
CASE REPORT

Endometrial carcinoma in a young patient with polycystic ovarian syndrome: first suspected at time of embryo transfer

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Adenocarcinoma of the endometrium is a rare condition in women under 40 years of age. However, patients with anovulatory polycystic ovarian syndrome are at risk of developing endometrial carcinoma due to the unopposed and prolonged effect of oestrogen on the endometrium. This case report discusses the dilemma of various treatment options for early disease in such patients.

Key words: endometrial adenocarcinoma/polycystic ovarian syndrome/infertility/IVF

Introduction

Endometrial carcinoma is the most common malignancy of the lower female genital tract. In 1994, the estimated incidence of endometrial cancer was 8% of all female cancers (Boring et al., 1994). However, only 5% of all patients who develop endometrial adenocarcinoma are under 40 years of age (Ostor et al., 1982). Anovulatory polycystic ovarian syndrome (PCOS) is associated with endometrial carcinoma due to the prolonged and unopposed effect of oestrogen on the endometrium (Wood and Boronow, 1976; Silverberg et al., 1977; Greenblatt et al., 1982; Tsoutsopilides, 1983). This was recently highlighted by Meirion and Schenker (1996), who analysed all case reports and epidemiological studies examining the link between infertility and endometrial cancer. They showed anovulation to be the main cause of the increased risk of endometrial carcinoma in infertile patients. PCOS is a common disorder which is thought to be present in up to 22% of all young women (Insler and Lunenfield, 1991; Balen et al., 1995). In addition, ovulatory dysfunction causes subfertility in 15–20% of couples (Hull et al., 1985). Furthermore, approximately 50% of all subfertile female patients diagnosed as having ‘unexplained’ infertility are subsequently found to have ovulatory dysfunction similar to that of PCOS. In this case report we emphasise the importance of having a high level of suspicion that endometrial disease may be present in such patients and discuss the various treatment options and their drawbacks.

Case report

A 32 year old woman with a five year history of primary subfertility was referred to the Assisted Conception Unit for investigation and treatment. Her menarche had been at the age of 14 years and her menstrual cycle was infrequent and irregular. Neither she nor any other member of her family had diabetes or hypertension. On examination she was hirsute and overweight, with a body mass index of 37 (normal range 19–25). Abdomino-pelvic examination was normal and her recent cervical smear test had been negative. Blood tests for thyroid function, random glucose and prolactin concentrations were normal. The plasma luteinizing hormone and free testosterone values were elevated and luteal phase progesterone was consistently anovulatory (Table I). A transvaginal ultrasound scan showed a normal looking endometrium but the ovaries had the characteristic ‘pearl necklace’ appearance, with peripherally-located follicles and dense echogenic stroma. The diagnosis of polycystic ovarian syndrome was thus confirmed. Laparoscopy and dye demonstrated a normal pelvis with patent tubes and her partner’s semen analysis was normal.

Administration of clomiphene citrate was unsuccessful in establishing ovulation. Gonadotrophin-induced ovulation was also unsuccessful in achieving a conception after three attempts. In-vitro fertilization (IVF) and embryo transfer were finally attempted. At baseline scan, performed early in the follicular phase of the cycle, the endometrium was noted to be 13 mm in thickness with otherwise normal morphology. Hence, down-regulation with buserelin was commenced. After 4 weeks of buserelin administration the patient menstruated which suggested a fall in endogenous oestradiol concentration and down-regulation of the pituitary. The endometrium, although still 8 mm in thickness, had diminished by this stage. Controlled ovarian hyperstimulation with 300 IU of urinary follicle-stimulating hormone daily was commenced. An adequate ovarian response was obtained and human chorionic gonadotrophin (5000 IU) was administered on day 11 of the stimulation phase. On the day of egg collection, 19 oocytes were collected, of which 14 were fertilized normally and 13 of these cleaved. Embryo transfer was planned 48 h post egg collection.

At the time of embryo transfer, a small but steady trickle of blood was noted as soon as the embryo transfer catheter was introduced into the uterine cavity. There had been no trauma in the insertion of the catheter which could have explained this loss. Hence this unprovoked bleeding was thought to be suspicious and merited further investigations. The embryo transfer was abandoned and all the embryos were frozen.

Cervical cytology and colposcopy were negative. Therefore, examination under anaesthesia, hysteroscopy and dilatation
and curettage (D&C) were performed. At hysteroscopy, three abnormal polypoid structures were identified and these were sampled. The histology was consistent with severe atypical endometrial hyperplasia and ‘intra-endometrial adenocarcinoma’, with no evidence of myometrial involvement (Figure 1). A pelvic ultrasound with Doppler studies and magnetic resonance imaging (MRI) did not demonstrate any extension of the tumour beyond the endometrium.

After counselling, the patient declined hysterectomy as she wished to retain her ability to conceive. Thus, oral medexyprogesterone acetate (Provera) 30 mg twice daily was prescribed for 3 months following which a repeat hysteroscopy and D&C was arranged. This revealed an atrophic endometrium from which no curettings were obtained. A repeat pelvic ultrasound as well as MRI were also reported to be normal. Progestagen therapy was continued for a further 6 months and a repeat hysteroscopy and D&C was advised. Unfortunately, at this second check, the endometrial histology was consistent with a well-differentiated adenocarcinoma with no myometrial invasion. Since the neoplastic lesion had failed to respond to conservative medical treatment, a total abdominal hysterectomy, bilateral salpingo-oophorectomy and pelvic node sam-

Table I. Biochemical data prior to infertility treatment

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Normal range</th>
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<tbody>
<tr>
<td>FSH</td>
<td>2.3 IU/l</td>
<td>2.0–6.0 IU/l</td>
</tr>
<tr>
<td>LH</td>
<td>12.4 IU/l</td>
<td>3.0–12.0 IU/l</td>
</tr>
<tr>
<td>Day 21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progesterone</td>
<td>&lt;2 nmol/l</td>
<td>30–90 nmol/l</td>
</tr>
<tr>
<td>Testosterone</td>
<td>2.7 nmol/l</td>
<td>0.3–2.5 nmol/l</td>
</tr>
<tr>
<td>Prolactin</td>
<td>184 mU/l</td>
<td>&lt;500 mU/l</td>
</tr>
</tbody>
</table>
The disease was confined to the endometrium as suggested (Lindahl, B. and Willen, R. (1985) Endometrial hyperplasia. Clinical, made, the dilemma arises of whether to recommend medical carcinoma permitting subsequent triplet pregnancy. 


Thereby removing endometrial tissue which might otherwise Farhi, D.C., Nosanchuk, J. and Silverberg, S.G. (1986) Endometrial adenocarcinoma, thereby removing endometrial tissue which might otherwise become hyperplastic. Furthermore, progesterone can reverse various degrees of hyperplasia to normal endometrial histology (Gambrell, 1984). 

Increased body mass index has also been found to be strongly related to the risk of endometrial cancer (Elwood et al., 1977; Kelsey et al., 1982; Henderson et al., 1983; Ron et al., 1987; Brinton et al., 1989; Escobedo et al., 1991; Brinton et al., 1992). It is well recognised that adipose tissue is the primary site for conversion of adrenal androstenedione to oestrone. Obesity has also been related to lower levels of sex hormone-binding globulin, leading to greater bioavailability of oestrogen. In women with PCOS, obesity and anovulation may contribute to the increased risk of endometrial carcinoma. 

Once the diagnosis of early endometrial carcinoma has been made, the dilemma arises of whether to recommend medical management (which retains fertility but might jeopardize prognosis) or definitive surgery. Diagnostic imaging using both transvaginal ultrasound and MRI were used to confirm that the disease was confined to the endometrium as suggested histologically. The preservation of fertility was of prime importance to this patient and conservative approach was therefore attempted in the first instance. 

Medical treatment with progestagens for extremely early disease has been reported in atypical endometrial hyperplasia (Lindahl and Willen, 1985) and in stage I endometrial carcinoma (Farhi et al., 1986). Patients with endometrial hyperplasia with atypia have been successfully treated with progestagens with a success rate of 70–100% after a 2-year follow-up (Kjosvat et al., 1978; Ferencyz and Gelfand, 1989). In a retrospective study of young patients with stage I endometrial cancer, 60% were successfully treated with progesterone therapy alone, allowing interval pregnancies (Farhi et al., 1986). Furthermore, Kimming et al. in 1995 reported a successful IVF treatment following medical treatment of a patient with stage I endometrial cancer. 

This case, however, illustrates that conservative treatment with progestogens may not always succeed in achieving a remission and prolonging the patient’s reproductive life. Close histological surveillance must therefore be maintained to detect treatment failure. 

**References**


**Endometrial carcinoma and polycystic ovarian syndrome**

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