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A Series of Ovarian Clear Cell and Endometrioid Carcinoma and their Association with Endometriosis

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ABSTRACT

Aim: To present our department's experience with clear cell carcinoma and endometrioid carcinoma of the ovary, paying particular attention to their relationship with endometriosis and concomitant endometrial pathology.

Method: Retrospective review of case records.

Results: From July 1986 to March 1995, 11 patients with clear cell carcinoma and 20 patients with endometrioid carcinoma of the ovary were treated. Of the patients with clear cell carcinoma, five (45%) had associated endometriosis. One patient (9%) also had endometrial adenomatous hyperplasia. Of the 20 cases of ovarian endometrioid carcinoma, four (20%) had endometriosis present during histopathological examination. Six patients (30%) had concomitant endometrial pathology (five cases of endometrial carcinoma and one with adenomatous hyperplasia).

Conclusion: Our series shows that the clear cell ovarian carcinoma may often be associated with endometriosis, more so than the endometrioid type of ovarian carcinoma. However, the patient with ovarian endometrioid carcinoma may also harbour a concurrent endometrial pathology.

Keywords: clear cell, endometrioid, carcinoma of ovary, endometriosis

INTRODUCTION

Endometriosis is a common gynaecological condition that has been reported to be present in up to 25% of women presenting with gynaecological symptoms in the United Kingdom and the United States[1]. The condition is classically associated with dysmenorrhoea, deep dyspareunia and infertility. Although itself a benign condition, endometriosis has been reported in association with certain epithelial ovarian tumours. Sampson[2] in 1925, was the first to report cases of endometrioid carcinoma of the ovary arising from endometriosis in the same organ. Scully and Barlow[3] in 1967 also established the close association between clear cell carcinoma, endometrioid carcinoma of the ovary and endometriosis. Since then, several authors have also reported on the incidence of endometriosis in patients with clear cell carcinoma and endometrioid carcinoma of the ovary[3-6]. Our study aimed to present our experience with clear cell carcinoma and endometrioid carcinoma of the ovary, paying particular attention to their relationship with endometriosis and concomitant endometrial pathology.

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MATERIAL AND METHODS

Between July 1986 and March 1995, 96 patients with primary epithelial ovarian tumours (excluding borderline tumours) were seen at the Department of Obstetrics and Gynaecology, National University Hospital, Singapore. Of these, there were 11 patients (11.4%) with clear cell carcinoma and 20 patients (20.8%) with endometrioid carcinoma of the ovary. Clinical records of these patients were reviewed and data concerning age, parity, tumour size, bilaterality, and initial International Federation of Gynaecology and Obstetrics (FIGO) 1988 stage were abstracted. All patients had a staging laparotomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy, and infracolic omentectomy. The histopathological reports were reviewed and the presence of endometriosis and concomitant endometrial hyperplasia and endometrial carcinoma were noted.

RESULTS

The mean age of presentation of the eleven patients with clear cell carcinoma of the ovary was 47.8 ± 8 years (range 31 to 61 years). Six patients (55%) were nulliparous while the remaining patients had parities ranging from 2 to 6. The mean diameter of the ovarian clear cell carcinomas was 10.9 ± 3 cm (range 4 to 15). The tumour was found to involve both ovaries in one (9%) patient. Nine patients (82%) presented with stage 1 tumours, one with stage 2 and another with stage 3 disease. Five (45%) patients had endometriosis associated with clear cell carcinomas. Of these, three had endometriotic deposits in the opposite uninvolved ovary, while 2 patients had endometriosis present in both ovaries. Only one patient (9%) had concomitant adenomatous hyperplasia in the uterus. There were no patients with concomitant endometrial carcinoma.

There were 20 patients with endometrioid carcinoma of the ovary. The mean age at presentation was 48.2 ± 9 years (range 28 to 67). Seven patients (35%) were nulliparous. The mean diameter of the ovarian endometrioid tumours was 12.3 ± 6 cm (range 3 to 25). Bilateral ovarian tumours were present in

10 patients (50%). There were five patients (25%) with stage 1 tumours, four patients (20%) with stage 2, eight patients (40%) with stage 3 and three patients (15%) with stage 4 disease. Endometriosis was also present during histopathological examination in 4 patients (20%). Of these, 3 had endometriosis present in the same ovary as the endometrioid tumour, while in one patient the endometriosis was present in the opposite uninvolved ovary. Six patients (30%) had concomitant endometrial pathology (5 cases of endometrial carcinoma and 1 case of adenomatous hyperplasia. Of the endometrial carcinomas, there were 3 well differentiated, one moderately differentiated and one poorly differentiated tumour. Four patients had endometrial tumours with minimal myometrial invasion (less than ⅓ thickness) while one patient had an endometrial tumour with full thickness myometrial involvement.

DISCUSSION

Clear cell carcinomas account for approximately 5% to 11% of all ovarian epithelial neoplasias[4]. In our series, 11.4% of primary ovarian epithelial tumours treated at our institution during the study period were clear cell carcinomas. The average age at the time of diagnosis range from 48 to 58 years[4] and is similar to the mean age of diagnosis (48 years) in our series. The prevalence of nulliparity in clear cell carcinoma appears to be higher than that seen in other primary ovarian epithelial tumours. Nulliparity of more than 50% has been reported by several authors[7,8]. This is comparable to the prevalence of nulliparity (55%) in our series. The reported incidence of bilaterality is less than 5% in stage 1 tumours[4]. This is less than the 11% of stage 1 tumours with bilateral ovarian involvement seen in our series. Several authors[5,9] have also noted that 50% - 60% of ovarian clear cell and endometrioid carcinomas present as stage 1 disease as opposed to 14% to 20% of serous epithelial tumours. In our series, 82% of clear cell carcinomas were stage 1 lesions at the time of diagnosis. At present, the majority of clear cell carcinomas of the ovary are believed to be derived from surface epithelial cells, and only in a few cases do the tumours actually arise from pre-existing endometriosis[4]. Endometriosis possesses some of the characteristics of cancer, such as the ability to invade into underlying stroma and the association with metastatic and sometimes, distant lesions. However, clear cell ovarian carcinomas are more often associated with pelvic and ovarian endometriosis than any type of ovarian tumour, including endometrioid carcinoma[3,5]. The presence of endometriosis in the same ovary has been reported in up to 24% of clear cell carcinomas[5] and pelvic endometriosis demonstrated in up to 50% of cases[4]. In our series, 5 patients (45%) with clear cell carcinoma had concomitant ovarian endometriosis identified on histopathological examination. In three patients, endometriosis was present in both ovaries while in 2 cases, endometriotic deposits were present only in the opposite, uninvolved ovary. It was Sampson[2] who first put forward, criteria to establish that a malignant tumour had developed from endometriosis: (1) That clear evidence of endometriosis should be present in close proximity to the tumour; (2) The histopathologic appearance should be such that the origin of the tumour from endometriosis is likely; and (3) no other primary sites are present. However, only a few authors have been able to document a direct continuous transition from the benign epithelium of endometriotic glands through atypia to carcinoma. Kurman and Craig[10] were able to document transition from endometriosis to carcinoma in only one patient with clear cell carcinoma. LaGrenade and Silverberg[11] were able to show the transition of benign to atypical endometriosis to malignancy in 3 cases of clear cell carcinoma and in one patient with endometrioid ovarian carcinoma. Unfortunately, in our series, we were unable to document such a transition from the ovarian endometriosis to clear cell or endometrioid carcinoma. This is probably understandable, for as tumour invasion and overgrowth occur, any evidence of such a transition may thus be destroyed.

Endometrioid carcinoma of the ovary was first recognised as an entity by Sampson in 1925[2], who also reported that in some cases, these neoplasms do arise in endometriotic deposits in the ovary. It has been reported that endometrioid carcinomas make up 16% to 30% of all ovarian carcinomas[4], compared to 20.8% of all ovarian epithelial tumours in our series. The incidence of nulliparity in patients with endometrioid carcinoma of the ovary has been reported to be about 37%[8] which is comparable to 35% seen in our series. The proportion of endometrioid carcinomas of the ovary presenting as stage 1 lesions has been reported to range from 50% to 60%[7,9]. In our series, only 25% of our patients presented with stage 1 lesions and more than 50% of cases already had stage 3 or 4 disease at the time of diagnosis. It has been estimated that up tso one-third of all endometrioid carcinomas involved both ovaries[4], which is lower than the 50% bilateral involvement of ovaries seen in our series. This could be due to the higher proportion of more advanced tumours seen in our series. Ovarian endometriosis has been reported to be present in 9% to 17% of cases with endometrioid carcinoma while pelvic endometriosis has been reported in up to 28% of patients[4]. In our series, four patients (20%) had concomitant ovarian endometriosis and endometrioid carcinoma. In three patients, the ovarian endometriosis was present in the same involved ovary while the remaining case had endometriotic deposits present only in the opposite uninvolved ovary. No pelvic endometriosis was detected in association with endometrioid carcinoma in our series. The occurrence of an endometrioid tumour developing from an endometriotic cyst has been demonstrated in only 5% to 10% of cases[6]. We were unable to document any case of an endometrioid carcinoma developing in an endometriotic cyst in our series. As in the case of endometriosis and clear cell carcinoma of the ovary, it is also difficult to prove that an endometrioid carcinoma has developed directly from endometriosis.

However, some authors[11] have been able to document a direct continuous transition from benign to atypical endometriosis through to endometrioid carcinoma. Thus, atypical hyperplastic changes in ovarian endometriosis may be precursors in some cases of endometrioid carcinoma[11,12]. Unfortunately in our series, there were no reports of atypical endometriosis and there were no transitional changes documented on histology. Interestingly, some investigators[5] have also reported that the concomitant occurrence of endometriosis did not seem to influence the prognosis for these patients.

Another interesting facet of ovarian endometrioid carcinoma is that it is frequently associated with endometrial hyperplasia and endometrial carcinoma. Up to 26% of patients with ovarian endometrioid carcinomas have concomitant endometrial carcinomas and an additional 12% may be associated with uterine endometrial hyperplasia[4]. By comparison, only 4% of ovarian carcinomas of all histological cell types are associated with endometrial carcinoma[13]. In our series, there were no concomitant endometrial carcinomas in the patients with clear cell carcinomas. In contrast, we had 5 cases (25%) of endometrial carcinoma and one case (5%) of endometrial adenomatous hyperplasia in association with ovarian endometrioid carcinoma. Although it remains difficult to establish whether these ovarian and endometrial tumours are independent primaries or metastatic from each other, the current view is that these tumours arise as two separate primary malignancies[14] and may be the result of a stimulus affecting both organs[8]. Several authors[8,15] have found that the 5-year survival of patients with endometrioid ovarian carcinoma, with or without concurrent endometrial tumours, was similar for all stages. If the endometrial lesions were truly metastatic and did not arise independently, then survival would be expected to be poorer for patients whose ovarian tumours would otherwise have been grouped as stage 1. This argument has been used to support the theory that the ovarian and endometrial tumours are probably synchronous, independent primaries. This view is further supported by the focal and minimally invasive nature of many of the concurrent endometrial tumours[8]. Czernobilsky et al[8] reported that patients with an endometrial carcinoma, in addition to an endometrioid ovarian tumour, had a mean age of 47.9 years. Although there was a statistically significant age difference between this subset of patients and that of all the patients with ovarian endometrioid carcinoma in that series, an explanation for this finding was not given. In our series, there was little difference between the mean ages of patients with ovarian endometrioid carcinomas (48.2 years) and those with concomitant endometrial carcinomas (48.0 years).

CONCLUSION

Although endometriosis is a benign condition, it may be associated with the development of ovarian clear cell and endometrioid carcinoma. Our series shows that clear cell ovarian carcinoma may often be associated with ovarian endometriosis, more so than the endometrioid type of ovarian carcinoma. However, the patient with ovarian endometrioid carcinoma may also harbour a concurrent hyperplastic endometrial lesion or even an endometrial carcinoma. The literature presently suggests that endometrial and ovarian tumours probably arise as separate, independent primary malignancies and do not worsen the overall prognosis.

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