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Rapidly progressive primary undifferentiated ovarian carcinoma: presentation of a rare case

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Summary

Ovarian cancer is the second most common gynecologic malignancy and is one of the leading causes of death among women. The disease course and the accurate diagnosis are correlated with the early detection of the lesion. About 5% of ovarian cancers are poorly differentiated and difficult to be classified, and are referred to as undifferentiated carcinomas. They are usually large, solid with haemorrhage and necrosis, bilateral, and very difficult to be histologically classified. Generally, cases with undifferentiated components are very rare. The authors present a case of a young female patient with a rapidly progressive undifferentiated ovarian carcinoma and a final unfortunate clinical result.

Key words: Ovarian cancer; Undifferentiated carcinoma; Necrosis.

Introduction

Ovarian cancer has the highest cancer mortality rate among women. According to Siegel *et al.*, in 2012 there were estimated 22,280 new cases of ovarian cancer and estimated 15,500 deaths [1]. Unfortunately, the majority (65%–75%) of women with ovarian cancer are diagnosed with advanced stage disease (III and IV), and only about 15%–20% of these women are free of disease recurrence at ten years [2-4]. The major histological subtypes of ovarian cancer, with several heterogeneous characteristics, include serous, endometrioid, clear cell, and mucinous [5]. Ovarian carcinomas often spread by direct extension, cell infiltration of the peritoneal cavity (tumour seeding), lymphatic infiltration to the pelvis and around the aorta, and finally, by haematogenous spread to distant organs [6]. The recent hypothesis regarding ovarian carcinogenesis supports that the carcinoma begins in the ovary by the dedifferentiation from a well to a poorly differentiated tumour, which subsequently spreads to the pelvic as well as to the abdominal cavity, before the further development of the distant metastasis. On the contrary, the development of secondary metastatic tumours, resistant to the conventional therapy, remains a major cause of morbidity and mortality [7]. The key to this evolution and, at the same time, to the increase of the survival rate is the development of the screening methods. Despite all efforts establishing screening methods for Stage I ovarian cancer early detection, there is no reliable screening system developed so far. Irregular wall thickening, large size of tumour, septa formation, presence of necrosis, and papillary protrusions only indicate the development of ovarian cancer [8-11]. The presence of papillary projections and solid portions in the tumour are known as the most predictive findings concerning the ovarian carcinoma. On the other hand, tumour size, depth of invasion, lymphatic infiltration, staging of the tumour, and Ca-125 count are correlating with prognosis of the lesion [12]. There are three types of tumour differentiation: high, middle, and poor types. The clinical characteristics of the poorly differentiated ovarian carcinomas are lymphadenopathy, organ infiltration, tumour seeding, and large amount of ascites [13]. Undifferentiated ovarian carcinomas have low survival rates and generally poor prognosis.

Case Report

The authors present a case of a 39-year-old female patient (gravida 1, para 1) with a history of one cesarean section. She came to the present Department complaining of pain located in the left inguino-femoral region and presence of edema at left talus. The physical examination revealed a solid palpable mass at her lower abdomen. A transvaginal ultrasound was performed and revealed the presence of an ovarian mass of a maximum diameter of nine-cm at the left ovary, filled with papillary protrusions and septa formations. The tumour markers were negative for malignancy. Additionally, the vein triplex ultrasound of the lower extremities showed an enormous mass at the left iliac fossa, which encircled the left external iliac vessels 5.5 cm in length. The left eternal iliac vein could not be depicted. The possibility of infiltration or thrombosis was high; therefore, the subject received low dose of heparin as inpatient. From the detailed preoperative tests,

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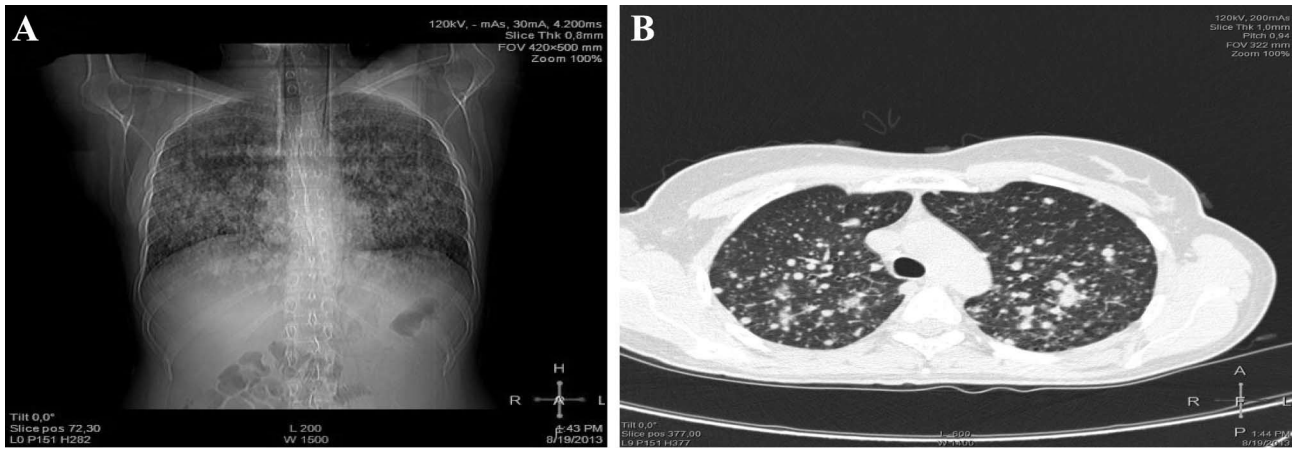

Figure 1. — (A) Thorax X-ray. Multiple metastatic lesions. (B) Thorax CT. Multiple metastatic lesions.

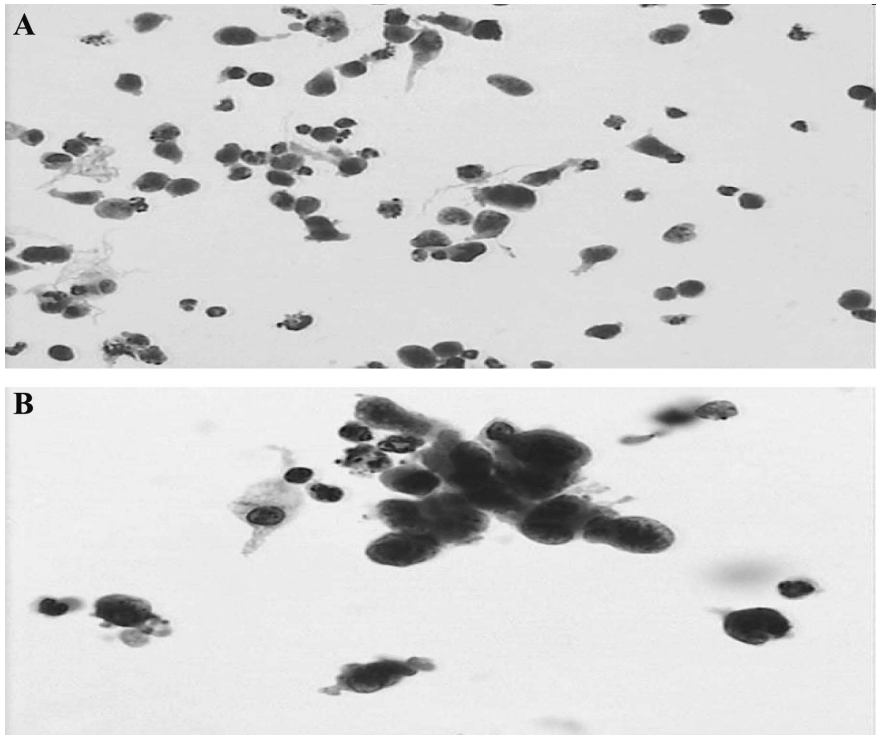

Figure 2. — Undifferentiated ovarian carcinoma. Very atypical cells, isolated, and in groups with lack of any architectural structure. (A) ThinPrep smear (Papanicolaou stain ×200). (B) ThinPrep smear (Papanicolaou stain ×400).

the chest X-ray revealed multiple and disseminated lesions in the lung fields bilaterally (Figure 1A). The thorax–CT confirmed the imaging findings from the chest X-ray and the presence of several secondary lesions (Figure 1B). Additionally, there were three hypodense lesions found on CT, at the region of the right hepatic lobe, without any other peripheral outbreaks. An ultrasound guided fine needle aspiration from the tumour region was performed. The cytological report revealed an undifferentiated ovarian carcinoma with extensive necrosis. The smears were dominated by small and medium sized cells, lying mostly singly and in small clusters, without evidence of serous or mucinous differentiation (Figure 2). Atypical mitoses were also present. Neoplastic cells were focally positive for EMA, whereas ER, PR, Ca-125, LCA, CD34, CD 117, p53, S-100, vimentin, desmin, calretinin, actin, and cytokeratins AE1/AE3, CK7, and CK20 were negative. The tumour markers and especially the Ca -125 were increased. (Ca -125=114.6 U/ml, with normal range 0-35 U/ml). The imaging findings confirmed the advanced stage of the lesion. On the other hand, the patient, due to lung infiltration, developed low oxygen saturation. The direct result was a feeling of breathlessness and signs of cyanosis. The following day the oxygen saturation was low enough and an oxygen mask was settled. On the third day, the patient attended the ICU. There was a great effort to stabilize the patient's situation, not only through colloid and vasoconstrictor solutions, but also through oxygen therapy, unfortunately without any remarkable results. The development of the lesion was so progressive and rapid that the patient passed away on the forth day of her visit to the hospital.

Discussion

Ovarian carcinoma is one of the most lethal malignancies among women. It is estimated that there are more than 140,000 deaths per year worldwide [14]. Although many surgical techniques and chemotherapies have been developed for the treatment of ovarian carcinoma, the prognosis remains poor, with a five-year survival rate of 45% [15]. The majority of patients present with an advanced stage disease (III/IV). Symptoms of ovarian cancer are usually vague and may resemble symptoms of other diseases. This may make it difficult to diagnose ovarian cancer at early stages. Pap smear cannot be used for detecting ovarian cancer. The cause of ovarian cancer is still unknown. However, the following factors increase the chances of a woman developing ovarian cancer: age, history of child birth, and hormonal factors. Approximately 5% to 10% of women who are diagnosed with ovarian cancer usually have a family history with analogue increase of the developing risk of this cancer type [16]. Regarding the grade of differentiation, there is a classification of ovarian cancer in three subtypes. Undifferentiated or poorly differentiated ovarian carcinomas are generally large, solid tumours with haemorrhage and necrosis, often bilateral, and most of all histologically difficult to be classified [17].

Cases with predominantly undifferentiated component are rare and may contain parts of a recognizable subtype of carcinoma, often serous or endometrioid adenocarcinoma [18]. When strict pathological criteria are used, this diagnosis is very rare, comprising less than 1% of ovarian carcinomas. This neoplasm is so little differentiated that immunohistochemical reactions are negative for almost any marker and only focally positive for epithelial markers, like in the aforementioned case. Undifferentiated ovarian carcinomas generally have poor prognosis and eventful clinical status. Amidst them, there are few cases which reported the rapid and progressive development of the lesion. The latter should undergo surgical staging followed by debulking, for their survival rate to be improved. The aim of this study was to emphasize on the rapid and progressive course of the lesion.

Conclusion

In summary, undifferentiated ovarian carcinomas represent uncommon neoplasms and generally are under-diagnosed. Not only the prognosis, but also the survival rate is poor, indicating the rapid and progressive development of the lesion.

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