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Mullerian Leiomyoma: Report of a Case and Review of Literature

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Abstract

Soft tissue tumors are a highly heterogeneous group of entities that are classified by the line of differentiation according to the adult tissue they resemble [1]. The smooth muscle tumors are the soft tissue tumors which shows smooth muscle differentiation. This group mainly comprises leiomyomas and leiomyosarcomas. But some smooth muscle tumors exist that cannot be exactly typed as benign or malignant and they are grouped as "smooth muscle tumors of uncertain biologic potential". Smooth muscle tumors are a common entity in female genital tract and in fact it is the most common tumor of uterus. The biologic categorization of smooth muscle tumors of uterus and smooth muscle tumors outside the uterus are based on different criteria. There has been very few studies on well differentiated smooth muscle tumors of deep soft tissue that show absence of cytological atypia and mitotic activity. Hence much of our knowledge is based on case reports only. Although exceptionally rare, leiomyomas do exist apart from somatic soft tissue, in retroperitoneum or abdominal cavity, which are considered as analogies of uterine leiomyoma (Mullerian Leiomyoma)

Keywords: leiomyoma, leiomyosarcoma, Mullerian leiomyoma

Introduction

Leiomyomas appear to be the most common uterine neoplasms. Around 20-30% of women above the age of 35 years have uterine leiomyomas [2]. Many of them may not be clinically detectable. In females, smooth muscle tumors occurring outside the uterus, inside the abdomen and pelvis, have to be typed by the criteria used for uterus rather than somatic soft tissue. These tumors are referred in literature as an analogue of uterine leiomyoma and criteria for grading has to be applied according to uterine smooth muscle tumors contrary to soft tissue smooth muscle neoplasm. The entity is described in literature as Mullerian smooth muscle tumor [3]. In some cases, leiomyomas occurring outside the uterus is diagnostically challenging. These tumors are graded benign and malignant using the criteria for uterus .These tumors exhibit positivity for hormone receptor ER and PR, hence they are diagnosed as Mullerian leiomyoma.

Here we present a case of Mullerian leiomyoma in a post-menopausal female.

Case Report

A 61-year-old female presented with abdominal discomfort for 1 month duration. Hysterectomy was done 13 years ago and ovaries were retained. Patient was asymptomatic till one year ago. She complained about occasional dull pain in the right side of lower abdomen.

Investigation

1. CT scan of abdomen showed a well-defined oval shaped mixed density mass measuring 10 x 8 cm in the right adnexa with enhancing solid components, cystic areas and adhesion with adjacent structures, bowel loops and

anterior abdominal wall. Radiologically suspected an ovarian cyst of epithelial nature.

2. The specimen was sent for histopathological examination ,her CA-125 level was estimated was normal.
3. The specimen consisted of fibro fatty soft tissue mass measuring 11x9x4 cm. Cut section showed solid grey white areas along with cystic areas intervened by areas of hemorrhage.

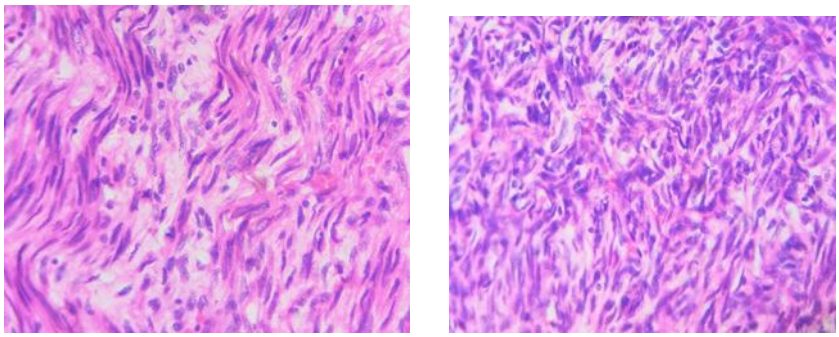

FIG.1, 2: Pathological findings

Microscopy showed a neoplasm composed of spindle cells arranged in interlacing long fascicles (FIG.1). Areas of increased cellularity seen. Focal areas of necrosis present. Cells are long, spindly, fusiform shaped with moderate amount of cytoplasm and pleomorphic nuclei. Nuclei exhibit minimal atypia in cellular areas, nuclei also shows nuclear inclusions (FIG.2). Mitotic figures are less than 10/10 HPF. Other areas show areas of hyalinization. Well differentiated smooth muscle areas also seen. Areas of vascular proliferation seen.

Immunohistochemistry

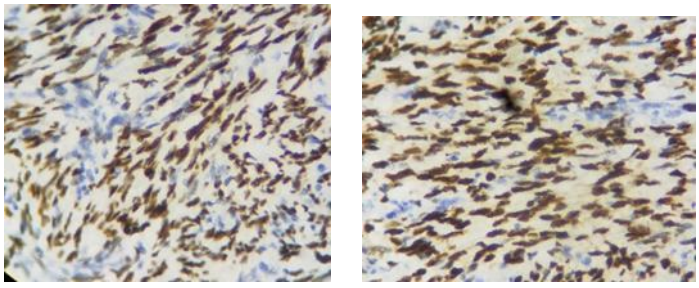

FIG-3, 4: Immunohistochemistry ER & PR

Figure 3,4 tumor cells exhibit diffuse, strong positivity for estrogen and progesterone receptors

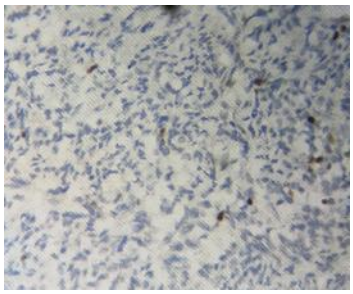

Fig 5: Ki67 index

Ki 67(proliferative index) shows varying positivity in different areas. Index ranges from 3-12 /10 HPF

Discussion

Somatic smooth muscle tumors of soft tissue consists of benign leiomyomas and malignant

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leiomyosarcomas. Tumors with both atypia and mitotic activity are diagnosed as leiomyosarcomas. These tumors often metastasize too. However a group of lesions exists that cannot be grouped under either category. These tumors are classified under "smooth muscle tumors of uncertain biologic potential".

Benign leiomyoma of somatic soft tissue comprises of smooth muscle hamartoma, pilar leiomyoma and angioleiomyoma. Along with this, a special category of leiomyoma which are estrogen receptor positive, occur anywhere in the abdomen and abdominal wall. This specific category of leiomyomas are similar to uterine leiomyomas. These ER positive leiomyomas are called Mullerian leiomyomas.

Estrogen receptor –positive leiomyomas (Mullerian leiomyomas)

These tumors occur specifically in women. They closely resemble uterine leiomyomas. These tumors occur in pelvis ,retroperitoneum and abdominal wall. Reports of Mullerian leiomyoma elsewhere in the retroperitoneum date back more than 10 years [4]. Other locations include omentum, peritoneal surface, mesentery, peri-intestinal or intestinal locations. Retroperitoneal leiomyomas can present as small nodules or they can grow into large masses of several kilograms.

The histological patterns of Mullerian leiomyomas include those seen in the uterus. They are solid, macrotrabecular, microtrabecular and hyalinized. Nuclear atypia is absent. Mitotic activity is very low usually less than 5/50HPF.

Immunohistochemically they are positive for SMA, desmin , heavy caldesmon, estrogen and progesterone receptor , nuclear WT1 immunoreactivity .

Another variant of Mullerian leiomyoma is peritoneal leiomyomatosis. In this case, numerous small nodules are present in the omentum or peritoneal surface.

The differential diagnosis of mullerian leiomyomas include PEComas, aggressive angiomyxomas, abdominal metastasies of uterine leiomyosarcomas, primary retroperitoneal leiomyosarcoma. PEComas are focally HMB-45 positive. Aggressive angiomyxomas are composed of oval cells that are positive for desmin and ER but focal SMA positive. Abdominal metastasis of uterine leiomyosarcomas shows nuclear atypia and greater mitotic activity.

General criteria for typing of soft tissue tumors according to the behaviour

Soft tissue tumors are divided into four categories, benign, intermediate (locally aggressive), intermediate (rarely metastasing) and malignant.

1. Benign-most benign soft tissue tumors do not recur locally. Those recur locally occur in a nondestructive fashion and are always cured by complete local excision.
2. Intermediate (locally aggressive) - they recur locally and have infiltrative and locally destructive growth pattern. They require wide excision with a margin of normal tissue
3. Intermediate (rarely metastasing) they are locally aggressive and show distant metastasis to lung or lymph node in occasional cases.
4. Malignant –they have local destructive growth and recurrence; Malignant soft tissue tumors are called soft tissue sarcomas. They have a substantial risk of developing distant metastasis depending on histological type and grade.

1 of the 3 criteria for leiomyosarcoma (coagulative tumor cell necrosis, cytologic atypia, elevated mitotic activity) should be present. Other useful parameters include atypical mitoses, vascular involvement and infiltrative/irregular margins.

Histologically leiomyosarcoma shows a smooth muscle-like appearance composed of irregularly intersecting fascicles and bundles of spindle cells. They have variable mitotic activity. Focal pleomorphism is seen. In some cases, leiomyosarcoma undergoes dedifferentiation. In case of somatic smooth muscle tumors, criteria for malignancy is very stringent. Even the presence of a single mitoses in smooth muscle tumors warrants malignancy. So in anatomical sites outside uterus these tumours if ER PR positive have to be typed by the criteria employed for the smooth muscle tumors of uterus.

Criteria for diagnosis of smooth muscle tumors in uterus [6]

The smooth muscle tumors of uterine leiomyomas are categorized based on tumor cell necrosis, atypia and mitoses.

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Tumor cell necrosis	Atypia	Mitoses*	Diagnosis
-	+	≥10	Leiomyosarcoma
+	+	≥10	
+	+	<10	
-	-	>15	STUMP
-	+	<10	
+	-	<10	
-	-	≥6 and ≤ 15	Mitotically active leiomyoma

*** Mitoses/mm2 (mitoses/10 HPF of 0.55 mm in diameter)**

TABLE-1: Differential Diagnosis in uterine spindle cell smooth muscle lesions

Smooth muscle tumour of uncertain malignant potential (STUMP) is a smooth muscle tumour with features that precludes unequivocal diagnosis of leiomyosarcoma, but that do not fulfill the criteria for leiomyoma, or its variants, and arise concern that the neoplasm may be having a malignant fashion.

Current diagnostic criteria for uterine leiomyosarcoma as per WHO FGT 2020 [6]

Conventional (Spindle cell) uterine leiomysarcoma

Two or more of the following:

- Marked cytological atypia (2+3+nuclear atypia)
- Tumor cell necrosis
- More than 4 mitoses/mm^2

Epitheloid uterine leiomyosarcoma

One or more of the following:

- Moderate to severe cytological atypia(2+3+atypia)
- Tumor cell necrosis
- ≥1.6 mitoses/mm^2

Myxoid uterine leiomyosarcoma

One or more of the following:

- Moderate to severe cytological atypia(2+3+atypia)
- Tumor cell necrosis
- >0.4 mitoses/mm^2
- Infiltrative borders/irregular margins

Thus, this criteria has to be applied for Mullerian leiomyomas to diagnose malignancy. Our case did not satisfy these criteria for malignancy. Patient is followed up closely for one year. She is asymptomatic without any treatment .

Conclusion

This case is reported as Mullerian leiomyoma using the above criteria .The patient was followed up .The patient is well preserved without any treatment. Awareness of this entity and application of this criteria is important to avoid unnecessary diagnosis of sarcoma in these type of tumors .These smooth muscle tumors should not be misinterpreted as their somatic counterparts. Here we are reporting this case to highlight the importance of differentiating Mullerian leiomyoma from somatic soft tissue smooth muscle tumors. One has to apply criteria for uterine smooth muscle tumors in leiomyomas with ER and PR positivity(Mullerian Leiomyomas).We also like to stress the importance of testing smooth muscle tumors in these locations for estrogen and progesterone receptors especially in females.

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