

Fine-needle aspiration of skin metastasis in ovarian cancer-report of two cases and review of the literature

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Abstract: Ovarian cancer is known to be the first cause of death of gynecological malignancy in Europe and United States. Skin metastases consist of an unusual event during the course of ovarian carcinoma and occur in 2–3.5% of the patients. We report two interested cases of patient with skin metastases, due to ovarian carcinoma, diagnosed by fine-needle aspiration (FNA). The clinical information, cytologic findings and immunocytochemical profile are described and further discussed, according to the relevant bibliographic data. The combination of FNA and thin layer cytology contribute to the accurate clarification of metastatic tumors with a known or unknown origin. It known that skin metastasis tend occurs in most ovarian carcinomas at a late stage course of the disease and it is usually associated with poor prognosis, in some cases the survival can be prolonged with appropriate therapy. So, an accurate cyto-immunodiagnosis is crucial for the best management of these patients.

Keywords: Ovarian cancer; fine-needle aspiration (FNA); skin metastasis

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Introduction

Ovarian cancer is known to be the first cause of death of gynecological malignancy in Europe and United States (1). The median age at diagnosis is 52 years (2). It has been observed that epithelial ovarian carcinoma is diagnosed at advanced stage with widespread intraperitoneal dissemination (3). It has been also observed that it can metastasize through the lymphatic channel and the hematogenous route (4). The most common sites of metastases are the pleura, liver, lung and lymph nodes (5). However, the ovarian cancers are usually confined to the peritoneal cavity, and rarely metastasize to the skin.

Skin metastases consist of an unusual event during the course of ovarian during the course of ovarian carcinoma and occur in 2–3.5% of the patients (5). They are mostly always situated at the skin of the abdominal wall. They can be diagnosed to the chest wall, the buttocks and the breast (5). This incidence invariably carries a poor prognosis in the course of an advanced stage ovarian carcinoma. As far as fine-needle aspiration (FNA) from skin metastasis in ovarian cancer is concerned, there are scarce bibliographic data, although FNA is a simple, useful, less invasive method, with a good sensitivity, specificity and accurate interpretation in the diagnosis of metastatic carcinoma, so that the appropriate therapeutic procedures

can be achieved. The aim of this study is to present two interested cases of ovarian cancer with skin metastasis and review of the relevant literature.

First case

We report a case of a 34-year-old woman who was admitted to our hospital with multifocal skin nodules (chest, abdomen, upper and low extremities) measuring 0.5–2 cm, but no other clinical manifestations. The patient had a previously established diagnosis of ovarian serous papillary carcinoma (pT3, FIGO III, grade 2) 2 years ago. The patient underwent surgery and she was admitted 6 cycles chemotherapy with Taxol and 1 cycle chemotherapy with Caelyx.

FNA of the skin nodule at the upper forearm with a 23o G needle was performed and the material was processed by conventional method and thin layer cytology (TninPrep technique). The cytologic examination revealed hemorrhagic and inflammatory material with a large amount of malignant neoplastic cells, in papillary structures, with hyperchromatic nuclei and prominent nucleoli. Cytoplasmic vacuoles were so evident.

The following findings were observed on the cytological specimen on the microscope: atypia, hyperchromatic nuclei, increased nuclear/cytoplasmatic ratio and 3D clusters of atypical cells. Immunocytochemistry showed strong positivity for CA-125 (3+) and mesothelin (3+) and moderate positivity for Glut-1 (2+) and p-53 (2+). The cytologic diagnosis was a metastatic adenocarcinoma of the ovary.

After 2 months the patient presented with more skin nodules. A CT scan of the chest/abdomen, showed lung and bone metastases as well. She was admitted 5 cycles chemotherapy with Caelyx and died after 1 year.

Second case

We report a case of a 64 years old woman, who was admitted to our hospital with an isolated skin nodule on the back measuring 1.9 cm × 1.8 cm. The patient had a known history of an ovarian serous papillary carcinoma grade II. Ten years ago she which was treated by a total abdominal hysterectomy, bilateral salpingo-oophorectomy and total omentectomy, as well as 6 cycles of chemotherapy with Taxol, Etyol and Emorzin. After 7 years of a disease-free interval an ECHO of the neck revealed enlarged lymph nodes and an FNA was performed showing a metastatic

adenocarcinoma of the ovary. Chemotherapy with Taxol and carboplatin followed and after 1 year brain metastasis and skin nodule on her back developed. An FNA with a 23o G syringe was performed and the material was processed by conventional method and thin layer cytology. The cytologic examination revealed inflammatory material with many malignant neoplastic cells, in papillary structures, with hyperchromatic nuclei prominent nucleoli and cytoplasmic vacuoles.

The following findings were observed on the cytological specimen on the microscope: atypia, hyperchromatic nuclei, increased nuclear/cytoplasmatic ratio and 3D clusters of atypical cells. Immunocytochemistry showed strong positivity for CA-125 (3+), vimentin (3+), mesothelin (3+) and CD-24 (3+) and the cytologic diagnosis was a metastatic adenocarcinoma of the ovary.

Radiotherapy of the skin nodule followed. The patient is still alive after 2 years of the skin nodule metastasis.

Discussion

It has been previously observed that ovarian carcinoma is the fourth most common origin of skin metastases in women after carcinoma of the kidney, breast and lung (5).

Clinical presentation of skin metastases differs from: isolated cutaneous nodule, multiple cutaneous nodules, cicatricial plaques and inflammatory metastasis (4). In other cases skin metastases have been observed in the periumbilical region as a “Sister Joseph’s nodules” (4). In our two cases, we had nontypical sites of metastasis: on the upper and lower extremities (1st case) and on the back of the patient (2nd case).

Several theories have been previously presented that explain the pathogenesis of skin metastases in ovarian cancer. These include the direct invasion from the underlying growth, accidental implantation of the tumor cells during surgical procedures and the contiguous extension of the tumor cells throughout lymphatics root. It has been observed in some cases direct development of skin metastases in surgical scars (6).

It has been previously reported that the median interval time between diagnosis of ovarian cancer and skin metastasis development is reported as 31.9 months (range, 4–77 months) in Dauplat’s series (5). However, there are cases where cutaneous metastasis is observed even 6 years after diagnosis of ovarian cancer (7). In our second case, we describe an even longer period (8 years) of the skin metastasis presentation.

It has been observed that skin metastasis is accompanied by a widespread intraperitoneal involvement in some cases and therefore, the appropriate approach to the patient should be the control of the abdominal disease. In the case of local cutaneous disease the best choice should be surgical resection (3). In the study by Cormio *et al.*, it was reported that a patient who had surgical excision of the skin metastasis had a prolonged median survival when compared to the median survival of a patient who treated with chemotherapy only (2). In the case of extensive cutaneous metastasis, the electrocoagulation has been successfully used. This method provides local control of pain, infection and hemorrhage, while on the other hand surgical excision might be impractical or there are cases where excessive morbidity was observed (8). Electron beam therapy has been applied in the case of large areas of the skin metastasis or, hematoporphyrin derivative injection with infrared phototherapy (8). However; these two treatment methods only provide local control (5). Until now there are no information regarding the efficiency of optimal treatment of ovarian cancer when diffuse cutaneous metastasis exists (5,9). Our two cases were treated by chemotherapy (1st case) and radiotherapy (2nd case), with good results in the second one.

It has been observed that the prognosis when skin metastases occur, is poor. The most important prognostic factor which is associated with survival is the interval time between diagnosis of ovarian cancer and documentation of cutaneous involvement (6). It has been reported that the overall survival after diagnosis of skin metastasis from ovarian cancer is given between 4 and 12 months (5,9). However; few patients had prolonged survived the diagnosis (7,10). In our cases, the survival time after the skin metastasis was 1 year in the first case and in the second case the patient is still alive after 2 years. Fine needle aspiration cytology (FNAC) is a safe, minimally invasive and rapid first-line investigation for assessing and confirming the diagnosis of skin metastasis from epithelial malignancies from known and unknown sites. A combination of FNAC and immunostaining may also help define the site of an unknown primary.

Cytological diagnosis of ovarian tumor is usually not difficult. Even in well-differentiated types of carcinoma, the smeared aspirate contains approximately spherical (papillary) groups of cancer cells, often with characteristic nuclear features, such as enlargement and hyperchromasia, large nucleoli and thickening of the nuclear membrane. Cytoplasmic vacuoles are often evident.

Immunocytochemistry often help to establish the

diagnosis of ovarian cancer with a panel of four main antibodies: CK7, Ca-125, vimentin and mesothelin. CK7 is an intermediate filament protein, found in most glandular and transitional epithelia. CK7 is expressed in epithelial cells of ovary, lung and breast. CA-125, a heterogenous cell membrane glycoprotein, is overexpressed in epithelial ovarian cancer cells (11). Vimentin is the characteristic intermediate filament type of mesenchymal cells and their corresponding tumors. In the ovarian serous papillary carcinomas vimentin is expressed in about 50–60% (11). Mesothelin is present on the surface of mesothelial cells, mesotheliomas, epithelial ovarian cancers and is expressed in about 85% of ovarian cancers. Other newly developed tumor markers expressed in ovarian cancer are: Glut-1 and CD-24.

Glut-1 is a useful marker that can be used as variable component of an antibody panel to distinguish reactive mesothelial cells from metastatic adenocarcinoma in particular adenocarcinomas of ovarian and pulmonary origin. Glut-1 is expressed in about 100% of ovarian cancers. CD-24 is a cell surface protein that appears to function as an adhesion molecule. High rates (83%) of CD24 expression detected by immunohistochemistry have been found in ovarian cancer. Its expression has been reported to correlate with poor prognosis in a variety of tumors (12). Also, immunocytochemistry could give more information about the type of ovarian carcinoma, while profile cytokeratins may be useful in this approach. Nonmucinous ovarian carcinomas typically showed a CK7+/CK20– phenotype while mucinous ovarian cancer are CK7+/CK20+ (11).

In our two cases immunoeexpression of the above mentioned markers (vimentin, CA-125, CK7, mesothelin), helped to establish the primary site. Thin layer cytology, due to the reproducibility of equivalent slides, facilitates the use of immunocytochemistry. The combination of FNA and thin layer cytology contribute to the accurate clarification of metastatic tumors with a known or unknown origin. Although, in most ovarian carcinomas, skin metastasis tend to appear late in the course of the disease and usually area associated with poor prognosis (13), in some cases the survival can be prolonged with appropriate therapy. So, an accurate cyto-immunodiagnosis is crucial for the best management of these patients.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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