High-grade ovarian serous carcinoma in a young woman -
case report and literature review

Carcinom ovarian seros cu grad înalt de malignitate la o femeie tânără -
prezentare de caz și revizuirea literaturii de specialitate

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<th>Abstract</th>
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<td><strong>Objective.</strong> Ovarian high-grade serous carcinoma is a type of malignancy that is rare among young adult women, being more frequent in postmenopausal women. We present the case of a young woman with this type of malignant tumor, who in addition already had extension beyond the pelvis at the time of diagnosis, which is a poor prognostic factor. <strong>Case report.</strong> We report the case of a 36-year-old woman who was admitted in our hospital with pelvic pain and ascites and also with suspicion of peritoneal carcinomatosis. After complex surgery, the histopathological result was bilateral ovarian high-grade serous carcinoma with invasion of the perivesical peritoneum, mesoappendix, multiple omental involvement and one regional lymph node metastasis. Afterwards, she was submitted for oncologic treatment. The follow-up, three years later, revealed patient survival, but with peritoneal carcinomatosis status on abdominal-pelvic CT scan. <strong>Discussions.</strong> Our work brings together reports of young women worldwide facing this form of cancer and underlines the fact that, regardless of age, reproductive women are at risk of developing an aggressive and deadly disease, and that clinical, biological and imaging screening should be increased from an early age. <strong>Keywords:</strong> high-grade serous carcinoma, young women, screening</td>
<td><strong>Obiectiv.</strong> Carcinomul ovarian seros cu grad înalt de malignitate este un tip de cancer rar întâlnit la femeile tinere, fiind mai frecvent la femeile în postmenopauză. Vă prezentăm cazul unei femei tinere cu această formă de tumură malignă, care se află deja într-un stadiu avansat cu extensie extrapelviană la momentul diagnosticului, cea ce reprezintă un factor de prognostic negativ. <strong>Prezentare de caz.</strong> Raportăm cazul unei femei de 36 de ani care s-a prezentat la spitalul nostru cu dureri pelviene și ascită, suspiciunea de carcinomă peritoneală. După intervenția chirurgicală (histerectomie totală cu anexectomie bilaterală, appendicetomie și evidarea gânglionară radicală), rezultatul histopatologic a fost: carcinom ovarian seros de grad înalt, bilateral, cu invazia peritoneului periveczial, mezoappendice, omentală, precum și a unui limfoganglion. Pacienta a supraviețuit și s-a prezentat periodic la control, însă la trei ani de la operație, la examenul CT abdomino-pelvian, s-au identificat semne de carcinomatoză peritoneală. <strong>Discuții.</strong> Lucrarea noastră aduce în prim plan raportări de cazuri ale unor paciente tinere din întreaga lume suferind de această formă de cancer și subliniază faptul că, indiferent de vârstă, femeile aflate în perioada reproductive sunt la risc de a dezvolta o afecțiune ovariană agresivă și subliniază faptul că aceea este important ca screeningul clinic, biologic și imagistic să fie început de la o vârstă timpurie. <strong>Cuvinte-cheie:</strong> carcinom seros de grad înalt, femeie tânără, screening</td>
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**Introduction**

High-grade serous carcinoma of the ovary is the most common type of ovarian cancer, representing 50-70% of all ovarian carcinomas\(^3\)\(^,\)\(^2\). Serous carcinoma is most often diagnosed in the sixth and seventh decade, with a mean age of high-grade tumors of 63 years old\(^3\). Diagnosis is often delayed because symptoms are non-specific and include: abdominal pain, distension, gastrointestinal symptoms (nausea, anorexia, constipation), high urinary frequency, vaginal bleeding\(^3\)\(^,\)\(^3\). High-grade ovarian serous carcinomas are more often bilateral, approximately in 60% of cases\(^4\). The most important predictor factor is the patient’s tumor stage\(^5\). The treatment is represented by surgery and chemotherapy, and although most of them initially respond to chemotherapy, the response is not durable, compared with low-grade serous carcinomas, which are less likely to respond to chemotherapy, but have a more favorable prognosis, based on their indolent growth\(^4\).

**Case report**

We report the case of a 36-year-old woman with previous complaints of abdominal pain and moderate abdominal distension who was admitted in our hospital. Following ultrasound examination (Figure 1), we detected

**Conflict of interests:** none declared.
a large left ovarian tumor multiple septa with intense vascularity during Doppler inspection and ascites. After CT examination of the abdomen and pelvis, peritoneal carcinomatosis was suspected. CA125 and HE4 markers were slightly elevated.

The patient was submitted for complex surgery with total hysterectomy with bilateral adnexectomy, omentectomy, appendectomy and peritoneal biopsies, together with regional lymph node dissection.

On macroscopy, both ovaries were enlarged, the left one measuring 90 mm in diameter and the other 5 cm. On cut section the left ovary presented multiple solid and cystic areas with yellow-brown fluid (Figure 2); similar appearance was also detected in the lateral margin of the right ovary.

The histopathological examination concluded bilateral ovarian high-grade serous carcinoma with invasion of the perivesical peritoneum, mesoappendix, multiple omental involvement and one regional lymph node metastasis (stage IIIC), with no evidence of metastasis to extraabdominal organs or parenchymal metastasis. The patient was submitted for further oncologic treatment. The histologic type was confirmed by positivity for p53 marker, and tumor proliferation index (Ki67) was 50%; estrogen receptors and androgen receptors were diffuse positive (Figures 3-7).
Discussions

Ovarian high-grade carcinoma in young women is rare and of unknown etiological factors, since current incriminated risk agents such as nulliparity, increased number of menstrual cycles, oral contraceptive use are long-term related accepted conditions, and that the carcinogenic process is developed upon a mutation-acquiring period. In a published study, A. Malpica et al. have reported cases of high-grade serous carcinomas of the ovaries in women with ages ranging from 27 to 76 years old, a mean of 55 years, suggesting that a wide range is possible in this malignancy.

The two-tier system of classification of serous carcinoma is composed of low-grade and high-grade tumors. The criteria for sub-classifying to one or the other are histological, represented by nuclear atypia and mitotic activity. According to age incidence, the low-grade tumors occur at younger age, with statistically declared one decade earlier than high-grade counterpart.

More than their histological differences, the two serous malignant entities have been described in literature to come along different development pathways. Type I carcinoma (low-grade) progresses from borderline or benign tumors and are thought to retain their low-grade appearance even after disease recurrence, and type II carcinoma (high-grade) were described mostly as de novo tumors, although a small percent appear to have evolved from a low-grade tumor. Supporting the different pathways are studies demonstrating different genetic alterations, low-grade tumors harbor KRAS and BRAF mutations, whereas high-grade tumors have p53 mutations and sometimes harbor BRCA mutations.

BRCA1/BRCA2 mutations are common in hereditary ovarian cancer. Other genetic alteration, like MMR genes in Lynch syndrome, is rarely seen in high-grade serous carcinoma, and is more frequent in non-serous types of ovarian cancer.

So, in our case, given the young age of the patient, it is possible that she had a genetic alteration of a hereditary ovarian cancer, even in the absence of known heredocolateral cancer, but she didn’t undergo genetic testing for subjective reasons.

In terms concerning screening, it is stated in literature that there are no documented effective screening methods that reduce the mortality in ovarian carcinoma. Although transabdominal or transvaginal ultrasonography examination, and serum CA125 can be used, they don’t have accepted levels of sensitivity and specificity, among screened women 70% presented an advanced stage disease, which was no different from unscreened populations. This supports the rapid onset and possible fulminant behavior of the disease, as de novo cancer, without detectable precancerous lesions. Additionally, Horvath L. et al., in their study performed on 110 patients diagnosed with epithelial ovarian cancer of different histologic types, found a statistically significant difference, with average measurement of 4.8 cm in advanced disease, and of 10.7 cm in early stage disease, suggesting that early stage grows locally and does not disseminate, and advanced stage disseminates while the tumor is still relatively
small\cite{13,14}. However, we strongly believe that some screening is better than no screening, and sustain the fact that classical “so-called” screening tools for ovarian cancers can be used among women, if the time period is enough frequent, using non-invasive methods. In our case, we have a big tumor dimension, up to 10 cm, and advanced stage disease, but we could not say when the metastasis began, and do not know if previous screening would have helped the patient in detecting earlier tumoral stage. What is sure is that the diagnosis was not incidental, and addressability to medical care was done when her quality of life was seriously affected. So, the need for reliable screening tests is an extreme necessity.

Conclusions

High-grade ovarian serous carcinoma is the most frequent ovarian cancer and it is found mostly in post-menopausal women, but cases of young women, at reproductive age, as in our case, have been reported in literature.

We found a higher tumor size accompanying advanced tumor stage at the time of diagnosis.

Regardless of age, reproductive women are at risk of developing an aggressive and deadly disease, but currently used screening tools need to be more studied regarding their effectiveness, on how often should they be performed or if there can be new screening tests for current use from an early age.

References