introduction

Aberrant cortical adrenal tissues might descend with the primordial gonads along the course of their supplying arteries but are not commonly encountered in adults.¹ We describe an unexpected case of gross hematuria caused by an ectopic adrenocortical adenoma located in the renal hilum of an otherwise healthy adult.

Case presentation

A 33-year-old man presented to the hospital with a complaint of sudden gross hematuria. He had no associated pain or additional complaints. His laboratory workup revealed normal levels of hemoglobin and tumor markers (CEA, CA19-9, NSE, SCC, sIL-2R, and IgG4). Atypical urothelial cells were not detected in the urinary cytological test. In a cystoscopic examination, gross hematuria from the left ureteral orifice was found, although no apparent abnormalities were observed in bladder mucosa. In contrast, enhanced CT revealed a 35-mm mass with slight enhancement, which significantly compressed the left renal vein (Fig. 1a,b). Collateral vessels were not apparent between renal parenchyma and inferior vena cava. Abdominal

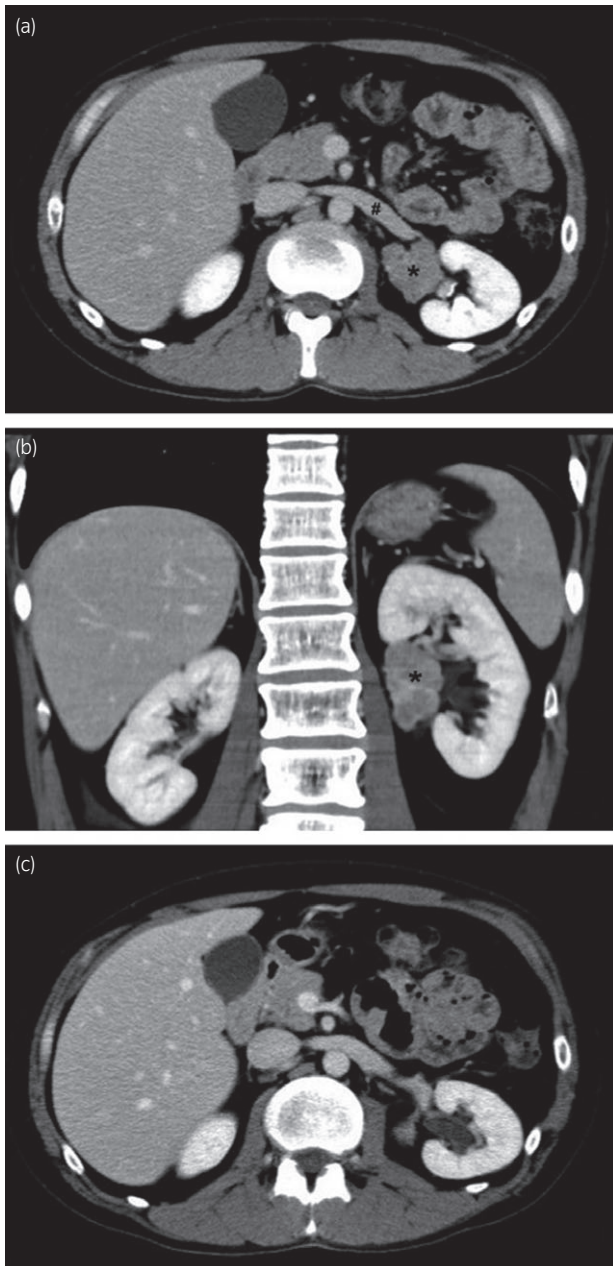


Fig. 1 Contrast-enhanced computed tomographic image. It shows anatomical tumor localization. A mass (*) is compressing the renal vein (#) (a: transverse view and b: coronal view). (c) Demonstrates postoperative transverse view of the same slice.

enhanced magnetic resonance imaging identified a low signal intensity of tumor at T1 as well as T2-weighted images with a slight enhancement and an almost normal intensity in diffusion weighted image suggesting a benign tumor. A CT-guided needle biopsy was not performed because the tumor was encroaching the renal vein, thus having a possible risk of hemorrhage. After obtaining the informed consent concerning surgery and subsequent publication, the patient underwent open tumor resection through retroperitoneal approach for easy extension of the resecting area in case the frozen section identified malignancy. During surgery, a yellowish, non-necrotic tumor compressing the renal vein was identified

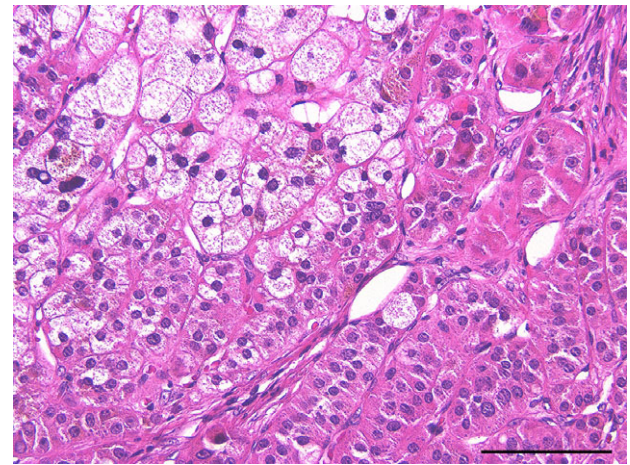


Fig. 2 Pathological features. The tumor consists predominantly of cells with eosinophilic cytoplasm in more than 75% of the mass (bottom right), while the remainder of the tissue consists of islands with vesicular or clear cytoplasm (upper left). Bar: 100 μ m.

corresponding to the CT findings. The result of the intraoperative rapid pathological analysis suggested a benign tumor. Therefore, the left kidney was spared and the surgery was completed.

Pathological examination identified the mass was directly surrounded by adipose tissue, lacking a distinct capsule, and was composed of adrenocortical-like cells. Medullary cells were not observed. The final pathological diagnosis was adrenocortical adenoma (Fig. 2).

According to the Weiss criteria,² the estimated malignant potential of the tumor was low, with only one of the nine criteria met, which was clear cells comprising $\leq 25\%$ of the tumor. Accordingly, the tumor was diagnosed as benign. The hematuria improved immediately after surgery, and no evidence of tumor recurrence was found during the 2-year follow-up, supporting the benign nature of the tumor.

To further investigate the etiology and hormonal function of the mass, we performed immunohistochemical analysis of key steroidogenic enzymes, as previously reported.^{3,4} 3β HSD, CYP11B2, CYP17, and CYP11B1 (Fig. 3). The PCA per TA of each stained section was measured by the Color Deconvolution software and the ImageJ software. The PCA/TA ratio of 3β HSD and CYP11B1 was 39.4% and 93.4%, respectively. The latter indicated that the tissue was of an adrenocortical origin. The PCA/TA of CYP17 was 10.0%, suggesting that some cells might have produced cortisol. The CYP11B2 staining result was positive only in a few cells (0.3%), indicating that the mass unlikely produced aldosterone.

After removal of the tumor, the narrowing of left renal vein disappeared in the CT image (Fig. 1c). At present, more than 2 years after the operation, there is neither recurrence nor even microscopic hematuria.

Discussion

We herein report an intriguing case of gross hematuria caused by an ectopic adrenocortical mass. Ectopic adrenocortical

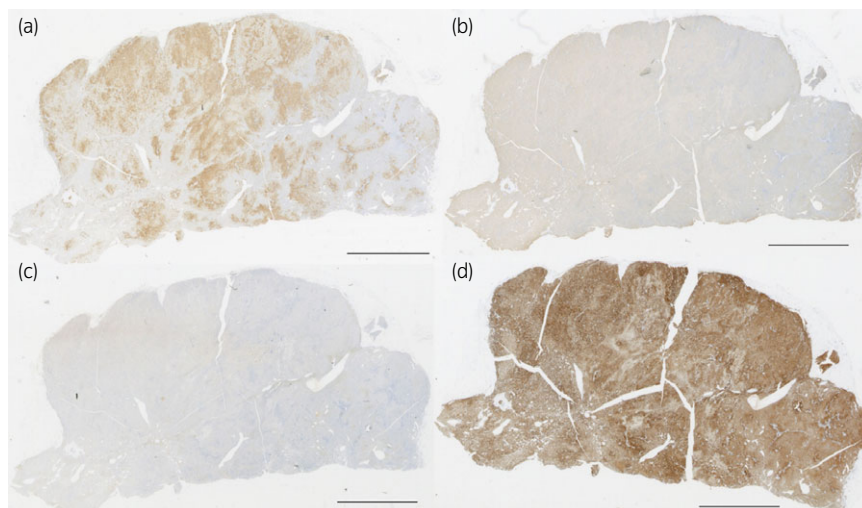


Fig. 3 Immunohistochemical analysis of key steroidogenic enzymes. High-resolution images (2400 dots/in) of immunostained sections for (a) 3βHSD, (b) CYP17, (c) CYP11B2, and (d) CYP11B1. Bars: 5 mm.

Table 1 Literatures related to ectopic adrenal adenoma in the renal hilum

Case	Title	Author	Journal	Age/sex	Symptoms	Complications endocrine disorder	Largest diameter
1	Ectopic adrenocortical adenoma in the renal hilum: a case report and literature review	Liu <i>et al.</i>	<i>Diagn. Pathol.</i> 2016; 11: 40	27/female	Amenorrhea	Borderline elevation of testosterone	2.5 cm
2	An ectopic adrenocortical adenoma of the renal sinus: a case report and literature review	Zhang <i>et al.</i>	<i>BMC Urol.</i> 2016; 16: 3	37/female	Hypertension Bilateral limb weakness	Possible primary aldosteronism with mild cortisol excess	3.4 cm
3	Ectopic cortisol-producing adrenocortical adenoma in the renal hilum: histopathological features and steroidogenic enzyme profile	Tong <i>et al.</i>	<i>Int. J. Clin. Exp. Pathol.</i> 2014; 7: 4415–21	53/female	Hypertension Weight gain Moon face Thin skin Systemic edema	Cushing's syndrome	3.5 cm
4	Laparoscope resection of ectopic corticosteroid-secreting adrenal adenoma	Wang <i>et al.</i>	<i>Neuro. Endocrinol. Lett.</i> 2012; 33: 265–7	38/male	Cushingoid appearance	Cushing's syndrome	5.3 cm
5	Corticotropin-independent Cushing's syndrome caused by an ectopic adrenal adenoma	Ayala <i>et al.</i>	<i>J. Clin. Endocrinol. Metab.</i> 2000; 85: 2903–6	63/female	Hirsutism Facial plethora Hypertension Centripetal obesity Proximal myopathy	Cushing's syndrome	3.5 cm
Current case	Ectopic adrenal adenoma causing gross hematuria: steroidogenic enzyme profiling and literature review	Ashikari <i>et al.</i>		33/male	Gross hematuria	No endocrinology disorders	3.5 cm

tissue can be found in children and usually regresses by puberty.¹ The most common sites of ectopic adrenocortical tumors are the celiac axis (32%), broad ligament (23%), adnexa of the testis (7.5%), and spermatic cord (3–8%).⁵ The growth of such ectopic adrenal rest tissue is promoted by excessive and sustained elevations of adrenocorticotropic hormone levels, such as those in patients with congenital adrenal hyperplasia, but is otherwise uncommon in adults. Presumably, ectopic adrenal tissue might undergo somatic mutations that led to adenomatous growth. Malignant transformation of

ectopic adrenal tissue has been previously reported; however, benign ectopic adrenal masses that cause hematuria have never been reported.

Based on image diagnosis and macroscopic findings during surgery, we assumed the nut-cracker mechanism would be the cause of hematuria in this case. Furthermore, the complete disappearance of hematuria after tumor removal also supported this assumption. In a typical case with nut-cracker phenomenon, the left renal vein is compressed between the superior mesenteric artery and the aorta. Therefore, it is easy

to detect left renal vein because its diameters before and after narrowing are relatively wide. In the present case, we could not measure renal venous pressures due to technical difficulty in detecting renal side of left renal vein.

We reviewed the summary of the manuscripts involved in ectopic adrenal tumor located in renal hilum. We identified five related articles and considered them (Table 1). Among the reported cases of ectopic adrenal tissue in the renal sinus, a 27-year-old woman presented amenorrhea with borderline elevation of testosterone,⁶ a 37-year-old woman with possible primary aldosteronism,⁷ a 38-year-old man with Cushing's syndrome,⁸ and a 63-year-old woman with Cushing's syndrome.⁹ Only one report, a 53-year-old woman with Cushing's syndrome, the mRNA levels of 3 β HSD, CYP17, CYP11B2, and CYP11B1 were analyzed by quantitative reverse transcription polymerase chain reaction and were suggestive of cortisol excess.¹⁰ All but this case has been identified because of hormonal symptoms accompanied by hormonally active tumors. We performed immunohistochemical analysis and obtained that 3 β HSD and CYP17 are highly expressed throughout the tumor. Conversely, in our case, the tumor had high 3 β HSD (39.4%) and CYP11B1 expression levels (93.4%) but low CYP17 (10.0%) and CYP11B2 expression levels (0.3%), indicating that the tumor was presumably non-functional. The immunohistochemical analysis of steroidogenic enzymes was useful for identifying true nature of the mass suggesting adrenal origin.

In conclusion, we here report for the first time a case of ectopic adrenal tumor in the renal hilum that was hormonally silent but, despite its benign nature, caused gross hematuria.

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Conflict of interest

The authors declare no conflict of interest.

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