Case report

Clear cell carcinoma arising from abdominal wall endometriosis – Brief report and review of the literature

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1. Introduction

Endometriosis is defined as an inflammatory condition characterized by the presence of endometrial-like tissue outside the uterus (Johnson et al. 2013), usually the pelvis, but it can even be found in the lung, bowel, ureter and abdominal wall. Endometriosis of the abdominal wall is one of the most common locations of endometriosis outside the peritoneal cavity; a prior history of surgery, whether laparotomy or laparoscopy, is usually mentioned. The malignant transformation is rare but, can occur (Horton et al. 2008).

We present a clinical case of clear cell carcinoma of the abdominal wall related to endometriosis neoplastic transformation.

2. Case description

A 47-year-old female presents for evaluation of a three-month pelvic pain exacerbating during the last month and a growing tumoral mass at the left side of a caesarean section scar. No relevant medical problems were referred other than three previous C-sections, at 23, 25 and 30 years old followed by a tubal ligation. No relevant family history was mentioned.

Physical examination revealed a smooth mass measuring 8 cm in diameter on the middle-left side of the caesarean median scar. At vaginal exam, a 8 cm tumor was palpable and seemed to be in continuity with the left abdominal wall. No pelvic tumor was detected by transvaginal ultrasound besides a cyst of the right ovary, but soft tissue ultrasound and computed tomography scan (CT-scan) revealed a heterogenous tumor, in the left abdominal rectus, extending from left flank until the Retzius space, measuring 11 cm (Fig. 1); no pelvic tumor mass in the intraperitoneal cavity or abdominal/pelvic lymph nodes were detected and laboratory tests revealed CA125 = 29 U/mL.

An initial operative approach by laparoscopy was performed: a haemorrhagic 4 cm right ovarian cyst, normal uterus and unremarkable pelvic cavity were observed; bilateral adnexectomy was performed. The surgery proceeded to total excision of the abdominal wall mass through the previous vertical infra-umbilical midline scar.

Histopathological examination revealed a clear cell carcinoma (CCC) suggesting malignant transformation from endometriosis of the abdominal wall, tumor free margin (Fig. 2). Positron emission tomography (PET) performed 6 weeks after surgery revealed a hypermetabolic image on the dependence of the left abdominal rectus; in abdominal magnetic resonance imaging (MRI) no lesions were found. Adjuvant chemotherapy treatment comprising six cycles of carboplatin plus paclitaxel was administered.

At evaluation after chemotherapy, the patient was asymptomatic and no other abdominal lesions were observed in MRI; CA125 levels decreased to 8.5 U/mL.

Nine months after, the patient complained about a new palpable tumor of 2 cm, at the same location. The MRI and PET revealed a local recurrence, in the abdominal wall, measuring 5.4 × 4.4 × 1.9 cm (Fig. 3). An abdominal hysterectomy, a wide resection of the abdominal recurrence and reconstruction of the abdominal wall with a mesh was performed. Histopathological analysis confirmed the recurrence of CCC, with adequate surgical margins. The post-operative course was complicated by an intestinal occlusion. A laparotomy was performed, the abdominal mesh was removed, the adherence between the small bowel and the abdominal wall conditioning the occlusion was identified and a new mesh was positioned. The treatment was complemented...
with 6 cycles of chemotherapy, carboplatin plus paclitaxel. The MRI post chemotherapy showed no secondary lesions.

The patient has been examined by gynecological oncologist every 6 months. Twenty-four months after the second surgery, 2 consecutive episodes of abscess succeeded, with no bacterial growth on cultures. A long course of antibiotic was administered and finally a complete clinical resolution was obtained. MRI confirmed a remaining liquid collection, although no signs of local recurrence.

Thirty-six months after the second surgery, no further evidence of the disease on imaging studies or clinical examination has occurred.

3. Discussion

Endometriosis of the abdominal wall can result from the contamination of subcutaneous tissue by endometrial cells during delivery or

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**Fig. 1.** Appearance of heterogeneous abdominal mass at CT-scan, measuring 11 × 7 × 4.1 cm. A- anterior, L- left.

**Fig. 2.** Clear cell abdominal wall carcinoma, with papilar and tubule-cystic pattern, with intra-cystic growing, related with previous endometriosis (H&E).

**Fig. 3.** MRI of recurrence at left rectus abdominis muscle level. Complex cystic formation, with 5.4 × 4.4 × 1.9 cm, which exceeds the muscular limit, bulging the transverse fascia.
clearing the endometrial cavity after removal of the placenta (Heaps et al. 1990). These implants are typically observed after caesarean section (0.03 to 1%) (Horton et al. 2008) or hysterectomy, although they have also been reported in association with episiotomy, trocar scars, appendectomy, and hernia repair scars (Taburiaux et al. 2015). Horton et al. (2008), described that abdominal endometriosis was associated with a previous caesarean section scar in 57% of patients although in 20% of patients it was not related with any abdominal scar. Malignant transformation of endometriosis associated with surgical scars is extremely rare, with an estimated incidence not exceeding 0.3–1.0% (Heaps et al. 1990) and 80% of endometriosis related cancer are referred to the ovary. The rectovaginal septum, the colon and the vaginal wall are the most frequent extraglandal sites of malignant endometriosis, comprising >50% of the cases (Bats et al. 2008). CCC is the histological subtype more often present in these cases; endometrioid carcinoma is the second most encountered (Taburiaux et al. 2015).

According to a systematic review, from Taburiaux et al. (2015), 27 clinical cases of abdominal wall adenocarcinoma related with endometriosis are reported in literature, until 2014. The mean age of presentation was 47 years (range 38–60) and the mean time between the first gynecological surgery and the diagnosis of carcinoma was 21 years (range 8–41 years), evidencing the slow evolution of these situations.

A mass in the abdominal wall, usually adjacent to a scar from previous surgery, is the typically complaint. A cyclical pain, correlated with the menstrual cycles, is largely described (Hensen et al. 2006). Considering the size of the lesion, in most of the cases, it was large at the time of diagnosis (Taburiaux et al. 2015). Clinical history with emphasis in previous gynecological surgeries is very important. Imaging techniques are very useful; soft tissue ultrasound is recommended, complemented, if necessary, with ultrasound-guided fine-needle aspiration of the mass. Sometimes, an MRI/CT scan is needed for additional information.

The clinical differential diagnosis of palpable masses in the abdominal wall includes hernia, hematoma, lymphadenopathy, lipoma, abscess, subcutaneous cyst, neuroma, soft tissue sarcoma, desmoid tumor or metastasis.

Surgical treatment of these situations is the definitive therapeutic approach. A wide and complete excision to obtain healthy margins has been frequently described. Usually, both ovaries are removed and, ideally, an endometrial biopsy should be done. Depending on the size of the tumor, a prosthetic mesh for abdominal wall repair is most often needed. Adjuvant chemotherapy and radiotherapy have been reported to improving outcomes, although no consensus is established regarding protocols. A chemotherapy based on a combination of carboplatin and paclitaxel has been reported as preferential, as we performed in this clinical case. Some series report an improvement in 5-year overall survival and progression free survival using abdominal radiation for ovarian carcinomas, especially for CCC (Hoskins et al. 2012; Macrie et al. 2014).

The prognosis of these patients seems to be poor; the median survival time is about 30 months (Taburiaux et al. 2015).

In 1925, Sampson (1925) proposed 3 criteria for the diagnosis of malignancy arising from endometriosis: (1) presence of both benign and neoplastic endometrial tissues in the tumor, (2) endometrial histology, and (3) absence of additional tumor. Further, in 1953, Scott (1953) added a fourth criterion: (4) the morphologic demonstration of benign endometriosis contiguous with the malignant tissue is a prerequisite for adjudication of a malignancy originating in endometriosis. All these criteria are fulfilled in this clinical case, although in this case the histological type is a CCC. Several studies have suggested the link between endometriosis and ovarian-type cancer. Pearce et al. (2012), concluded that self-reported endometriosis was associated with significantly increased risk for CCC [odds ratio (OR) 3.05], endometrioid cancer (OR 2.21), and low-grade serous invasive ovarian cancers (OR 2.21).

Little is known about the mechanisms involved in the neoplastic progression endometriosis. Genetic, immunological, and hormonal factors have been implicated. It is becoming clear that epigenetics and genomic instability associated with the particular microenvironment of endometriosis characterized by oxidative stress, inflammatory process and high estrogen levels contribute to the process of malignant transformation of endometriosis (Pearce et al. 2012; Nezhat et al. 2014).

The long-term endometriosis, endometriosis diagnosed at an early age, endometriosis associated with infertility, and the presence of enlarging ovarian endometrioma or changing characteristics and mural nodule formation are risk situations for the malignant transformation of endometriosis (Nezhat et al. 2014).

Given the increasing rates of caesareans around the world, it is very likely that abdominal wall endometriosis also increases. It is important to keep scar endometrioma in mind in order to facilitate an early and timely diagnosis and treatment.

4. Conclusion

Endometriosis-associated abdominal wall cancer is rare, but usually very aggressive. A few cases are reported and there is no standardized treatment. The pathogenesis of the malignant transformation of endometriosis is largely unknown and further studies are needed. Attention should be placed in a proper treatment of endometriosis, identification of the patients at risk and a suitable monitoring in order to allow the prevention the occurrence of a malignant lesion or the diagnosis and treatment at an early stage.

Conflicts of interest

None.

Acknowledgments

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

References

Bats, A.S., et al., 2008. Malignant transformation of abdominal wall endometriosis to clear cell carcinoma: case report and review of the literature. Fertil. Steril. 90, 1197–1206.
Heaps, J.M., et al., 1990. Malignant neoplasms arising in endometriosis. Obstet. Gynecol. 75, 1023–1028.
Hensen, J.H., et al., 2006. Abdominal wall endometriosis: clinical presentation and imaging features with emphasis on sonography. AJR. Am. J. Roentgenol. 186, 616–620.
Horton, J.D., et al., 2008. Abdominal wall endometriosis: a surgeon’s perspective and review of 445 cases. Am. J. Surg. 196, 207–212.
Hoskins, P.J., et al., 2012. Low-stage ovarian clear cell carcinoma: population-based outcomes in British Columbia, Canada, with evidence for a survival benefit as a result of irradiation. J. Clin. Oncol. 30, 1656–1662.
Johnson, N.P., et al., 2013. Consensus on current management of endometriosis. Hum. Reprod. 28, 1552–1568.
Macrie, B.D., et al., 2014. Patterns of recurrence and role of pelvic radiotherapy in ovarian clear cell adenocarcinoma. Int. J. Gynecol. Cancer 24, 1597–1602.
Nezhat, F.R., et al., 2014. The link between endometriosis and ovarian cancer: clinical implications. Int. J. Gynecol. Cancer 24, 623–628.
Pearce, C.L., et al., 2012. Association between endometriosis and risk of histological subtypes of ovarian cancer: a pooled analysis of case-control studies. Lancet Oncol. 13, 385–394.
Sampson, J., 1925. Endometrial carcinoma of the ovary arising in endometrial tissue in that organ. Arch. Surg. 10, 1–72.
Scott, R.B., 1953. Malignant changes in endometriosis. Obstet. Gynecol. 2, 283–289.
Taburiaux, L., et al., 2015. Endometriosis-associated abdominal wall cancer: a poor prognosis? Int. J. Gynecol. Cancer 25, 1633–1638.