CASE REPORT

Endometrioma of uterine serosa in a woman with mosaic Turner’s syndrome receiving hormone replacement therapy

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Endometriosis in Turner’s syndrome patients has only been reported in five isolated cases. We present here an endometrioma on the uterine serosa and pelvic endometriosis arising in a mosaic Turner’s patient receiving hormone replacement therapy (HRT). The 24 year old patient with mosaic Turner’s syndrome [45,X; 46,X pseudo dicentric Y (q11.23)], on cyclic HRT after laparoscopic gonadectomy 5 years previously, was found to have an adnexal mass on routine examination. Given her history, due to the fear of a malignant process arising from a potential gonadal remnant, she underwent a laparoscopy and was found to have a 5 cm serosal endometrioma arising on a stalk from the uterine fundal surface as well as pelvic endometriosis. De-novo endometrioma and endometriosis occurred in a mosaic Turner’s patient after gonadectomy on cyclic HRT. The presentation was also unusual with a pedunculated endometrioma arising from the uterine serosa. Due to the fact that the patient did have cyclic menstrual flow, her endometriosis may have arisen from retrograde menstruation or coelomic metaplasia induced by exogenous hormones.

Key words: adnexal mass/endometrioma/endometriosis/hormone replacement therapy/Turner’s syndrome

Introduction

Endometriosis is a common disease in menstruating women (Olive and Schwartz, 1993; Berger, 1994) but has been also reported in postmenopausal or surgically castrated women on hormone replacement therapy (HRT) (Kempers et al., 1960; Djursing et al., 1981). Endometriosis has even been described in men receiving high doses of hormone therapy for bladder or prostate cancer (Oliker and Harris, 1971; Pinkert et al., 1979). The common denominator of all such cases is exposure to female hormones, although endometriosis has rarely been described in prepubertal girls (Lauf, 2000).

Endometriosis in patients with Turner’s syndrome has rarely been reported in the literature. There are only five case reports describing endometriosis in patients with gonadal dysgenesis (Doty et al., 1980; Peress et al., 1982; Binns and Banerjee, 1983; Bosze et al., 1987; Meinen et al., 1989). Currently, the medical management of patients with Turner’s syndrome includes the prepubertal use of growth hormone, which has been shown to result in a significant increase in adult height (Rosenfeld, 1998; Saenger, 1996). HRT is then started around the age of 15 years to attain maximum secondary sexual characteristics and to prevent later osteoporosis as the result of a hypoestrogenic state (Rosenfield et al., 1998). This paper presents a case report of an endometrioma in an atypical site occurring subsequent to the initiation of HRT in a patient with mosaic Turner’s syndrome.

Case report

The medical records, including clinic notes, operative reports, ultrasound images and video taken during laparoscopy, pathology of surgical specimen, and peripheral leukocyte karyotype were reviewed. Literature search was performed using PubMed (National Library of Medicine) with the key words ‘Turner’s syndrome’, ‘gonadal dysgenesis’, ‘hypoestrogenism’, ‘hormone replacement therapy’ and ‘endometriosis’.

The patient presented initially to us at the age of 19 years with the chief complaint of primary amenorrhoea. She appeared to be a phenotypic female. Childhood history was unremarkable except for short stature. She reported breast bud development at age 11 and sparse pubic hair growth subsequently. At age 15 years, she consulted a gynaecologist, but could not tolerate a pelvic exam and did not seek further evaluation. At that time she was told that her blood pressure was elevated.
The remainder of her history including family history was unremarkable.

On physical examination, she appeared anxious. She was 154 cm tall and weighed 52 kg. Her initial blood pressure was 130/100 mmHg but was repeatedly normal at 120/80 mmHg on subsequent exams. Her breasts were small and undeveloped and were assessed to be at Tanner stage 2. There was minimal pubic hair. On pelvic exam, the length of the vagina was found to be normal at 8 cm and a hypoplastic uterus was palpated. The uterus measured 3 cm in length, using a transvaginal ultrasound. Adnexa were free of masses and no distinct ovaries could be visualized by ultrasound. There was no webbing of the neck, increased carrying angles, nor a shield chest. The measurement of peripheral gonadotrophins revealed the FSH level to be >100 mIU/ml and LH level to be 70 mIU/ml. The karyotype of 16 out of 20 peripheral leukocytes analysed was 45,X, and the karyotype of the remaining four leukocytes was 46,X pseudodicentric Y(q11.23). Due to the presence of a Y chromosome component, which put her at an increased risk for developing a gonadoblastoma or dysgerminoma, the patient underwent laparoscopic bilateral gonadectomy. Both streak gonads were removed and histological analysis revealed that these gonads had atrophic ovarian cortex, medulla and hilum. The uterus was hypoplastic but normal in gross appearance (Figure 1a).

Post-operatively, she began sequential HRT with Premarin 1.25 mg per day for 25 days of each month with the addition of Provera 10 mg per day during the last 10 days (Saenger, 1996). She reported regular cyclic menses on her annual follow-ups. There was breast development to Tanner stage 3. However, which may explain the most commonly seen cases of endometriosis in reproductive age women. However, cases of endometriosis arising in men receiving high doses of estrogen treatment (Oliker and Harris, 1971; Pinkert et al., 1979) or de-novo endometriosis in women with rudimentary non-cavitated uterus (Rosenfeld and Lecher, 1981) cannot be adequately explained by Sampson’s theory of retrograde menstruation. Such conditions support the alternative theory of coelomic metaplasia which hypothesizes that the tissue derived from the fetal coelomic cell transforms into endometrial cells under certain conditions, such as exposure to female sex hormones (Batt and Smith, 1989). The third theory, known as the induction theory, combines the first two theories and suggests that substances released from exfoliated endometrium induce the formation of endometriotic tissue in undifferentiated mesenchymal cells (Olive and Schwartz, 1993).

In the literature, there are only five case reports of endometriosis in patients with gonadal dysgenesis (Table I) (Doty et al., 1980; Peress et al., 1982; Binns and Banerjee, 1983; Bosze et al., 1987; Meinen et al., 1989). Additionally, there is one report of endometriosis occurring in a woman with primary hypogonadism (Cavins, 1968). It is of particular interest that all cases reported in the literature received exogenous cyclical HRT and all but one had menstrual flow. The dosages of estrogen and progesterone used were in the range for post-menopausal HRT in four patients, with oral contraceptive pills used in the fifth. Since these young women were given HRT in amounts that typically induce menstrual flow, endometriosis could have developed from retrograde menstruation. Alternatively, coelomic metaplasia could be the

Discussion

The aetiology of endometriosis remains poorly understood. The most commonly accepted theory (Sampson, 1927) proposes transplantation of endometrial tissue via retrograde menstrual flow, which may explain the most commonly seen cases of endometriosis in reproductive age women. However, cases of endometriosis arising in men receiving high doses of estrogen treatment (Oliker and Harris, 1971; Pinkert et al., 1979) or de-novo endometriosis in women with rudimentary non-cavitated uterus (Rosenfeld and Lecher, 1981) cannot be adequately explained by Sampson’s theory of retrograde menstruation. Such conditions support the alternative theory of coelomic metaplasia which hypothesizes that the tissue derived from the fetal coelomic cell transforms into endometrial cells under certain conditions, such as exposure to female sex hormones (Batt and Smith, 1989). The third theory, known as the induction theory, combines the first two theories and suggests that substances released from exfoliated endometrium induce the formation of endometriotic tissue in undifferentiated mesenchymal cells (Olive and Schwartz, 1993).

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Figure 1. Laparoscopic view of (a) the uterus during the initial surgery, and (b) an endometrioma arising from the fundal uterine serosa at the second surgery, 5 years later.
Table I. Previous reports of endometriosis in Turner’s syndrome patients

<table>
<thead>
<tr>
<th>Author</th>
<th>Age (years)</th>
<th>Karyotype</th>
<th>HRT</th>
<th>Presentation</th>
<th>Findings and outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meinen et al. (1989)</td>
<td>20</td>
<td>45,X</td>
<td>OCP ×5 years</td>
<td>Cyclic menses, severe dyspareunia, progressive weight loss, diarrhea,</td>
<td>5 litres of ascites, diffuse endometriosis on all serosa, small fixed uterus,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>obstipation, abdominal distension</td>
<td>gonads, obliterated cul-de-sac, rectovaginal endometriosis, rectal stenosis at 10 cm from the anus</td>
</tr>
<tr>
<td>Bosze et al. (1987)</td>
<td>26</td>
<td>44.X; t(13:14)</td>
<td>Cyclic HRT ×10 years</td>
<td>Cyclic menses, progressive pelvic pain, dyspareunia</td>
<td>Status-postgonadectomy: fixed uterus with infantile tubes, endometriotic mass on the left cornu, no other pelvic endometriosis. Pathology: endometrial glands and stroma</td>
</tr>
<tr>
<td>Binns and Banerjee</td>
<td>28</td>
<td>45,X/46,XXq</td>
<td>Cyclic HRT, Mestranol 0.05 mg and norethisterone 1 mg qd×9 years</td>
<td>Cyclic menses, painless 2 cm mass and norethisterone 1 mg qd×9 years</td>
<td>Returns with enlargement of mass</td>
</tr>
<tr>
<td>(1983)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Streak gonads, small uterus, tubes, no endometriotic lesions identified, mobile recto-vaginal mass, felt to be Wolffian duct remnant not removed. Transvaginal biopsy(endo)metriosis, submucosal and intramural rectal endometriosis</td>
</tr>
<tr>
<td>Peress et al. (1982)</td>
<td>37</td>
<td>45,X</td>
<td>Cyclic HRT, Premarin 0.625 mg (days 1–25) and Provera 10 mg (days 16–25) for 23 years</td>
<td>Irregular menses, pelvic pain</td>
<td>Streak gonads, hypoplastic uterus, tube, endometriosis of uterosacral ligaments, atrophic endometrial glands and stroma (intrauterine)</td>
</tr>
<tr>
<td>Doty et al. (1980)</td>
<td>17</td>
<td>46.XY with gonadal dysgenesis</td>
<td>Cyclic ERT, conjugated estrogen and Provera for 2 years</td>
<td>Primary amenorrhoea</td>
<td>Enlarged clitoris (5–6 cm) normal vagina, small cervix hypoplastic uterus and tubes streak gonads (dysegenetic testes), endometriosis of mesosalpinx</td>
</tr>
</tbody>
</table>

OCP = oral contraceptive pills; HRT = hormone replacement therapy; ERT = estrogen replacement therapy.
mechanism of pathogenesis of endometriosis in these Turner’s patients. One of the cases with pelvic endometriosis had persistent amenorrhoea (Doty et al., 1980) and another had an endometrial biopsy on HRT, which revealed atrophic endometrial glands and stroma (Peress et al., 1982). Thus, at least in these two patients, retrograde menstruation is unlikely to be the cause of endometriosis.

The true incidence of endometriosis in Turner’s syndrome patients on HRT is not known but may be more common than previously supposed. Indeed, our patient and two out of the five women in the case reports were asymptomatic at the time of surgical intervention. The particular location of this endometrioma, arising from the uterine serosa, like a pedunculated fibroid, is highly unusual. This atypical location would in itself be quite interesting to observe in any patient with endometriosis and not just in the setting of Turner’s syndrome.

The multiple benefits of HRT in young women with hypogonadism and the relatively low incidence of endometriosis in Turner’s syndrome patients warrant initiation and continuation of HRT in these patients (Saenger, 1996). Unopposed estrogen use has been implicated in the development of an endometrioma in a post-menopausal woman (Bellina and Schenck, 2000) and has been associated with the occurrence of adenocarcinoma arising in endometriosis (Heaps et al., 1990). Endometrial growth in various tissues has been purported to occur when an estrogen threshold has been surpassed by a combination of endogenous and exogenous estrogen source (Barbieri, 1992). The addition of progestins to HRT is endorsed in all women with intact uterus to prevent the development of endometrial hyperplasia and adenocarcinoma (Manson and Martin, 2001), and has been suggested to reduce the incidence of pain recurrence and malignant transformation of residual endometriosis following hysterectomy and gonadectomy (Corson, 1992). However, the literature lacks studies comparing continuous combined HRT with cyclical HRT with regards to the development of endometriosis. Still, it seems prudent to use a continuous combined regimen in a patient with a history of endometriosis and an intact uterus, in order to minimize cyclic menstruation and potential retrograde endometrial flow. Accordingly, we have recently changed our patient’s HRT regimen from a cyclical to a continuous combined therapy with oral conjugated equine estrogen 0.625 mg and medroxyprogesterone 5 mg daily.

The incidence of endometriosis in Turner’s syndrome patients on HRT appears to be very low. However, our case report, together with a handful of prior reports, should remind physicians to be aware and screen for this possibility during follow-up visits and physical examinations.

References

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