Rare disease

Endometrial stromal sarcoma of uterus with metastasis to the lung and brain

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Summary

Endometrial stromal sarcomas are rare tumours of the uterus and account for 10% of uterine sarcomas. Most of such tumours are low grade, although even these types can spread to the extrauterine areas; however, brain metastasis is very uncommon. This case report presents a 43-year-old Iranian woman with synchronous lung and brain metastases.

BACKGROUND

Endometrial stromal sarcomas (ESSs) are the least common types of uterine sarcomas and constitute about 10% of these neoplasms.^{1–3} Endometrial stromal tumours are classified by the WHO (2003) as follows: endometrial stromal nodules (ESN) (the benign lesion), ESSs (previously referred to as low-grade ESSs, ESSs-LG) and undifferentiated endometrial sarcomas (UESs) (previously referred to as high-grade ESSs).⁴ Although ESSs are often indolent, they have metastatic potentials.^{5–10} Abdomen, pelvis and lungs are common sites of metastases¹⁰; however, brain metastasis is unusual. This case report presents a patient with ESSs and lung and brain metastases.

CASE PRESENTATION

The patient was a 43-year-old housewife and was referred to our centre for whole-brain radiation therapy, subsequent to surgical resection of a brain lesion. Her medical history revealed that her problem had started from 7 years earlier with abnormal vaginal bleeding and physical examination had shown apparently cervical polyp and

pathology had reported it as adenofibroma. Since excluding of adenosarcoma is not possible on curettage material, hysterectomy was proposed but the patient refused to accept this procedure. One year later, cervical polypectomy and endometrial curettage specimens showed the same pathology. Two years later, her problem reappeared and finally she accepted hysterectomy. This time the pathological examination revealed a polypoid tumour originating from the posterior part of the endometrial cavity and extending radially to more than half of the myometrium and inferiorly to the endocervical epithelium. The tumour showed characteristics of ESS (low grade) with three mitosis in the 10 high-power field. Since at that time we did not have immunohistochemistry (IHC) facility in Yazd, all pathology blocks and sections were given to the patient for performing IHC study in Tehran, capital of Iran. IHC was positive for oestrogen receptors (ER), progesterone receptors (PR), Ki-67 (10%) smooth muscle actin (SMA), cytokeratin (CK) and negative for CD34 and was compatible with ESS. Unfortunately, the patient lost all samples she had taken from our centre and

Figure 1 MRI showing a lobulated mass lesion located in the left occipital lobe.

Figure 2 H&E showing malignant pleomorphic cells with numerous mitotic figures.

now they are not available anymore. The patient's condition was fairly satisfactory until last month when she complained of a headache.

INVESTIGATIONS

Brain MRI with gadolinium revealed a lobulated mass lesion located in the left occipital lobe with the greatest diameter of 5 cm and significant enhancement (figure 1). Surgery was performed in another centre and pathological examination showed that brain tissue was infiltrated by malignant pleomorphic cells with numerous mitotic figures and foci of necrosis (figure 2). IHC staining was positive for vimentin (figure 3), SMA (figure 4), ER (figure 5), CD10 (figure 6), Ki-67 (20%) (figure 7) and weakly positive for CK and PR and negative for CD34

Figure 4 Smooth muscle actin.

(figure 8) and caldesmon. Chest CT scanning showed multiple lung metastases (figure 9).

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of ESS includes ESN, UES, highly cellular leiomyoma, highly cellular intravenous leiomyomatosis, cellular endometrial polyp, sex-cord stromal tumours, low-grade Mullerian adenosarcomas and adenomyosis.¹¹ ESS must be distinguished from ESN and UES. The size of ESN is variable from less than 1 to 22 cm with a mean of 7 cm. It is frequently polypoid. Although non-capsulated, it is well circumscribed and is the main gross differentiating feature between ESN and ESS. In contrast, ESS has infiltrating irregular margin. Although ESN does not show myometrial and vascular invasion, in microscopic examination both features are seen in ESS

Figure 3 Vimentin.

Figure 5 Oestrogen receptors.

Figure 6 CD10.

and these are the two main distinctions between these two entity subgroups.^{11 12} Almost always, distinction between them is impossible on curettage specimens and hysterectomy is essential for accurate diagnosis. It is an important issue in women in reproductive age who desire to have babies. On the other hand, on gross examination UES show a destructive infiltrative growth into the myometrium, which contrasts with the permeative invasion of the myometrium and myometrial vessels seen in low-grade ESS. This tumour has marked nuclear atypia, high mitotic activity and necrosis.

TREATMENT

The patient received 3000 cGY whole-brain radiation dose and then was referred for chemotherapy.

Figure 7 Ki-67.

Figure 8 CD34.

OUTCOME AND FOLLOW-UP

Now 2 months postradiation therapy, she is receiving chemotherapy regimen including docetaxel and cisplatin.

DISCUSSION

ESSs are composed of cells closely resembling normal proliferative endometrial stromal cells and usually have an indolent course with an 80–100% 5-year survival.^{11–13} Women with ESSs are usually younger than those suffering from other types of uterine sarcomas, the disease most often occurring in women between 40 and 55 years; however, there are reports of this disease in adolescents.¹⁴ As mentioned above, diagnosis of ESS from benign conditions such as ESN is impossible in curettage specimens. There is no real possibility of confusing a pure stromal neoplasm with a typical mixed Mullerian tumour; however, if a stromal sarcoma envelops and includes non-neoplastic glands resembling to a mixed Mullerian tumour may result. This only poses a problem in biopsy material for hysterectomy specimens. It is usually apparent that the entrapped glands are confined to the periphery or base of the tumour. We think that in our patient the tumour was ESS from the beginning when the patient was 36 years old. Some cases have been reported in patients with ovarian polycystic disease.¹² An association with prolonged oestrogenic stimulation, tamoxifen treatment or previous pelvic irradiation has been observed in some patients.¹⁴ Patients commonly present with abnormal vaginal bleeding and pelvic or abdominal pain; however, up to 25% of women are asymptomatic.^{1 3 12 14} Vaginal bleeding was the chief complaint of our patient and it was repeated a few months postcurettage. More than 30% of women with ESS have extrauterine disease at presentation and the ovary is often involved in such cases.^{3 12 14} Thus, when evaluating an ovarian tumour with histological features consistent with an endometrial stromal tumour, it is important to exclude a history of uterine ESS.^{12 14} These tumours are usually

Figure 9 CT scanning showing multiple lung metastases.

immunoreactive for ER, PR, vimentin, muscle-specific actin, α -smooth muscle actin and frequently keratin as in our patient. Desmin and h-caldesmon are generally negative or at most focally positive.¹² In our patient, in metastatic samples caldesmon was negative. Amant *et al* reported transition of ESS into high-grade sarcoma in two cases during several years. They used increased cellular atypia, absence of spiral arterioles and an increased mitotic index and proliferation index as a reason for their proposal.¹⁵ UES designates when sarcomatous cells lack specific differentiation and shows myometrial invasion, severe nuclear pleomorphism, high mitotic activity and/or tumour cell necrosis. These tumours lack immunoreaction for ER and PR, but a high proportion are epidermal growth factor receptor immunoreactive.¹² Sometimes these tumours have an ESS component indicating that high-grade component is presumably of endometrial stromal derivation. Classifying these tumours remains a controversial approach.^{12 14 16} In the meantime, designation of high-grade ESS arising from low-grade ESS may be acceptable. We think that this transition happened in our case because the tumour with three mitotic figures and low-grade characteristics and Ki-67=10% were converted to a high-grade tumour with numerous mitotic figures and Ki-67=20% although at the same time they showed immunoreactivity for SMA, ER and PR. Kurihara *et al* classified non-low-grade ESSs into two groups: UES with nuclear uniformity (UES-U) and UES with nuclear pleomorphism (UES-P), and compared their molecular genetic and immunohistochemical profiles. They suggested that UES-U shares some molecular genetic and immunohistochemical characteristics with ESS-LG, but UES-P considerably differs from ESS-LG.¹⁷ Thus, it seems that an intermediate group of uterine sarcomas with only modest endometrial stromal differentiation, higher mitotic rate and greater nuclear atypia than low-grade ESSs, but lacking the nuclear pleomorphism of undifferentiated sarcomas exist, most likely they represent the old 'high-grade ESSs'.¹⁸ Although ESSs have an indolent course they can recur and metastasise to regional and distant organs. Most recurrences are limited to pelvis. Lung, bone and liver are the most common sites of distant metastases.^{10 13 19 20} Brain metastasis is very uncommon and as per our knowledge only two cases have been reported before^{13 19} and our case is the third one.

Learning points

- Endometrial stromal sarcomas (ESSs) are usually indolent and limited to pelvis; however, in rare situations and even in rarer situations brain metastases may occur.
- Since some cases of undifferentiated endometrial sarcomas have a low-grade ESS component and non-low-grade endometrial sarcomas are not unique in their genetic profiles and clinical behaviour, it seems that may be adding an intermediate group to the present classification would be helpful.
- Transformation of uterine ESS to a tumour with characteristics of a higher-grade disease may happen over time.

Competing interests None.

Patient consent Obtained.

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