


Case Report

Undifferentiated pleomorphic sarcoma of the retroperitoneum mimicking a cortisol- and catecholamine-secreting adrenal tumor

Takayoshi Fuu,  Akihiro Yano and Shinji Urakami

Department of Urology, Toranomon Hospital, Tokyo, Japan

Abbreviations

DST = dexamethasone suppression test
 MIBG = ¹²³I-metaiodo benzylguanidine
 RPS = retroperitoneal soft tissue sarcoma
 UPS = undifferentiated pleomorphic sarcoma

Correspondence: Takayoshi Fuu M.D., Department of Urology, Toranomon Hospital, 2-2-2 Toranomon, Minato-ku, Tokyo, 105-0001, Japan. Email: gjerryfuu@gmail.com

How to cite this article: Fuu T, Yano A, Urakami S. Undifferentiated pleomorphic sarcoma of the retroperitoneum mimicking a cortisol- and catecholamine-secreting adrenal tumor. *IJU Case Rep.* 2022; **5**: 195–198.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

Received 14 December 2021; accepted 4 March 2022.
 Online publication 22 March 2022

Introduction: Retroperitoneal tumors with endocrine abnormalities are suspected to be functional adrenal tumors. Retroperitoneal soft tissue sarcomas are rare tumors, without endocrine potential.

Case presentation: A 60-year-old male was referred for a 15 cm mass in the left suprarenal space. His plasma cortisol and catecholamine levels were elevated. He underwent open left adrenalectomy with radical nephrectomy and his endocrinological abnormalities were improved. Pathological findings suggested that it had originated from the retroperitoneal fat tissue, and a diagnosis of undifferentiated pleomorphic sarcoma was made based on the results of immunohistochemical analysis and fluorescence in situ hybridization. Interestingly, neither cortisol nor catecholamine was elevated when, 6 months after surgery, local recurrence developed.

Conclusion: This is the first reported case of undifferentiated pleomorphic sarcoma accompanied by high levels of cortisol and catecholamine. We should keep in mind the possibility of tumors like retroperitoneal soft tissue sarcomas inducing endocrine abnormalities.

Key words: catecholamine, cortisol, mimicking tumor, retroperitoneal tumor, undifferentiated pleomorphic sarcoma.

Keynote message

Retroperitoneal tumors with endocrine abnormalities are normally suspected to be functional adrenal tumors. There are unique cases of other tumors like sarcomas mimicking cortisol- and catecholamine-secreting adrenal tumors. We should keep in mind the possibility of non-adrenal tumors inducing endocrine abnormalities.

Introduction

Retroperitoneal masses around adrenal lesion with endocrine abnormalities are suspected to be functional adrenal tumors, which may be malignant or benign. A differential diagnosis is adrenal cortex adenoma or carcinoma with oversecreting of cortisol, or pheochromocytoma with oversecreting of catecholamine.¹ Initial diagnosis includes radiological phenotypical evaluation and biochemical assessment of tumor hormonal activity.² Most advocate resection of a mass larger than 4 cm if the patient is a surgical candidate, unless there is clearly a transient, infectious, or benign cause.¹

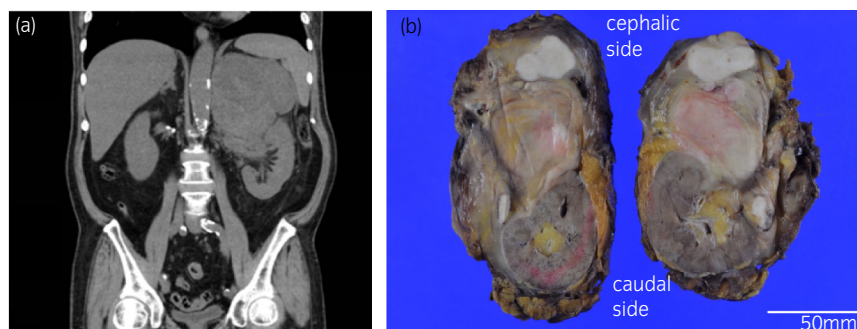
RPSs are rare tumors that account for approximately 12–15% of all soft tissue sarcomas with an incidence rate of 2.7 per million.³ RPSs are frequently incidental findings in the work-up for non-related diseases and can grow to an extremely large size in the retroperitoneum before symptoms of abdominal pain, back pain, bowel obstruction or a palpable abdominal mass.⁴ Surgical resection is the only hope for a cure and is therefore the treatment of choice for localized disease.⁴ Here we report a unique case of suprarenal RPS mimicking a cortisol- and catecholamine-secreting adrenal tumor.

Case presentation

A 60-year-old male presented with malaise and 10 kg weight loss over a period of 1 year. He also had a fever of over 38° and tachycardia. He had a history of hypertension, but no

Table 1 Laboratory findings on admission

Hematology			Biochemistry		
White blood cell	12 900	/ μ L	Total protein	7.6	g/dL
Neutrophil	77.2	%	Albumin	2.3	g/dL
Eosinophil	0.3	%	Blood urea nitrogen	9	mg/dL
Monocyte	7.2	%	Creatinine	0.53	mg/dL
Lymphocyte	14.7	%	Sodium	133	mEq/L
Red blood cell	3.78	$\times 10^6$ / μ L	Potassium	4.4	mEq/L
Hemoglobin	8.3	g/dL	Chloride	97	mEq/L
Platelet	769	$\times 10^3$ / μ L	Calcium	8.6	mg/dL
Coagulation			Total bilirubin	0.4	mg/dL
Prothrombin time	69.7	sec	Aspartate aminotransferase	46	IU/L
Activated partial thromboplastin time	29.8	sec	Alanine aminotransferase	53	IU/L
D dimer	0.4	μ g/mL	Alkaline phosphatase	1299	IU/L
			γ glutamyl transpeptidase	252	IU/L
			Lactate dehydrogenase	226	IU/L
			HbA1c	7.5	%
			C reactive protein	15.8	mg/dL
			Ferritin	954	μ g/dL
			Iron	12	μ g/L
			Tumor necrosis factor α	2.19	pg/mL
			Interleukin 6	97.9	ng/L

**Fig. 1** (a) Computed tomography of sagittal abdomen on admission (b) Macro image of the whole resected specimen. The tumor is on the cephalic side and the left kidney is on the caudal side.

transient elevation of blood pressure, headache or profuse sweating. Blood tests revealed inflammatory findings (C reactive protein 15.8 mg/dL), anemia (hemoglobin 8.3 g/dL) and deterioration of glucose tolerance (HbA1c 7.5%) (Table 1). Computed tomography showed a heterogeneous mass 15 cm in size in the left suprarenal space (Fig. 1a). Magnetic resonance imaging scan showed an internal heterogeneous mass with mixed high and low signal on T2-weighted images and fluorodeoxyglucose-positron emission tomography showed hyperintensity in the mass. For further assessment, detailed blood and urine tests were performed, the results of which are shown in Table 2. Briefly, serum cortisol levels were elevated at midnight and were not suppressed by 1 mg dexamethasone. Plasma adrenocorticotropic hormone level was markedly suppressed. In addition, 24-h urinary noradrenaline and normetanephrine levels were greater than three times the normal upper limit. These results indicated that the suprarenal tumor was an adrenal tumor, secreting both cortisol and catecholamine, although MIBG-scintigraphy showed no uptake in

Table 2 Endocrinological data on admission

Endocrinology	Value unit (reference value)
24 h urince catecholamine	984 μ g/day (34–198)
24 h urince dopamin	2730 μ g/day (280–1100)
24 h urince noradrenaline	960 μ g/day (31–160)
24 h urince metanephrine	1.12 mg/day (0.14–0.46)
24 h urince normetanephrine	0.97 mg/day (0.10–0.28)
24 h urince vanillylmandelic acid	5.47 mg/day (1.50–4.90)
Plasma adrenocorticotropin hormone	3.7 pg/mL (7.2–63.3)
Plasma cortisol	21.4 μ g/dL (4.5–21.1)
Plasma adrenocorticotropin hormone (DST 1 mg)	<1.0 pg/mL (7.2–63.3)
Plasma cortisol (DST 1 mg)	7.7 μ g/dL (4.5–21.1)
Plasma dehydroepiandrosterone sulphate	1022 ng/mL (270–1400)
Plasma testosterone	50.4 ng/dL (142.4–923.1)
Plasma aldosterone	6.4 ng/dL (3.0–15.9)
Plasma renin activity	18.5 ng/mL/h (0.2–2.3)

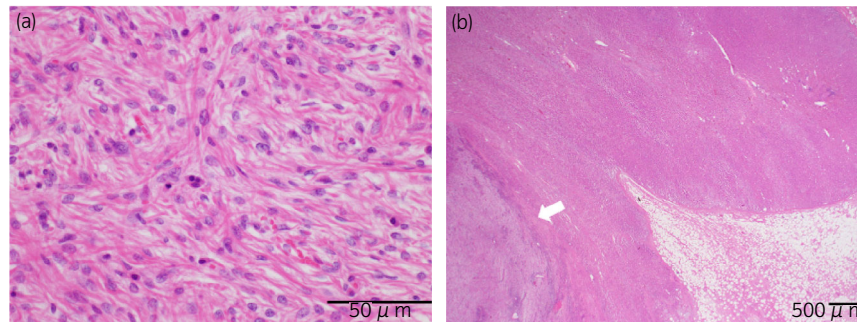


Fig. 2 (a) Diffuse proliferation of spindle and multi-forming cells with large hyperchromatic nuclei and narrow eosinophilic cytoplasm on hematoxylin and eosin-stained sections (original magnification $\times 400$) (b) Image of left adrenal gland and infiltrating tumor (white arrow) on hematoxylin and eosin-stained sections (original magnification $\times 20$).

the tumor. For more definitive diagnosis and treatment, we performed open left adrenalectomy with radical nephrectomy, with blood transfusions and 12 mg of oral doxazosin mesylate as preoperative preparation. No intraoperative hypertension was observed.

The tumor was a tan-colored, multilobulated solid mass $30 \times 25 \times 13$ cm in size, situated in the retroperitoneum around the superior pole of kidney, and it extended to the hilum of the left kidney (Fig. 1b). Histology revealed atypical spindle cells with a fascicular architecture intermingled with lymphoplasmacytic infiltrates (Fig. 2a). On immunohistochemistry, the tumor cells were positive for CD34 and negative for AE1/3, EMA, desmin, SMA, S100, c-KIT, SF-1, chromogranin A, synaptophysin, MDM2, and CDK4. The Ki67 labelling index was 12%. Fluorescence in situ hybridization revealed no amplification of MDM2. A definitive diagnosis of UPS was made. The left adrenal gland was slightly invaded, and hyperplasia was observed in the adrenal cortex but not in the adrenal medulla on hematoxylin and eosin-stained sections (Fig. 2b).

The patient was discharged 10 uneventful days following surgery, after recovering from fever and tachycardia. Catecholamine and cortisol levels had been normalized prior to discharge. Unfortunately, the patient developed local recurrence 6 months after the operation. Intriguingly, neither catecholamine nor cortisol levels were elevated at recurrence. The patient received radiotherapy to the local recurrent site with a total dose of 60 Gy in 25 fractions, and has since remained in stable condition without distant metastasis for a period of 5 months since the end of the radiotherapy.

Discussion

In the present case, suprarenal RPS mimicked a cortisol- and catecholamine-secreting adrenal tumor. To our knowledge, this is the first reported case of UPS accompanied by high levels of cortisol and catecholamine. UPS, formerly called malignant fibrous histiocytoma and declassified by the World Health Organization in 2002, is a rare and malignant subtype characterized by a lack of specific immunohistochemical markers for any specific lineage of differentiation.^{5,6} It represents the fourth most common soft

tissue sarcoma and has an incidence of about 0.08–1 per 100 000.⁷ In the present case, both preoperative imaging modalities and hormonal studies indicated a possible functional adrenal tumor secreting cortisol and catecholamine. Many case reports have described adrenal tumors, including malignant ones, that over-secrete these two hormones.^{8,9} In this case, however, pathological examination revealed that the tumor was UPS, without potential of producing the hormones. In addition, neither catecholamine nor cortisol levels were elevated when the local recurrence occurred. This implies that the tumor itself had not caused the elevations in these hormones that were seen when the patient first presented. One possible explanation for the high preoperative cortisol levels is adrenal cortex hyperplasia. Some soft tissue sarcomas have been reported to cause paraneoplastic syndrome, in which the tumor-derived growth factors and cytokines produced by these tumors induce adrenal cortex hyperplasia, which causes the adrenal gland to over-secrete cortisol.^{10–12} Some previous reports have described retroperitoneum tumors that mimicked pheochromocytoma.^{13–17} One hypothesis proposed by Ajmi *et al.* is that paracrine stimulation of adrenal secretion by the RPS results in elevated catecholamine.¹³ In the present case, however, imaging studies including MIBG scintigraphy did not show the presence of any neuroendocrine tumors such as paraganglioma. An alternative explanation is that catecholamine was overproduced due to compression of the renal vessels or the surrounding nerves by the large tumor. The former hypothesis has been proposed previously in connection with several other cases, indicating that the over-secretion of catecholamine is triggered by the renin-catecholamine pathway.^{13,14} The latter hypothesis is based on the anatomical observation of the sympathetic nerves surrounding the renal vessels.¹⁸

Conclusion

We presented a unique case of suprarenal UPS mimicking a cortisol- and catecholamine-secreting adrenal tumor. Even when we strongly suspect functional adrenal tumors, we should keep in mind the possibility of other tumors like RPS inducing endocrine abnormalities.

Acknowledgements

We thank Chris Rowthorn, from Eibunkousei.net (www.eibunkousei.net) for editing a draft of this manuscript.

Author Contributions

Takayoshi Fuu: Data curation; Writing – original draft. Akihiro Yano: Writing – review & editing. Shinji Urakami: Supervision.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Written informed consent was obtained from the patient and can be supplied on request.

Registry and the Registration No. of the study/trial

Not applicable.

References

- Nieman LK. Approach to the patient with an adrenal incidentaloma. *J. Clin. Endocrinol. Metab.* 2010; **95**: 4106–13.
- Cyrańska-Chyrek E, Grzymisławska M, Ruchała M. Pułapki w diagnostyce incydentaloma nadnerczy. *Endokrynol. Pol.* 2017; **68**: 360–77.
- Bonvalot S, Rivoire M, Castaing M *et al.* Primary retroperitoneal sarcomas: a multivariate analysis of surgical factors associated with local control. *J. Clin. Oncol.* 2009; **27**: 31–7.
- Messiou C, Moskovic E, Vanel D *et al.* Primary retroperitoneal soft tissue sarcoma: imaging appearances, pitfalls and diagnostic algorithm. *Eur. J. Surg. Oncol.* 2017; **43**: 1191–8.
- Doyle LA. Sarcoma classification: an update based on the 2013 World Health Organization classification of tumors of soft tissue and bone. *Cancer* 2014; **120**: 1763–74.
- Zhu Y, Hao D, Tang X, Sun L. Undifferentiated high-grade pleomorphic sarcoma of ethmoid sinus: a case report and literature review. *Braz. J. Otorhinolaryngol.* 2018; **84**: 389–92.
- Demetri GD, Antonia S, Benjamin RS *et al.* Soft tissue sarcoma. *J. Natl. Compr. Canc. Netw.* 2010; **8**: 630–74.
- Alexandraki KI, Michail OP, Nonni A *et al.* Corticomedullary mixed adrenal tumor: case report and literature review. *Endocr. J.* 2009; **56**: 817–24.
- Alsabek MB, Alhmaidi R, Ghazzawi B, Hamed G, Alseoudi A. Mixed corticomedullary adrenal carcinoma – case report: comparison in features, treatment and prognosis with the other two reported cases. *Int. J. Surg. Case Rep.* 2017; **31**: 254–61.
- Dorn C, Bugl S, Malenke E *et al.* Paraneoplastic granulocyte colony-stimulating factor secretion in soft tissue sarcoma mimicking myeloproliferative neoplasia: a case report. *BMC Res. Notes* 2014; **7**: 313.
- Des Guetz G, Mariani P, Freneaux P, Pouillart P. Paraneoplastic syndromes in cancer. *J. Clin. Oncol.* 2004; **22**: 2242–3.
- Angelousi A, Kyriakopoulos G, Nasiri-Ansari N, Karageorgou M, Kassi E. The role of epithelial growth factors and insulin growth factors in the adrenal neoplasms. *Ann. Transl. Med.* 2018; **6**: 253.
- Trimeche Ajmi S, Marmouch H, Trabelsi A *et al.* Retroperitoneal liposarcoma mimicking pheochromocytoma. *Pathologica* 2008; **100**: 470–2.
- Pekic S, Damjanovic S, Djurovic M *et al.* Retroperitoneal malignant fibrous histiocytoma mimicking pheochromocytoma. *Endocrine* 2004; **24**: 99–104.
- Kiriakopoulos A, Papaioannou D, Linos D. Adrenal cortical oncocytoma mimicking pheochromocytoma. *Hormones* 2011; **10**: 76–9.
- Caliskan S, Yencilek E. Large B-cell lymphoma mimicking adrenal pheochromocytoma. *Indian J. Med. Res.* 2013; **138**: 276.
- Lu J, Xiong XZ, Li L, Cheng NS. An unusual retroperitoneal tumour mimicking adrenal pheochromocytoma. *Dig. Liver Dis.* 2015; **47**: e18.
- García-Touchard A, Sañudo JR. Renal denervation. Importance of knowledge of sympathetic nervous system anatomy in refining the technique. *Rev. Esp. Cardiol.* 2019; **72**: 531–4.