

CASE REPORT

Uterine Epithelioid Leiomyosarcoma Arising Within Leiomyoma in A Postmenopausal Woman: A Case Report

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ABSTRACT

Uterine leiomyosarcoma is a malignant smooth muscle tumour of the uterus. It is rare and accounting for less than 2% of cases in malignant gynaepathology. To date, only a few reported cases of leiomyosarcoma arising from leiomyoma documented in the literature. We shared an uncommon occurrence of leiomyosarcoma arising from leiomyoma. Presented herein is a case of a 'rare epithelioid subtype' of leiomyosarcoma arising from a leiomyoma in a postmenopausal woman. We highlighted the importance of recognizing the possibilities of this event to allow for a timely diagnosis of leiomyosarcoma and to provide insights on management of patients presented with clinically presumed fibroid.

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INTRODUCTION

Leiomyosarcoma is a rare malignant myometrial smooth muscle tumour. The incidences of malignant transformation of leiomyoma into leiomyosarcoma are even extremely rare. There are only a limited number of case reports documenting the occurrence of leiomyosarcoma arising from leiomyoma. To the best of our knowledge, this is the second reported case of the 'rare epithelioid variant' of leiomyosarcoma arising from a leiomyoma. We emphasize the significance of recognizing the possibility of this phenomenon to ensure timely diagnosis and guide further management of patients presented with clinically presumed fibroids.

CASE REPORT

A 61-year-old postmenopausal lady presented with a history of on-and-off postmenopausal bleeding. An initial ultrasound showed multiple uterine fibroids,

with a recent scan found progressive increase in the size of the largest fibroid. A preoperative diagnosis of leiomyoma with cystic degeneration was made for the largest fibroid. Abdominal hysterectomy and bilateral salpingo-oophorectomy were performed due to symptomatic multiple large fibroids. Histopathology diagnosis of epithelioid leiomyosarcoma arising within leiomyoma was made for the largest clinically presumed fibroid.

Macroscopically, the uterus was enlarged with the presence of multiple intramural uterine fibroids. All these fibroids were well circumscribed and displayed white to tan cut surfaces with a whorled trabeculae pattern. However, in the largest fibroid, despite its circumscription, showed a central area of variegated fleshy cut surface and necrosis (Fig. 1).

Microscopically, all the fibroids showed the classic histomorphology features of leiomyoma except for the largest, which displayed the classic characteristic of leiomyoma only at the periphery. In the centre of this largest fibroid, we noticed the presence of an area that exhibited features of epithelioid leiomyosarcoma infiltrated into the surrounding leiomyoma (Fig.



Figure 1: Uterus shows well circumscribed intramural mass with variegated and fleshy cut surface. Other smaller fibroids are not seen in this cut section.

2 A). A focus of necrosis observed (Fig. 2 B). The leiomyosarcoma showed sheet of cells displaying an increase in cellularity, composed of round cells in eosinophilic to clear cytoplasm accompanied with frequent mitotic figures (5 to 7/10 HPF) (Fig. 2 C). SMA immunohistochemistry was lost in the epithelioid leiomyosarcoma component and only highlighted the leiomyoma component at the periphery (Fig. 3 A). The leiomyosarcoma showed positivity for CKAE1/AE3 immunohistochemistry (Fig. 3 B), and patchy positivity for vimentin and ER. The cells were negative for CD10, desmin, caldesmon, and cyclin D1. Ki-67 proliferative index was 20% (Fig. 4). The epithelioid leiomyosarcoma component was confined within the leiomyoma.

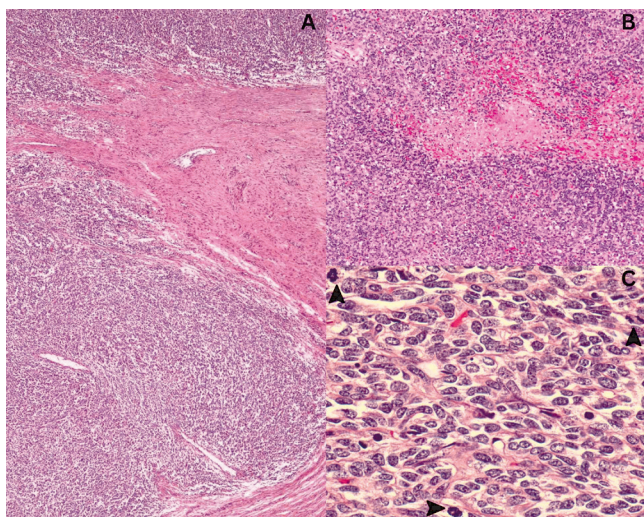


Figure 2: A The epithelioid leiomyosarcoma (left) shows infiltrative margin to the surrounding leiomyoma (right) (H&E, 40x). B The leiomyosarcoma displays increase in cellularity with presence of a focus of necrosis at the centre (H&E, 100x). C The leiomyosarcoma is composed of mild to moderately pleomorphic round cells with clear to eosinophilic cytoplasm. Mitosis is frequent. Arrowhead shows mitosis (H&E, 600x).

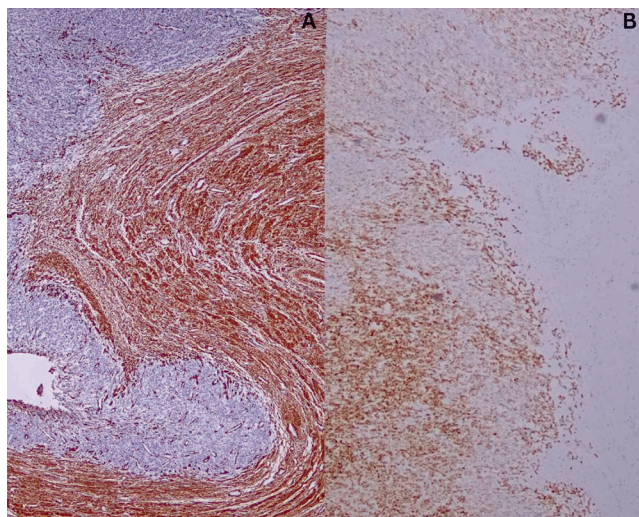


Figure 3: A Diffuse and strong immunoreactivity for SMA in the leiomyoma component (right). The epithelioid leiomyosarcoma component shows loss of SMA staining (left) (SMA, 40x). B The epithelioid leiomyosarcoma component (left) is positive for CKAE1/AE3. The leiomyoma component (right) is negative for CKAE1/AE3 (CKAE1/AE3, 40x).

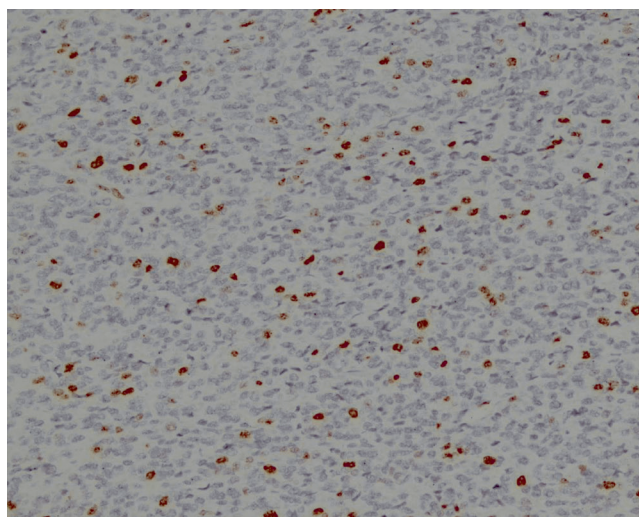


Figure 4: Ki-67 proliferative index shows 20% staining in the epithelioid leiomyosarcoma component. (Ki-67, 200x).

The patient had completed brachytherapy and pelvic radiotherapy, and recent follow up at the thirty-sixth month revealed no disease recurrence or distant metastasis.

DISCUSSION

Leiomyoma almost never transforms into leiomyosarcoma, and it is generally recognized that leiomyosarcoma occurs de novo with no precursor lesion. Only a few reported cases of leiomyosarcoma arising from leiomyoma have been published in the literature. Indraccolo et al. (1) described a patient with three uterine fibroids in which two of the fibroids transformed into leiomyosarcoma after menopause (Table I). These findings suggest the possibilities of a subgroup of leiomyoma that can progress and transform into leiomyosarcoma after a certain period. Molecular

Table I: Summary of the cases of uterine leiomyoma transformed into leiomyosarcoma

Authors	Age of onset	Age of diagnosis	Size (cm)	Follow up (months)	Histology subtype	Radiology (no MRI available)
Indraccolo et al. [1]	41	53	4.0 and 3.5	DOD (NA)	NA	USG shows hypoechoic lesion
Yanai et al. [4]	NA	54	20.5	NED (*)	NA	NA
	NA	56	8.0	NED (*)	NA	NA
	NA	40	NA	NED (*)	NA	NA
	NA	64	4.0	NED (*)	NA	NA
Present Study	53	61	6.0	NED (36)	Epithelioid	CT scan shows leiomyoma with degenerative change

NA, not available; DOD, died of disease; NED, no evidence of disease; *, three out of four patients had been followed up for 8 to 43 months.

studies, however, are limited. A study by Levy et al. (2) shows the absence of common genetic aberration and fails to prove the relationship between leiomyoma and leiomyosarcoma.

Leiomyosarcoma occurs in older individuals when compared to leiomyoma, where the majority of the cases have occurred in patients aged 50 years and over (3). Many of the reported cases of leiomyoma transforming into leiomyosarcoma occurred in postmenopausal women (1,4). Patients in eight out of ten cases reported by Yanai et al. (4), including the new four cases in their article, were aged 50 and over (Table I). Leiomyoma typically shrinks after menopause, with enlargement in postmenopausal women commonly resulting from degenerative changes. However, we believe that the possibility of malignant transformation of the leiomyoma should be considered in older patients who are clinically presented with rapidly growing fibroid. We suggest histopathological diagnosis should be made in this subset of patients to avoid delay in the management of undiagnosed uterine sarcoma.

It is difficult to distinguish the early stage of leiomyosarcoma from leiomyoma as both may have common presentations, including pelvic mass associated with abdominal pain and abnormal vaginal bleeding. However, making an accurate preoperative diagnosis of leiomyosarcoma is of pertinent importance to avoid patients from being managed conservatively for uterine fibroid. At the moment, there is no standard or validated criteria to confidently diagnose the early stage of leiomyoma that transforms into leiomyosarcoma. Unless the patient is presented with tumour extension beyond the uterus, involvement of other organ or lymph node metastasis, radiological distinctions between leiomyosarcoma and leiomyoma with degenerative changes are challenging since both may share overlapping features at their early stage. Computed tomography (CT) plays a limited role in the diagnosis of a myometrial lesion. Using an algorithm of combined sets of radiology characteristics of magnetic resonance

imaging (MRI) is helpful in risk-stratifying patients to decide the treatment options. The MRI criteria that favour leiomyosarcoma include focal area of non-enhancement, a high signal intensity on the T2-weighted image, and an area of high signal intensity within the lesion on the T1-weighted image (5).

Careful histology examination should be performed in all rapidly enlarging leiomyoma especially in postmenopausal women, since preoperative imaging study could miss the diagnosis of leiomyosarcoma. Leiomyosarcoma has three histology subtypes: 1. spindle cell, 2. myxoid, and 3. epithelioid subtype. The conventional spindle cell uterine leiomyosarcoma is composed of markedly pleomorphic spindle cells arranged in long interlacing fascicles. The diagnosis of conventional leiomyosarcoma requiring the presence of two out of three diagnostic criteria including marked nuclear atypia, tumour cell necrosis and increase mitosis; $\geq 10/10$ HPF of 0.55 mm in diameter. Diagnosing the less common subtypes of leiomyosarcoma, myxoid and epithelioid, are challenging as they only need the presence of one out of three of the diagnostic criteria with a lower mitotic count; $\geq 4/10$ HPF of 0.55 mm in diameter for epithelioid subtype and $\geq 1/10$ HPF of 0.55 mm in diameter for the myxoid subtype. The malignant neoplastic cells express desmin, SMA and h-caldesmon however these can be weak and patchy in the less common subtype, with positivity towards EMA and cytokeratin frequently seen in the epithelioid subtype (3). Epithelioid leiomyosarcoma is characterised by at least 50% of the component displaying epithelioid appearance with round to polygonal cells in eosinophilic or clear cytoplasm (3). In our case, the epithelioid leiomyosarcoma component exhibited only mild to moderate pleomorphism, but the presence of frequent mitosis, tumour necrosis and increase in Ki-67 proliferative index staining enabled us to exclude the benign counterpart. In a case series reported by Yanai, none of the leiomyomata show Ki-67 proliferative index staining more than 5% (4). Although leiomyosarcoma is an aggressive tumour with poor prognosis (3), the

prognosis of the early stage of leiomyosarcoma that is confined within leiomyoma is generally better than for de novo leiomyosarcoma (4).

CONCLUSION

Rapid growth in a previous clinically diagnosed fibroid, particularly in postmenopausal women, should raise a suspicion of a malignant transformation. Extensive sampling and thorough histological evaluation are crucial since preoperative imaging studies might miss the diagnosis of leiomyosarcoma. This case report emphasizes the significance of recognizing the possibility of diagnosing 'rare epithelioid subtype' of leiomyosarcoma arising within leiomyoma.

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