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Case Report

Choriocarcinoma of the Lung

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ABSTRACT

Primary choriocarcinoma of the lung is an extremely rare condition with a fatal outcome in most patients. We report the case of a 31-year-old woman with cough, chest pain, and hemoptysis, whose chest radiograph displayed nodules in the right upper lobe. After study and an unsuccessful attempt at histological characterization of the lesions, exploratory surgery was indicated. The patient underwent lobectomy and lymphadenectomy after diagnosis of a malignant process in the intraoperative biopsy. The definitive diagnosis was choriocarcinoma. Gonadal involvement was ruled out and the patient was referred to the oncology department for adjuvant therapy. She remains free of disease after 42 months.
Although choriocarcinoma of the lung is extremely rare and it is hard to establish a standard treatment, in cases of localized disease, surgical resection followed by chemotherapy seems to be useful and can achieve long survivals.

Coriocarcinoma de pulmón

Palabras clave:
Coriocarcinoma pulmonar
ß-HCG
Tratamiento

RESUMEN

El coriocarcinoma primitivo de pulmón es una entidad extraordinariamente infrecuente, con evolución fatal en la mayoría de los pacientes. Se presenta el caso de una mujer de 31 años con tos, dolor torácico y hemoptisis, en cuya radiografía se apreciaron nódulos en el lóbulo superior derecho. Tras estudio e intento de filiación histológica de las lesiones, sin resultado, se indicó exploración quirúrgica y se practicó una lobectomía más linfadenectomía tras el diagnóstico de malignidad en la biopsia perioperatoria. El diagnóstico definitivo fue de coriocarcinoma. Se descartó que hubiera afectación ginecológica y se remitió a la paciente a oncología para tratamiento complementario. No hay evidencia de enfermedad a los 42 meses.
Si bien esta enfermedad es muy rara y resulta difícil establecer un tratamiento estandarizado, en la enfermedad localizada parece útil la resección quirúrgica seguida de quimioterapia, con las que pueden conseguirse supervivencias elevadas.

Introduction

Choriocarcinoma is a malignant germ cell tumor characterized by a proliferation of syncytial cells and cytotrophoblasts, and by secretion of β-human chorionic gonadotropin (β-hCG). It can present in a gonadal site (associated with gestation) or, less often, in extragonadal sites. It affects young people of either sex though it is more common in women.

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Primary choriocarcinoma of the lung is an extremely uncommon variant of this tumor. A search of the medical literature yielded 28 cases, of which 16 were in women and 12 in men. We present the case of a woman diagnosed with such a tumor.

Case Description

A 31-year-old woman with no relevant history was referred to the pulmonology department with cough and pleuritic pain in the right subscapular region. She had also twice produced blood-tinged sputum. She reported no other symptoms and did not present wasting syndrome. The results of physical examination were normal. A nodule and infiltrate were apparent in the right upper lobe on the chest radiograph (Figure 1) and were studied further. Computed tomography (CT) revealed 3 pulmonary lesions in the right upper lobe—the largest measuring 2×2 cm in an anterior segment and the other 2 measuring 1×1 and 1.8×2 cm—and a hilar lymph node on the same side measuring 1.5 cm. The results of all laboratory analyses performed (complete blood count, coagulation, biochemistry, and urine) were normal and smear microscopy, culture, and sputum cytology, as well as the Mantoux text, and serology for atypical bacteria and human immunodeficiency virus were all negative or normal. The levels of carcinoembryonic antigens, α-fetoprotein, neurospecific enolase, cancer antigen [CA] 125, CA19/9, and CA15/3 were all normal, and antinuclear, antimitochondrial, and (antiproteinase-3 and myeloperoxidase) antineutrophil cytoplasmic antibodies were all negative. No lesions were apparent by bronchoscopy and both cytology and cultures of bronchial aspirate were negative. Necrotic material was found in fine-needle aspiration biopsy although this result did not aid diagnosis.

Tuberculosis treatment was started empirically and a positron emission tomography (PET)-CT scan was requested (Figure 2). Uptake was observed in the pulmonary nodules and the enlarged hilar lymph node but not in the rest of the body. The lesions had grown compared to the previous CT scan and so, given the lack of diagnosis, exploratory surgery was indicated, which was not contraindicated by the lung function tests. Right posterolateral thoracotomy was done and a biopsy was taken of one of the nodules. The intraoperative pathology report indicated a malignant tumor and so, as all lesions were located in the same lobe, a right upper lobectomy was performed, along with hilar-mediastinal lymphadenectomy. The pathology study revealed proliferation of cytotrophoblast-like cells with pronounced atypia, surrounded by syncytiotrophoblasts and accompanied by necrotic areas. Immunohistochemistry was positive for β-hCG. With this information, choriocarcinoma was diagnosed. The lymph nodes showed no histological abnormalities. When questioned about her gynecological history, the patient reported 1 normal pregnancy and birth and 1 miscarriage. The β-hCG level immediately after surgery was 643 (normal level <5).

The clinical outcome after surgery was satisfactory, and the patient was discharged and referred to the gynecology department to rule out gynecological disease and to the medical oncology department for adjuvant therapy. After confirming that there was no gynecological involvement, she received chemotherapy cycles of modified EMA-CO (etoposide, vincristine, and cyclophosphamide) until 1 month after β-hCG levels had returned to normal, which occurred 2 months after surgery. She attended regular follow-up visits during which she was asked about changes since the last visit, and underwent a physical examination and imaging studies (radiography, CT, PET-CT) and measurement of β-hCG. The patient is currently asymptomatic and in a good state of health. There was no evidence of malignant disease 42 months after starting treatment.

This was considered a primary tumor of the lung because we were unable to find any other affected organs and because concentrations of β-hCG returned to normal after treatment.

Discussion

Primitive extragonadal choriocarcinoma is very rare and when it does occur, it is usually in the mid-line structures, mainly the retroperitoneum, mediastinum, or cranial cavity, although other sites have been reported. One of the least common sites is the lung.[1-3] Unemori et al[1] reviewed all 25 cases of primary choriocarcinoma of the lung reported up until the time of writing and described a new case. We have found a further 2 cases described by Parikh et al in 2005[4] and Shintaku et al in 2006.[5] Such cases tend to occur slightly more often in women—of the cases reported 16 were in women and 12 in men, and our case also presented in a woman. The right lung is the one most often affected.

The origin of this type of tumor is not clear, although a range of theories have been put forward. Autopsies performed on women who died during birth or after miscarriage have found trophoblastic cells in pulmonary arteries, suggesting that choriocarcinoma of the lung in women could be due to pulmonary embolization caused

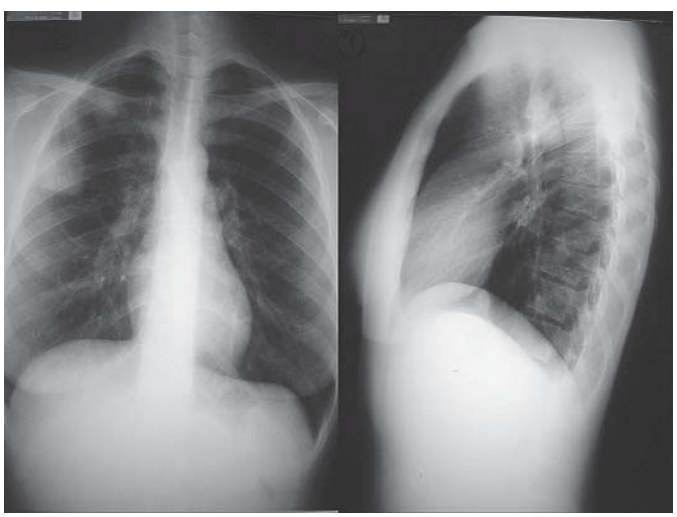

Figure 1. Plain chest radiograph.

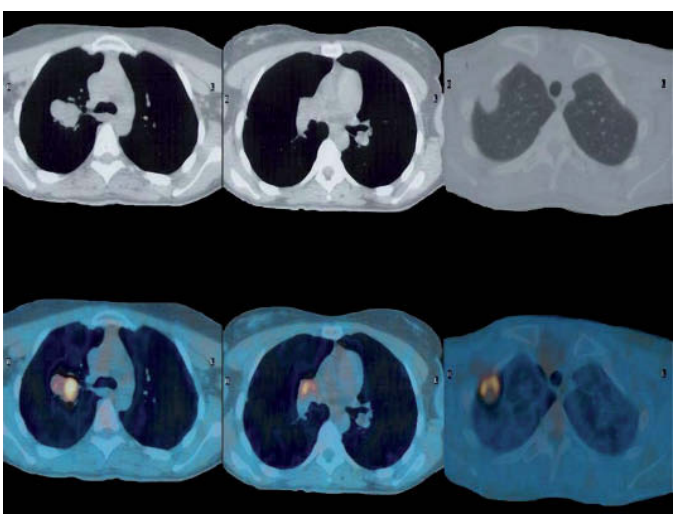

Figure 2. Positron emission tomography-computed tomography scan showing pulmonary lesions.

—during birth or miscarriage—by these cells, which might subsequently become malignant.[1,2] The tumor may even appear years later. On the other hand, there have been reports of such tumors in women who have never been pregnant and in men. This suggests that there is some other possible source, probably a gonadal tumor that had spontaneously regressed but not before metastasizing to the lung,[1,3,6] although the tumor should not strictly be considered as primary in this case. Another possibility would be the incomplete migration of germ cells during embryonic development; these cells would be retained in other organs and could then give rise to this type of tumor.[1,3,6] They might also originate from teratomas.[2,7] Finally, they might be a primitive carcinoma of the lung whose cells have differentiated into trophoblasts, a possibility supported by the observation that some pulmonary tumors produce β-hCG, as does choriocarcinoma.[1,2,8] Cases have been reported of coexistence of choriocarcinoma with other types of tumor such as pulmonary adenocarcinoma[8,9] and tumors of the digestive tract, particularly gastric tumors.[2]

The symptom most often reported is hemoptysis with or without cough, chest pain, and progressive dyspnea. Other signs such as gynecomastia or testicular atrophy in men, as well as wasting syndrome may also be present. Preoperative diagnosis is usually extremely difficult. Nodules, diffuse or micronodular infiltrates, and even pleural effusion may be observed on the chest radiograph. CT can identify the lung lesion better and assess whether enlarged lymph nodes are present. Fiberoptic bronchoscopy can also be done, although the result may be negative. Fine-needle percutaneous biopsy will often reveal cells considered as squamous. Definitive diagnosis is histological, after lung biopsy, although it is not uncommon to reach a diagnosis after analyzing the resected specimen when another type of tumor with a more common histology had been suspected. Sometimes, diagnosis is made at autopsy.

Treatment is the same as for non-small cell lung cancer. Surgery is the treatment of choice when locally advanced or distant disease is not present and there are no contraindications.[3,6] Surgery alone has not been associated with long survival,[1] and so chemotherapy is indicated whether or not surgery has been performed.[1,6] The most appropriate regimen seems to be bleomycin, etoposide, and cisplatin,[6-8] or EMA-CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine), and this was the regimen administered to our patient (in modified form). As this is an uncommon disease, there are no standardized chemotherapy regimens.[6,7] This tumor is not very radiosensitive,[6,8] perhaps because of its limited differentiation.[8]

Measurement of β-hCG production is useful for diagnosis, follow-up, and prognosis of this tumor. Tsai et al[10] reported the case of a patient with suspected primary choriocarcinoma of the lung in whom measurement of β-hCG in urine aided diagnosis. In our case, we did not measure β-hCG before surgery because diagnosis had not been reached at that time and choriocarcinoma was not suspected. From a practical point of view, it is not perhaps a test that should be done systematically, as the tumor is extremely rare and its clinical course and radiological signs coincide, in principle, with any other primary lung tumor. A return to normal β-hCG levels after therapy is indicative of good response, and increasing levels may point to recurrence.[6] For monitoring and detection of recurrences, regular β-hCG measurements and radiological examinations should be performed.[8] We have not found any reference in the literature to the use of PET-CT as a diagnostic technique, although it seems a useful way to determine the extent of the disease, and may be used in the future to monitor these patients.

Unlike gonadal choriocarcinoma associated with gestation, prognosis of primary tumor of the lung is worse in view of its rapid progression and spread,[1] mainly in the lung and to the brain and kidneys.[6] The outcome is usually fatal and the prognosis poor despite treatment,[1,3,8] with survival of less than 1 year in most cases. According to Umemori et al,[1] mean survival is 5 months and the survival at 1 year 34.6% (9 patients). The 2 cases described previously also had a fatal outcome.[4,5]

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