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Ovarian endometrioid carcinoma associated with diffuse pulmonary endometriosis: a case report

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Summary

Endometriosis is generally assumed to be a benign disease, but it shares many characteristics with malignancy, such as invasive and unrestrained growth and a tendency to metastasize and recur. Although not yet fully delineated, there is a relationship between endometriosis and specific types of epithelial ovarian carcinomas (EOC). A case of an endometrioid ovarian carcinoma in a previously hysterectomized postmenopausal woman, associated with diffuse pulmonary endometriosis is presented. After series of diagnostic and therapeutic procedures, a patient was successfully treated with surgery, chemotherapy, and resection of the suspicious pulmonary lesions which led the authors to a final diagnosis. Most likely such patients with endometriosis-associated ovarian cancers represent different types of patients than traditional ones with ovarian cancer and may require a different therapeutic approach.

Keywords: Ovarian endometrioid carcinoma; Pulmonary endometriosis.

Introduction

Epithelial ovarian carcinomas (EOC) represent the sixth most commonly diagnosed cancer among women in the world, and cause more deaths per year than any other cancers of the female reproductive system.

Endometriosis is a common, benign, chronic, and estrogen-dependent disorder and is defined as the presence of endometrial-like glandular epithelium and stroma in ectopic locations. These ectopic endometrial implants are usually located in the pelvis, but can occur practically anywhere in the body. Despite the fact that endometriosis cannot be termed a premalignant condition, epidemiologic, histopathologic, and molecular data suggest that endometriosis does have malignant potential.

The prevalence of endometriosis in patients with epithelial ovarian cancer, specifically in endometrioid and clear cell types, has been confirmed to be higher than in the general population [1].

The authors report a case of diffuse pulmonary endometriosis that mimicked metastases in postmenopausal women having undergone surgery and chemotherapy for ovarian endometrioid carcinoma.

Case Report

A 63-year-old Caucasian woman, gravida 4, para 2 was hospitalized in August 2008 with symptoms of an acute abdomen and excessive, nonproductive cough. Anamnestically, she had a total hysterectomy without bilateral salpingo-oophorectomy back in 1988 due to uterine fibroids. A diagnosis of acute appendicitis was set and appendectomy via laparotomy was performed. The histopathology report of the resected appendix showed no abnormalities. Several months later identical symptoms reappeared. A preoperative abdominal computed tomography (CT) scan demonstrated presence of a 14-cm solid mass in abdomen with minimal ascites and few suspicious nodules up to one cm on both pulmonary bases. Tumor markers were as following: CEA 7.5 ng/ml, CA 15-3 13.0 U/ml, CA 125 91.2 U/ml, and CA 19-9 85.6 U/ml (Figure 1).

The patient underwent an exploratory laparotomy, adhesiolysis, bilateral salpingo-oophorectomy, and infracolic omentectomy were performed. An approximate 14-cm solid, encapsulated tumor belonging to left ovary, was completely removed, while ascitic fluid contained malignant cells. There were no macroscopically visible metastatic implants intraabdominally. Histopathologic report was: ovarian endometrioid adenocarcinoma, well-differentiated (gr I); (pTNM: pT1a, pNx, pMx), FIGO Stage IC.

After three cycles of systemic chemotherapy (paclitaxel/carboplatin protocol) Ca 125 was within reference range. However, positron emission tomography/computed tomography (PET CT) scan revealed more pulmonary nodules in comparison to previous chest CT scan (seven nodules up to one cm; the largest two were metabolically active) (Figure 2). Unilateral pulmonary metastasectomy through right thoracotomy was performed. Six nodules up to 1.5 cm from the right lung were resected but numerous small nodules previously not visible on PET CT scan were described by surgeon. Histopathology revealed diffuse pulmonary lesions consisting of mesenchymal and epithelial components. Mesenchymal layers of smooth muscle cells surrounded islands of endometrial stroma with endometrial glands. Immunohistochemical staining revealed SMA and estrogen and progesterone positive muscle cells. Endometrial stroma was CD10 and vimentin positive while SMA and estrogen negative (Figure 3). Less than 10% of endometrial cells were progesterone positive. Endometrial epithelia were cytokeratin positive. Low proliferative activity was reported (Ki-67 1%). A diagnosis of pulmonary endometriosis was obtained. An additional three cycles of sys-

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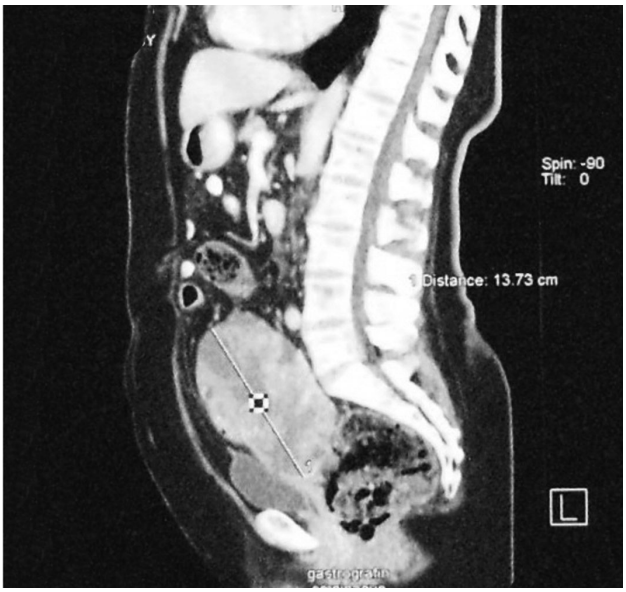

Figure 1. — Preoperative abdominal/pelvic computed tomography imagining revealed a large (14 cm), encapsulated tumor originating from left ovary.

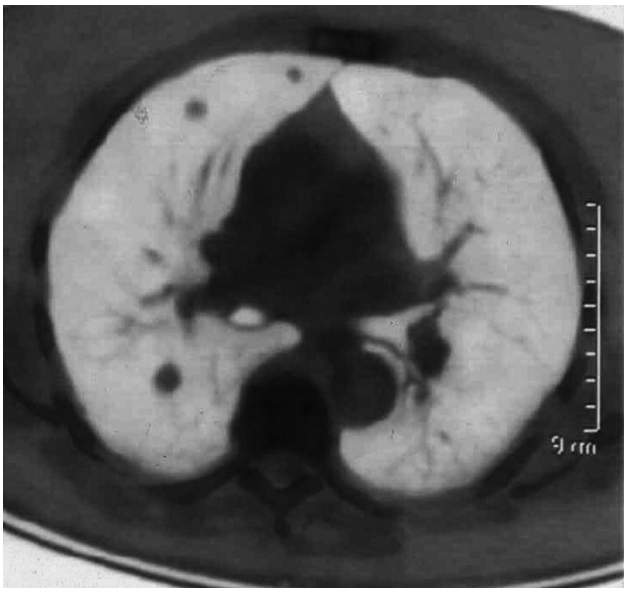

Figure 2. — Positron emission tomography/computed tomography demonstrating pulmonary lesions.

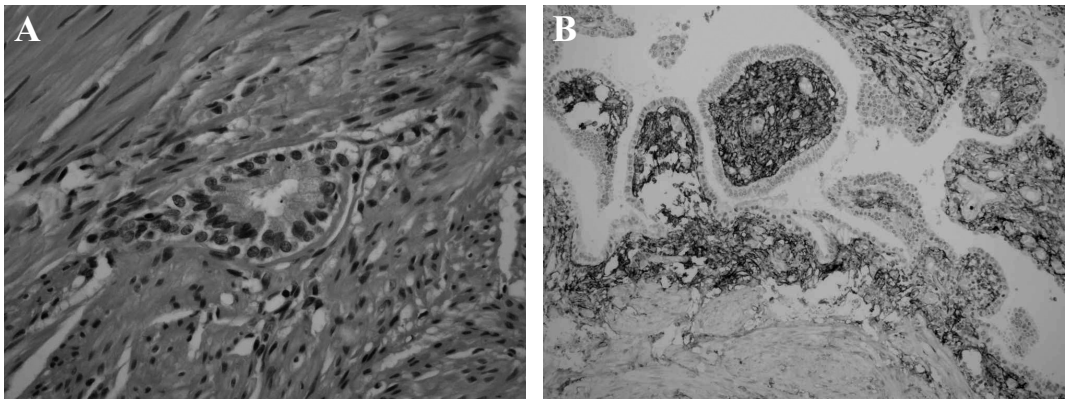

Figure 3. — Staining of pulmonary lesions; (A) gland, hematoxylin eosin staining ×60 and (B) CD 10 staining.

temic chemotherapy (paclitaxel/carboplatin protocol) were administered. The patient had no evident recurrence or metastatic disease seven years after the operation.

Discussion

An association between endometriosis and cancer was reported back in 1925 when Sampson proposed that endometrial carcinoma of the ovary develops from endometrial tissue, based on classic microscopic observation using several strict criteria [2]. Numerous studies have confirmed histologic transition from benign endometriosis to ovarian malignancy, including malignant transformation of extraovarian endometriosis.

Evaluation of the medical literature gives sufficient evidence to conclude that women with endometriosis have an increased risk of EOC, predominantly of the endometrioid and clear-cell subtypes [3]. Relationship between EOC and endometriosis was clearly demonstrated in a meta-analysis of 13 case-control studies that included nearly 8,000 women with EOC and found a statistically significant association between a self-reported history of endometriosis and an increased risk of clear cell (OR 3.05, 95% CI 2.43−3.84), endometrioid (OR 2.04, 95% CI 1.67−2.48), and low grade serous (OR 2.11, 95% CI 1.39−3.20) EOC, but not high-grade serous (OR 1.13, 95% CI 0.97−1.32) or mucinous (OR 1.02, 95% CI 0.69−1.50) EOC [4].

The clinical characteristics of endometriosis-associated ovarian cancers (EAOCs) are somewhat distinct from those of typical ovarian cancer [5]. It appears that they tend to develop in younger and nulliparous women, which was not

the case in the present patient [6].

The literature and the present case illustrate that EAOC tends to present at an earlier stage and with lower grade lesions than non-EAOC [6]. Furthermore, after surgical resection these patients also tend to have less residual disease then non-EAOC; thus, overall survival is better [6, 7].

Malignant extraovarian endometriosis is accountable for a quarter of all malignant transformations of endometriosis and 80% of endometrioid subtype [8]. Different mechanisms have been proposed to explain a relationship between endometriosis and ovarian cancer: (1) endometriosis cells may undergo transformation to cancer or/ (2) the coexistence of endometriosis and ovarian cancer may be due to shared risk factors/antecedent mechanisms, such as genetic predisposition, immune dysregulation, and environmental factors [9]. The observation that the risks of malignant transformation of endometriosis and eutopic endometrium are similar supports the notion that there is a cellular or genetic predisposition [10].

Numerous genetic alterations (loss of heterozygosity on p16, overexpression of p53, oncogenic Kras Pten deletion, mutations in the tumor suppressor gene ARID1A) which associate endometriosis with clear cell and endometrioid carcinomas were described in literature [3].

The presence of diffuse pulmonary endometriosis mimicking metastasis on PET CT scan is particularity of the presented case. Another particularity lies in the fact that the present patient had episodes of excessive, non-productive cough for many years and these episodes were perceived as asthma exacerbations and treated accordingly. However, unexpectedly the histopathological report revealed diffuse pulmonary endometriosis which mimicked metastatic lesions and caused episodes of uncontrolled coughing. Consequently, asthma medications were discontinued. Interestingly, the patient did not consult a gynecologist since 1988 (after total hysterectomy due to uterine fibroids); a fact which underlines the necessity of regular gynecological checkups.

In such patients, due to the rarity of malignant transformation of endometriosis at gonadal and extragonadal sites, it is difficult to establish standard treatment protocol. The treatment plan for each EAOC patient should be individualized, based on patient's findings, age, and medical and family history. Surgery remains the most effective treatment, although the role of chemotherapy, radiotherapy, and hormonal therapy are not clearly defined; these treatment modalities have been associated with prolonged overall survival.

At this time, screening women with endometriosis for ovarian cancer is not a requisite because of the low incidence and the lack of an effective screening test. Additional evidence is needed before generalizing any mutation screening test or changing the treatment of endometriosis to include radical excision in case of positive genetic mutation [11].

References

[1] Nezhat F.R., Pejovic T., Reis F.M., Guo S.W.: "The link between endometriosis and ovarian cancer: clinical implications". *Int. J. Gynecol. Cancer*, 2014, *24*, 623.

[2] Sampson J.A.: "Endometrial carcinoma of the ovary, arising in endometrial tissue in that organ". *Arch. Surg.*, 1925, *10*, 1.

[3] Heidemann L.N., Hartwell D., Heidemann C.H., Jochumsen K.M.: "The relation between endometriosis and ovarian cancer - a review". *Acta Obstet. Gynecol. Scand.*, 2014, *93*, 20.

[4] Pearce C.L., Templeman C., Rossing M.A., Lee A., Near A.M., Webb P.M., *et al.*: "Association between endometriosis and risk of histological subtypes of ovarian cancer: a pooled analysis of case-control studies". *Lancet Oncol.*, 2012, *13*, 385.

[5] Boruban M.C., Jaishuen A., Sirisabya N., Li Y., Zheng H.G., Deavers M.T., Kavanagh J.J.: "Ovarian endometriosis associated with carcinoma and sarcoma: case report". *Eur. J. Gynaecol. Oncol.*, 2008, *29*, 393.

[6] Erzen M., Rakar S., Klancnik B., Syrjänen K.: "Endometriosis-associated ovarian carcinoma (EAOC): an entity distinct from other ovarian carcinomas as suggested by a nested case-control study". *Gynecol Oncol.*, 2001, *83*, 100.

[7] Melin A., Lundholm C., Malki N., Swahn M.L., Sparen P., Bergqvist A.: "Endometriosis as a prognostic factor for cancer survival". *Int. J. Cancer*, 2011, *129*, 948.

[8] Benoit L., Arnould L., Cheynel N., Diane B., Causeret S., Machado A., *et al.*: "Malignant extraovarian endometriosis: a review". *Eur. J. Surg. Oncol.*, 2006, *32*, 6. Epub 2005 Nov 11.

[9] 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". *Gynecol. Oncol.*, 2006, *101*, 331.

[10] Viganò P., Somigliana E., Parazzini F., Vercellini P.: "Bias versus causality: interpreting recent evidence of association between endometriosis and ovarian cancer." *Fertil Steril.*, 2007, *88*, 588.

[11] Kobayashi H., Sugimoto H., Onishi S., Nakano K.: "Novel biomarker candidates for the diagnosis of ovarian clear cell carcinoma". *Oncol. Lett.*, 2015, *10*, 612.

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