Case Report

Primary Adrenal Leiomyosarcoma: Case Report and Review of Literature

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Primary adrenal leiomyosarcomas are rare and usually symptomatic at presentation. The presentation of a large adrenal mass should raise suspicion of adrenal leiomyosarcoma as a differential diagnosis. To our knowledge, primary adrenal leiomyosarcoma has been reported in 20 cases in the English literature. Here we describe a case of primary adrenal leiomyosarcoma in a 76-year-old Caucasian female. The patient complained of right upper quadrant abdominal pain for 2 months. Contrast-enhanced magnetic resonance imaging showed a heterogeneous 10.5 cm adrenal mass with a suspected inferior vena cava tumor thrombus without lymph node enlargement or distant metastasis. The patient underwent a right adrenalectomy, partial resection of the inferior vena cava and reconstruction of the inferior vena cava with a pericardial patch. Histopathologic examination was consistent with leiomyosarcoma. At 3 months postoperatively, a follow-up computed tomography scan of the chest, abdomen and pelvis without intravenous contrast was done that showed multiple bilateral pulmonary metastatic lesions, bilateral hilar and mediastinal lymphadenopathy, liver metastasis, a new mass at the head of the pancreas, and a new mass at the lower pole of the right kidney. The patient was deemed to be unfit for systemic chemotherapy, and was referred to the hospice service for palliative care. The patient died 4 months after surgery.
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Key Words: *primary adrenal leiomyosarcoma, retroperitoneal sarcoma*

INTRODUCTION

Primary adrenal leiomyosarcoma (LMS) is rare. Twenty cases have been reported in the English literature since 1981.[1-19] Typically, the disease presents as a symptomatic retroperitoneal mass more than 10 cm in diameter. It can be associated with a mass effect on surrounding organs, involvement of the inferior vena cava (IVC) by a tumor thrombus, local organ invasion or distant metastasis. In the absence of effective chemotherapy and radiotherapy, the best treatment is surgical resection of the mass along with involved organs and metastatic lesions, if possible. In this paper, we report a case of primary adrenal LMS that has recently been diagnosed and treated at our institution, and provide a review of the literature.

CASE REPORT

A 76-year-old Caucasian female was referred to our institution with a diagnosis of right adrenal mass, diagnosed on abdominal ultrasound. The main complaint was right-sided flank and upper quadrant abdominal pain for 2 months. The patient denied constitutional symptoms. Past medical and surgical histories were significant for celiac disease, a bowel resection, multiple laparotomies for intestinal obstruction, history of necrotizing fasciitis from a spider bite requiring debridement, and intravenous iodinated contrast allergy. On physical examination, the patient was obese and no palpable abdominal masses could be appreciated. Non-contrast abdominal computed tomography (CT) scan showed a large heterogeneous retroperitoneal mass with foci of calcifications, inseparable from IVC (**Figure 1A**). Contrast-enhanced magnetic resonance imaging (MRI) showed a heterogeneous 10.5 cm adrenal mass with a suspected IVC tumor thrombus without lymph node enlargement or distant metastasis (**Figure 1B**). A comprehensive metabolic and endocrine workup was within normal range. The patient underwent a right adrenalectomy, partial resection of the IVC and reconstruction of the IVC with a pericardial patch. Intra operative trans-esophageal echocardiogram was performed to monitor the IVC thrombus.

The tumor was found to be invading the right posterior aspect of the IVC, between the entry points of the renal and hepatic veins. Grossly, the mass was 285 grams and 13x8x5.5 cm in dimensions. A soft lobulated white tumor was protruding from one side of the mass where it directly invaded the IVC (**Figure 2A**, arrow). The adrenal gland was replaced with a soft to mucoid tan-pink to rubbery white tumor with central necrosis (**Figure 2B**, arrow) and hemorrhage (**Figure 2B**, star). Microscopically, the tumor showed spindle cells with a spectrum of differentiation ranging from well-differentiated to poorly-differentiated cells, consistent with conventional leiomyosarcoma (**Figure 2C**). The tumor showed high nuclear pleomorphism (**Figure 2D**, right-pointing arrow),

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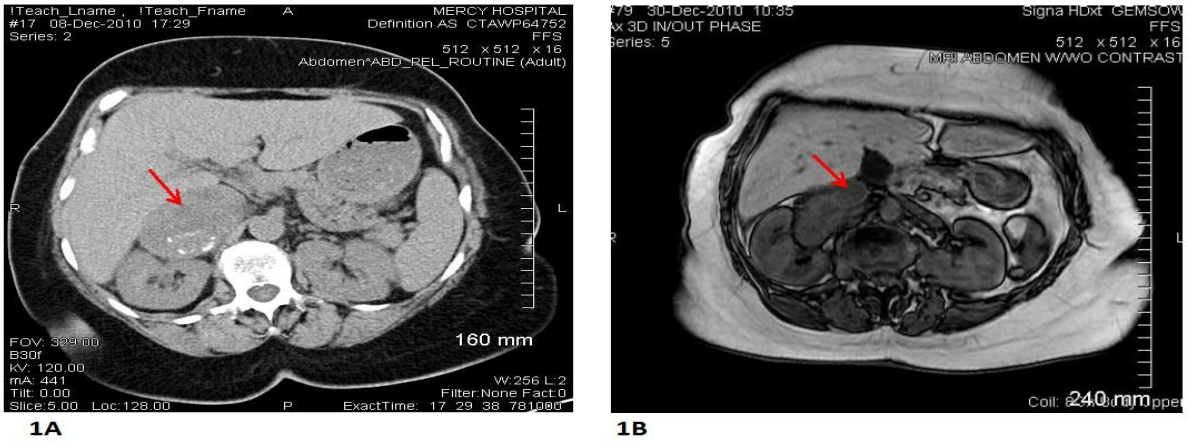

Figure 1.
A. Noncontrasted abdominal CT scan: Large heterogeneous right retroperitoneal mass (arrow) with foci of calcifications, inseparable from the IVC.
B. Abdominal MRI: heterogeneous mass (arrow) surrounding the IVC.

frequent atypical mitotic figures (**Figure 2D**, left pointing arrow) and areas of necrosis (**Figure 2F**, star). Tumor grade was 2 on the Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system. On immunohistochemistry, tumor cells were positive for smooth muscle actin (SMA), vimentin, desmin (**Figure 2E**) and smooth muscle myosin heavy chain. It was negative for S100 and α-inhibin.

At 3 months postoperatively, a follow-up CT scan of the chest, abdomen and pelvis without IV contrast showed multiple bilateral pulmonary metastatic lesions, bilateral hilar and mediastinal lymphadenopathy, liver metastasis, a new mass at the head of the pancreas, and a new mass at the lower pole of the right kidney. The patient was deemed to be unfit for systemic chemotherapy and was referred to the hospice service for palliative care. The patient died 4 months after surgery.

DISCUSSION

To our best knowledge, 20 cases of primary adrenal LMS have been reported in the English literature. A review of these cases can be found in **Table 1**.[1-19] Most patients were adults (range, 30-73 years) except for one patient who was a 14-year-old female.[2] The male to female ratio was 1:1. In most patients, the disease was unilateral with equal distribution among right and left adrenal glands. Four patients had acquired immunodeficiency syndrome. A literature search revealed only 1 case of secondary adrenal LMS that was reported in a 10-year-old boy who had bilateral adrenal metastasis from an ileal LMS.[20]

Primary adrenal LMS are usually larger than 10 cm at presentation and are symptomatic. Symptoms include abdominal/flank pain and manifestations of local organ involvement. Obstruction of the IVC can lead to lower limb swelling, cold feet, venous gangrene and pulmonary embolism.[7,14] Metastasis to the liver, lungs and bone is common and can cause shortness of breath, jaundice, bone pain and paresis.[8,9,15,17]

Preoperative diagnosis of primary adrenal LMS is difficult due to the absence of definitive biomarkers. Radiological features that help differentiate between adrenal adenomas and nonadenomas are well described, including size cutoff, growth rate and imaging characteristics on CT and MRI.[21] Radiological features, however, cannot differentiate among the different types of adrenal malignancies e.g. metastasis, adrenocortical carcinoma, malignant pheochromocytoma and malignant adrenal mesenchymal tumors. Features such as calcification, necrosis, heterogeneity, outline and distinctness are non-specific and can be found in benign and malignant adrenal lesions.[21]

Morphologically, LMS are usually large and of rubbery firm consistency. They are soft if necrosis, hemorrhage and cystic degeneration are present.[22] LMS may project into lumen of major vessels or be intramural. Microscopically, the tumor shows spindle cells with a spectrum of differentiation ranging from well-differentiated to poorly differentiated cells. The typical cells of LMS are elongated and have abundant cytoplasm. The color varies from pink to deep red on hematoxylin-eosin staining. The nucleus is either centrally located and blunt-ended or cigar-shaped.[22] Immuno-histochemically, the tumor cells are positive for SMA, vimentin, desmin and smooth muscle myosin heavy chain, and are negative for S100 (marker of malignant melanoma and malignant peripheral nerve sheath tumors), α-inhibin (marker of gonadal stromal tumors of ovary) and CD117 (marker of gastrointestinal stromal tumors).

Primary adrenal LMS are of two types: the conventional and the pleomorphic.[4] The former is more common and shows positive immunohistochemical staining for SMA and muscle specific actin (MSA) in 90-95% of cases and to desmin in 70-90% of cases. The pleomorphic variant has been reported in 4 patients in the literature and shows marked variability in the expression of smooth muscle markers. In a study of pleomorphic leiomyosarcomas of various sites by Oda, 37.5% of cases were positive for desmin, 46.4% were positive for MSA, and 50% positive for SMA.[23]

Table 1. Summary of published cases of primary adrenal leiomyosarcoma.

Author	Gender	Age	Type	HIV status	Tumor site	Tumor size (cm)	Metastasis	Treatment modalities	Survival (in months)
Zetler PJ et al	Male	30	Conventional	+	left	11	None	Adrenalectomy	20 (alive w/o mets)
Boman F et al	Male	29	Conventional	+	left	0.8	None	None	Not available
Boman F et al	Male	48	Conventional	+	right	2	None	None	Not available
Lack EE et al	Male	49	Conventional	-	right	11	None (preop) Bone (postop)	Adrenalectomy, nephrectomy, XRT (bone), CRT (ADR)	9 (alive w mets)
Nakanishi M et al	Male	63	Conventional	-	right	10	None (preop) Local relapse (postop)	Adrenalectomy, CRT after relapse	5 (dead)
Choi SH et al	Female	50	Conventional	-	left	12	None	Adrenalectomy	12 (alive w/o mets)
Lujan MG et al	Male	63	Pleomorphic	-	right	25	Locally invasive	Adrenalectomy, nephrectomy, partial hepatectomy	Dead shortly after Sx
Lee CW et al	Male	49	Not specified*	-	left	3	None	Laparoscopic Adrenalectomy	10 (alive w/o mets)
Goto J et al	Female	73	Conventional	-	right	8	None	Adrenalectomy, nephrectomy, IVC resection/grafting	10 (alive w/o mets)
Mencoboni M et al	Female	75	Conventional	-	right	5	None	Adrenalectomy	12 (alive w/o mets)
Matsui Y et al	Female	61	Conventional	-	right	> 10	IVCT	Adrenalectomy, nephrectomy and thrombectomy	1 (dead)
Candanedo-Gonzalez FA et al	Female	59	Pleomorphic	-	left	16	Locally advanced, Relapsed in liver	Adrenalectomy CRT (ADR, IFO), XRT, Sx	>36 mo after1st Sx (alive at last f/u)
Hamada S et al	Female	62	Conventional	-	bilateral	R:8 L: 4	None (preop), R pleura, R iliac bone, B femurs, liver, L kid, pancreas (postop)	Staged adrenalectomy, PN, CRT (CYVADIC) XRT, RFA	16 mo after 1st surgery (died due to mets)
Wong C et al	Male	57	Not specified*	-	Left	> 15	Locally advanced, IVCT	Adrenalectomy, nephrectomy, thrombectomy, XRT	> 6 (then died from mets)
Etten B et al	Female	73	Conventional	-	right	27	Fixed to liver, IVCO	Laparatomy only	3 weeks (dead)
Thamboo TP et al	Female	68	Conventional	-	right	10	None	Adrenalectomy, nephrectomy	12 (alive w/o mets)
Mohanty SK et al	Female	47	Pleomorphic	-	left	10	None, Multiple mets (postop)	Adrenalectomy, nephrectomy, XRT, CRT (GEM+ DOC)	9 (alive w mets)
Linos D et al	Female	14	Conventional	+	bilateral	R: 3.5 L: 4	None	Bilateral Laparoscopic Adrenalectomy	Not available
Kato T et al	Male	59	Pleomorphic	-	left	10	None (preop) Bone, liver (postop)	Adrenalectomy, nephrectomy and thrombectomy. XRT (bone)	6 (dead)
Karasmanoglu A et al	Male	63	Not specified*	-	Right	>20	IVC thrombus	Inoperable	3 (dead)

Preop, pre-operation; postop, post-operation; L, left; R, right; B, bilateral; IVCT, inferior vena cava thrombus; IVCO, inferior vena cava obstruction; XRT, radiotherapy; CRT, chemotherapy; Sx, surgery; PN, partial nephrectomy; RFA, radiofrequency ablation; ADR, adriamycin; IFO, ifosfamide; CYVADIC, cyclophosphamide, vincristine, adriamycin, dacarbazine; GEM, gemcitabine; DOC, docetaxil; w/o, without; w, with; f/u, follow-up; mets, metastasis

*, type not specified and no image provided by authors

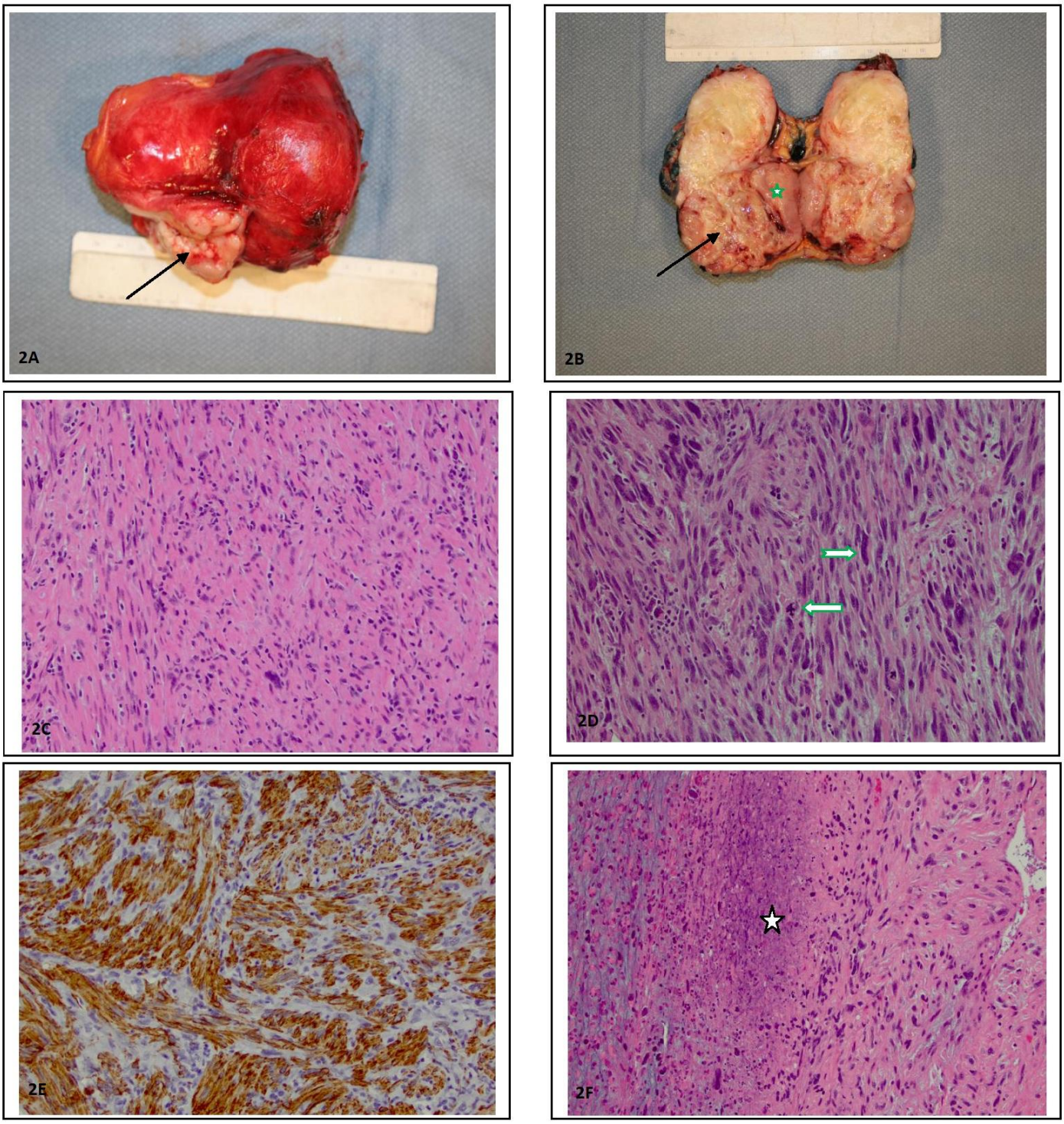

Figure 2.
A. Bulky encapsulated mass, partially encapsulated except for the area attached to the IVC (arrow).
B. Cut tumor is white tanned with storiform surface, foci of necrosis (arrow) and hemorrhage (star).
C. The lesion is composed of spindle cells with nuclei of various size and shape in the background of infiltrative inflammatory and mast cells (hematoxylin and eosin [H/E] stain).
D. Tumor showing high nuclear pleomorphism (right pointing arrow) and frequent atypical mitotic figures (left pointing arrow, H/E stain).
E. Immunostaining for Desmin highlights the cytoplasm of malignant cells.
F. Higher magnification of tumor with necrosis (star).

There are two grading systems for soft tissue sarcomas - the French (FNCLCC, table 2) and the NCI systems.[24] Both are 3-grade systems and are based on histologic type, subtype, mitotic activity and necrosis. These grading systems are not suitable to samples obtained by core-needle biopsies and fine-needle aspirations since these samples may not be representative of the whole tumor. The two systems have been compared head to head and the French system performed better on a multivariate analysis in terms of predicting metastasis-free and overall survival.[25] In our case, sub-scores for tumor differentiation, mitotic count and tumor necrosis were 2, 1 and 1, respectively, and the histologic grade was 2.

Surgical resection with microscopically negative margins represents the best chance of cure. However, this is seldom achievable given the usual advanced stage at presentation.[26,27] Published data on responses of primary adrenal LMS to chemotherapy and/or radiotherapy are inconsistent. The prognosis for primary adrenal LMS is generally poor. The most important prognostic factor is the ability to achieve a microscopically negative surgical margin.[26,27] Other prognostic factors include histologic type, grade, size, age, local control and metastasis.[28]

In all reported cases of adrenal LMS, the distinction between primary and secondary adrenal LMS depended on the results of clinical staging at presentation. All patients, including our case, who were diagnosed with primary adrenal LMS had a solitary adrenal mass at presentation, except for a 14-year-old female patient who had bilateral metachronous adrenal LMS. Workup of this patient at presentation and during follow-up revealed the lack of abnormal masses elsewhere. Her adrenal masses could have been a unilateral adrenal LMS that metastasized to the other adrenal gland or bilateral metachronous primary adrenal LMS. The 10-year-old boy diagnosed with secondary adrenal LMS had an ileal and simultaneous bilateral adrenal masses. Histopathologic examination confirmed the same diagnosis (LMS) in the ileal and adrenal masses; hence the diagnosis of secondary adrenal LMS.

Among 12 patients who presented with localized disease and underwent surgical resection, 6 patients remained in remission at the last follow-up without adjuvant therapy. However, the duration of follow-up was short (range 10-20 months, mean 12.6 months).[1,3-7] Five patients developed local and/or systemic recurrence after surgical resection for localized disease; 3 died after a mean of 9 months post surgery, and 2 were alive with disease after a mean of 9 months. Postoperative follow-up was not available for 1 patient who presented with bilateral adrenal LMS and underwent bilateral laparoscopic resection.[2] Our patient presented with locally advanced disease and underwent complete surgical resection. Three months postoperatively, widespread metastatic disease was discovered, and the patient died 4 months after surgery.

Table 2. The French grading system for soft tissue sarcomas (FNCLCC).

Histologic Grade Score:
Sum of (tumor differentiation + mitotic count + tumor necrosis)
Total score range: 2-8
Total score 2-3: grade 1
Total score 4-5: grade 2
Total score 6-8: grade 3

Tumor differentiation:
Score 1: Sarcomas closely resembling normal adult mesenchymal tissue (e.g. well-differentiated liposarcoma)
Score 2: Sarcomas for which histologic typing is certain (e.g. myxoid liposarcoma)
Score 3: Embryonal and undifferentiated sarcomas, sarcomas of doubtful type, synovial sarcomas, osteosarcomas, PNET

Mitotic count:
Score 1: 0-9 mitoses/10 HPF
Score 2: 10-19 mitoses/10 HPF
Score 3: ≥20 mitoses/10 HPF

Tumor necrosis:
Score 0: No necrosis
Score 1: < 50% tumor necrosis
Score 2: ≥ 50% tumor necrosis

FNCLCC, Federation Nationale des Centres de Lutte Contre le Cancer; PNET, primitive neuroectodermal tumor; HPF, high-power field.

CONCLUSIONS

We described a case of primary adrenal leiomyosarcoma, and summarized the clinical, radiologic, histologic and immunophenotypic features of this rare entity. The presentation of a large adrenal mass should raise suspicion for a primary adrenal LMS as a differential diagnosis. The prognosis is generally poor. Early diagnosis and surgical resection are critical, since long-term survival depends mostly on the ability to achieve microscopically negative resection margins.

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CONFLICT OF INTEREST

None.

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