Case Report

RECURRENT PRIMARY ADRENAL LEIOMYOSARCOMA: A COMPLETE LITERATURE REVIEW AND PRESENTATION OF A RARE ADRENAL TUMOR

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ABSTRACT

Objective: Leiomyosarcomas are mesenchymal tumors that very rarely present as a primary adrenal malignancy.

Methods: We present the complete clinical presentation, imaging, and anatomicopathologic features of a unique case of recurrent primary adrenal leiomyosarcoma (PAL) after initial surgery. This case is accompanied by an updated literature review.

Results: A 63-year-old Hispanic female referred to our clinic 4 months after having right adrenalectomy. Eight months prior to this encounter, she started to notice bilateral lower extremity edema with skin changes. Computed tomography of the abdomen revealed a large 6.8 × 4.4 cm adrenal mass that appeared to be encroaching in the inferior vena cava with hypodense areas, irregular borders, and a necrotic center. A preoperative hormonal evaluation failed to reveal evidence of a functional adrenal tumor. Microscopic examination revealed spindle cell neoplasia. Immunohistochemistry of the surgical specimen revealed positive staining for desmin, smooth muscle actin, and focal myogenin (MYF-4). S-100 protein and inhibin were negative. The diagnosis of intermediate-grade leiomyosarcoma was confirmed. Two months after surgery, surveillance positron emission tomography scan revealed another right adrenal mass measuring 5.6 × 5 cm, with a standardized uptake value of 2.1.

Conclusion: PAL is excessively rare. To our knowledge, this is only the second case of PAL with documented recurrence and the 19th case reported in the current medical literature. Surgical removal of the tumor is the first step in treatment. Adjuvant therapies are still not well standardized based on the low incidence of cases. **(AACE Clinical Case Rep. 2015;1:e8-e11)**

Abbreviations:
CT = computed tomography; **PAL** = primary adrenal leiomyosarcoma; **SMA** = smooth muscle actin

INTRODUCTION

Leiomyosarcomas are mesenchymal tumors that very rarely present as a primary adrenal malignancy. Our patient is a 63-year-old female who presented with worsening bilateral lower extremity edema, skin discoloration, and abdominal discomfort. Computed tomography (CT) showed a large right adrenal mass encroaching the inferior vena cava. Initial biopsy showed features of spindle cell neoplasia, and surgical specimens revealed similar histologic description. Immunohistochemistry was positive for desmin and smooth muscle actin (SMA) and negative for S-100 protein, and the Ki-67 proliferation index was focally greater than 50%. Follow-up imaging studies after surgery showed a new mass in the right adrenal fossa and evidence of prominent retroperitoneal lymph nodes.

CASE REPORT

A 63-year-old Hispanic female was referred to our clinic 4 months after having right adrenalectomy. Eight months prior to this encounter, she started to notice bilateral lower extremity edema with skin changes. She also reported diffuse nonspecific abdominal pain. She denied weight loss, fever, or vomiting. Her past medical history

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was significant for type II diabetes mellitus, diabetic retinopathy, peripheral neuropathy, dyslipidemia, coronary artery disease, and postablative hypothyroidism. Human immunodeficiency virus testing was negative. A CT scan of the abdomen revealed a large adrenal mass that appeared to be encroaching in the inferior vena cava and measured 6.8 × 4.4 cm with hypodense areas, irregular borders, and a necrotic center (Fig. 1). A preoperative workup did not reveal evidence of a functional adrenal mass. She underwent a CT-guided adrenal biopsy that showed spindle cell neoplasia with positive SMA in all tumor cells. Exploratory laparotomy was performed; the right mass arising from the adrenal gland was cut in half and resected with difficulty.

Two months after surgery, a surveillance positron emission tomography (PET) scan revealed another right adrenal mass measuring 5.6 × 5 cm, with a standardized uptake value of 2.1. Twenty-four-hour urine collection showed a metanephrine level of 21 μg/24 hours (normal, 90 to 315 μg/24 hours), normetanephrine level of 231 μg/24 hours (normal, 122 to 676 μg/24 hours), and total metanephrine level of 252 μg/24 hours (normal, 224 to 832 μg/24 hours). Repeat surgical intervention and radiotherapy were reconsidered, but ultimately the patient was treated with gemcitabine and Taxotere. A follow-up abdominal and pelvic CT scan showed rapid growth of the known right adrenal lesion, now measuring 9.5 × 8.5 × 9.5 cm, with prominent retroperitoneal lymph nodes.

Histopathology

A histologic report from another institution showed a reconstructed mass measuring 8.7 × 5.2 × 5 cm, with heterogeneous borders and areas of internal necrosis. Microscopic examination revealed spindle cell neoplasia (Fig. 2). Mitotic index was focally 7 mitoses per 10 high-power fields; atypical mitosis and necrosis were present.

Immunohistochemical Analysis

Immunohistochemical analysis of the initial right adrenal biopsy was positive for actin and desmin and negative for S-100. Ki-67 was present in 40% of proliferating cells.

Immunohistochemical analysis of the surgical specimen was positive for desmin, SMA, and focal myogenin (MYF-4). The analysis was negative for S-100 protein and inhibin. The Ki-67 proliferative index was focally greater than 50%. The diagnosis of intermediate-grade leiomyosarcoma was confirmed.

DISCUSSION

Primary leiomyosarcomas of the adrenal gland are exceedingly rare. Our literature review identified 18 reported cases including the current case (1-17), with the first reported by Lack et al (2) in 1991. Primary adrenal

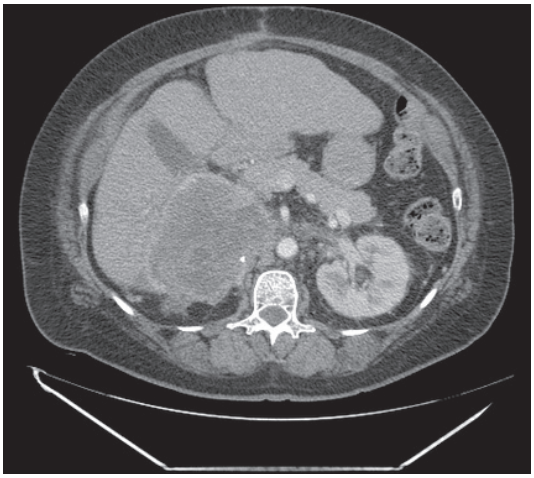

Fig. 1. 6.8 × 4.4 cm right adrenal mass with irregular borders and necrotic center.

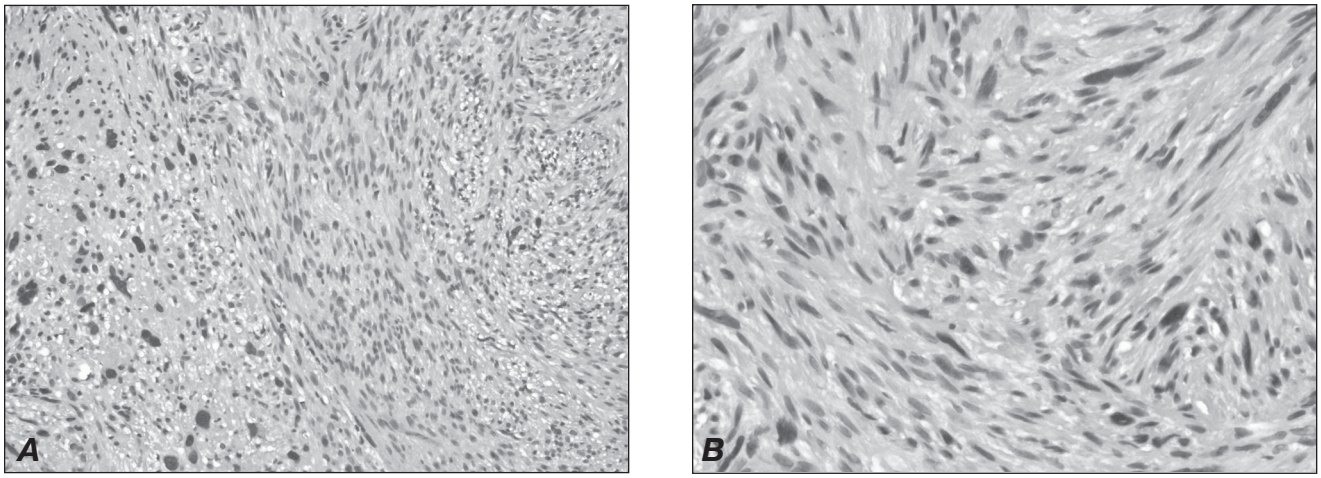

Fig. 2. (*A)* Biopsy of the adrenal gland, showing malignant spindle cell neoplasm. (*B)* Interlacing bundles and fascicles of spindle cells with elongated nucleus.

leiomyosarcoma (PAL) is a subgroup of mesenchymal tumors. When presenting as an adrenal lesion, the differential diagnosis includes malignant peripheral nerve sheath tumors (MPNSTs), metastatic sarcoma, metastatic carcinoma, malignant melanoma, primary retroperitoneal sarcoma, and gastrointestinal stromal tumors (3).

Adrenal leiomyosarcoma may derive from the smooth muscle wall of the central adrenal vein and/or its branches (4,5), presenting as a unilateral mass. No clear genetic predisposition or age distribution have been described, but human immunodeficiency virus and Epstein-Barr virus infections have been associated with this type of tumor (6,7). Linos et al (16) reported the first case of bilateral adrenal leiomyosarcomas in a 14-year-old patient with known acquired immunodeficiency syndrome.

Various imaging studies are used in the initial evaluation of adrenal masses. When a larger adrenal mass with decreased vascular flow is seen on ultrasound, PAL becomes part of the differential diagnosis. Dedicated screening of the inferior vena cava (IVC) is recommended, as invasion of the IVC is associated with poor prognosis (15). The CT and magnetic resonance imaging characteristics of PAL are indistinct from adrenal cortical carcinomas (ACCs) and metastatic cancers of adrenal glands (8). However, ACC may be functional, a feature that distinguishes these tumors from PAL.

Interlacing bundles of smooth muscle cells with variable uniformity and an increased number of mitoses per high-power field are the common initial histologic findings of leiomyosarcomas (3). Immunohistochemical muscle markers such as SMA, muscle-specific actin, and desmin are present in 90 to 95% and 70 to 90% of cases, respectively (1,4). The immunohistochemical characteristics of the right adrenal mass affecting our patient are presented in Table 1. The absence of S-100 protein along with muscle-specific markers helped differentiate PAL from MPNST in our case.

We report the second case of primary leiomyosarcoma with clearly documented disease recurrence. Given the few cases reported in the literature, disease progression and prognosis are difficult to estimate. Tumor size does not seem to be a good predictor of morbidity, as suggested by Etten et al (18), who reported a patient with a 27-cm adrenal leiomyosarcoma without evidence of metastasis

Table 1
Primary Adrenal Leiomyosarcomas: Clinical and Immunohistochemical Findings From the Literature

Case	Age (years)/ Sex	Initial Presentation	Imaging Studies	Tumor Size (cm)	Follow- Up	SMA	MSA	Desmin	S-100
Present case	63/F	Lower extremity edema and abdominal pain	Large right adrenal mass encroaching the IVC	8.7	Recurrent tumor in same area in 2 months F/U PET scan	+	ND	+	–
Gulpinar et al 2014 (14)	48/M	Frequent urination and nocturia	Right adrenal mass extending to liver border	9	No evidence of disease 8 months after surgery	+	ND	ND	–
Deshmukh et al 2013 (1)	60/F	Left abdominal mass on exam	Left upper abdominal mass posterior to pancreas and anterior to kidney	5.2	No metastasis in 21 months after surgery	+	ND	+	–
Tomasich et al 2008 (5)	48/F	Abdominal pain and mass on exam	Heterogeneous left adrenal mass	9	Died 53 months after surgery	+	+	+	NR
Lujan and Hoang, 2003 (4)	63/M	Painless growing abdominal mass	Adrenal tumor that invaded the superior pole of kidney and liver	25	Had lung metastasis; died shortly after surgery	–	–	+	–
Zetler et al 1995 (7)	30/M	Upper abdominal pain	Heterogeneous mass superior to left kidney	11	No evidence of disease 20 months after surgery	+	+	ND	–
Lack et al 1991 (2)	49/M	Severe right flank pain	Heterogeneous suprarenal mass	11	Had bony metastasis; no evidence of disease 9 months after surgery	+	+	ND	Weakly +

Abbreviations: F = female; F/U = follow-up; IVC = inferior vena cava; M = male; MSA = muscle-specific actin; ND = not done; NR = not reported; PET = positron emission tomography; S-100 = S-100 protein; SMA = smooth-muscle actin.

on autopsy. Ferrario et al (9) postulated that morphologic grading (presence of mitotic activity, necrotic areas, nuclear atypia) can be predictors of survival. The longest disease-free survival in a patient with PAL is 21 months (1).

The use of serum neuron-specific enolase (NSE), a protein produced by neuroendocrine tissues, has been reported in cases of adrenal leiomyosarcoma that presented with severe hypertension. Interestingly, NSE levels decrease after resection of this adrenal tumor, suggesting that this neuropeptide may be a useful marker for the detection of early recurrence (19).

Radical surgical resection of the tumor is the main goal of therapy. Some authors advocate postsurgical adjuvant radiation therapy for locally advanced malignant disease (10,11). In a recent report, Murart et al (14) suggested that radical surgical resection without adjuvant therapies might be an alternative approach for low-grade leiomyosarcomas. The efficacy of chemotherapy is limited, and only a few patients have responded to agents such as gemcitabine and taxanes (11,13-14). Hamada et al (17) used the combination of cyclophosphamide, vincristine, Adriamycin, and dacarbazine in a case of bilateral adrenal leiomyosarcomas. On the other hand, radiotherapy alone is reportedly not an effective therapy for adrenal leiomyosarcomas (20). Radiofrequency ablation may be an effective therapy for local control of adrenal leiomyosarcomas, but complete ablation is difficult to achieve. Therefore, combined radiotherapy and radiofrequency ablation should likely be used in combination for the treatment of metastatic lesions (17).

Following 3 cycles of chemotherapy, our patient returned to the clinic with clear findings of disease progression. A CT scan of the abdomen and pelvis revealed enlargement the right adrenal mass, measuring 20 cm and compressing the IVC. After discussion with the patient and family members, palliative care was initiated.

CONCLUSION

Although exceedingly rare, PALs are potentially aggressive tumors that result in high morbidity and mortality. We present the 19th case reported in the medical literature and the second with documented recurrence. Surgical removal of the tumor is the first step in treatment. Adjuvant therapies including chemotherapy, radiotherapy, and radiofrequency ablation are not standardized and are mostly palliative. Future studies that focus on immunohistochemical and molecular diagnostic markers that could predict disease behavior will be essential to identity select novel combination therapies.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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