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COMMUNICATION

A case of unsuspected leiomyosarcoma diagnosed following laparoscopy-assisted vaginal hysterectomy performed for presumed myoma after GnRH treatment

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Abstract A 37-year-old woman who had received two courses of gonadotropin-releasing hormone (GnRH) analogue for preparation to hysteroscopic resection of a presumed submucous myoma after a benign endometrial sampling had no improvement of bleeding episodes and no regression in the size of the myoma. The patient chose to have a hysterectomy and laparoscopic hysterectomy was performed uneventfully. The mass, consisting of haemorrhagic and necrotic tissues, was found to be located intramurally with dimensions 8×6 cm. Pathological diagnosis was leiomyosarcoma, as examination of the specimen showed diffuse cytologic atypia with coagulative necrosis and 7–8 mitosis per high-power field. The possibility of delaying the definitive treatment of leiomyosarcoma by giving GnRH analogue to patients who were presumed to have myomas should be considered, even in young patients.

Keywords Leiomyoma · Leiomyosarcoma · GnRH analogue · Laparoscopy-assisted vaginal hysterectomy (LAVH)

Introduction

Smooth muscles of the uterus encompass a variety of neoplasms, either benign or malignant. These include leiomyomas, leiomyosarcomas and smooth muscle tumour of uncertain malignant potential (STUMP). Leiomyomas are the most common gynaecologic neoplasms in women of reproductive age [1, 2]. Leiomyosarcoma, on the other hand, constitutes approximately 1% of all uterine malignancies [3]. The overall incidence of uterine sarcoma has been estimated to be 0.67 per 100,000 women per year [4]. These tumours usually grow as solitary, irregular, bulky masses that invade the uterine wall. The median age of women with leiomyosarcomas (50–55 years) is about 10 years greater than that of the women with leiomyomas [5, 6]. Patients with uterine leiomyosarcomas may present with abnormal vaginal bleeding, lower abdominal pain and pelvic or abdominal mass. The diagnosis is frequently made by the pathologist after primary hysterectomy performed by the gynaecologist for presumed leiomyomas [7]. The majority of patients are diagnosed at clinical stage 1, although most patients do not receive adequate staging at the time of primary surgery, due to a lack of preoperative suspicion of malignancy [8].

A case of leiomyosarcoma that was presumed as submucous leiomyoma and, thus, planned to be managed conservatively and received gonadotropin-releasing hormone (GnRH) analogue for preparation to hysteroscopy is presented in order to draw attention to the possibility of the presence of leiomyosarcoma, even in young patients who are diagnosed to have leiomyomas by using routine diagnostic tests.

Case report

A 37-year-old woman with Gravida:4, Para:4 was referred to MoH Ankara Etlik Maternity and Women's Health Hospital with a history of intractable bleeding for 6 months. The hystopathological evaluation of the specimen obtained by endometrial sampling showed chronic endometritis. On transvaginal ultrasonographic evaluation, the dimensions of

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the uterus were measured as 90×58×78 mm and a fibroid of 48×47 mm was detected. She had received antibiotics and progestins, and then combined oestrogen and progestin therapy consecutively for 6 months without any improvement in her bleeding episodes. The haemoglobin level on admission was 7.0 gr/dl.

Vaginal examination showed an enlarged uterus with the size of a pregnant uterus of 8 weeks. On transvaginal ultrasonography, the dimensions of the uterus were found to be 90×62×78 mm, with a submucous myoma of 49×46 mm filling the cavity. Saline sonohysterography showed that the myoma was predominantly submucous, with an intramural component <1/3. All of the treatment modalities were discussed with the patient and a hysteroscopic resection of the submucous myoma after suppression with GnRH analogue was planned. The patient was given GnRH analogue, gosarelin acetate (Zoladex Depot 3.6 mg subcutaneous, AstraZeneca), for 2 months as preparation to hysteroscopic resection and was put onto iron supplementation therapy. The ultrasonographic evaluation after two doses of GnRH analogue administration showed a uterine size of 84×66×64 mm, but the size of the submucous myoma remained unchanged (48×47 mm), with an increased intramural component of >2/3. The patient also complained about ongoing bleeding during this treatment. Hysteroscopic myomectomy was cancelled and detailed information about myomectomy via laparotomy and hysterectomy were given. The patient refused to have myomectomy and requested a hysterectomy for definitive treatment. She was scheduled for laparoscopic hysterectomy for leiomyoma uteri and intractable uterine bleeding. Laparoscopy-assisted vaginal hysterectomy (LAVH) was uneventful. Hystopathological evaluation of the specimen was reported as leiomyosarcoma, as diagnosed by the presence of necrotic and haemorrhagic areas with cellular atypical and 7–8 mitosis per high-power field. After confirmation of the hystopathological diagnosis, the patient was re-operated for surgical staging and bilateral salpingooophorectomy and bilateral pelvic para-aortic lymph node dissection with omentectomy were performed. No residual tumour was found. Due to the aggressive nature of the tumour, the patient received chemotherapy (ifosfamide, mesna and adriamycin). Eighteen months after the initial surgery, the patient is still alive without any consequences.

Discussion

Uterine leiomyoma is the most common benign tumour of the female reproductive tract. Although many women with fibroids are asymptomatic, some cases may present with menorrhagia, pelvic pain, obstructive symptoms, infertility or pregnancy loss. Submucous myomas are often associated with menorrhagia [9]. After palpation of the mass during bimanual examination, translational ultrasonography, sonohysterography, hysteroscopy and magnetic resonance imaging (MRI) can be helpful in confirming the presence and identifying the localisation of these benign tumours. The treatment modalities in symptomatic patients vary, from the surgical removal of the mass (myomectomy, hysteroscopic resection of the fibroid or hysterectomy) to conservative methods, such as uterine artery embolisation, ablative techniques, myolysis or medical treatment. Hysterectomy can be offered as a definitive treatment option in symptomatic women with leiomyomata who do not want to preserve their fertility. According to the Canadian Society for Obstetrics and Gynecologists, hysteroscopic myomectomy—with 1-B level of evidence—is considered as the first-line conservative surgical therapy for the management of symptomatic intracavitary fibroids. GnRH analogues or agonists can be used preoperatively for reducing the tumour size prior to hysteroscopic resection of predominantly submucous fibroids. Pretreatment with GnRH analogue may be particularly indicated for all myomas with a diameter of more than 3 cm and/or with an intramural portion, or for patients with secondary anaemia [10]. On the other hand, there are seldom reports showing that these medications may also lead to substantial degeneration and infarction of the leiomyoma, making the preoperative diagnosis of leiomyosarcomas even more difficult [11, 12].

With the consistent improvement in conservative treatment modalities of leiomyomas, distinguishing leiomyosarcomas from benign leiomyomas before selecting a conservative approach is becoming more important, as these therapies may lead to a delay in the diagnosis of this aggressive tumour. There are reports of unexpected mesenchymal uterine tumours diagnosed following the pathologic review of specimens obtained during hysteroscopy performed for the resection of endometrial polyp or submucous myoma [13]. Studies showed that leiomyosarcoma incidence in hysterectomies that were presumed to be leiomyoma is low (0.13– 0.3%), but a rise between the ages of 30 and 70 years from 0.2 to 1.7% is demonstrated [14, 15].

The preoperative diagnosis of leiomyosarcoma is difficult and there is no pathognomic sign for differential diagnosis. The most common sign encountered in cases with leiomyosarcoma, prolonged uterine bleeding, is also seen in leiomyomata. A rapidly growing uterus is believed to be indicative of malignancy, but various studies had shown that the rapid growth of a fibroid defined by Parker as an increase by 6 weeks gestational size over a 1-year period does not always prove the presence of a leiomyosarcoma [3, 14]. Leiomyosarcomas are most likely to be solitary than myomas, and they do not resemble a leiomyoma macroscopically with ill-defined margins and loss of the whorl pattern seen in leiomyomas. On the other hand, leiomyomas frequently resemble leiomyosarcomas

due to benign degenerative changes and tumour necrosis that is pathognomic for leiomyosarcomas is frequently observed in fibroids greater than 10 cm in diameter. Diagnostic imaging techniques are not very successful in distinguishing these malignant tumours from leiomyomas. The combined use of dynamic MRI and serum lactate dehydrogenase levels has a relatively better sensitivity in distinguishing leiomyosarcomas from leiomyomas [16].

Endometrial biopsy is successful in diagnosing leiomyosarcoma in only one third of the cases [12] and up to 50% of leiomyosarcoma cases are found in a submucous mass [15]. Beside these difficulties, even frozen section can only diagnose 3 out of 16 patients with leiomyosarcoma [3]. Meyer et al. [17] described the GnRH analogue challenge test for the identification of leiomyosarcoma based on the hypothesis that leiomyosarcomas will not respond to GnRH analogue, whilst leiomyomas will shrink. There are case reports in the literature reporting patients with leiomyosarcomas who received GnRH analogues for the treatment of presumed leiomyomas [18, 19]. Changes attributed to GnRH analogues, i.e. improvement of the symptoms and histological changes observed in cases with leiomyoma, can also be seen in these leiomyosarcoma cases. The GnRH analogue test is not routinely advocated for diagnosis, as, contrary to what is expected, there are reported cases showing shrinkage of the leiomyosarcoma during GnRH treatment [20, 21].

In conclusion, a diagnostic method to distinguish malign uterine masses from benign leiomyomas is needed, but, due to the rarity of leiomyosarcomas, concrete recommendations for differential diagnosis has not yet been established. The clinicians must be aware of the occurrence of leiomyosarcoma in patients who are mistakenly diagnosed to have leiomyoma and, thus, assigned for conservative management. The patients who are assigned for conservative management should be monitored closely in order to avoid the possibility of a delay in the diagnosis of leiomyosarcoma that might effect the patient's survival.

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