

Axillary lymph node metastasis as first presentation of peritoneal carcinomatosis from serous papillary ovarian cancer: case report and review of the literature

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Summary

Ovarian cancer usually spreads into abdominal cavity and to the loco-regional lymph nodes. Extra-abdominal metastases are less frequent and isolated axillary metastases are very rare. The authors describe the case of a 49-year-old woman who was diagnosed with a peritoneal carcinomatosis from ovarian cancer by mean of an enlarged axillary lymph node biopsy, whose histological examination identified as a ovarian cancer metastasis. Patient was treated by peritonectomy and intraperitoneal chemohyperthermic perfusion (HIPEC). Although patients with axillary lymph node metastasis from ovarian cancer are though to be metastatic (FIGO Stage IV), surgical radical treatment and adjuvant systemic chemotherapy can achieve the same prognosis of Stage IIIb-c patients, suggesting they could be a particularly good prognosis subset of patients. Early differential diagnosis between ovarian or breast cancer in axillary lymph node metastasis is crucial but not always very simple, because of the very different course and treatment of these tumours.

Key words: HIPEC; Peritonectomy; Ovarian carcinoma; Axillary lymph node metastasis.

Introduction

Ovarian cancer usually spreads into the abdominal cavity as the first site of extraovarian diffusion. Due to the peritoneal fluid circulation pattern, during its clinical history the disease involves the greater omentum, pelvic and paracolic gutter peritoneum, diaphragm, liver capsule and the serosal surface of small and large bowel, and often can be confined into the abdominal cavity for many years. Symptoms are generally related to intrabdominal compression by the growing pelvic mass, ascites or bowel obstruction due to peritoneal implants on bowel wall or rectal involvement by a pelvic mass.

However, more often later in the patient's course, metastasis of ovarian cancer to retroperitoneal organs such as kidney, or distant metastasis to liver, lung or brain are seldom reported. Pelvic and para-aortic lymph nodes are usually affected by ovarian cancer with a rate reaching 67%, while extra abdominal lymph node involvement is less common. Although this pattern of spread can be possible in N+ patients, the involvement of supradiaphragmatic lymph nodes without metastases in para-aortic or iliac ones is exceptional.

Isolated axillary metastasis as first sign of ovarian carcinoma without other loco-regional or distant lymph nodes metastases is a rare condition [1]; the authors describe the case of a 49-year-old woman who was diagnosed an axillary isolated enlarged lymph node during a screening ultrasound for breast cancer prevention, which was the first

and only sign of a serous papillary ovarian carcinoma with peritoneal carcinomatosis without abdominal or other extra-abdominal lymph node metastases.

Case Report

A 49-year-old woman was diagnosed an enlarged right axillary lymph node during an ultrasound examination for breast cancer screening. A fine needle aspiration of the lymph node was done and the diagnosis was metastasis from unknown primary carcinoma. Breast ultrasonography and nuclear magnetic resonance (NMR) examination were negative for lumps. Patient medical history was negative for previous gynaecological or breast diseases.

Histological examination of surgical specimen from the excisional biopsy of the enlarged lymph node showed microscopic lymph node structure disrupted by neoplastic cells proliferation characterized by papillar architecture of columnar epithelium with hyperchromatic nuclei (Figure 1, hematoxylin and eosin [H/E] x2.5 high-power field [HPF]). Several psammoma bodies were present. At immunohistochemical evaluation, neoplastic population was found positive to anti CK-7 and WT-1 (Figure 2, x40 HPF) antibodies and negative for anti vimentin antibodies, thus suggesting an ovarian origin. Haematological tests were all unremarkable, with normal haemoglobin and WBC count, except for serum CA125 levels, (750 um/ml). A contrast enhanced whole body computed tomography (CT) scan was then performed and showed a bilateral ovarian neoplasm with involvement of the uterus and the pelvic peritoneum with mild ascites. No other enlarged lymph node was seen in abdominal or extra abdominal stations.

Patient underwent surgical treatment; cytological examination of ascites confirmed malignancy and a radical hysterectomy with bilateral salpingo-oophorectomy, complete omentectomy, appendectomy, and pelvic peritonectomy were performed. A complete iliac, para-aortic, and inferior mesenteric artery lymphadenectomy was

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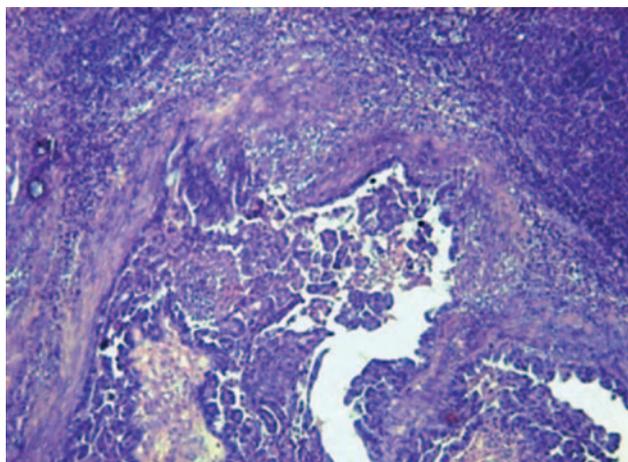


Figure 1. — Axillary node metastasis of epithelial tumour with prevalent papillary pattern (H/E, x2.5 HPF).

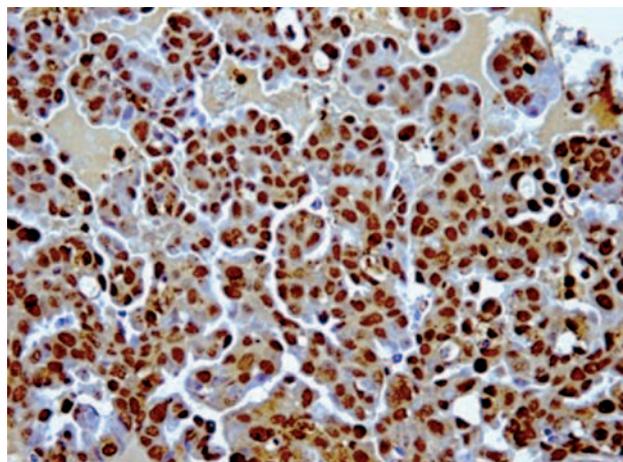


Figure 2. — Axillary node metastasis: marked positivity with antibody WT-1, in the area with closely packed papillae, most of which lack fibrous cores (x20 HPF).

also performed. A number of scattered peritoneal implants on right paracolic gutter and Douglas pouch were ablated by means of an argon beam coagulator, and a three-cm bulky implant of the bladder peritoneum was excised. The remaining peritoneal surfaces, as well as the diaphragms, the liver capsule, and the small bowel loops were free from disease. Final peritoneal cancer index (PCI), according to Sugarbaker's scoring system, was 9. Completeness of cytoreduction was considered optimal (CC-0 at CC-score by Sugarbaker). At the end of the surgical procedure, the patient underwent hyperthermic intraperitoneal chemotherapy (HIPEC) with the closed technique, using a 75 mg/m²/l cisplatin (CDDP) solution at 43°C for 60 minutes, following Sugarbaker's criteria [2].

Histological examination of the surgical specimen confirmed the diagnosis of a poorly differentiated serous papillary cystadenocarcinoma of the ovary (Figure 3, H/E x5 HPF), with implants on the left adnexa, on the uterus surface with early myometrial infiltration and with peritoneal carcinomatosis on omental surface, on the Douglas, and right paracolic gutter peritoneum. The 34 lymph nodes removed were all negative for neoplastic involvement.

Immunohistochemical evaluation of the sample confirmed anti CK-7, CK-20, WT1 positive staining, anti vimentin, and GCDPF-15 negative staining of the neoplastic population.

Postoperative course was uneventful and the patient was discharged after 18 days in good general conditions.

She underwent an adjuvant six courses systemic chemotherapy with carboplatin and paclitaxel. Ca125 normalized during therapy, reaching the final value of five um/ml. Patient underwent a six-month periodical follow-up, including clinical evaluation, serous markers determination, and a whole body contrast-enhancement CT scan for the first two years and then every year.

To date, she is alive and disease free after seven years of follow-up.

Discussion

It is well known that the principal and earliest way of diffusion of ovarian carcinoma is the peritoneal spread. Peritoneal fluid circulation "drives" the neoplastic cells towards their final destinations on the peritoneal surface [3]. Limited or diffused peritoneal carcinomatosis is present at the first

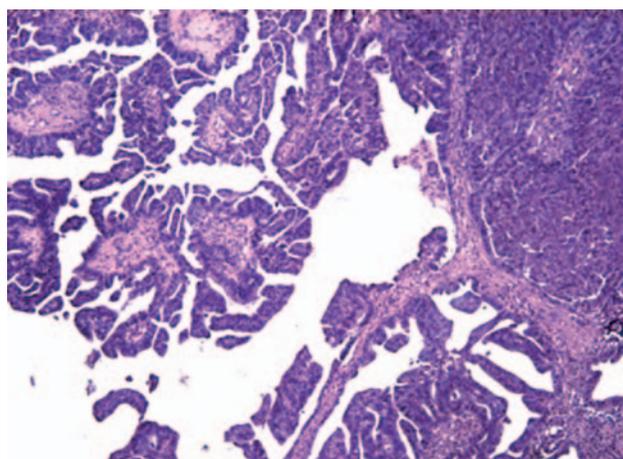


Figure 3. — Ovarian lesion: serous papillary adenocarcinoma, composed of papillae with abundant fibrous core, left, and area with solid papillary aggregates without fibro-vascular cores, right (H/E, x5 HPF).

diagnosis in more than 75 percent of patients. Iliac and para-aortic lymph node metastases are less frequent, although not exceptional [4, 5]. Systemic metastases are present in 38 percent of patients late in disease history [6] and in eight to 22 percent at the time of first diagnosis [7]. One of the first clinical signs of the presence of an ovarian carcinoma is the development of high volumes of ascites, together with variable signs of intestinal obstruction due to small bowel implants or the development of a pelvic mass with involvement of the sigmoid colon. Extra-abdominal lymph node metastases are less frequent, especially in serous carcinoma, and follow the lymphatic way involving progressively the loco-regional lymph nodes and the para-aortic chains [3, 7-9].

The presence of an extra-abdominal lymph node metastasis alone as first and unique sign of the disease is very rare [1]. The diagnosis of ovarian carcinomatosis from an axillary lymph node metastasis is exceptional. In a recent article by Euscher *et al.*, on a sample of 35 patients affected by ovarian carcinoma, peritoneal carcinoma or carcinoma of the fallopian tube with loco-regional lymph node metastases, the incidence of axillary metastases in patients with ovarian carcinoma was 0%, while more frequent were metastases to supraclavicular or inguinal lymph nodes [3]. Zang *et al.*, in their series of patients affected by ovarian cancer with extra-abdominal diffusion, found only six and five patients with supraclavicular and inguinal lymph node metastases, respectively. [8]

Literature report very scarce data about extra-abdominal lymph nodes involvement in primary advanced ovarian cancer. In a review by Cormio *et al.* [7], five cases of extra-abdominal lymphatic spread are reported on a group of 162 patients with epithelial ovarian cancer.

The neoplastic involvement of supra-diaphragmatic lymph nodes without loco-regional ones is not easy to explain. Some studies proposed that serous carcinoma could follow the central lymphatic duct without interesting iliac or para-aortic stations [10, 11]. However the real anatomic or physiopathological basis of this pattern of spread is still unknown.

Synchronous axillary lymph nodes involvement in ovarian cancer is not exceptional, reaching in some studies the rate of 60% to 70% of the patients [12,13], but the presence of an isolated axillary metastasis in an asymptomatic patient has been reported only in a few patients [1, 3].

In the present patient, the only metastatic lymph node was the axillary one, without any involvement of iliac, para-aortic or supra-diaphragmatic chains. In such a patient, to assess whether the lymph node is a primary cancer or is a metastasis from an ovarian cancer or of a primary undiagnosed breast cancer, seems to be an issue of primary importance. Immunohistochemical studies, especially the evaluation of the WT-1 expression, seem appropriate for such differential diagnosis [14]: in the present patient positivity was found both in axillary lymph node and in the ovarian surgical sample. Other authors have focused on the key role of the GCDFP-15 evaluation to rule out the ovarian or breast origin [15]. In agreement with the present finding, Monteagudo *et al.* demonstrated that more than 71 percent of metastatic breast cancers express the GCDFP-15, while it is always negative in primary ovarian carcinoma [16].

The presence of psammoma bodies or calcifications is also important to determine the origin of the primary cancer: in the present patient, they were present both in the axillary lymph node and in the ovarian carcinoma, suggesting, together with a negative mammography, the ovarian origin of the axillary metastasis. Nevertheless, diagnostic problems may arise because in fact axillary metastatic ovarian

cancer may sometimes appear as lymph node calcifications at mammography [17].

Although prognosis in patient with axillary or breast metastasis from ovarian carcinoma is poor and the reported median survival rate accounts for 13 months (range 7-66) [12], the present patient is still alive and disease free after seven years.

In conclusion, metastatic ovarian carcinoma presenting with an isolated axillary lymph-node metastasis is an uncommon event; its recognition and differential diagnosis with metastatic breast carcinoma to the ovary is of great importance because of the very different prognosis and treatment.

Patients with peritoneal carcinomatosis and single extra-abdominal lymph node metastasis from ovarian carcinoma are a particular subset of ovarian cancer patients who are able to be treated by radical surgery, intraperitoneal hyperthermic chemotherapy, and systemic adjuvant chemotherapy with a reasonable hope of good prognosis and long life expectancy. Clinical history and histological and immunohistochemical accurate comparison of the WT-1 and of the GCDFP-15 expression between the ovarian cancer and axillary metastasis are helpful to determine the correct diagnosis and therefore the more appropriate treatment.

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