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Case Report

Pathology Section

Primary Adrenal Leiomyosarcoma: A Rare and Unusual Cause of a Flank Mass

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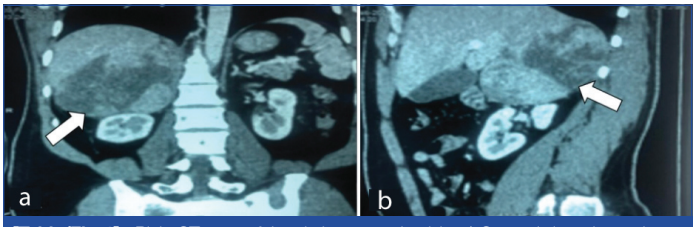
ABSTRACT

Leiomyosarcoma (LMS) is a very rare malignant mesenchymal tumour of the adrenal gland that originates from the smooth muscle cells of the central adrenal vein and/or its branches. The tumour has an equal incidence in both males and females. The presentation and diagnosis of LMS in the adrenal gland are usually late and are associated with a poor prognosis. Typically, patients do not present with any specific laboratory or radiological findings; rather, only compressive effects on adjacent structures are noted. Fewer than 50 cases of LMS of the adrenal gland have been reported in the scientific literature. In this case report, a 40-year-old male patient presented with complaints of intermittent right loin pain for one year. Computed Tomography (CT) of the abdomen and pelvis revealed a mass measuring 10.1×8.9×9.6 cm in the right suprarenal region. A right adrenalectomy was performed and histopathological analysis along with the Immunohistochemistry (IHC) profile confirmed the diagnosis of primary adrenal LMS.

Keywords: Adrenal gland, Adrenalectomy, Malignant tumour, Suprarenal mass

CASE REPORT

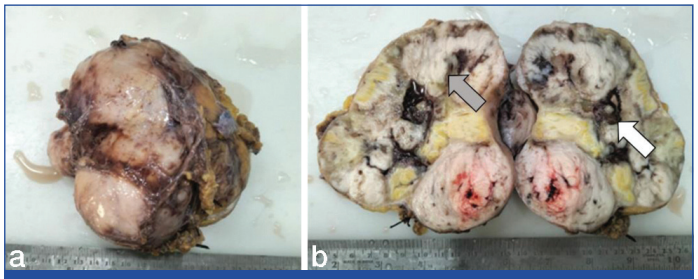
A 40-year-old male presented with complaints of intermittent pain in the right loin for the past one year. No other symptoms were noted by the patient. A routine clinical examination of the patient was unremarkable. A plain CT of the abdomen and pelvis revealed a well-defined, heterogeneously hyperintense mass lesion measuring 10.1×8.9×9.6 cm in the right suprarenal region, causing a mass effect over the right kidney and the inferior surface of the right lobe of the liver [Table/Fig-1a,b]. The left adrenal gland was unremarkable. A differential diagnosis of pheochromocytoma or adrenal cortical carcinoma was considered based on the CT scan findings. However, laboratory findings such as complete blood count, renal function tests, liver function tests, plasma metanephrine levels, 24-hour urine tests for metanephrine, normetanephrine, 17-ketosteroids and an overnight 1 mg dexamethasone suppression test were all within normal limits. Nonetheless, the right adrenalectomy procedure was performed, and the entire specimen was sent for Histopathological Examination (HPE).



[Table/Fig-1]: Plain CT scan of the abdomen and pelvis: a) Coronal view showed a well-defined heterogeneously hyperintense mass lesion (white arrow) measuring 10.1×8.9×9.6 cm in right suprarenal region; b) Sagittal view showing the mass pointed by white arrow.

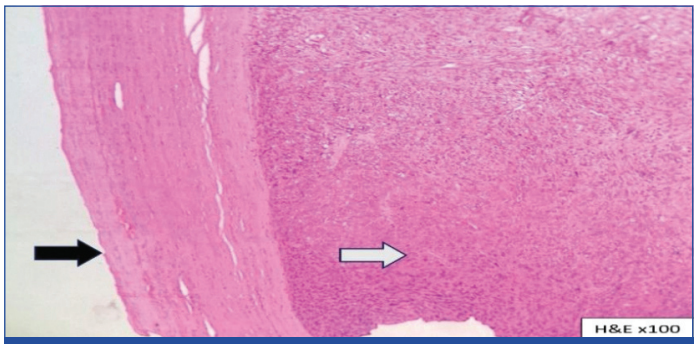
Gross pathology: On gross pathological examination, the adrenalectomy specimen [Table/Fig-2a,b] measured 12×10×6 cm and weighed 490 grams. The external surface was well encapsulated with no breaches of the capsule or growth noted. The external surface was also bosselated. The cut surface of the specimen showed many nodules that were gray-white to gray-brown, with areas of necrosis and focal areas of haemorrhage noted.

Microscopic examination: A well-encapsulated and highly cellular neoplasm composed of spindle cells arranged in longitudinal and interlacing fascicles was observed. The tumour cells exhibited elongated nuclei with blunt ends and mild to moderate eosinophilic cytoplasm, along with moderate to marked nuclear pleomorphism,



[Table/Fig-2]: Gross image of the retrieved specimen: (a) Gross image of adrenalectomy specimen showed a well encapsulated mass; (b) Cut surface showed many nodules which were grey white to grey brown with areas of necrosis (grey arrow) and haemorrhage (white arrow).

hyperchromatism, many bizarre nuclei and multinucleate tumour giant cells. Numerous mitotic figures were noted (10-12/10 HPF), and a few atypical mitotic figures were also observed. Large areas of coagulative tumour cell necrosis were noted. The capsule was not involved by the tumour and no normal residual adrenal parenchyma was identified. The above microscopic findings are represented in [Table/Fig-3,4a,b].

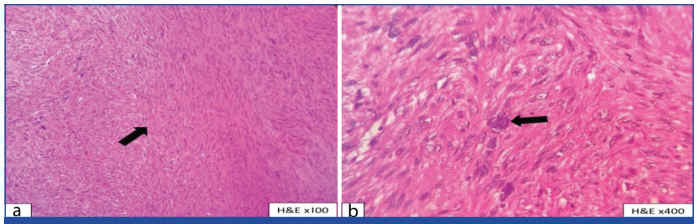


[Table/Fig-3]: Suprarenal mass histology: Microscopic examination of mass in low power (H&E stain, 100x) revealed a well encapsulated (Black arrow) tumour (Grey arrow).

Histopathological differential diagnosis: These histopathological findings were suggestive of a high-grade malignant spindle cell tumour with morphological differentials of:

1. Leiomyosarcoma (LMS)
2. Malignant Peripheral Nerve Sheath Tumour (MPNST)

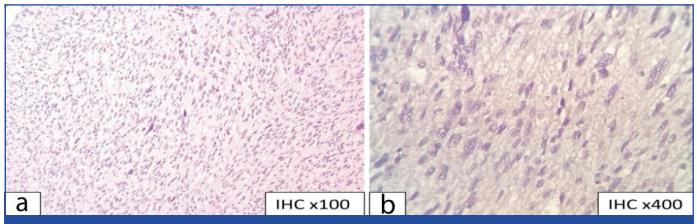
For further analysis and confirmation, an IHC study was performed, and the following profiles were observed.



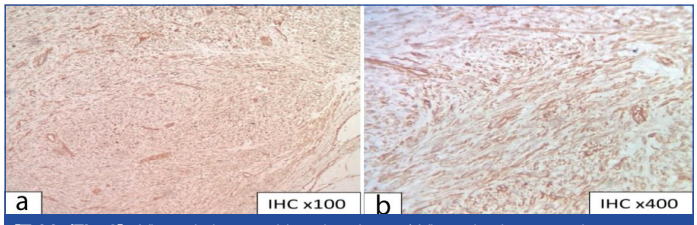
[Table/Fig-4]: Suprarenal mass histology: (a) Spindle cells arranged in longitudinal and interlacing fascicles shown by black arrow (H&E stain, 100x); (b) These cells have elongated nuclei with blunt ends and mild to moderate eosinophilic cytoplasm with moderate to marked nuclear pleomorphism, hyperchromatism, with many bizarre nuclei shown by black arrow (H&E stain, 100x).

Immunohistocehmical study:

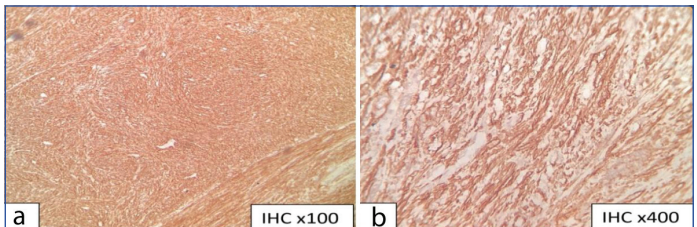
1. Pan-CK (cytokeratin) was negative in tumour cells [Table/Fig-5a,b], while Vimentin [Table/Fig-6a,b] showed strong and diffuse cytoplasmic positivity in tumour cells, confirming the mesenchymal origin of the tumour and indicating that the tumour is not of epithelial origin.
2. Smooth Muscle Actin (SMA) was diffuse and strongly positive (cytoplasmic and membranous) in tumour cells [Table/Fig-7a,b], whereas S-100 [Table/Fig-8a,b] was negative in tumour cells, indicating a smooth muscle origin of the tumour.
3. Ki-67 was 5% in tumour cells [Table/Fig-9a,b].



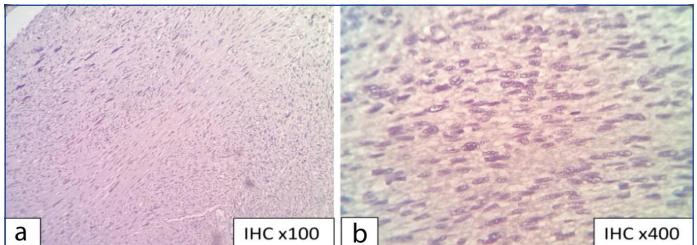
[Table/Fig-5]: Pan-CK immunohistochemistry: a) Pan-CK is negative in tumour cells (Pan-CK stain, 100x); b) Pan-CK is negative in tumour cells (Pan-CK stain, 400x).



[Table/Fig-6]: Vimentin immunohistochemistry: a) Vimentin shows moderate to strong cytoplasmic positivity in tumour cells (Vimentin stain, 100x); b) Vimentin shows moderate to strong cytoplasmic positivity in tumour cells (Vimentin stain, 400x).

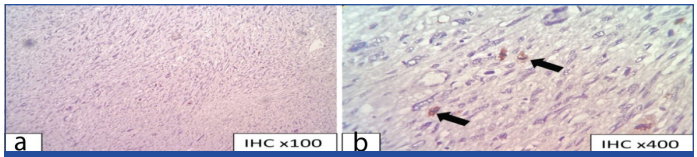


[Table/Fig-7]: Smooth Muscle Actin (SMA) immunohistochemistry: a) SMA shows diffuse, strong cytoplasmic positivity in tumour cells (SMA stain, 100x); b) SMA shows diffuse, strong cytoplasmic positivity in tumour cells (SMA stain, 400x).



[Table/Fig-8]: S-100 immunohistochemistry: a) S-100 is negative in tumour cells (S-100 stain, 100x); b) S-100 is negative in tumour cells (S-100 stain, 400x).

The final impression was that the HPE and IHC profile of the tumour confirmed the diagnosis of primary LMS of the adrenal gland. The capsule was not involved. No other treatment was given to this patient. He did not present with local or distant metastasis, and no recurrence has been noted within the past two years after surgical resection. The patient is in active follow-up.



[Table/Fig-9]: Ki-67 immunohistochemistry: a) Ki-67 was 5% positive in tumour cells (Ki-67 stain, 100x); b) Ki-67 was 5% positive in tumour cells (Ki-67 stain, 400x).

DISCUSSION

Common adrenal gland neoplasms include adrenal cortical adenoma, cortical carcinoma, pheochromocytoma and paragangliomas [1]. Primary mesenchymal tumours of the adrenal gland are extremely infrequent, usually consisting of benign tumours such as myelolipomas or haemangiomas [2]. Two rare smooth muscle tumours of the adrenal gland that occur without any predisposing conditions or risk factors are leiomyoma and LMS [3]. LMS is a soft-tissue tumour that is malignant and derived from smooth muscle cells. While primary LMS typically arises from the uterine myometrium, retroperitoneum, or dermal extremities, its occurrence in the adrenal gland is extremely rare [4]. The first description of LMS in the adrenal gland was provided by Choi SH and Liu K in 1981 [4]. Primary adrenal LMS is an infrequently occurring mesenchymal tumour that presents as a retroperitoneal mass and constitutes less than 0.5% of intra-abdominal soft-tissue malignancies in adults [3,5]. Within the adrenal gland, LMS seems to arise from the adrenal vein and/or its branches and is non functional [6]. In the literature, fewer than 50 cases have been documented [3]. There is an equal incidence among males and females and it is also equally common on both the right and left-sides [7]. Only two cases with bilateral presentation have ever been reported to date [8].

Although the aetiology is not clearly understood, associations with Human Immunodeficiency Virus (HIV) and Epstein-Barr Virus (EBV) have been suggested. Morphological changes as well as clinical behaviour may pertain to aberrations in chromosomes [2]. It is important to mention that this patient was negative for HIV and HBsAg. Patients often show no distinct clinical or laboratory findings, making preoperative diagnosis challenging [3]. Imaging studies typically show large heterogeneous masses without any specific characteristics, rendering them indistinguishable from other tumours of the adrenal gland [9]. The present patient also presented with no distinct clinical, laboratory, or radiological findings. Histopathology and IHC examination are significant in determining tumour type and predicting its biological behaviour [2]. Well-encapsulated, small adrenocortical tumours weighing less than 50 grams and resembling the appearance of the zona fasciculata and/or zona glomerulosa are usually benign tumours [2]. LMSs of the adrenal gland, on the other hand, may grossly attain larger sizes, have a rubbery consistency and often exhibit necrotic foci, being generally soft. Cystic degeneration and haemorrhage can also be noted [2].

Microscopically, LMS demonstrates a fascicular pattern of growth with intersecting bundles at wide angles. Individual cells have blunt-ended elongated nuclei, acidophilic cytoplasm and varying degrees of nuclear atypia [10]. Primary adrenal LMS can be classified as either conventional or pleomorphic types [2]. About 90 to 95% of conventional LMS show positivity for smooth muscle markers, including smooth muscle actin, while 70 to 90% of cases show positivity for desmin. Pleomorphic LMSs exhibit variable expression of these smooth muscle markers [4]. Histologically, all cases reported to date have been of the conventional type, except for five cases that were of the pleomorphic variety [7]. A high incidence of local recurrence has been noted in LMS, although these tumours grow slowly and metastasise late [2].

Differential diagnosis that should be considered include MPNST, gastrointestinal stromal tumour, malignant melanoma, sarcomatoid renal cell carcinoma, pleomorphic undifferentiated sarcoma, primary retroperitoneal sarcoma and metastatic tumours that could have infiltrated the adrenal gland [2]. Myeloid components and fat are noted in myelolipomas, while proliferating vascular components are seen in haemangiomas. Inhibin, synaptophysin, calretinin and Melan-A are positive in both benign and malignant adrenocortical tumours. MPNST, gastrointestinal stromal tumour, malignant melanoma, malignant fibrous histiocytoma and sarcomatoid renal cell carcinoma are positive for markers such as S100, c-KIT (CD117), HMB45, CD68, and renal cell carcinoma marker, respectively, but they are negative for the aforementioned IHC markers. Pheochromocytomas are usually positive for synaptophysin as well as chromogranin and they exhibit nests of cells with abundant cytoplasm that is basophilic to amphophilic [2].

Although the most positive biomarker for LMS is smooth muscle actin, a few patients may show positivity for S100, CD34 and CD117 [3]. In this case, Pan-CK was negative, vimentin and smooth muscle actin were positive, S100 was negative and CD117 was focally positive. The unilateral occurrence of the tumour, along with complete replacement of normal adrenal parenchyma by the tumour and the absence of other mass lesions elsewhere in the patient, supported its primary nature in this case. Based on histopathology and IHC profiling, the present case was classified as a conventional type adrenal LMS.

The mainstay of therapy is complete resection with negative surgical margins [2]. Generally, no additional chemotherapy or radiotherapy is necessary. Long-term follow-up is recommended [3]. In cases of metastatic disease, chemotherapy or radiotherapy is proposed, but their benefits have not yet been proven [11]. Invasive disease and distant metastases carry a poor prognosis [12]. The longest survival period ever documented for this condition was three years [13]. This patient did not present with local or distant metastasis, and no recurrence has been noted within the past two years following surgical resection. The patient is currently in active follow-up.

Similar to the findings of Oshidari B et al., Zhou Y et al., and Onishi T et al., the present patient presented with the non specific symptom of intermittent loin pain [3-5]. Unlike the case reported by Onishi T et al., where the patient had lymph node metastasis [5], and the case by Matsui Y et al., where the tumour extended to the right atrium, the present patient had no metastasis [12].

CONCLUSION(S)

In conclusion, with relatively few cases documented in the scientific literature, primary adrenal LMS is a mesenchymal neoplasm with an extremely rare incidence. It exhibits neither specific symptoms nor specific radiological findings but is associated with aggressive behaviour and poor prognosis. Therefore, HPE and IHC profiling play vital roles in confirming the diagnosis of LMS in the adrenal gland. The mainstay of therapy is surgical resection with negative margins. Generally, no additional therapy is required. Long-term follow-up is necessary.

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