

Primary Ovarian Leiomyoma: A common tumor in rare location and report of eight cases

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Abstract

Background: Leiomyomas are the most common pelvic tumors in fertile women and rare conditions of them have extrauterine locations. Ovarian Leiomyoma accounts only for 0.5 to 1% of all benign ovarian tumors with fewer than 60 cases reported in a manner of case report. Here we present a series of eight patients over a six-year period(2012-2018). The clinico-pathological features, diagnosis and management were discussed. Case presentation: We had experienced eight cases of ovarian leiomyoma. The clinical features, pathologic findings, diagnosis, treatment were reviewed. The mean age of these patients was 38.5 years. The majority of these patients may be asymptomatic and usually diagnosed incidentally during pelvic examination or pathologic examination after surgery. Six cases presented only with pelvic mass sized from 2 to 20 cm and even some patients persisted for more than twenty years while the other two were diagnosed due to four years of primary infertile or three months of irregular vagina bleeding. Three patients coincident with uterine leiomyoma while the others not. Three had ovarian leiomyoma degenerated and one case had a evidence of atypical 4/10. Conclusions : ovarian leiomyoma was very rare but it should be considered in the diagnosis of pelvic or ovarian solid masses. Magnetic resonance imaging was provital in its different diagnose while fast frozen pathology during operation was very necessary for its surgical decision. A proper surgical decision should be made according to patients age.

Background

Leiomyoma is one of the rarest ovarian benign tumors, accounting for 0.5-1% overall[1]. Since the first case was described in 1862[2], less than sixty cases had been reported so far and the overwhelming of them were case reports with or without literature review as summarized in Table 1. The age of reported cases ranged from 17 to 79 years old and most of them were small in size, asymptomatic and diagnosed incidentally during routine pelvic examination, at surgery or even at autopsy[3, 4]. Few cases can also manifest with lower abdominal pain[5], ascites[6], pelvic mass, elevated cancer antigen 125(CA125) or Meigs' syndrome[4, 7]. They occurred in unilateral ovary mostly while bilateral ovarian leiomyoma were mainly reported in young patients aged 16 to 25 and no has been reported in patients >35 years old[5]. Due to its rarity and its similarities to pelvic solid mass, the ovarian leiomyoma was rarely diagnosed pre-operatively, and thus the purpose of this paper was to summarize and analyze the clinical data of these ovarian leiomyoma patients during the recent six years along with a review of the literature with all cases to guide the clinical practice.

Methods

A six-year retrospective study of primary ovarian leiomyoma diagnosed in the Pathology Department of Women's Hospital, Zhejiang University School of Medicine was carried out during year 2012-2018. The data were collected mainly by searching on medical records and department of pathology databases. The clinico-pathological features, diagnosis and management were discussed.

Results

Ovarian leiomyoma was noted in eight cases. The mean age at presentation was 38.5 years with the youngest 17 and the oldest 65. Pelvic mass was the most common presenting sign (6/8 cases) (Fig 1,2), while one case presented with four years of primary infertile and the other presented with three months of irregular vagina bleeding. Duration of signs ranged from 1 month to 20 years. The level of CA125 was all in normal range and no patient was diagnosed with ovarian leiomyoma before operation. The oldest two had bilateral salpingo-oophorectomy with or without hysterectomy and the rest of them all had myomectomy. These tumor sized from 2 to 20 cm and most of them come from one side of the ovaries except one from the left ovarian inherent ligament. Accidental surface with or without vascular engorgement was also found in these tumors and the youngest patient even had 100ml ascites who was proved to have nuclear division (4/10) (Fig3). Leiomyoma degeneration such as hyaline and calcification could also be seen and frozen section during operation contributed to its nature diagnoses or differentiating benign from malignant tumors. Clinical details of the cases are summarized in Table 1 and their macro and/or microscopic features were summarized in Table 2.

Table 1 Clinical details of the patients with ovarian leiomyoma

Case	Age (years)	Symptoms and signs	USG/CT/MRI	surgical approach	concomitant ovary cyst or uterine leiomyoma
1	24	pelvic mass for 2 months follicular cyst	sex-cord stromal tumors	myomectomy	left ovary
2	65	pelvic mass for 20 years	subserous myoma	salpingo-oophorectomy	multi-leiomyoma with hysterectomy
3	34	pelvic mass for 1 months	ovarian tumor? myoma?	Myomectomy	no
4	57	pelvic mass for 1 months	subserous myoma	salpingo-oophorectomy	multi-leiomyoma with hysterectomy
5	17	vaginal bleeding 3 months	sex-cord stromal tumors	myomectomy	no
6	29	pelvic mass for 1 months	sex-cord stromal tumors	myomectomy	no
7	31	primary infertile for 4 years	ovarian tumor? myoma?	myomectomy	no

8 51 pelvic mass for 10 years subserous myoma myomectomy multi-leiomyoma

USG: ultrasonography ;CT: computer tomography;MRI: magnetic resonance
imagine

Table 2 Macro and microscopic features of ovarian leiomyoma

Macroscopic features		Microscopic features	
Case Location & size section	Gross appearance	Degeneration	Frozen
1 right,diameter 6.0cm leiomyoma	clear border, uneven surface	hyaline,calcification	
2 left,diameter 6.0cm	uneven surface	hyaline,calcification	leiomyoma
3 left inherent ligament, 3*2*2cm leiomyoma		ovary inherent ligament	leiomyoma
4 right,diameter 20cm, mesenchymal origin	vascular engorgement	fibro-leiomyoma,edema,hyaline	
5 left,diameter 8.0cm origin	rich blood supply,	nuclear division(4/10)	mesenchymal
	ascites 100ml		
6 left,2*2*2cm,	uneven surface	no	leiomyoma considered
7 right,diameter 6cm	uneven surface	no	fibroma or leiomyoma
8 right, diameter 8cm	myoma fusion,tortuous vessels	no	leiomyoma

Table 3 [A review of the literature with ovarian leiomyoma cases proved by pathology](#)

Reference	Age	Clinical characteristics	Reference	Age	Clinical
Presented with Meigs' syndrome polymyositis			Presented with ascites and		
Kurai M (2005)[8]	79	chest pain & dyspnea ,CA125 163U/L	Van Winter JT(1992)		
[9]		ascites & polymyositis			
Erdemoglu E(2006)[10]	45	ascites and elevated CA125 levels	Presented with		
		inguinal hernia			
Presented with virilization/elevated T level into labium majus			Prasad KR(1993) [11]		indirect
Carpen O(1996)[12]	64	almost male type baldness,T level 20.4nmol/L	With abnormal histologic features		
Parish JM(1984)[13]	68	virilization , depression,T level 1082ng/dl	Moulla A(2017)		
[14]	58	with areas of myxoid stroma			
Mallya S(1990)[15]	56	virilization,marked hirsutism,T level49nmol/L	Ye zhao(2018)		
[16]	58	ovarian atypical leiomyoma			
Presented with abnormal menstruation			Emovon EU (1999)[17]	24	nuclear pleomorphism,
Abdel-Gadir A(2010)[18]	35	9 years secondary amenorrhoea			mitotic
		activity			
small uterus	LH 19.5 IU/l,FSH 3.8 IU/L		Erkaya S(2000)[19]	56	3-4
		mitotic activity			
Ozcimen EE(2006)[20]	32	dysmenorrhea for six months	Blue NR(2014)[21]	14	
		4 cm grew to 6.5 cm over			
		two years,slight nuclear enlargement			
Lema VC (2013) [22]	29	secondary amenorrhea, big, bilateral	Accompy other		
		tumor			
Presented with urinary symptoms			Dworniak T (2002) [23]	70	left
		kidney cancer			
Serenat Eris (2015) [24]	59	frequent micturition, uterin lipoleiomyoma	Kojiro S(2003)		
[25]	84	rectal cancer			
Alshalabi O (2016)[24]	53	constipation, urinary hesitation, mass between	Khangar		
B(2017)[26]	42	LPD,6 years ago had			
		vagina and rectum, myxoid leiomyoma,			total
		hysterectomy for a 20cm fibroid			
Khaffaf N (1996)[27]		acute abdomen,bilateral hydronephrosis,	Bayram I(2007)		
[28]		PSTT			
		mass 11.65 kg,	Adolescence		
Presented with appendicitis-like symptoms			Wei C(2008)[29]	13	abdominal
		pain,nausea& vomiting			

Tomas D(2009)[30] 31 appendicitis-like symptoms,associated with Guney M (2007) [31] 17 asymptom, 15 cm x 12 cm,
 an endometriotic cyst unilateral salpingo-
 oophorectomy

Al-Shaikh AF(2015)[32] 52 right-lower abdominal pain,consistent with Lim SC(2004) [33] 17 huge, bilateral ,
 acute appendicitis,goblet cell carcinoid of the appendix salpingo-
 oophorectomy

Presented with paraneoplastic syndrome San marco L(1991)[34] 16
 bilateral, left ovary

Yumru AE (2010)[35] 55 epileptic seizure ,abdominal pain,30 x 28 preserved
 x 15 cm ,CA-125 48 77 U/ml

Seinera P(1997) [36] 25 epilepsy for 3years, bilateral,total 15 small nodules

Akizawa Y(2016)[37] 21 Gorlin syndrome, with a second hit in PTCH1 region

Presented with torsion

Guzel AI(2014)[38] 64 severe acute abdominal pain,peritoneal irritation

Kim M(2015)[39] 35 abdominal pain,peritoneal irritation,10-week gestation

Diagnosed during pregnancy

Zhao X(2014)[39] 28 acute abdominal pain following activity, 12-week gestation
 4.1×3.2cm grew to10.4×10cm,laparoscopic ovarian tumorectomy

Zorlu CG (1993)[40] 32 6-week gestation, 14*9cm ,cycst left salpingo-oophorectomy

Daniel Y(1997)[41] 31 bilateral,multiple,diagnosed during caesarean section

HsiaoCH(2007)[42]41 diagnosed during caesarean section, left oophorectomy

T: testosterone ;LH:luteinizing hormone; FSH: follicle stimulating hormone;CA125: cancer antigen 125;
 LPD: leiomyomata peritonealis disseminata; PSTT :placenta site trophoblastic tumor

Discussion

Leiomyoma arising from ovary was considered a rare type of solid benign tumor and it could happened to people of all ages, but nearly eighty percent of them occurred in pre-menopausal women[43]. Our department was one of the largest top three specialized hospitals in China and the total number of gynecological surgery was about 17000-20000 per year,while only 8 patients were diagnosed with ovarian leiomyoma during the past six years.The youngest pediatric girl aged only 17, 4 fertile and 2 pre-menopausal women while the other one had been diagnosed 20 years ago when she was 45. Ovarian leiomyoma usually sized millimeters or a few centimeters and rarely exceeded 3 cm in diameter meanwhile both ovaries had the same morbidity[44]. Tumor diameter of our cases ranged from 2 to 20

cm which mainly measured 6-8cm that can be easily visible by ultrasound. Just because of their small size, the majority of them were usually asymptomatic and incidentally found when having pelvic examination or surgery for oophorectomy. However, the symptoms such as pelvic pain, abnormal uterine bleeding, constipation and frequent urination were associated with tumor size [45, 46]. Literature had also revealed the relationship between ovarian leiomyoma and infertile [47]. All our cases had normal CA125 level, the pediatric girl was diagnosed for menstrual disorder with ascites 100 ml and another one was diagnosed for four years of primary infertile. Rare symptoms including Meigs' syndrome, elevated T level and virilization, abnormal menstruation, urinary symptoms, appendicitis-like symptoms, paraneoplastic syndrome and acute abdomen caused by torsion had also been reported as summarized in Table 3.

To date, the histological origin of ovarian leiomyoma had not been excluded. Some studies had stated that it possible originated from smooth muscle in ovarian hilar blood vessel, ovarian ligament, ovarian stroma, mature cystic teratomas and the wall of mucinous cystic tumour and so on [48], while the most accepted one was that it arised from the smooth muscle of the ovarian ligament where they enter the ovary from the ovary vascular smooth muscle [49]. It could be implied from the enlarged ovarian ligament of our tissue photo. They frequently accompanied with other ipsilateral or contralateral ovarian lesions such as endometriotic cyst [49] although only one patient had contralateral ovarian follicular cyst in present report, thus careful exploration for both ovary was very necessary.

Strictly speaking, primary ovarian leiomyoma had to be entirely within the ovary with no similar lesions in the uterus or elsewhere [50]. However, literature had reported that about eighty percent cases accompanied with uterine leiomyomas [48]. Without exception, three patients aged more than fifty also had multiple uterine leiomyomas. As reported in the literature, leiomyoma degeneration such as hyaline and calcification could also be seen especially in larger tumors, even nuclear mitosis was observed in the pediatric girl (4/10HPF). By literature review, there were five reports revealing abnormal histologic features such as areas of myxoid stroma, atypical leiomyoma, nuclear pleomorphism, mitotic activity and nuclear enlargement in ovarian leiomyoma. Thus frozen section and immunohistochemistry could help in its right diagnose and making decision for surgical approach. Though 4 mitosis could be found in very 10 high power field (HPF) in case 5 (in Fig 3), she had an ovary-preserving surgery for adolescence with 2 years no recurrence so far.

When diagnosing ovarian leiomyoma, it should be distinguished from sex-cord stromal tumors including ovarian fibroma, thecoma, leiomyosarcomas while uterine leiomyomas parasiting on the ovary should also be considered. Intra-operative immunohistochemical analysis and frozen section were very helpful in its right diagnosis and surgical decision-making. It would be better if a definite diagnosis could be made before surgery. The majority of our cases had been diagnosed with sex-cord stromal tumors and seldom had a correct diagnosis before operation as showed in Table 1 which was in accordance with the existing literature. The imaging features of ovarian leiomyoma had seldom been described due to its rarity, there were few literatures reporting that intravenous administration of Gd-DTPA and the supplying vessels arising directing from the myometrium as a flow void could both contribute to the differentiation of it from uterine leiomyomas. A good example of this was case 8 (in Fig1, 2) who had both right ovarian

leiomyoma and left uterine subserous leiomyomas. On axial diffusion-weighted image(TR/TE: 4000/72.4ms,b value=500s/mm²) the two masses showed the same intermediate signal intensity. On axial fat-saturated T2-weighted(TR/TE:3020/70.5ms)image, the signal intensity of the left mass was continued with the myometrium while the right mass was well-circumscribed and sharply demarcated from the uterus.On sagittal or axial T1-weighted with gadolinium administration(TR/TE:3.9/1.7ms) the left mass showed low intensity identical to the uterus myometrium and flow voids could only be seen in left uterine subserous leiomyomas. Although these tumors were benign and rare of them had abnormal histologic features, radical surgeries were usually done for their complete removal because the ovary might become almost completely absorbed by the tumor or just persist portions[50]. A common surgical approach was salpingo-oophorectomy or an oophorectomy with or without hysterectomy,but an ovary-preserving surgery should be suggested in young and fertility-sparing women[51].

Conclusions

primary ovarian leiomyoma was very rare in clinic and should be considered in the differential diagnosis of ovary solid tumors and subserous myoma .Magnetic resonance imaging was provital in its definite diagnose before operation while fast frozen pathology during operation was very necessary for its surgical decision. Hysterectomy in conjunction with bilateral salpingo-oophorectomy were preferred in middle-aged to elderly patients but an ovary-preserving surgery should be considered in young and child-bearing patients.

Abbreviations

CA125: cancer antigen 125 ;USG: ultrasonography ;CT: computer tomography;MRI: magnetic resonance imagine

Declarations

Ethics approval and consent to participate

This research conformed to the provisions of the Declaration of Helsinki and was approved by the ethics committee of Women's hospital Zhejiang University.The patients were informed and provided her written informed consent.

Consent for publication

Written informed consent has been obtained from all the cases or her guardian of 17 years old for publication of this paper report.The authors declare that they have no competing interests.

Availability of data and materials

The data-sets used and /or analyzed during the current study are available from the authors on reasonable request.

Competing interests.

The authors declare that they have no competing interests.

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Authors' contributions x

WZG collected the clinical data, analysis these data and drafted the manuscript. DMY helped to draft the manuscript and revised the manuscript. All authors read and approved the final manuscript.

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Figures

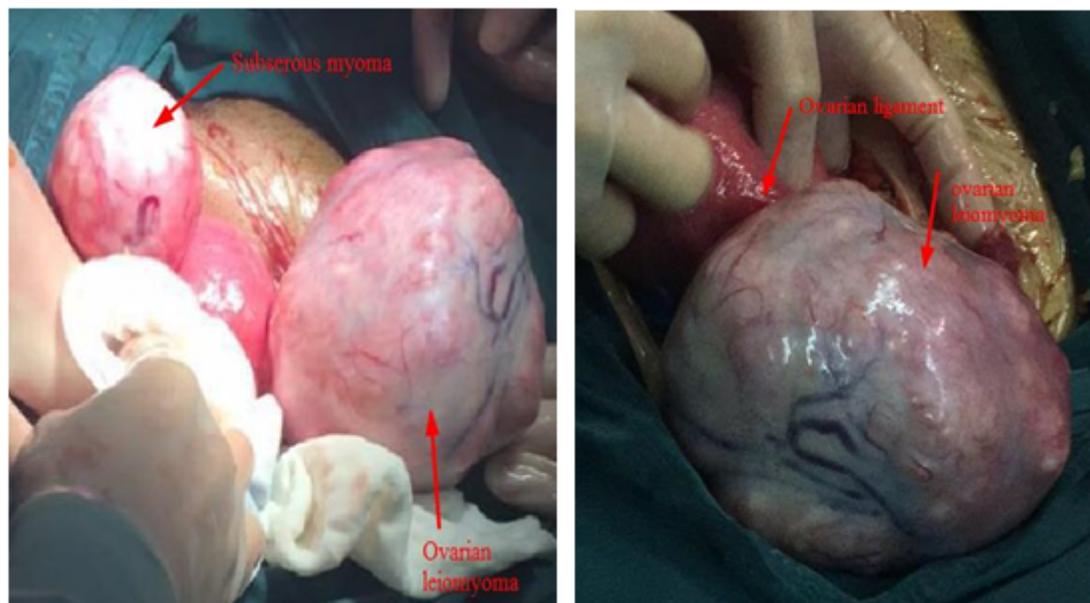


Figure 1

Transabdominal intraoperative view of case 8 the right ovary and part of the uterus with the left subserous myoma(left). The right ovary is noted to be enlarged with a 8cm hard mass in diameter

separated from the uterus not adherent to or infiltrating the surroundings(right) .

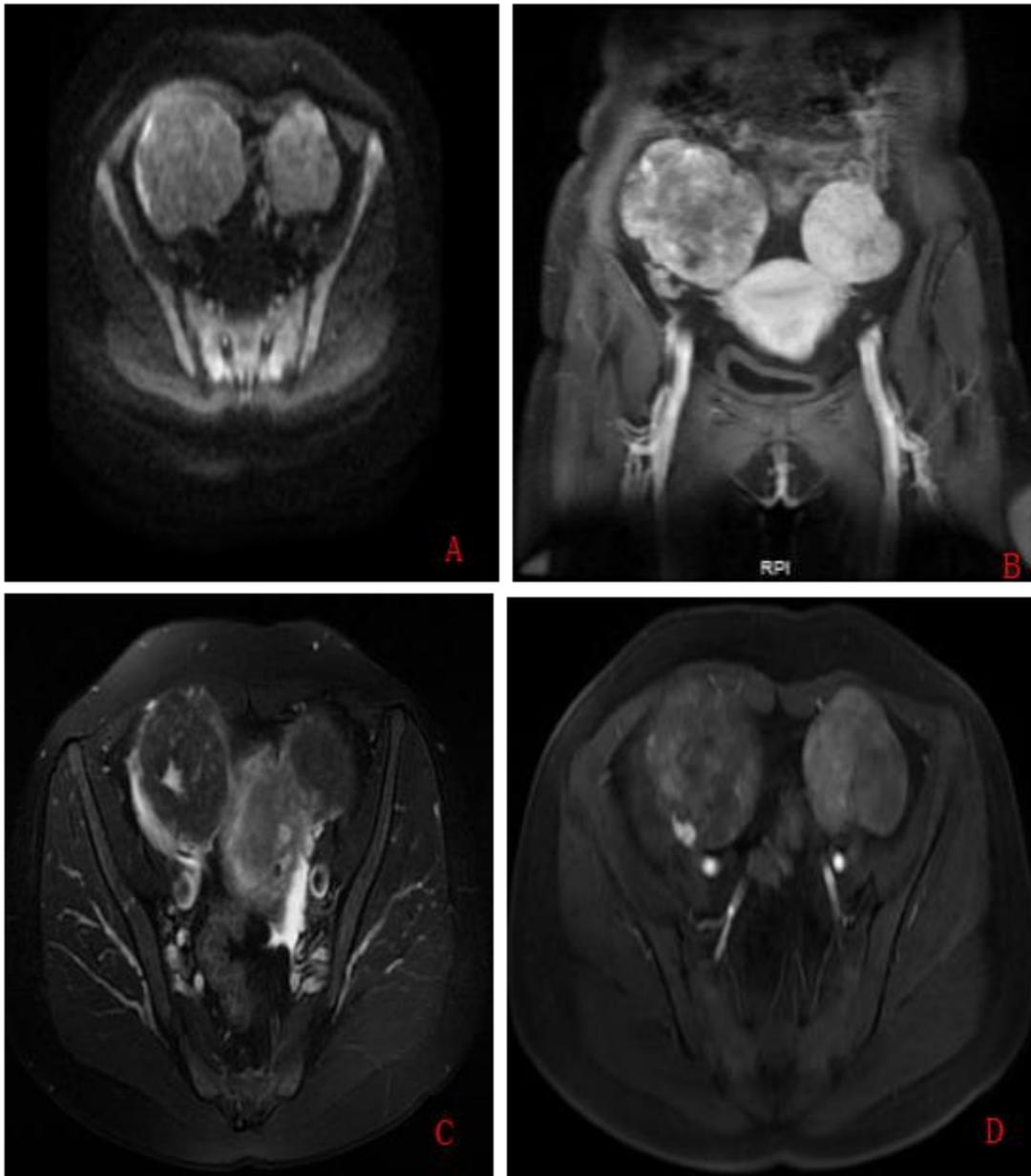


Figure 2

Magnetic resonance imaging of the pelvis from case 8. On axial diffusion-weighted image(TR/TE: 4000/72.4ms,b value=500s/mm²) the two masses showed the same intermediate signal intensity(A). On sagittal T1-weighted with gadolinium administration(TR/TE:3.9/1.7ms) the left mass showed low intensity identical to the uterus myometrium(B). On axial fat-saturated T2-weighted(TR/TE:3020/70.5ms)image, the signal intensity of the left mass was continued with the myometrium while the right mass was well-circumscribed and sharply demarcated from the uterus(C).On axial T1-weighted with gadolinium administration(TR/TE:3.9/1.7ms) ,flow voids could only be seen between the tumor and uterus myometrium on the left mass(D).

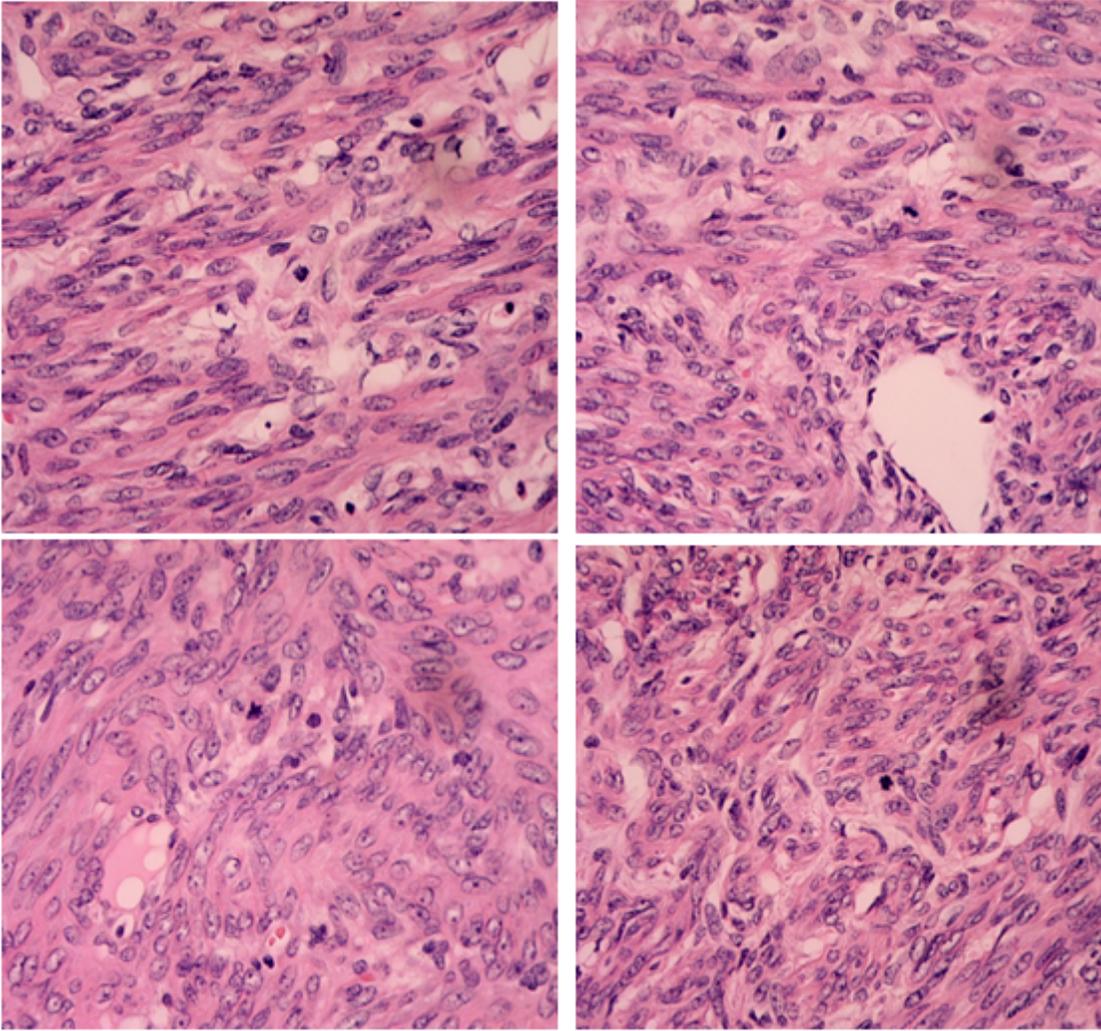


Figure 3

4 mitosis could be found in every 10 high power field (HPF) from case 5 (H&E×400)