CASE REPORT

Endometriosis and uterine leiomyomata with ovarian granulosa cell tumour

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We report the first known case of right endometrial cyst and multiple uterine leiomyomata complicated by an ovarian granulosa cell tumour of adult type. A 42 year old woman had an adult type left granulosa cell tumour. Laparoscopy 13 years earlier had revealed a small endometrial implant on the peritoneum, without uterine leiomyomata or bilateral ovarian tumours. Findings in this case suggest that the aetiology of endometriosis and uterine leiomyomata are related to the presence of an oestrogen-secreting neoplasm and that the presence of a state of hyperoestrogenaemia due to granulosa cell tumour over several years might have stimulated the development of endometriosis and leiomyomata.

Key words: endometriosis/granulosa cell tumour/leiomyoma/oestrogen effect/uterine malformation

Introduction

The development of endometriosis and uterine leiomyomata are known to be stimulated by elevated levels of oestrogen. Granulosa cell tumours, the most common type of hormone-secreting ovarian neoplasm, are almost always oestrogenic when endocrine manifestations are present (Roth and Czernobilsky, 1985). The relationship between these gynaecological diseases and congenital uterine malformation has not been confirmed before. We present what is believed to be the first documented case of ovarian endometrioma and leiomyomata of a bicornuate uterus in a patient with an ovarian granulosa cell tumour of the adult type.

Case report

A 42 year old nulligravida Japanese woman was hospitalized for the diagnosis and treatment of abnormal uterine bleeding and left lower abdominal pain on December 9, 1996. She had no history of pregnancy. She had been treated for infertility 13 years earlier (between September 10, 1982 and January 22, 1985) at our university hospital. At that time, her menstrual cycles were regular and not associated with pelvic pain or dysmenorrhoea. The results of hormonal examination in the early follicular phase were normal. No male factor in the infertility was recognized. Her medical history included a congenital urological malformation, left renal agenesis, and hepatic haemangioma. But she did not have any symptoms of precocious puberty. Hysterosalpingography (Figure 1) and laparoscopy (Figure 2) revealed a bicornuate uterus and in the pelvic cavity, small endometrial implants classified as stage I, according to the scoring system of the revised American Fertility Society classification (AFS, 1985). However, the ovaries and the uterine corpora showed no abnormalities. We treated her by intrauterine insemination of husband’s spermatozoa due to bicornuate uterus. After being treated for 2 years and 4 months, she gave up the effort to conceive a child and ceased attending our clinic. In November 1994, she noticed abnormal uterine bleeding after menstruation and irregular menstruation. She consulted us on April 5, 1995, complaining of uterine bleeding and left lower abdominal pain. Multiple uterine leiomyomata and bilateral endometrial cysts were diagnosed by bimanual examination and ultrasound. Although their surgical removal was recommended, the patient initially refused to undergo the procedure. Subsequently, increasing pelvic pain, hypermenorrhoea associated with severe dysmenorrhoea, and abnormal uterine bleeding led her to decide on surgery. She was re-admitted to our hospital on December 9, 1996. A pelvic examination then revealed bilateral enlarged uterine bodies, approximately three times normal size, and fixed bilateral ovarian cysts. A transabdominal ultrasound examination showed suspected multiple leiomyomata, a right endometrioma, and a left abnormal heterogeneous tumour (Figure 3). Magnetic resonance imaging (MRI) demonstrated multiple leiomyomata of the right uterine corpus, a degenerated leiomyoma of the left uterine corpus, and a right endometrioma (Figures 4 and 5). Serum concentrations of CA-125 and 17β-oestradiol on the 38th menstrual day (December 9, 1996) were 25 IU/ml and 1746 pmol/ml (conversion factor to SI unit, 3.699), respectively. Laparotomy on December 24, 1996, revealed two enlarged uterine bodies with multiple leiomyomata and bilateral ovarian cysts, but no evidence of a degenerated leiomyomata of the left uterine corpus, as suggested by MRI. While dissecting the tissue between the left uterine corpus and a left ovarian tumour enlarged to the size of an adult fist (10 cm), the left ovary was ruptured. This tumour contained mainly old blood. A total hysterectomy and bilateral salpingo-oophorectomy were performed. Histopathological examination revealed a left granulosa cell tumour, adult type (Figure 6), a right ovarian endometrioma and multiple leiomyomata of the uterine corpus bilaterally.
Figure 1. Hysterosalpingogram taken 13 years earlier shows bicornuate uterus (50% actual size).

Figure 2. Laparoscopy demonstrates bicornuate uterus with a small endometrial implant (arrows). (A) No uterine leiomyoma and normal ovaries (70% actual size). (B) Enlarged figure of endometrial implant.

Although high cellularity of endometrial gland was detected, there was no typical hyperplastic change, only secretory phase endometrium with blood on the 1st menstrual day. Clinically, she was diagnosed as stage Ic of granulosa cell tumour according to Petterson (1988) and stage III of endometriosis classified according to the revised AFS scoring system (AFS, 1985). After confirmation of no evidence of distant metastasis by computerized tomography (CT) and MRI, combination chemotherapy consisting of cisplatin, vinblastine, and pepleomycin (PVP), a modification of the chemotherapeutic regimen, consisting of cisplatin, vinblastine, and bleomycin (PVB) (Colombo et al., 1986), was started on the 35th postoperative day. Dosage was as follows: cisplatin, 75 mg/m² of body surface area on day 1, i.v.; vinblastine, 0.07 mg/kg of body weight on days 1 and 2, i.v.; and pepleomycin, 5 mg/m² on days 1–5, continuous s.c.; this regimen was given every 28 days for three cycles, together with granulocyte colony-stimulating factor. Complications during chemotherapy included gastrointestinal symptoms and myelosuppression. After confirmation of recovery of her general condition, the patient was discharged on April 24, 1997. She is being followed monthly in our outpatient clinic.

Discussion

Endometriosis and leiomyomata commonly affect women of child-bearing-age. Adult granulosa cell tumours account for ~1–2% of all ovarian tumours, and 95% of all granulosa cell tumours (Young and Scully, 1987) are usually unilateral. Granulosa cell tumours occur more often in post-menopausal than in pre-menopausal women, with a peak incidence at 50–
Figure 5. Magnetic resonance imaging of right endometrioma, which was compatible with typical endometriosis (fat-saturated T1-weighted imaging). Scale bar = 1 cm.

Figure 6. Histological features of granulosa cell tumour (adult type) (stained with haematoxylin and eosin; original magnification ×200). The tumour cells exhibit abundant cytoplasm and bizarre nuclei.

55 years of age. The typical endometrial alteration associated with hormone-secreting tumours in this category is simple hyperplasia (Gusberg and Kardon, 1971). However, our patient was a 42 year old pre-menopausal woman who had no endometrial hyperplasia. In women of child-bearing age, granulosa cell tumours may cause a variety of symptoms related to oestrogen effects such as menometrorrhagia and oligomenorrhoea. Post-menopausal patients frequently complain of uterine bleeding (Jones, 1993). Uterine abnormalities are common in women with granulosa cell tumours, usually manifested as myohypertrophy and leiomyomata (Jones, 1993). Furthermore, a congenital urological malformation (her left renal agenesis) is not a rare anomaly complicated with uterine anomaly (Wiersma et al., 1976).

However, there are few cases of endometriosis with granulosa cell tumours. This scarcity may be related to the discrepancy in time of peak incidence of endometriosis, leiomyoma and granulosa cell tumour, although the aetiology of endometriosis is related to high levels of oestrogen, as is that of uterine leiomyomata. Ferrara et al. (1993) reported a case of non-cicatricial endometriosis of the thoracic skin affected by an ovarian granulosa cell tumour, adult type. They suggested that, in the presence of an oestrogen-secreting neoplasm, foci of endometriosis might turn out to be more common than expected, if only clinicians and pathologists would look for them carefully. In our case, the presence of a small endometrial implant, without uterine leiomyomata and ovarian tumours had been identified 13 years earlier. Furthermore, her precocious puberty and other symptoms had not been recorded. When the symptoms of menometrorrhagia occurred in November 1994, the evidence of high oestrogen activity was first revealed. At this time, a granulosa cell tumour may have begun to grow. The onset of juvenile type of granulosa cell tumour has been detected occasionally at <20 years of age (Young et al., 1984). Our patient was 29 years old when she underwent the first laparoscopy which did not reveal any ovarian tumours. She had noticed abnormal uterine bleeding at age 40. Histological findings of this tumour were compatible with adult type. Therefore, we suggested that her adult type granulosa cell tumour had grown as endometriosis, increasing under hyperoestrogenemia during the 13 years following the first laparoscopy. Although endometriosis, leiomyomata, and granulosa cell tumours have independent aetiologies, high oestrogen concentrations caused by granulosa cell tumours may play a central role in the pathogenesis of uterine leiomyomata and endometriosis. Although a few cases of endometriosis and granulosa cell tumours are alluded to (Ferrara et al., 1993), it would be interesting to examine in more detail the stage of endometriosis, the amount of oestrogen secreted and the duration of the presumed association.

Varma et al. (1990) suggest that when a granulosa cell tumour exhibits typical appearance on gross examination, preoperative diagnosis by MRI may be possible, with appropriate clinical findings. However, in the present case, the radiologists had diagnosed the granulosa cell tumour preoperatively as a degenerated leiomyoma of the left uterine corpus. We recognize once more that it is difficult to diagnose a granulosa cell tumour associated with multiple gynaecological tumours.

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References


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