

A case report of incidental primary leiomyosarcoma of the fallopian tube and a review of the recent literature

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Abstract

Primary leiomyosarcoma (LMS) of the fallopian tube (PLFT) is a very rare neoplasm with descriptions limited to case reports. We present the case of a 46 year old lady with a history of renal transplantation in whom a PLFT was identified incidentally following hysterectomy and bilateral salpingectomy undertaken for a uterine fibroid. The tumour demonstrated classical morphological and immunohistochemical features of a LMS. It appeared localised to the fallopian tube and was completely resected. Adjuvant therapy was not given but active surveillance initiated. After fourteen months of follow up, there was no evidence of disease recurrence. We review cases from the past twenty years with a focus on management and outcomes. Given the rarity of this disease, continued publication of case reports and the creation of a centralised case registry would be of benefit.

Keywords: fallopian tube, leiomyosarcoma, malignancy

Introduction

Primary leiomyosarcoma (LMS) of the fallopian tube (PLFT) is an extremely rare neoplasm thought to arise from the smooth muscle of the wall of the fallopian tube. Given the rarity of this condition, description of each identified case is important to facilitate expansion in our understanding of the variation in presentation, clinical and pathological features, management approaches and outcomes of this entity. We therefore present a new case report of a patient with a PLFT identified incidentally post hysterectomy and bilateral salpingectomy undertaken for a uterine fibroid and we review the literature with a focus on recent case descriptions.

Case Report

A 46 year old lady, with a history of cadaveric renal transplantation following renal failure due to childhood Henoch-Schönlein Purpura was referred to gynaecology after the incidental identification of a pelvic mass during routine clinical examination and ultrasound. The clinical and ultrasonographic impression was of a likely fibroid uterus of 22 weeks in size. This was confirmed on MRI which showed the fibroid to measure $140 \times 130 \times 75$ mm, arise from the ventral uterine wall and extend to the level of the umbilicus. There were no radiologically suspicious features suggestive of malignancy. The endometrium was noted to be slightly thickened at 9 mm but no other abnormalities were observed. The patient had a history of two elective Cesarean sections but no other relevant past medical history. Drug history included tacrolimus, azathioprine and low dose prednisolone for immunosuppression and anti-hypertensives. Hysteroscopic examination was unremarkable and endometrial biopsy showed inactive endometrium. The patient received Zoladex (goserelin acetate) to reduce the size and vascularity of the fibroid pre-operatively.

The patient underwent an open total abdominal hysterectomy and bilateral salpingectomy. Intra-operatively, an incidental lesion on the right fallopian tube was noted. Macroscopic examination of the surgical excision specimens demonstrated the uterus to be distorted by an intramural fibroid measuring 95

× 93 × 85 mm with no macroscopic features of malignancy present (Figure 1). The serosal surface of the uterus appeared intact. The cervix appeared unremarkable. Along the length of both fallopian tubes there were a number of small paratubal cysts. The left fallopian tube appeared otherwise unremarkable. At the fimbrial end of the right fallopian tube was a multi-lobulated lesion measuring 50 × 33 × 20 mm with overlying serosa which appeared intact. The cut surface of the lesion was homogenous and off-white in colour (Figure 2). Histological examination of the specimens showed a benign endometrial polyp, a uterine leiomyoma with hyaline degeneration and foci of endometriosis within the cervix, both fallopian tubes and a separately submitted peritoneal biopsy. The uterus and fibroid were extensively sampled to exclude the presence of a primary uterine LMS. Examination of the right fallopian tube mass revealed a well-circumscribed tumour covered by tubal type ciliated columnar epithelium (Figure 3A). The tumour had a fascicular architecture composed of moderately atypical spindle cells with blunt ended nuclei and eosinophilic cytoplasm. There were greater than 54 mitoses per 10 high power fields (Figure 3B). There was no evidence of necrosis. The immunohistochemical profile of the tumour cells was as follows: SMA (focal +), EMA (focal +), desmin (+), h-caldesmon (+) (Figure 3C), ER and PR (+ in approximately 70% of cells), MNF-116 (-), calretinin (-), inhibin (-), CD10 (-), CD117 (-) and DOG1 (-). The ki-67 proliferation fraction was very high (Figure 3D). In situ hybridisation with the Epstein-Barr virus (EBV)-encoded small RNA (EBER) was negative.

Overall the morphological and immunohistochemical features were those of a primary high grade LMS of the fallopian tube. The lesion appeared to be completely excised and there was no evidence of lymphovascular invasion. The case was reviewed by the specialist regional sarcoma histopathology team who agreed with the diagnosis. The absence of the lesion on the pre-operative MRI was thought to either be due to it being obscured by the enlarged fibroid uterus or due to it having arisen in the intervening ten months between imaging and surgery.

The patient was referred to the regional sarcoma unit for oncological review. It was decided that no further treatment, such as adjuvant chemotherapy or radiotherapy, was necessary as the tumour was completely excised and a CT chest, abdomen and pelvis showed no evidence of metastatic disease. Furthermore, the option of pelvic radiotherapy was undesirable as this would irradiate the renal transplant and ovaries. A strategy of regular surveillance including clinical examination, MRI of the abdomen and pelvis and chest X-ray was instigated. The patient is currently fourteen months post diagnosis and is well with no signs of disease recurrence.

Discussion

Primary malignancies of the fallopian tube are rare with an incidence of approximately 0.4 per 100,000 women. Of these, adenocarcinomas account for over 85%¹. Fallopian tube sarcomas include synovial sarcoma, rhabdomyosarcoma, liposarcoma and LMS; these are all exceedingly rare with observations limited to case reports². As with other LMS, PLFT is characterised histologically by a proliferation of atypical spindle cells and numerous mitoses. It is classically described as being highly aggressive with a significant rate of local recurrences and distant metastases². Primary uterine LMS has an incidence of approximately 0.86 per 100,000³ and adnexal invasion or metastasis has been reported to occur in approximately 3% of cases⁴. Although rare, this is more probable than PLFT and thus if resected, the uterus requires careful exclusion by gross and microscopic examination before diagnosing PLFT.

Determining with precision the number of reported cases of PLFT in the literature is difficult owing to variation in morphological descriptions and a lack of immunohistochemistry in early publications; however, it is thought to be less than 30 at the present time ⁵. Immunohistochemical analysis forms an important part of the diagnostic work up of LMS to exclude potential morphological mimics, including extragastrointestinal stromal tumours (eGISTs) ⁶. Over the past twenty years there have been seven publications describing nine cases of PLFT confirmed by immunohistochemical analysis (Table 1) ^{5,7-12}. The average age of onset of these cases was 51 years with a range of 33-70 years. The majority of cases presented with abdominal pain and/or an abdominal mass. Intraoperative frozen section was employed in all but two cases. In four of the cases, the tumour was limited to the fallopian tube. By definition, at least one smooth muscle marker (usually Desmin) was positive on immunohistochemical analysis in all cases, with notable variation. Progesterone and estrogen receptor were positive in two of five cases in which they were reported. All but the earliest of the cases (which was confined to the fallopian tube) received adjuvant chemotherapy. A second look laparotomy and completion surgery was performed in two cases, both with localised disease, with no change in disease stage. The duration of follow up varied from one to six years; in five of the patients (three of whom had localised disease) there was no evidence of local recurrence, metastases or death at the time of publication. The remaining patients (including one with localised disease) developed metastases and/or died within eight months to four years following diagnosis.

The case presented herein shows a number of similarities to those previously described. Of note, however, it was discovered incidentally. In a series of 6,360 hysterectomies undertaken for benign indications, approximately 1% of patients were reported to have had unexpected ovarian, peritoneal, or fallopian tube malignancy ¹³. This highlights the importance of careful histopathological examination of surgical resection specimens and sampling of all suspicious macroscopically identified lesions. In addition, in contrast to all but one of the examined cases from the past twenty years, adjuvant chemotherapy was not given. The use of adjuvant chemotherapy has been justified based on the highly aggressive nature of PLFT and by extrapolation from uterine LMS ⁷. However, importantly one case ¹² of localised PLFT was not managed with adjuvant therapy and showed no signs of recurrence or metastases after four years of follow up. Furthermore, in the context of uterine LMS, recent data argues against the need for adjuvant therapy in completely resected stage I disease ¹⁴. Needless to say, frequent and careful surveillance is required to enable prompt identification and management of recurrent disease, should this occur.

It is interesting to note that in this case, the patient was immunosuppressed following renal transplantation. Immunosuppression is a known risk factor for many malignancies and solid organ transplant recipients have a higher incidence of malignancy than the general population ¹⁵. There are several case reports of leiomyosarcoma occurring in solid organ transplant recipients and many, but not all, were associated with EBV infection (for example ¹⁶⁻¹⁸). None of the cases of PLFT reviewed (Table 1) were immunosuppressed. Although EBV was negative in the present case, the fact the patient was immunosuppressed may be of aetiopathogenic significance; further research in this field is required.

Given the rarity of this disease, it has previously been suggested that a centralised case registry documenting the course of disease, treatment, and outcome would enable a more comprehensive assessment to guide management of such cases ¹¹. Such an initiative and the continued publication of case reports would be of value.

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Figure 1 - Total hysterectomy specimen showing the uterus distorted by the presence of a large intramural fibroid with no macroscopic features of malignancy. The serosa of the uterus was intact.

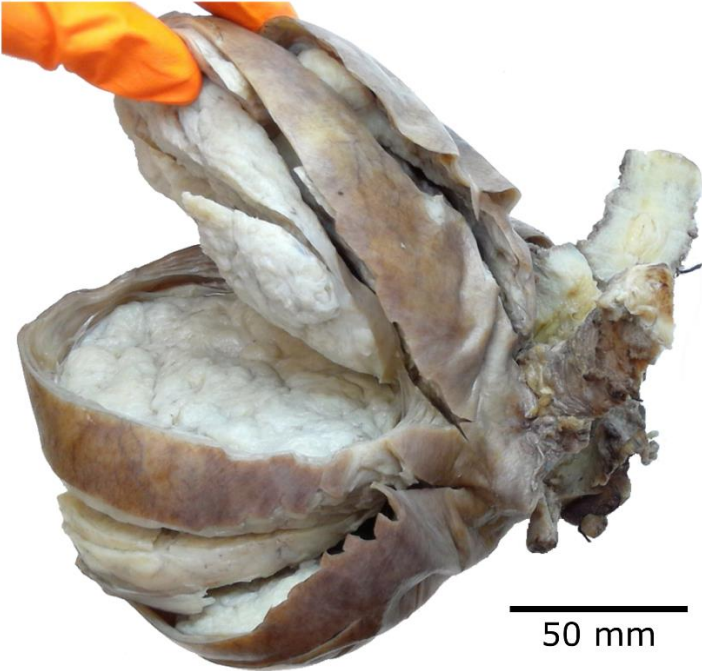


Figure 2 - Incidentally identified lesion attached to the right fallopian tube. A) External surface of the lesion; the arrow indicates the transected fallopian tube. B) Cut surface of lesion.

A



B

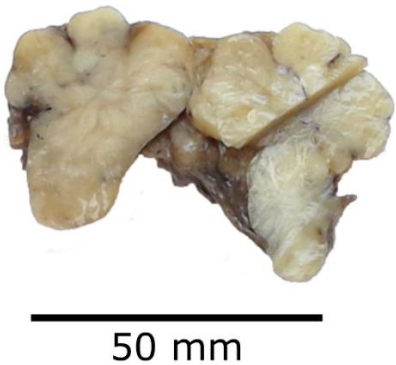
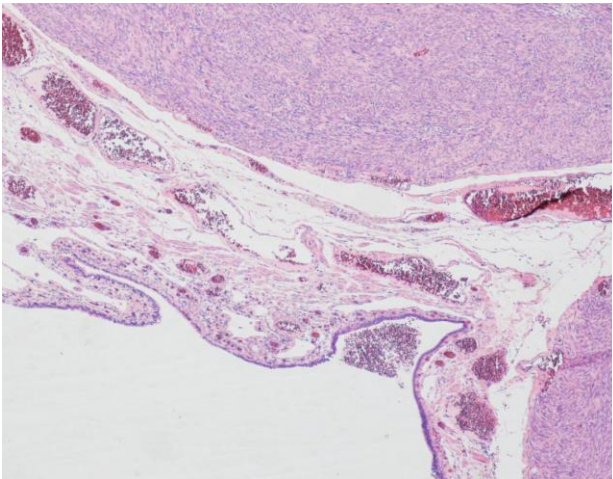
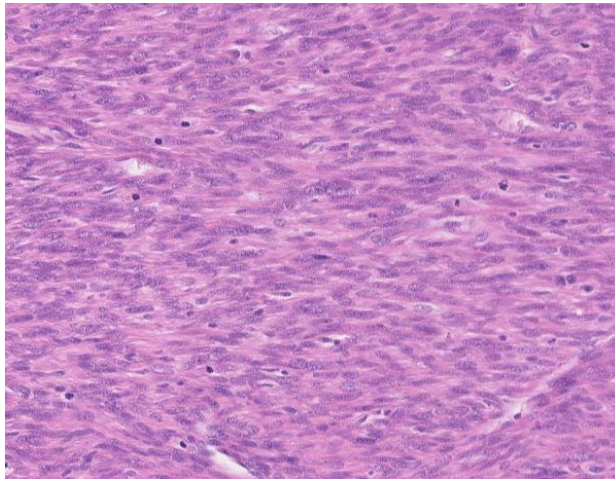


Figure 3 - H&E stained sections of the lesion. A) The lesion is seen to be covered by surface tubal type ciliated columnar epithelium consistent with it arising within the fallopian tube. B) The lesion has a fascicular architecture with moderately atypical spindle cells and numerous mitoses. C) Immunohistochemical staining is positive for h-Caldesmon. D) The Ki67 proliferation index is very high.

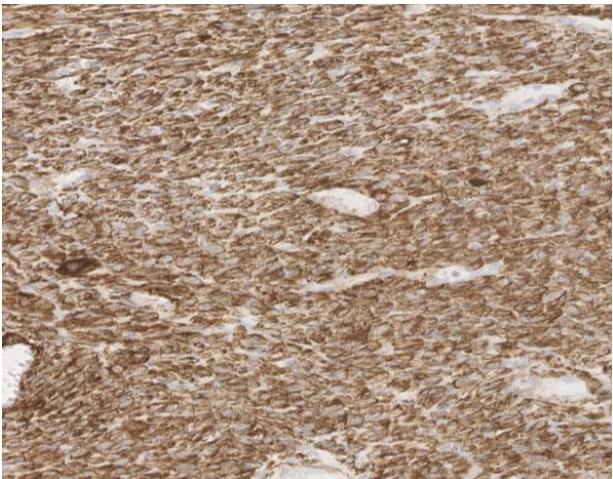
A



B



C



D

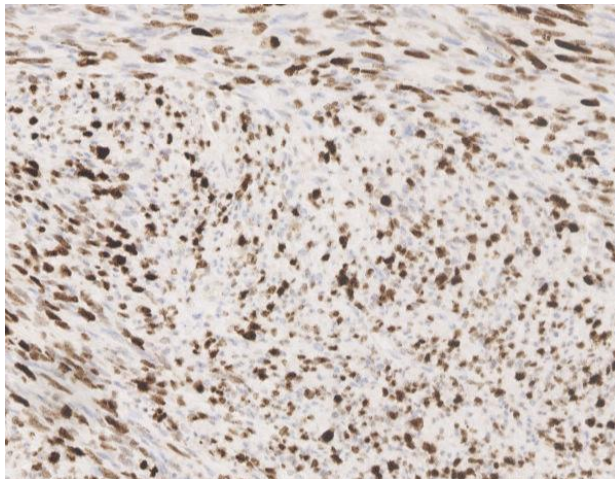


Table 1 – Clinical characteristics of the nine cases of PLFT confirmed by immunohistochemical analysis from seven publications over the past 20 years

Publication	Age	Presenting complaint	Initial surgery	IHC(+)	IHC(-)	Stage at diagnosis	Follow up surgery	Adjuvant therapy	Outcome
Xia LF, 2018 ⁷	47	Abdominal pain	FS, TAH, BSO, peritoneal washing	Caldesmon, vimentin, desmin, Ki67 (40%)	CK7, ER, PR	IA	Nil	Cyclophosphamide, cisplatin, doxorubicin	Lung/liver metastases at 4 years, gemcitabine and docetaxel, alive at 6 years
Xia LF, 2018 ⁷	52	Abdominal and pelvic masses on imaging	FS, BSO, omentectomy, partial diaphragm resection, PLNS, appendicectomy, resection of tumour on surface of intestine/mesentry	Caldesmon, desmin, SMA, Ki67 (2%)	ER, PR, AE1/AE3	IV (lung and peritoneal metastases)	Nil	Gemcitabine, docetaxel	Alive at 2 years
Xia LF, 2018 ⁷	33	Abdominal pain	LS	Desmin, SMA, ER, PR, Ki67 (40%)	AE1/AE3, CD34, Inhibin, S100, CD117, DOG-1	IA	TAH, LO, peritoneal washing, node exploration	Ifosfamide, cisplatin	Alive, no recurrence or metastases at 2 years
Orsaria M, 2018 ⁹	35	Abdominal pain	FS, TAH, BSO, PLNS, omentectomy, appendicectomy, peritoneal washing	Desmin, CD34, WT-1, calretinin, ER, PR	h-Caldesmon, SMA, CD117, DOG-1	IA	Nil	Chemotherapy, type not stated	Alive, no recurrence or metastases at 1 year
You D, 2010 ⁵	44	Abdominal pain	FS, LS, peritoneal washing	Desmin, SMA, Vimentin	CK7, CK20	IC (tumour rupture)	TAH, LO, RSO, partial omentectomy, PLNS	Dacarbazine, cisplatin	No regular follow up, died at 27 months
Ueda T, 2010 ⁸	69	Abdominal pain	FS, TAH, BSO, PLNS, partial omentectomy, low anterior resection of rectum, peritoneal washing	SMA, Alpha-SMA	Desmin, CD34	IIC (rectal invasion, positive washings)	Nil	Pirarubicin, ifosfamide	Liver, lung, supraclavicular LN metastases at 30 months, further chemotherapy, died at 39 months
Jacobs VR, 2010 ¹¹	59	Abdominal pain, constipation	FS, BSO	Desmin, Vimentin, SMA, S100, Ki67 (80%)	ER, PR, CD34	IV (liver metastases)	Bowel resection, rectovaginal fistula closure	Pamidronate, radiotherapy, gemcitabine, docetaxel	Wide spread metastases, died at 8 months

Kobayashi Y, 2010 ¹⁰	70	Abdominal pain	TAH, BSO	Vimentin, CD10, SMA	Cytokeratin, h-Caldesmon, HMB45, Melan A, epithelial common antigen	IIC (peritoneal metastases)	Nil	Cisplatin (intraperitoneal), etoposide	Alive, no recurrence or metastases at 6 years
Mariani L, 2005 ¹²	48	Abdominal pain, pelvic mass	FS, TAH, BSO, omentectomy, random biopsy	Desmin, Actin	Cytokeratin, neuroendocrine markers	IA	Nil	Nil	Alive, no recurrence or metastases at 5 years

Publication: first author, year. Age: age at diagnosis. Surgery: FS frozen section, TAH total abdominal hysterectomy, RSO right salpingo-oophorectomy, LS(O) left salpingo-(oophor)ectomy, BSO bilateral salpingo-oophorectomy, PLNS pelvic ± para-aortic lymph node sampling. IHC: Immunohistochemistry. Stage at diagnosis: as reported in the original manuscript, as per the International Federation of Gynecology and Obstetrics (FIGO) Committee on Gynecologic Oncology¹⁹.