Case Reports

Ovarian clear cell carcinoma associated with endometriosis: a case report with immunohistochemical study

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Summary

Endometriosis is a frequent benign gynecological disease; nonetheless, it can demonstrate some aspects that resemble malignant disease. Malignant transformation of endometriosis occurs mainly in the ovary. A rare case of transition between typical endometriosis and clear cell carcinoma with immunohistochemical study is presented. The patient, a 30-year-old Caucasian woman (para 0), was diagnosed with endometriosis ten years before. Six months later she developed a left cystic ovarian tumor (58 cm^3) that persisted after two ultrasounds in a four-month period. Tumor markers were normal (CA125, CA 15.3, CA 19.9, alpha-fetoprotein, carcinoembrionary antigen Al). There was no ascites. The left ovarian mass was removed by laparotomy and endometriosis in continuity with carcinoma positive for cytokeratin 7 and estrogen receptor was revealed. CD10 was positive in the stromal cells of the endometriosis. Clear cell carcinoma grade 3 was diagnosed. In conclusion, although a rare event, the association of typical endometriosis and clear cell carcinoma of the ovary should be kept in mind, mainly in patients with a persistent ovarian cyst.

Key words: Ovary; Clear cell carcinoma; Endometriosis; Immunohistochemical study.

Introduction

Endometriosis is a frequent benign gynecological disease, nonetheless, it can demonstrate some aspects that resemble a malignancy disorder. Based on clinical, epidemiological and molecular biological studies, endometriosis has been associated with an increased risk of various cancers as ovarian, breast and non-Hodgkin's lymphoma [1, 2].

Extragonadal sites of malignant tumors in the pelvis, are the rectovaginal septum and colon/rectum in the form of endometrioid carcinoma [1, 3, 4]. Other unusual sites that have been described are carcinosarcoma arising from atypical endometriosis in a ceserean section scar [5] and an endometrioid adenocarcinoma arising from ureteral endometriosis in a patient with no history of gonadal endometriosis [6].

Malignant transformation of endometriosis occurs mainly in the ovary. The most common histopathological finding is an association of ovarian endometriosis and endometrioid carcinoma. Extragonadal sarcoma [1] and ovarian clear cell carcinoma [7] are the second most frequent associations. The figure transition between ovarian endometriosis and carcinoma is rarely shown in the literature. To our knowledge, the uncommon cases demonstrated in the English literature are a progressive transition between endometriosis and endometrioid adenocarcinoma [1, 7], an abrupt transition between endometriosis and endometrioid adenocarcinoma, and endometrioid adenocarcinoma with a clear cell carcinoma component [7]. Nonetheless, rare cases of an association between the transition from endometriosis to clear cell carcinoma have been reported [8]. We present a rare case of transition from typical endometriosis to clear cell carcinoma with immunohistochemical study.

Case Report

The case of 30-year-old caucasian woman, para 0, with endometriosis diagnosed ten years before is presented. She was taking oral contraceptives and was admitted to an other department with the complaint of a cyst in the left ovary. Six months later she developed a left cystic ovarian tumor (58 cm^3) that persisted after two ultrasonounds in a four-month period. The tumor was painless and had a cystic consistency. Tumor markers were normal (CA125, CA15-3, CA19-9, alpha-fetoprotein, carcinoembryonic antigen Al). There was no ascites. The patient underwent exploratory laparotomy, revealing multiple adherences in the pelvic organs due to endometriosis. After removing the adherences, a left ovarian cystic tumor was diagnosed. The uterus, tubes and right ovary were normal. The ovarian mass showed endometriosis in continuity with large cells with voluminous amounts of clear cytoplasm (Figure 1A) positive for mucicarmine, high iron colloid and alcian blue staining. The carcinoma was positive for cytokeratin 7 and estrogen receptor. There was expression for CD10 in the stromal cells of endometriosis (Figure 1 B-D). A clear cell carcinoma grade 3 was diagnosed.

The patient to our department where she underwent peritoneal washing, total hysterectomy, left salpingo-oophorectomy, pelvic lymphadenectomy, omentectomy and peritoneal biopsies. All anatomopathological exams were normal. The postoperative course was uncomplicated. The patient was submitted to six cycles of platinum-based chemotherapy and now well without any symptoms of recurrence.

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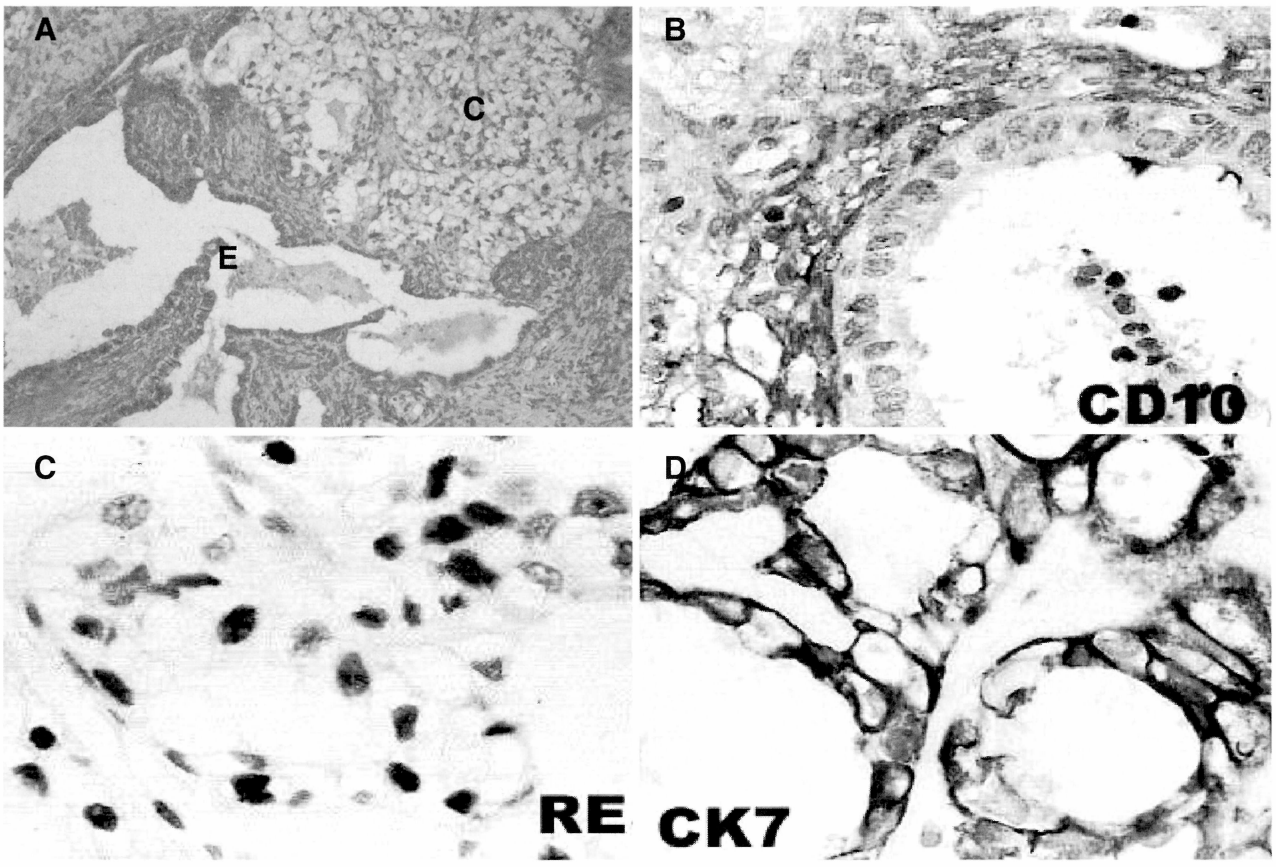

Figure 1. — A. Endometriosis (E) with clear cell carcinoma (C) directly arising from it (HE x100), B. Cells of the endometrial stroma positive for CD10 in foci of endometriosis and glandular epithelium, C. Nuclear expression of estrogen receptor in clear cell carcinoma (x400), and D. Cytoplasmic positivity for cytokeratin 7 in cells of clear carcinoma (x400).

Discussion

We described a rare case of endometriosis in continuity with clear cell carcinoma in a 30-year-old patient. Few cases of the transition from ovarian endometriosis to carcinoma have been reported in the literature. Patients with endometriosis associated with malignant ovarian neoplasms are frequently in postmenopause and have a long history of endometriosis. In this case, the patient was in premenopause, but she did have a long history of endometriosis [7].

The rare cases demonstrated in the English literature involve a progressive transition from endometriosis to endometrioid adenocarcinoma [1, 7], an abrupt transition from endometriosis to endometrioid adenocarcinoma, and an endometrioid adenocarcinoma with a clear cell carcinoma component [7]. Nonetheless, few cases of an association between the transition of typical endometriosis and clear cell carcinoma have been reported. In a study of 22 cases of endometrioid adenocarcinoma, endometriosis and clear cell carcinoma were found in three patients. In one, transition from endometrioid adenocarcinoma to a clear cell carcinoma component was found. The authors compared the presence of a clear-cell component in patients with or without endometriosis, and a statistically significant relationship between endometriosis and a clear-cell component was found [7]. Epithelial atypia in endometriosis has frequently been found to be associated with ovarian carcinoma [9].

An immunohistochemical study showed our case was positive for estrogen receptor and cytokeratin 7, and then clear cell carcinoma was confirmed. A study by Ogawa *et al.* [9] showed that an immunohistochemical study for Ki-67 index revealed it was higher in atypical endometriosis than in ovarian carcinoma. Gene mutational studies are rare in this context and the causal link between endometriosis and ovarian carcinomas remains to be defined [10].

The criteria still in use to identify malignant neoplasia arising from endometriosis was proposed by Sampson in 1925. The criteria are: 1) endometriosis must be adjacent to the neoplasia; 2) the histological type of the neoplasia must be compatible with an endometrial origin; and 3) no other primary site should be found [1, 3]. An additional criterion was proposed by Scott [1], the demonstration of a histological transition from benign endometriosis to malignant neoplasm. Our patient had all the criteria proposed by Sampson and Scott. The use of these four criteria has rarely been fulfilled [1]. This shows that this event is very rare, nonetheless, in our case, the malignant transformation is unquestionable.

Although the extent of endometriosis and clear cell carcinoma was significant, CA125, CA 15.3, CA 19.9, alpha-fetoprotein, carcinoembrionary antigen were normal. A high level of CA125 is a marker of serous ovarian cancer and endometriosis, but in our case the level of CA125 was normal.

Our patient was submitted to left salpingoo-ophorectomy that histologically showed clear cell carcinoma. It was then decided to complete the first surgery with peritoneal washing, total hysterectomy, right salpingoo-ophorectomy, pelvic lymphadenectomy, omentectomy and peritoneal biopsies. After those surgeries, the malignant neoplasia was FIGO Stage IC. A platinum-based chemotherapy regimen was chosen because of initial stage of the neoplasia [11].

In conclusion, although a rare event, the association of typical endometriosis and clear cell carcinoma of the ovary should be kept in mind, mainly in patients with a persistent ovarian cyst.

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References

[1] Somigliana E., Vigano P., Parazzini F., Stoppelli S., Giambattista E., Vercellini P.: "Association between endometriosis and cancer: A comprehensive review and a critical analysis of clinical and epidemiological evidence". *Ginec. Oncol.,* 2006, *101,* 331.

[2] Melin A., Sparén P., Persson I., Bergqvist A.: "Endometriosis and the risk of cancer with special emphasis on ovarian cancer". *Human Reprod.,* 2006, *21,* 1237.

[3] Yazbeck C., Poncelet C., Chosidow D., Madelenat P.: "Primary adenocarcinoma arising from endometriosis of the rectovaginal septum: a case report". *Int. J. Gynecol. Cance.,* 2005, *15,* 1203.

[4] Ulrich U., Rhiem K., Kaminski M., Wardelmann E., Trog D., Valter M., Richter O.N.: "Parametrial and rectovaginal adenocarcinoma arising from endometriosis". *Int. J. Gynecol. Cancer,* 2005, *15,* 1206.

[5] Leng J., Lang L., Guo H., Liu Z.: "Carcinosarcoma arising from atypical endometriosis in a caesarean section scar". *Int. J. Gynecol. Cancer,* 2006, *16,* 423.

[6] Salerno M.G., Masciullo V., Naldini A., Zannoni G.F., Vellone V., Scambia G.: "Endometrioid adenocarcinoma with squamous differentiation arising from ureteral endometriosis in a patient with no history of gonadal endometriosis". *Gynecol. Oncol.,* 2005, *99,* 749.

[7] Valenzuela P., Ramos P., Redondo S., Cabrera Y., Alvarez I., Raiz A.: "Endometrioid adenocarcinoma of the ovary and endometriosis". *Eur. J. Obstet. Gynaecol.,* 2006, *30,* 4.

[8] Stern R.C., Dash R., Bentley R.C., Snyder M.J., Haney A.F., Robboy S.J.: "Malignancy of ovarian and extraovarian types". *Int. J. Gynecol. Pathol.,* 2001, *20,* 133.

[9] Ogawa S., Kaku T., Amada S., Kobayashi H., Hirakawa T., Aryoshi K. *et al.*: "Ovarian endometriosis associated with ovarian carcinoma: a clinicopathological and immunohistochemical study". *Gynecol. Oncol.,* 2000, *77,* 298.

[10] Vigano P., Somigliana E., Chiodo I., Abbiati A., Vercellini P.: "Molecular mechanisms biological plausibility underlying the malignant transformation of endometriosis: a critical analysis". *Hum. Reprod. Update.,* 2005, *19,* 77.

[11] Pather S., Quinn M.A.: "Clear-cell cancer of the ovary is it chemosensitive?". *Int. J. Gynecol Cancer,* 2004, *15,* 432.

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