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Leiomyosarcoma of the Broad Ligament With Fever Presentation: A Case Report and Review of Literature

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Abstract

Introduction: Leiomyosarcoma is a rare gynecologic malignancy that accounts for less than 1% of gynecological malignancies. Leiomyosarcoma of the broad ligament is an even rarer condition. According to Gardner's criteria, the diagnosis is made when the mass is completely separated from the uterus and adnexa. So far, 23 cases of primary leiomyosarcoma of the broad ligament have been reported in the literature published in English.
Case Presentation: In September 2014, a 55-year-old, gravida 3, para 3 woman with a BMI of 30 and a chief complaint of fever and dizziness was admitted to the infectious-diseases ward of the Pars general hospital affiliated with Iran University of Medical Sciences in Tehran, Iran. Her symptoms had begun two weeks before. The results of a fever workup and examination for infectious, metabolic, and immunologic problems were all negative. Imaging modalities revealed an endometrial polyp, two calcified myoma in the body of the uterus, and a solid, heterogeneous 70-mm mass in the right para-cervical space, posterior to the broad ligament, and far from the ovary. After surgery, a histologic report revealed leiomyosarcoma.
Conclusions: Although a leiomyosarcoma of the broad ligament is rare, practitioners should consider it when dealing with masses in the region of the broad ligament. If there is any suspicion of malignancy, especially in the presence of fever, it is recommended to avoid morcellation during laparoscopy.

Keywords: Broad Ligament, Leiomyosarcoma, Laparoscopy, Laparotomy, Fever

1. Introduction

Leiomyosarcoma accounts for 3.7% of uterine malignancies and less than 1% of gynecological malignancies (1). The most frequent solid tumor of the broad ligament is leiomyoma, and leiomyosarcoma of this region is very rare. It seems that the microscopic pattern plays an important role in the prognosis of this disease. According to Gardner's criteria (2), to make a diagnosis of broad ligament tumor, the mass should be completely separated from the uterus and adnexa. Since very few cases have been reported, treatment of broad ligament leiomyosarcoma is based on the criteria used for uterine leiomyosarcoma. The first sarcomas of this region were reported in the latter part of the nineteenth century and were not diagnosed using the criteria of Gardner et al. (2, 3). Since then, only 23 cases of primary leiomyosarcoma of the broad ligament have been reported in the literature published in English, with the most-recent case reported in 2015 by Gupta et al. (1). According to Gardner et al., primary leiomyosarcoma of the broad ligament occurs in or on the broad ligament, with no connection to the uterus and ovaries (3).

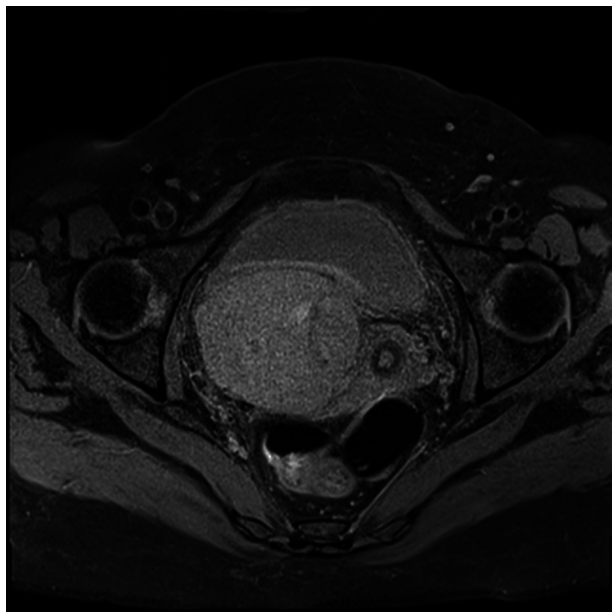
This neoplasm occurs mainly among postmenopausal women, but a few reports show that it also may also occur in women of reproductive age. This extremely malignant tumor behaves unpredictably and has nonspecific clinical manifestations. It often has an insidious course and a poor prognosis, similar to ovarian cancer (1). Since primary leiomyosarcoma of the broad ligament is very rare, its treatment is based on the criteria used for the uterine leiomyosarcoma (1, 2).

None of the previous cases of leiomyosarcoma of the board ligament reported in the literature were correctly diagnosed before surgery and the final histopathology report, which indicates the importance of considering this rare disease. Here, we describe the 24_{th} case, that of a postmenopausal woman who presented with the unusual manifestation of fever, and the management of the case. The case includes histological diagnosis, management, and a thorough literature review.

2. Case Presentation

In September 2014, a 55-year-old, gravida 3, para 3 woman, 5 years postmenopausal, with chief complaints of fever and dizziness, was admitted to the infectious disease ward of Pars general hospital, a private hospital affiliated with Iran University of Medical Sciences in Tehran, Iran. Her symptoms had begun two weeks before. Her past history included cardiac surgery at age 8, and diabetes and hypertension beginning 12 years before. She was under 60 U of NPH, 14 U of regular insulin, 10 mg of Enalapril, and 6.25 mg of oral Carvedilol daily. Physical exam results were as follows: head, neck, chest, and cardiac exams were normal. She was ill, pale, and having cold sweats and chills. Her oral temperature was 38.6°C. Results of a chest X-Ray and ECG were normal. There was no tenderness or organomegaly in the abdomen. After gynecologic consultation and bimanual exam, we detected a top normal and myomatous uterus, normal left adnexa, and a big, firm mass in the right adnexa. The lab results were as follows: HB: 7.4 gm/dL, WBC: 13600/mcL, Platelet: 929000/mcL, ESR: 130 mm/hour., FBS: 223 mg/dL, HbA1c: 10.5. Tumor markers, such as LDH, AFP, HCG, CA125, CA19-9, CA15-3 and CEA, were all normal. The result of a fever workup were negative, as were all examinations for infectious, metabolic, and immunologic problems, including malaria, brucellosis, 2ME, Wright, ANA, ds DNA, blood and urine cultures, Gamma Glutamyl Transferase, C3, C4, CRP, SGOT, and SGPT. Bone-marrow aspiration was hyper-cellular, with 6% -7% plasmacytosis. The upper and lower gastrointestinal endoscopies were normal. A pelvic ultrasound showed an endometrial polyp, two calcified myomas with diameters of 27 and 24 mm in the body of the uterus, and a 60 × 65 hypo-echoic mass with areas of necrosis adjacent to the right aspect of the uterus. An axial CT scan of the abdomen and pelvis with IV and oral contrast showed a 9-mm, calcified gallstone and a 70-mm solid, heterogeneous mass in the right para-cervical space, posterior to the broad ligament, and far from the ovary. Table 1 summarizes the patient's findings. The differential diagnoses were subserosal myoma and right ovarian mass. Magnetic resonance imaging (MRI) showed a broad ligament mass (Figure 1). As her general condition did not change, insulin, empirical antibiotics, and four units of packed cells were administered. A laparotomy confirmed a 7 ×7-cm right broad-ligament mass, adhering to the right pelvic side-wall, closely attached to the bladder and the right ureter. The uterus, tubes, and both ovaries were grossly normal and completely separated from the mass. The liver, sub-diaphragmatic area, para-aortic lymph nodes, gut, omentum, and peritoneum were all normal. Pelvic and para-colic washings were taken for cytological assessment. After the mass was separated from the attached structures, it was entirely excised. Frozen sections revealed leiomyosarcoma. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed, as were multiple lymph node, omental, and peritoneal biopsies. The cytology of para-colic washing was negative for malignancy. The uterus, adnexa, lymph nodes, omentum, and peritoneum revealed no metastasis, but the pathology of the mass showed a highly atypical neoplastic growth, composed of spindle and epithelioid cells with highly pleomorphic nuclei and large foci of necrosis (Figure 2).

Figure 1. There Was a Large 70 × 65-mm Solid Mass in the Right Pelvis With Heterogeneous Enhancement After Gd Injection



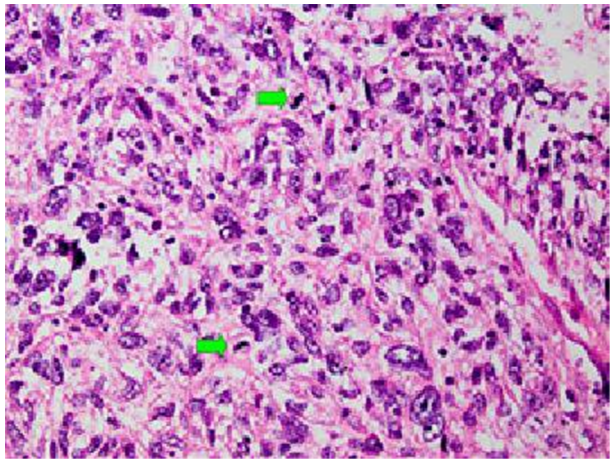
There was mass effect on the bladder and uterus, without obvious invasion, and internal, non-enhancing parts in favor of necrosis. Ovarian mass was ruled out by other cuts.

In immunohistochemistry, the neoplastic cells showed positive staining for smooth muscle actin (SMA) antibodies (Figure 3). In the aftermath, the patient received 25 courses of radiotherapy and 5 courses of adjuvant chemotherapy. At the end of 12 months of follow up, she was disease-free.

3. Discussion

Leiomyosarcoma of the broad ligament is a very rare tumor and mainly involves postmenopausal women. Leiomyosarcoma behaves unpredictably and has nonspecific clinical manifestations, including abdominal pain, mass, distension, and anorexia (2, 3). Therefore, leiomyosarcoma has sometimes been accepted as the

Figure 2. Leiomyosarcoma With Marked Nuclear Atypia and Abnormal Mitotic Shapes



(H and E + 400). (Arrows): fascicles of spindle and devoid cells with large pleomorphic nuclei and abnormal mitotic shapes.

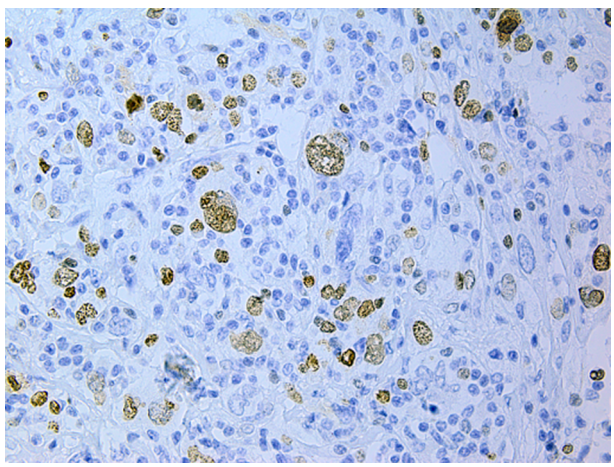


Figure 3. Ki67 Marker Showing Prominent Nuclear Staining of Tumor Cells, Indicating High Proliferative Index (X 400)

Table 1. Patient's Characteristics and Exam and Laboratory Findings

Patient's Characteristics	Findings
Age	55
Sex	Female
Chief complaints	Fever, dizziness
Past medical history	Cardiac surgery at age 8, diabetes, hypertension
Drug history	60 U of NPH and 14 U of regular insulin, 10 mg of Enalapril, 6.25 mg of oral Carvedilol
Physical exam results	Patient was ill, pale, and had cold sweats and chills, oral temperature was 38.6°C, big, firm mass in the right adnexa
Laboratory findings	HB: 7.4 gm/dL, WBC: 13600/ mcL, Platelet: 929000/ mcL, ESR: 130 mm/hour, FBS: 223 mg/dL, HbA1c: 10.5, tumor markers, such as LDH, AFP, HCG, CA125, CA19-9, CA15-3 and CEA, were all normal
Results of fever workup	All following investigations were negative: Malaria, Brucellosis, 2ME, Wright, ANA, ds DNA, blood and urine cultures, Gamma Glutamyl Transferase, C3, C4, CRP, SGOT, SGPT
Other Findings	Chest X-Ray and ECG results were normal, upper and lower gastrointestinal endoscopies were normal
Pelvic Sonography	Endometrial polyp, two calcified myomas with diameters of 27 and 24 mm in the body of the uterus, A 60 × 65 hypo-echoic mass with areas of necrosis adjacent to the right aspect of the uterus
CT scan of abdomen and pelvic	A 9-mm calcified gallstone, A 70-mm solid, heterogeneous mass in the right para-cervical space, posterior to the broad ligament, and far from the ovary
Magnetic resonance imaging	A broad ligament mass

differential diagnosis of ovarian tumors. The present case was admitted to the infectious ward due to fever and sweating. After a comprehensive literature review on Medline and a search for hard copies of older articles in the oregon health and sciences university, we found the full text of 23 previously reported cases of leiomyosarcoma, none of which indicated fever without pain as the main presentation (Tables 2, 3).

Leiomyoma is the most prevalent primary tumor of the broad ligament, and myolipoma, angioleiomyoma, and solitary, fibrous tumors are rare, benign tumors of this region (5-7). Malignant fibrous histiocytomas, alveolar soft-part sarcomas, and hyalinizing spindle-cell tumors are other examples of rare malignant tumors of this region. The histological differential diagnoses are endometrial stromal sarcomas, uterine carcinosarcomas, and gastrointestinal stromal tumors (4). None of the previous cases of leiomyosarcoma of the broad ligament reported in the literature were correctly diagnosed before surgery and the final histopathology report. Schmidt reported the first sarcoma of this region in 1887 (8), followed by a few cases documented by German and French authors around the turn of the twentieth century (9), which were not diagnosed using the criteria of Gardner et al. (2). According to Gardner et al., primary leiomyosarcoma of the broad ligament occurs in or on the broad ligament, with no connection to the uterus and ovary (2). Today, it seems that the microscopic pattern plays an important role in prognosis. But the reliance on mitotic counts has been

Table 2. [Part 1] Cases of Leiomyosarcoma of the Broad Ligament and the Manifestation Reported for All Cases[a]

Cases	Age	Clinical Manifestation	Side of Tumor	Mitoses 10 HPF	Initial Treatment	Subsequent Treatment	Survival
1	50	N/S	Rt	0 - 4	TAH + BSO		> 12 months
2	50	N/S	Lt	15	TAH + BSO	RT, CT	DOD > 7 months
3	50	N/S	Lt	12	TAH + BSO	CT	DOD > 19 months
4	48	Rapidly enlarging pelvic mass	Lt	10	TAH + BSO		No report
5	70	N/S	Lt	< 10	Enucleation		No report
6	73	Low back pain, Constipation, Anorexia,Wt loss, Rt shoulder pain	Lt	21	TAH + BSO		DOD > 1 month
7	31	Rt adnexal mass, Rt lower quadrant abdominal pain	Rt	8	Enucleation	RT, CT	> 30 months
8	36	N/S	Lt	> 10	TAH + BSO	RT, CT	> 33 months
9	65	N/S	Lt	> 10	Subtotal hysterectomy + BSO	CT	DOD > 30 months
10	59	Rt lower abdominal pain	Rt	< 10	TAH + BSO		Alive > 12 months
11	56	Rt lower abdominal pain, Abdominal distention	Rt	14	TAH + BSO	RT	Alive > 12 months
12	55	Lower abdominal pain	Lt	> 10	TAH + BSO	CT	Alive > 1 year

[a]Modified from: Shah et al. (4).
Abbreviations: BSO, bilateral salpingo-oophrectomy; CT, chemotherapy, DOD: dead of disease; HPF, high power-field; LSO, left salpingo-oophrectomy; N/S, not specified; RT: radiotherapy; TAH, total abdominal hysterectomy.

Table 3. [Part 2] Cases of Leiomyosarcoma of the Broad Ligament and the Manifestation Reported for All Cases[a]

Cases	Age	Clinical Manifestation	Side of Tumor	Mitoses 10 HPF	Initial Treatment	Subsequent Treatment	Survival
13	87	Poor appetite, Tiredness, Breathlessness	Rt	30 - 40	TAH + BSO		DOD > 2 months
14	53	Pelvic pain, Dysuria	Rt	< 10	TAH + BSO		Alive > 15 months
15	52	Pelvic pain, Metorrhagia	Rt	> 10	TAH + BSO		DOD > 3 months
16	50	n/m	Rt	> 10	TAH + BSO		DOD
17	73	Rt pelvic pain, Low back pain	Lt		TAH + BSO		DOD > 30 days
18	49	N/S	Rt	> 10	TAH + BSO + Appendectomy + Omentectomy		DOD > 5 months
19	45	Lower abdominal pain, Lump		10	Resection	CT	Alive > 15 months
20	26	Pelvic pain, Metorrhagia, Poor appetite, Fatigue	Lt	30 - 40	LSO + partial Omentectomy		Alive > 3 years
21	35			> 10	TAH + BSO	RT, CT	Alive >12 months
22	52	Pelvic pain	Rt	< 10	TAH + BSO		Alive > 42 months
23	41	Lower abdominal pain	Lt	12 - 14/10	TAH + BSO	RT, CT	Presently alive
24	55	Fever	Rt	> 10	TAH + BSO	RT, CT	Alive > 9 months

[a]Modified from: Shah et al. (4).
Abbreviations: BSO, bilateral salpingo-oophrectomy; CT, chemotherapy, DOD: dead of disease; HPF, high power-field; LSO, left salpingo-oophrectomy; N/S, not specified; RT: radiotherapy; TAH, total abdominal hysterectomy.

questioned due to adjacent necrosis, the influence of hormones, and an increased appreciation for the lack of reproducibility among observers (9). The criteria used by Zaloudek and Norris are mitotic figures ($\geq$ 5 versus < 5 per 10 high-power field (HPF)), cellularity (hyper-cellular versus normo-cellular), and nuclear atypia (yes-no) (10). Coindre et al. advocated a three-grade system, using mitotic figures, tumor differentiation, and necrosis; this is very important, because of the prognostic and therapeutic implications (11). Immunohistochemically, these tumors have significant reactivity for actin, myosin, desmin, and estrogen receptors, which increase the possibility of the hypothesis of tumor hormonal responsiveness (12). Since very few cases have been reported, treatment of broad ligament leiomyosarcoma is based on the criteria used for uterine leiomyosarcoma. Standard management for uterine sarcoma includes total abdominal hysterectomy and bilateral salpingo-oophorectomy, but pelvic and para-aortic lymphadenectomy is recommended only for carcinosarcoma and not for leiomyosarcoma, despite the fact that some cases of the latter show a higher incidence of nodal involvement (13). Occasionally, the tumor is large, adheres to surrounding structures, and has areas of hemorrhage or necrosis. The role of frozen section in the diagnosis can be omitted (13), but in our case, frozen section revealed an accurate diagnosis. In nulliparous, pre-menopausal women or in the case of a tumor in early its stages, the ovaries should be conserved. Adjuvant chemotherapy with or without radiotherapy can be used in selected cases (14). Some authors believe that when mitoses are less than 10 per 10 HPF, no further therapy is needed after surgical intervention (15). Mirsadraee et al. reported a unique case: a 26-year old woman who, despite 30 - 40 mitosis in 10 HPF, was treated surgically without adjuvant treatment and remained disease free for more than 3 years. Furthermore, she had a successful pregnancy, and the uterus and adnexa were found to be unremarkable during cesarean section (16).

It is well-known that malignancies can cause a fever. In some series, fever underlying malignancy accounts for up to 25% of cases of fever of underdetermined origin (17). The pathophysiology of a tumor-induced fever may be caused by several mechanisms, including the release of cytokines (tumor necrosis factor and interleukin-1), tumor, or infiltrating mononuclear cells (18). Other causes include tumor necrosis or obstruction of a hollow duct or viscous, resulting in proximal infection; drug fever; TTP; DVT; and Trousseau's syndrome. Although ovarian cancers commonly cause a fever, there is no previous report of a fever being caused by a leiomyosarcoma of the broad ligament. Our case indicates that fever might be present in patients with this very rare disease and should be considered in their diagnoses. A recent Food and Drug Administration (FDA) safety communication (19) discouraged the use of laparoscopic, uterine power morcellation in hysterectomy and myomectomy because of the chance of the presence of an underlying, unsuspected uterine sarcoma. In patients with such sarcomas, there is a risk that the procedure will spread cancerous tissue within the peritoneal cavity, significantly reducing the patient's long-term survival. Our case shows that this consideration should be extended to cover patients who present with fevers and broad ligament masses. The most important point of this case is that a patient who presented with a chief complaint of fever actually had an unusual manifestation of leiomyosarcoma of the broad ligament. The patient's follow up was relatively short, 12 months, which might be considered a shortcoming of this presentation.

Although a leiomyosarcoma of the broad ligament is very rare, practitioners should consider it when dealing with tumoral masses in this region, particularly if the disease manifestation includes a fever. If there is any suspicion of malignancy, especially in the presence of fever, it is recommended to avoid power morcellation during laparoscopic treatment.

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Footnote

Authors' Contribution: Shahla Chaichian , study design, data interpretation, manuscript preparation; Abolfazl Mehdizadehkashi, data collection, manuscript preparation; Kobra Tahermanesh, data interpretation, manuscript preparation; Bahram Moazzami, study design, manuscript preparation; Fatemeh Jesmi, literature search, data interpretation; Moezedinjavad Rafiee, manuscript preparation, literature search; Katayoun Goharimoghaddam, literature search, manuscript preparation.

References

1. Gupta D, Singh G, Gupta P, Mendonca S, Singh KK. Primary leiomyosarcoma of the broad ligament: A case report with review of literature. *Hum Pathol.* 2015;**2**(3):59–62. doi: 10.1016/j.ehpc.2015.02.005.
2. Turnbull HL, Duncan TJ. Management of a pelvic mass. *Obstet Gynaecol Reprod Med.* 2013;**23**(9):279–85. doi: 10.1016/j.ogrm.2013.06.004.
3. Gardner GH, Greene RR, Peckham B. Tumors of the broad ligament. *Am J Obstet Gynecol.* 1957;**73**(3):536–54. [PubMed: 13402824] discussion, 554-5.

4. Shah A, Finn C, Light A. Leiomyosarcoma of the broad ligament: a case report and literature review. *Gynecol Oncol.* 2003;**90**(2):450–2. [PubMed: 12893217].
5. Eltabbakh GH. Broad ligament lipoma presenting as a pelvic mass: a case report. *J Reprod Med.* 2007;**52**(6):543–4. [PubMed: 17694978].
6. Cobellis L, Pecori E, Rigatti F, Scaffa C, Rotondi M, Messalli EM. A rare case of female pelvic mass: angioleiomyoma of the broad ligament. *Eur J Gynaecol Oncol.* 2007;**28**(5):418–20. [PubMed: 17966227].
7. Zubor P, Kajo K, Szunyogh N, Galo S, Danko J. A solitary fibrous tumor in the broad ligament of the uterus. *Pathol Res Pract.* 2007;**203**(7):555–60. doi: 10.1016/j.prp.2007.02.005. [PubMed: 17493768].
8. Schmidt K. Leiomyosarcoma of the broad ligament. *Prag Med Wschr.* 2008;**1878**(35):260.
9. Bell SW, Kempson RL, Hendrickson MR. Problematic uterine smooth muscle neoplasms. A clinicopathologic study of 213 cases. *Am J Surg Pathol.* 1994;**18**(6):535–58. [PubMed: 8179071].
10. Zaloudek C, Hendrickson MR, Soslow RA. Blaustein's pathology of the female genital tract. Springer; 2011. pp. 453–527.Mesenchymal tumors of the uterus.
11. Coindre JM, Nguyen BB, Bonichon F, de Mascarel I, Trojani M. Histopathologic grading in spindle cell soft tissue sarcomas. *Cancer.* 1988;**61**(11):2305–9. [PubMed: 3365658].
12. Zaloudek C, Brenda WN. The ovary and fallopian tube. Churchill Livingstone/Elsevier,[Edinburgh]; 2006.
13. Scurry JP, Sumithran E. An assessment of the value of frozen sections in gynecological surgery. *Pathology.* 1989;**21**(3):159–63. [PubMed: 2626269].
14. Duhan N, Singh S, Kadian YS, Duhan U, Rajotia N, Sangwan N. Primary leiomyosarcoma of broad ligament: case report and review of literature. *Arch Gynecol Obstet.* 2009;**279**(5):705–8. doi: 10.1007/s00404-008-0777-2. [PubMed: 18777035].
15. Stita W, Trabelsi A, Hmissa S, Sriha B, Mokni M, Korbi S. Leiomyosarcoma of the broad ligament: a case report and literature review. *Eur Clinics Obstet Gynecol.* 2008;**3**(3-4):127–9. doi: 10.1007/s11296-008-0076-2.
16. Mirsadraee S, Mansouri A, Ataei R, Kakhi S. Leiomyosarcoma of the broad ligament: case report and review of literature. *IJP.* 2008;**3**(2):104–8.
17. Hayakawa K, Ramasamy B, Chandrasekar PH. Fever of unknown origin: an evidence-based review. *Am J Med Sci.* 2012;**344**(4):307–16. doi: 10.1097/MAJ.0b013e31824ae504. [PubMed: 22475734].
18. Cunha BA. Fever of unknown origin: clinical overview of classic and current concepts. *Infect Dis Clin North Am.* 2007;**21**(4):867–915. doi: 10.1016/j.idc.2007.09.002. [PubMed: 18061081] vii.
19. Laparoscopic Uterine Power Morcellation In Hysterectomy And Myomectomy: Fda Safety Communication [cited 10/27/2014]. Available from: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm393576.htm.