A mediastinal germ cell tumor mimicking an ectopic pregnancy

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The objective is to report the case of a 36 year-old female with a primary mediastinal germ cell tumor mimicking an ectopic pregnancy. The patient under birth control pill presented, at seven weeks of amenorrhea, a β-human chorionic gonadotropin (β-hCG) level of 850 UI and uterine vacuity with left lateral uterine heterogeneous mass but no bleeding and no pain. She received left adnexectomy, uterine curettage and further treatment by methotrexate because of persistent high β-hCG markers. Computed tomography scan finally permitted to discover a voluminous anterior mediastinal tumor. We may recommend investigating patients with a simple chest X-ray that present with persistent increased β-hCG despite efficient ectopic pregnancy treatment.

Keywords: Ectopic pregnancy, Germ cell tumor, Mediastinum

INTRODUCTION

Mediastinal germ cell tumors are very rare, less than 0.5% of thoracic tumors. They occur in young patients, middle-aged 31, and only 3% are females (Epithor, database of the French Society of Thoracic and cardiovascular Surgery). They have poor prognosis, especially for the nonseminomatous germ cell tumors (NSGCT) with primary mediastinal localization [1].

Two theories have been proposed to explain the origin of these tumors. The first one is based on a stop of embryonic germ cells during their migration along the median line, and the second involves a reactivation of genes normally active only during the embryonic life that confers pluripotent properties to a few number of cells.

Germ cell tumors include three different histological entities: teratoma, with mature and immature forms, seminoma and NSGCT, with embryonic carcinoma, choriocarcinoma, responsible for secretion of β-human chorionic gonadotropin (β-hCG); and yolk sac tumors, which produce α-fetoprotein (αFP) [2]. Mixed tumors are frequent. The case herein reported emphasizes that mediastinal tumors may be responsible for pregnancy syndrome in women.

CASE REPORT

A 36-year-old smoking woman (16 pack years) with a past medical history of three pregnancies, appendectomy and cholecystectomy, referred to her physician with symptoms remembering her previous pregnancies. She was under birth control pill but presented with a 7-week amenorrhea and a β-hCG level of 850 UI. Her body mass index was of 18 and the physical examination revealed breast enlargement. A pelvic ultrasound exploration showed a uterine vacuity with a left lateral uterine heterogeneous mass. Even with no bleeding and no pain, ectopic pregnancy was suspected. She was referred to a
first gynecologic center where she underwent surgical treatment. Laparoscopic exploration detected a 4 cm left ovarian cyst, a voluminous hematoma of the left broad ligament of uterus nearby the left suspensory ligament, and voluminous left pelvic varicose veins. The hematoma was spreading along the left salpinx. To rule out ectopic pregnancy and as the hematoma was extensive, left adnexectomy followed by uterine curettage were performed. Despite surgical treatment, \( \beta \)-hCG increased from 850 to 900 UI, therefore medical treatment by methotrexate was prescribed.

Pathologic examination found no signs of ectopic pregnancy or malignancy.

Despite methotrexate treatment, \( \beta \)-hCG still increased to 1,335 UI two weeks later. She was referred to our center from this moment. An extragonadal germ cell tumor was suspected and a computed tomography (CT) scan was performed. It showed a voluminous anterior mediastinal tumor with no radiological compressive signs and no other extension site. \( \alpha \)FP and angiotensin-converting enzyme were negative. The review of the chest X-ray showed an evident anterior mediastinal tumor (Fig. 1).

After multidisciplinary agreement, biopsy through the mini-invasive right anterior video assisted thoracotomy was performed for neo-adjuvant chemotherapy adaptation to histological proof. Pathologic examination concluded a NSGCT with choriocarcinoma characteristics and reported positivity of \( \beta \)-hCG and placental alkaline phosphatase.

First line chemotherapy was based on etoposide, ifosfamide and cisplatin (VIP). In the meantime, we completed explorations with bone scintigraphy and cerebral scan. These detected no secondary localizations. Serum tumor markers were unchanged. Compliance to the four cycles of VIP was good under cover of antiemetic treatment. However, evaluation after four cycles of chemotherapy showed progression with appearance of liver metastasis in spite of decrease in \( \beta \)-hCG level (830 UI) and mediastinal mass volume to 30% of its previous volume. A second line salvage chemotherapy based on taxol and carboplatin was delivered. The tumor continued to aggressively metastasize throughout brain and bone. The patient died 16 months after her initial presentation as ectopic pregnancy (12 months after applying first line chemotherapy).

DISCUSSION

Germ cell tumors of the mediastinum are rare and are a very heterogeneous entity; they have poor prognosis and occur in young people. In addition, our patient presented the unusual characteristics. \( \beta \)-hCG is increased in only 30% to 35% of patients with NSGCT [3]. Therapeutic strategy is multimodal and is based on tumor markers. Two situations: 1) The level of \( \beta \)-hCG is over 5,000 UI or the level of \( \alpha \)FP is over 1,000 UI: no histological proof is required, diagnosis is NSGCT, and the treatment consists in preoperative chemotherapy (usually four cycles of bleomycin, etoposide and cisplatin [BEP]), followed by surgical resection; 2) The level of \( \beta \)-hCG is negative or under 5,000 UI and the level of \( \alpha \)FP is negative or under 1,000 UI: if the tumor is small and extricable at once, then surgical...
Treatment is recommended in the first place; if, the tumor is voluminous or inextricable, then it is necessary to proceed to a surgical biopsy to adapt multimodality treatment of the histology. The treatment combines chemotherapy; classically four cycles of BEP for NSGCT or four cycles of cisplatin for seminoma, with surgery, and sometimes further treatment by radiotherapy in case of seminomatous tumors [4].

Concerning our patient, surgical biopsy was doubtful since histological proof is no more required for administrating first line chemotherapy to patients with increased specific serum tumor markers and mediastinal anterior mass. Multidisciplinary tumor board decided an invasive biopsy because of the extremely low incidence of primary germ cell tumors of the mediastinum in females and because of a level of β-hCG under 5000 UI. In most of the patients with poor and intermediate-risk germ cell tumors, four cycles of BEP remain the standard therapy. The VIP regimen may be considered an alternative treatment for patients with underlying pulmonary disease [5]. In order to avoid pulmonary complications in this 16 pack years smoking young patient, oncologists proposed the VIP regimen, but this strategy may be discussed.

Determining relevant prognosis factors has been difficult to date, largely because of the low incidence of mediastinal germ cell tumors, but our patient definitely belonged to a poor prognosis group because of the non seminomatous histology [6]. This was consistent with her one-year survival. The most important single institution experience is Kesler’s one, published in 2002 and then in 2008 with a more important follow-up [7]. This study concerns 158 patients over 25 years and only three of them were women. No analysis was performed in this study in order to determine whether gender was a prognostic factor or not, nor in other series [8-10].

Our patient was treated for ectopic pregnancy [11]. According to the operative report, the surgeon who initially managed this patient considered that keeping the left adnexa was not an option because of the large spreading of the hematoma observed during the laparoscopic exploration. This strategy may be disputed. Ectopic focus was doubtful in the operative findings. A non-visualy confirmed diagnosis should be managed carefully. The surgical treatment applied to this patient involving salpingo-oophorectomy may be considered excessive. Another therapeutic strategy would have been to realize an ovarian cystectomy in order to manage the left ovarian lesion and to preserve the ovary in this young woman.

Persistently increased β-hCG during post treatment follow-up forced us to explore other hypothesis with a CT scan: abdominal pregnancy, germ cell tumor. Most patients who present with mediastinal germ cell tumors have symptoms of chest pain, short breath, cough, superior vena cava syndrome, asthenia or weight loss. Our 36-year old patient was asymptomatic. We did not mention the right diagnosis before the CT scan, while a simple chest X-ray would have been sufficient. We may also discuss to propose to include a preoperative chest X-ray for early detection of mediastinal tumors in the ectopic pregnancy management strategy. Even though this malignant pathology is extremely rare, the benefit of early detection may be worth the small dose of radiation induced by the chest X-ray in a woman that cannot carry a pregnancy for the moment anyway. However to date the French Society of Anaesthesiologists does not recommend systematic preoperative chest X-ray before this type of procedure in young patients with no history of pulmonary disease. Moreover, in our case there were four months between the first symptoms of pregnancy and the beginning of the suitable treatment (first line chemotherapy). This is a too long period to apply a treatment in such an aggressive and poor prognosis disease. Having a chest X-ray immediately after the unsuccessful surgical treatment of ectopic pregnancy may have saved two to three months. Chemotherapeutic agents may have been administered more promptly and may have limited the quick progression of the disease.

In conclusion, mediastinal primitive germ cell tumors are very rare in woman and evidently should not be considered as a differential diagnosis of ectopic pregnancy. But we may recommend investigating patients that present with persistent increased β-hCG despite efficient ectopic pregnancy treatment with a simple chest X-ray in order to rule out this rare but poor prognosis disease. This strategy may improve overall survival in these young patients by treating them earlier.

**CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

**REFERENCES**

1. Mead GM, Stenning SP. The International Germ Cell Consensus Classification: a new prognostic factor-based staging classification for metastatic germ cell tumours. Clin Oncol (R Coll Radiol) 1997;9:207-9.
2. Wakely PE Jr. Cytopathology-histopathology of the mediastinum: epithelial, lymphoproliferative, and germ cell neoplasms. Ann Diagn Pathol 2002;6:30-43.
3. Rivera C, Arame A, Jougon J, Velly JF, Begueret H, Dahan M, et al. Prognostic factors in patients with primary mediastinal...
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1. Kesler KA, Einhorn LH. Germ cell tumors, a surgical multicenter retrospective study. Interact Cardiovasc Thorac Surg 2010;11:585-9.

2. Kesler KA, Einhorn LH. Multimodality treatment of germ cell tumors of the mediastinum. Thorac Surg Clin 2009;19:63-9.

3. Kesler KA, Rieger KM, Hammoud ZT, Kruter LE, Perkins SM, Turrentine MW, et al. A 25-year single institution experience with surgery for primary mediastinal nonseminomatous germ cell tumors. Ann Thorac Surg 2008;85:371-8.

4. Kang CH, Kim YT, Jheon SH, Sung SW, Kim JH. Surgical treatment of malignant mediastinal nonseminomatous germ cell tumor. Ann Thorac Surg 2008;85:379-84.

5. Hinton S, Catalano PJ, Einhorn LH, Nichols CR, David Crawford E, Vogelzang N, et al. Cisplatin, etoposide and either bleomycin or ifosfamide in the treatment of disseminated germ cell tumors: final analysis of an intergroup trial. Cancer 2003;97:1869-75.

6. Hainsworth JD. Diagnosis, staging, and clinical characteristics of the patient with mediastinal germ cell carcinoma. Chest Surg Clin N Am 2002;12:665-72.

7. Kesler KA, Rieger KM, Hammoud ZT, Kruter LE, Perkins SM, Turrentine MW, et al. A 25-year single institution experience with surgery for primary mediastinal nonseminomatous germ cell tumors. Ann Thorac Surg 2008;85:371-8.

8. Kang CH, Kim YT, Jheon SH, Sung SW, Kim JH. Surgical treatment of malignant mediastinal nonseminomatous germ cell tumor. Ann Thorac Surg 2008;85:379-84.

9. Ganjoo KN, Rieger KM, Kesler KA, Sharma M, Heilman DK, Einhorn LH. Results of modern therapy for patients with mediastinal nonseminomatous germ cell tumors. Cancer 2000;88:1051-6.

10. Hartmann JT, Nichols CR, Droz JP, Horwich A, Gerl A, Fossa SD, et al. Prognostic variables for response and outcome in patients with extragonadal germ-cell tumors. Ann Oncol 2002;13:1017-28.

11. Farquhar CM. Ectopic pregnancy. Lancet 2005;366:583-91.