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An Ovarian Tumor Like No Other

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Case Report

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Abstract: Mixed ovarian tumors are rare. The association of a granulosa tumor with a mucinous adenocarcinoma is exceptional and has never been reported to our knowledge in the literature. We report the case of a 44 year old patient, who consulted for an abdominal mass. The radiological explorations showed the presence of an enormous ovarian tumor, after hysterectomy the diagnosis of mixed ovarian tumor was made by histological and immunohistochemical study. The treatment is essentially surgical.
Keywords: ovary, adenocarcinoma, granulosa, mucinous, immunohistochemistry

INTRODUCTION

BACKGROUND

Ovarian cancer is the second most common cancer of the female reproductive system and the leading cause of death from gynecologic malignancies.

The most common ovarian tumors are the epithelial ones, they mainly occur in women of childbearing age .Mixed ovarian tumors are rare, the coexistence of mucinous and granulosa cell tumor is more rare, only four such cases have been reported in the literature [1]. These four cases described an association of a granulosa tumor and mucinous cystadenoma. To our knowledge no cases of granulosa tumor associated with mucinous adenocarcinoma has been reported. We describe an unusual case of a mixed mucinous adenocarcinoma and granulosa cell tumor of the ovary, and discuss: the clinical and radiological characteristics, the histopathological results, and particularly the difficulties of the immunohistochemical analysis.

CASE PRESENTATION

Clinical history: A 44-year-old woman, flight attendant, with no past medical history, presented an abdominal discomfort associated with diffuse abdominal pain. Physical examination revealed a pelvic mass of hard consistency, fixed to both planes, very painful on palpation, without inflammatory signs or gynecological signs.

Radiologic and histopathologic findings: The ultrasound showed the presence of a cystic lesion measuring 35 x 12 cm and endocystic vegetationof the right ovary. The abdominal computed tomography showed the presence of a cystic lesion of the right ovary measuring 40 x 13 cm with endocytic vegetations without rupture of the ovarian capsule (Fig-1).

The carbohydrate antigen 125 (CA 125) was 139 U/mL (normal range <35 U/mL) and the alpha foetoprotein (AFP) was 25 ng/ml (normal range: 10-200 ng/ml).

The therapeutic decision was a radical hysterectomy with pelvic lymph node dissection completed with histological study.

Macroscopic examination revealed a cystic lesion of 38 x 13 cm with brownish content, the wall contains fleshy areas measuring between 3x4 and 5x7 cm, with no exocystic vegetation, the capsule seems intact. Histological examination in a large sample (Fig-2) showed the presence of a tumor proliferation in double differentiation:

- First a papillary structures lined by cells with abundant eosinophilic cytoplasm and nuclei with marked cytonuclear atypia.
- Second a microfollicular architecture with abundant eosinophilic cytoplasm, hyperchromatic nuclei and some incised coffee bean, the nuclei were vesicular with numerous mitoses (10 mitoses per 10 high power fields x40)associated to call-exner bodies.

The ovarian capsule was intact

The tumor cells of the two sectors presented diffuse immunoreactivity for Cytokeratin (CK AE1/AE3). Epithelial membrane antigen (EMA) was positive for tubular structures, the inhibin was strongly positive for the second component. The Tumor cells showed no staining with calretinin (Fig 3 & 4). Thus, the diagnosis of mixed ovarian tumor associating mucinous adenocarcinoma and granulosa tumor was made

The surgical limits and the post-operative follow-up after adjuvant chemotherapy, were simple with a good clinical and radiological evolution.

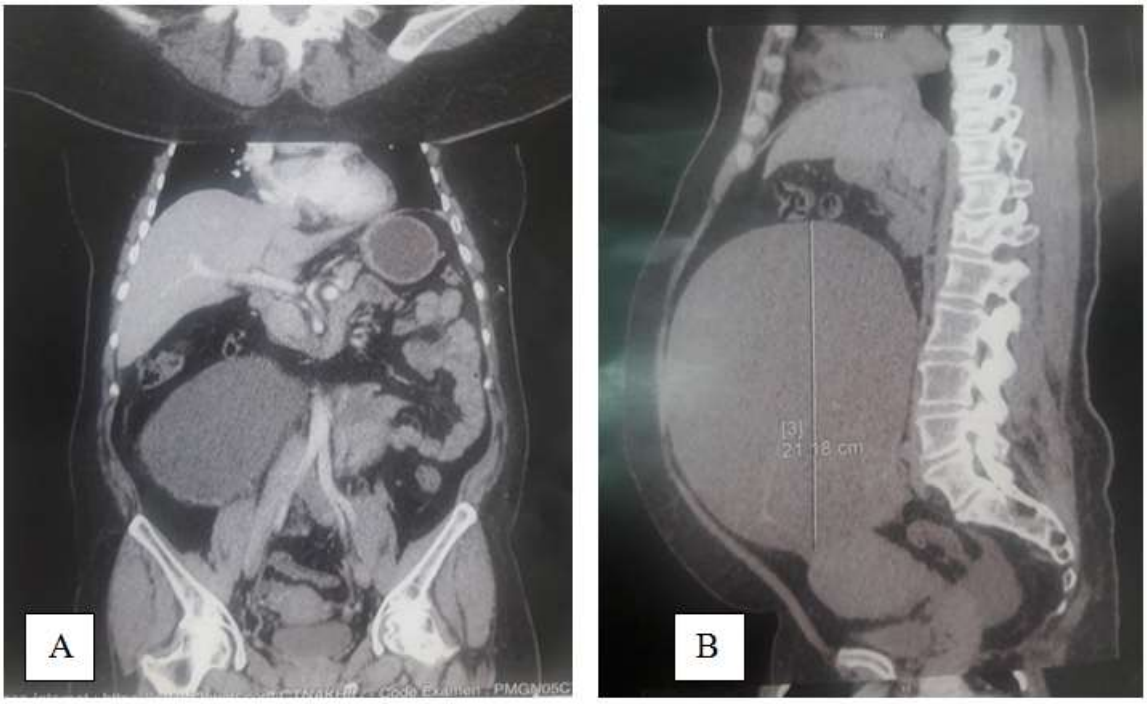

Fig-1: Abdominal scanner: Enormous right ovarian tumor A: Frontal section, B: Sagittal Section

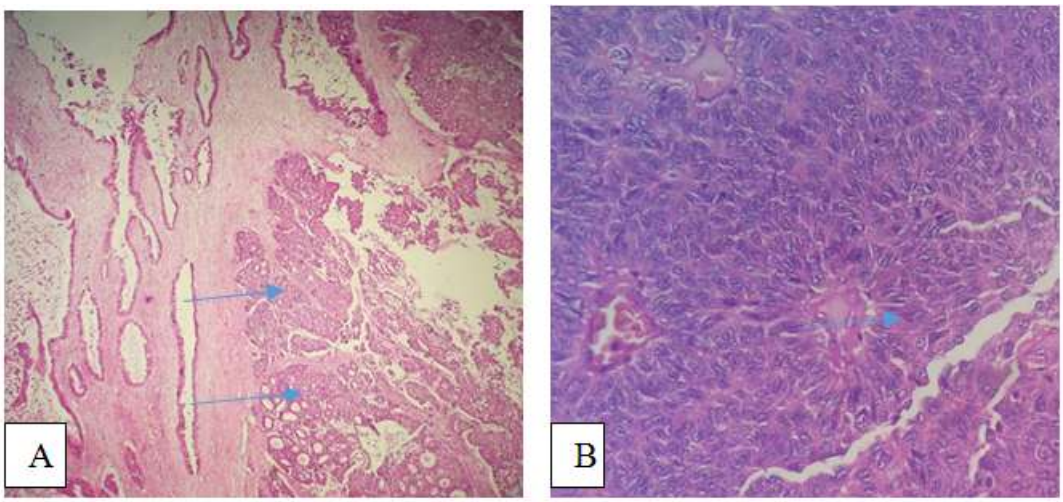

Fig-2: Microscopic appearance of the ovarian tumor. A: tumor proliferation by double differentiation in low magnification(x100) Granulosa tumor is indicated by the arrows. B: granulosa tumor showing the 'call exner 'bodies indicated by the arrow (x400)

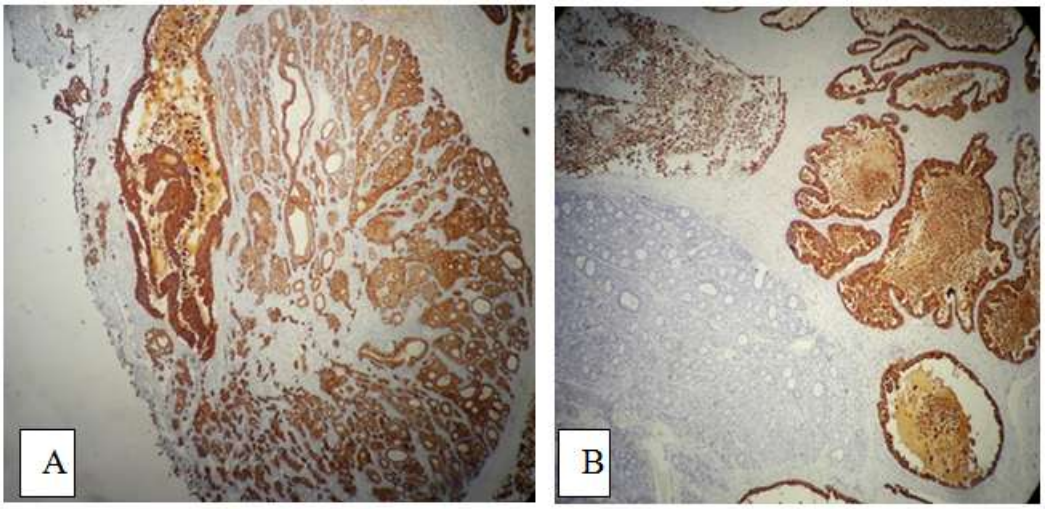

Fig-3: The tumor cells showed positivity in the membrane for (A) CKAE1/AE3, however (B) EMA is expressed solely by the adenocarcinomatous component.

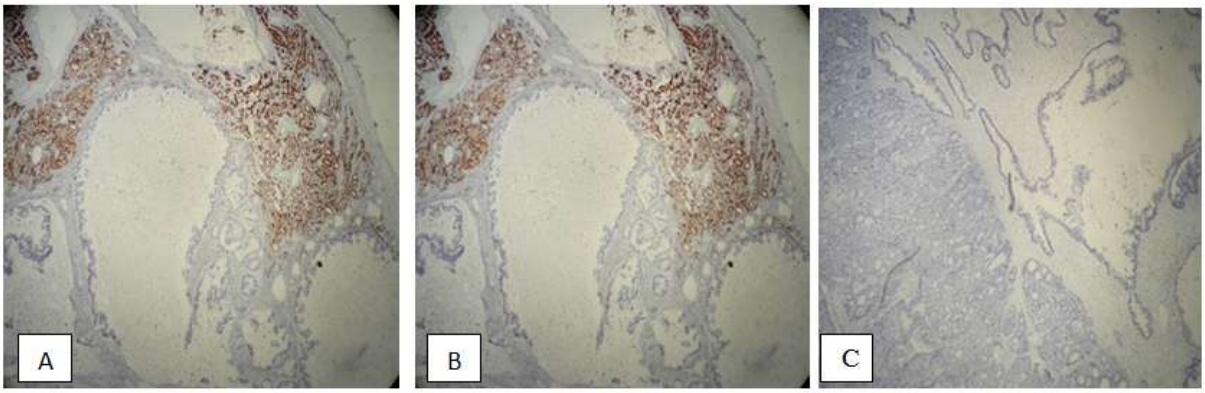

Fig-4: The tumor cells showed positivity in the membrane for vimentin (A) and inhibin (B) however, they showed negativity for (C) calretinin.

DISCUSSION

Ovarian tumors are more common in middle-aged women, given their retroperitoneal localization, these tumors are often diagnosed late, which complicates the treatment and the prognosis. Epithelial tumors are the most frequent and represent 2/3 of all ovarian tumors, they come from the surface coating, serous and mucinous tumors are the most common. Mucinous adenocarcinomas are proliferations of cells suggestive of the endocervical mucinous epithelium or intestinal surface. The cytological criterias of malignancy are associated with a stromal reaction, which is indicative of the invasive nature of carcinoma. The presence of invaded territories is often difficult to assert and requires the realization of multiple samples, because of the frequent association of benign, borderline and malignant lesions within the same tumor.

Granulosa tumors are rare neoplasms characterized by long natural history [2], which are seen especially in young adults, developed from cords and sexual stroma, these tumors are associated with a good prognosis compared with epithelial ones. They exist in two histological forms: an adult form (95%) and a juvenile form (5%), the last being observed mainly in young women, with more pronounced signs of malignancy and a high risk of recurrence [3, 4]. Histologically the adult form has five subtypes; the most frequent is the Microfollicular, characterized by the presence of "Call Exner" bodies with nuclei "coffee beans" [5, 6], there is often a reaction accompanying the proliferation of theca cells.

The coexistence of mucinous and granulosa tumor are extremely rare and only four such cases have been reported in the literature [1, 2], and these four cases reported an association of a granulosa tumor to mucinous cystadenoma or borderline. To our knowledge no cases of granulosa tumor associated with mucinous adenocarcinoma has been reported.

Histogenesis of associated mucinous tumors to granulosa tumors is not yet elucidated. Several studies suggest that the granulosa tumors originate from reactive stromal hyperplasia in the wall of the pre-existing mucinous neoplasm [7].

The diagnosis of mucinous adenocarcinoma is evident in our case, characterized by the presence of invasives papillar and tubular structures, however, the diagnosis of a granulosa tumor most often requires the use of immunohistochemistry. The main markers expressed by the granulosa cells are: Inhibin which is the most intensely positive marker, other markers are: desmin (2/3 of cases), CK AE1AE3 (1/3 of cases), SP100 (1/3 of cases). Calretinin may be positive but is less specific than inhibin. Recently, it was found that the cells in 90% express E-cadherin [4]. In our case the granulosa tumor strongly expressed the inhibin, wich is the most specific marker of this type of tumors, and the cytokeratin with a diffuse and intense staining, the tumor cells showed no expression to calretinin. The particularity of our case is the presence of an infiltrating component of adenocarcinoma that has never been described in the mixture mucinous and granulosa tumors. The prognosis depends on the adenocarcinomatous component: tumor stage, patient age, cytological atypia, mitotic index and capsule status.

Our patient is a flight attendant, the aircrews are a population exposed to a high dose of ionizing radiation, if the United Nations Scientific Committee for the Study of Ionizing Radiation estimates that the average annual dose of natural radioactivity per capita is 2.4 millisievert (mSv) [8], 16% of Aircraft crews are exposed to an average annual dose of more than 3 mSv in a study conducted by the French National Institute of Research and Security (IRNS) in 2012 [9]. The carcinogenic effect of ionizing radiation strongly demonstrated [10]. The histopathogenic study of radio-induced tumors could make it possible to describe new histological entities or associations that are still unclear.

The therapeutic management of this type of tumor requires a total hysterectomy with lymph node dissection followed by adjuvant chemotherapy and active monitoring [11]. The use of minimally invasive surgery has been increasingly used for the management of patients with mucinous ovarian tumors, even when they are quite large [12].

CONCLUSION

Mixed ovarian tumors are rare; the association of a granulosa tumor with a mucinous adenocarcinoma is exceptional. The diagnosis is anatomopathological, evoked by the histology and confirmed by the immunohistochemical study. The treatment include surgery and adjuvant chemotherapy. The prognosis is variable.

Competing interests: The authors have declared that no competing interest exists.

Author's contributions: MY drafted the manuscript and all authors read and approved the final manuscript.

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