Rare disease

Uterine adenosarcoma in a patient with history of breast cancer and long-term tamoxifen consumption

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Summary

Adenosarcoma is a rare tumour which usually originates from endometrium. This paper presents a 69-year-old woman with adenosarcoma of uterus and a history of breast cancer and 10 years tamoxifen therapy.

BACKGROUND

Mullerian adenosarcomas consist of a malignant stromal sarcoma and a benign epithelial component and account for only 8% of uterine sarcomas.¹⁻² Tamoxifen is used in breast cancer due to its antioestrogenic properties; however, it has a weak oestrogenic effect which can increase the risk of endometrial and especially mixed Mullerian tumour.¹⁻⁸ A 69-year-old Iranian woman with uterine adenosarcoma following long-term tamoxifen consumption is presented in this paper.

CASE PRESENTATION

A 69-year-old woman referred to our emergency ward because of vaginal bleeding and a protruding mass through her vagina. At examination, a large grey necrotic mass was seen in the vagina that originated from the uterus and the uterus was larger than normal. The patient was gravid 9 para 9. She had a history of hypertension, hyperlipidaemia and diabetes. The most important point in her medical history was a hormone-receptor-positive breast cancer diagnosed 11 years earlier. Mastectomy, chemotherapy and radiation therapy had been done and tamoxifen 20 mg daily had been started and continued until the patient's recent problem had begun. Unfortunately, regular pelvic examination and pap smear test had not been performed. Her family history was unremarkable. The patient underwent sonographic study when admitted to the hospital. It showed a large heterogenous 167×80×100 mm uterus with endometrial thickening of about 48 mm. Chest CT scanning was normal. Abdominopelvic CT scanning showed enlarged uterus with heterogenous density and a 52 mm hypodense mass inside it (figure 1).

Cervical mass removal and endometrial curettage was done. Pathology examination revealed low-grade adenosarcoma with extensive haemorrhagic necrosis (figure 2).

DIFFERENTIAL DIAGNOSIS

Adenosarcoma is differentiated from adenofibroma by the presence of stromal mitotic figures of 1 or more per 10 high-power field, marked stromal cellularity with periglandular

Figure 1 CT scanning shows enlarged uterus with increased thickness.

Figure 2 Image shows benign neoplastic glands among a sarcomatous background. Few mitotic figures and pleomorphic nuclei are seen.

cuffing or more than mild nuclear atypia of the stromal cells. Benign endometrial polyps have stroma similar to adjacent endometrium and there is no prominent cellularity around the glands.⁹ Further differential diagnosis includes adenomyoma, polyp in uterine cavity, low-grade endometrial stromal sarcoma, malignant mixed Mullerian tumours (MMMTs) and embryonal rhabdomyosarcoma.¹⁰

TREATMENT

Total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph nodes sampling from obturator, internal and external iliacs and inguinal, peritoneal washing and omental biopsy were performed. On macroscopic examination, a 7 cm polypoid mass originating from the anterior part of the endometrium was seen. Microscopic evaluation revealed a mesenchymal tumour confined to the endometrium. Neither of 10 resected lymph nodes nor omental biopsy showed any evidence of malignancy, peritoneal washing did not show malignant cells and, therefore, the stage of tumour was stage one A (IA).

OUTCOME AND FOLLOW-UP

The patient's postoperative course was uneventful. Since the tumour was low-grade stage, IA adjuvant radiation therapy and chemotherapy was not performed. After 3 months postoperation, the patient condition was fair.

DISCUSSION

Tamoxifen is a partially agonist of oestrogen. It has both oestrogenic and anti-oestrogenic activity depending on the target organs. Since it exhibits anti-oestrogenic effects on breast, it is used in different situations: for risk reduction in persons with high probability of breast cancer, for treatment of ductal carcinoma in situ (DCIS) and for treatment of hormone-receptor-positive breast cancer in adjuvant and metastatic settings. Tamoxifen reveals oestrogenic effects on bone, liver and uterus. It improves bone density and lipid profile; however, it increases the risk of thromboembolic disease. Oestrogen receptors exist in the endometrial epithelium and in the stroma; therefore, tamoxifen can influence both these tissues and induce endometrial proliferation and condensation of periglandular stroma.¹¹ On the contrary, tamoxifen, despite oestrogen, induces genes that produce adrenomedullin, a growth factor for endothelial cells and an angiogenetic factor. Adrenomedullin also upregulates Bcl2 and enhances carcinoma cell survival under hypoxia.¹² In the uterus, it can produce a spectrum of proliferative abnormalities such as endometrial hyperplasia, endometrial polyps, endometrial carcinoma and endometrial sarcoma.⁷ The first evidence of carcinogenesis of tamoxifen comes from the Stockholm trial in which postmenopausal patients with early breast cancer were given 40 mg tamoxifen for 2–5 years and the relative risk of endometrial cancer was 6.4 and this risk decreased to about 3 when daily dose of tamoxifen was decreased to 20 mg.¹³ According to Dr Ismail, endometrial malignancies were confined to women who had taken a cumulative dose of more than 35 g of tamoxifen irrespective of the daily dose of the drug.¹⁴ Our patient had been receiving more than 73 g of the drug. Although most of the endometrial cancers in association with tamoxifen are adenocarcinomas, relative risk for MMMTs may be higher. As shown by Curtis *et al*,³ the relative risk is substantially higher for

MMMTs (O/E=4.62, O=34, 95% CI 3.20 to 6.46) than for endometrial adenocarcinomas (O/E=2.07, O=306, 95% CI 1.85 to 2.32). MMMTs of uterus are composed of a malignant epithelial component and mesenchymal sarcoma. Adenosarcoma is a rare variant of these tumours having a benign epithelial component instead of malignant ones.² There are few case reports of adenosarcoma on the patients who have been using tamoxifen.^{1 2 4-6 8} The sarcomatous component in more than 75% of cases is homologous and composed of non-specific fibroblastic stroma and endometrial stromal sarcoma or undifferentiated sarcoma. Heterologous type of sarcomatous element contains rhabdomyosarcoma, liposarcoma or chondrosarcoma.⁹ Adenosarcomas are usually low grade and their reported mitotic activity, according to different studies, varies from 1⁹ to 15¹⁰ per 10 high-power field. Myometrial invasion is seen in 15% of cases and is mainly restricted to the inner layer.^{9 10} When more than 25% of adenosarcoma is composed of pure sarcoma, it is named: 'adenosarcoma with sarcomatous overgrowth'.^{9 10} Adenosarcoma usually presents as a solitary lesion arising from uterine fundus projecting to the endometrial cavity and may contain necrosis such as what is seen in our patient.⁵ This tumour usually occurs in the endometrium; however, less common sites are myometrium, cervix, ovary and peritoneum.^{1 10} Clement and Scully¹⁵ evaluated 100 patients whose median age was 58 years. In this study, vaginal bleeding was the most common symptom, and protruding mass from the external os was the most common sign, as in our patient. Definitive staging surgery for uterine endometrial adenosarcoma comprises total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph node sampling, omentectomy and peritoneal washing¹⁰ such as what was performed for our patient. The role of adjuvant chemotherapy and radiotherapy is not clear⁹; however, those patients with poor prognostic factors such as deep myometrial invasion or sarcomatous overgrowth may benefit from adjuvant chemotherapy and radiotherapy.¹⁰ It seems that prognosis for patients with adenosarcoma in association with tamoxifen is similar to the other cases of adenosarcoma.

Learning points

- ▶ Adenosarcoma is a rare tumour that maybe seen in patients who have been receiving tamoxifen.
- ▶ Taking a cumulative dose of more than 35 g tamoxifen may increase the risk of endometrial cancer.
- ▶ The role of adjuvant treatment in treating adenosarcoma is not clear.

Competing interests None.

Patient consent Obtained.

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