Choriocarcinoma with pulmonary and cerebral metastases

Sierra-Bergua B, Sánchez-Marteles M, Cabrerizo-García J L, Sanjoaquin-Conde I

ABSTRACT

Choriocarcinoma is an aggressive tumour. Uncommonly, it spreads distantly, and rarely results in pulmonary and brain metastases. Its prognosis is generally good when treated. We report a 33-year old woman with fever, haemoptysis and asthenia. One month after the appearance of metrorrhagia, she was diagnosed to have choriocarcinoma with pulmonary metastasis. After chemotherapy, pulmonary images disappeared and human chorionic gonadotropin returned to normal. She was re-admitted with neurological signs ten months later, confirming recurrence of the disease with brain metastasis. She was treated with surgery and polychemotherapy, with a favourable outcome and disappearance of the disease.

Keywords: choriocarcinoma, human chorionic gonadotropin, metrorrhagia, trophoblastic disease

Singapore Med J 2008;49(10):e286-e288

INTRODUCTION

Trophoblastic disease is considered to be a condition that generally has a benign clinical outcome. Choriocarcinoma is part of this disease and acts as an aggressive tumour. It has the ability of local invasion in the uterus, and less frequently, at distance for blood spread to other organs. Consequently, the clinical signs can be very different, depending on the site of the lesions. It is characterised by causing autonomous secretion of human chorionic gonadotropin (HCG). The diagnosis can be complex, as the symptoms are varied. The treatment is mainly based on polychemotherapy, but sometimes surgery is required. The prognosis is usually favourable.

CASE REPORT

Our patient is a 33-year-old Caucasian woman, with a history of active smoking, and no other current disease. Date of her last vaginal childbirth was twelve months before the onset of symptoms, with two previous uncomplicated deliveries. Before the appearance of metrorrhagia after eight months from the last delivery, she had been referred to the gynaecology clinic, with regular examinations and diagnosis of uncomplicated uterine myoma with consistent endometrial biopsy. She was admitted to the hospital for fever, haemoptysis and asthenia starting two weeks before. Upon obtaining a complete clinical history, the patient reported regular contact with a kestrel at home.

A complete physical examination was performed, and laboratory and urine tests were requested, providing

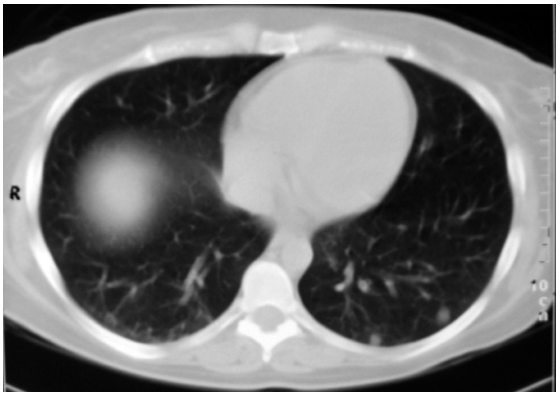

Fig. 1 Axial chest CT image shows multiple bilateral pulmonary nodules.

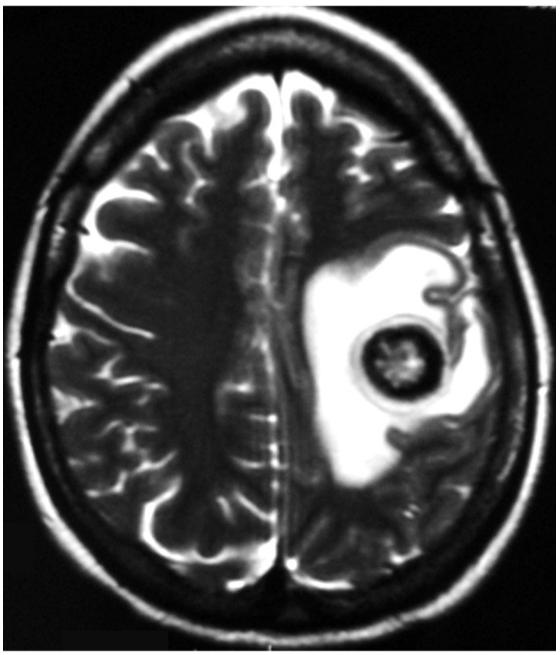

Fig. 2 Axial T2-W MR image shows a large left cerebral brain metastasis.

Department of Internal Medicine, Hospital Clínico Universitario "Lozano Blesa", Avda San Juan Bosco 15, Zaragoza 50009, Spain

Sierra-Bergua B

Sánchez-Marteles M

Cabrerizo-García JL

Department of Infectious Diseases

Sanjoaquin-Conde I

Correspondence to:
Dr M Sánchez-Marteles
Tel: (349) 9 7613 4823
Fax: (34) 9 765 645 61
Email: correomarta@inicia.es

Table I. WHO Classification and FIGO staging.

WHO CLASSIFICATION[7,8]

- Molar lesions
  - Hydatiform mole
    - Complete
    - Partial
  - Invasive mole
- Non-molar lesions
  - Choriocarcinoma
  - Trophoblastic tumour at the site of implantation
  - Other trophoblastic tumours
  - Exaggerated reaction at the site of implantation
  - Node at the site of placental implantation

FIGO STAGING*

Stage	Findings
I	Disease limited to the uterus.
II	Disease out of the uterus but limited to the female genital tract.
III	Metastasis in the lung with or without involvement of female genital tract.
IV	All metastasis at other locations.

* Stages I–IV are subdivided into A and B depending on the prognostic marker.
The classification is based on that adopted by FIGO in 1992, updated in the year 2001.[7,8]

no findings. The chest radiograph showed diffuse peripheral infiltrates in both lungs, and the thoracic computed tomography (CT) confirmed the existence of peripheral nodules of 15 mm diameter and areas of ground glass pattern (Fig. 1). Sputum samples were taken and several serological tests that were performed were negative. Given the respiratory symptoms and the radiological findings, respiratory function tests were ordered, which showed only reduced CO diffusion (DLCO). Bronchoscopy was normal. Given her past medical history of metrorrhagia, a gynaecological examination was requested, and revealed only a uterine myoma. The patient improved clinically without treatment and the symptoms leading to admission subsided, and radiologically, the lesions were more attenuated. She was discharged with hygiene measures at home and the kestrel was removed, given the suspect hypersensitivity pneumonitis, and pending serology tests to establish serum precipitins and perform challenge tests.

The patient was admitted again, this time to the intensive care unit, for fever, severe bleeding, severe anaemia and signs of low cardiac output. Nodules persisted on the chest radiographs. Beta-HCG levels were 151,000 mIU/ml, and together with biopsy of the cervix with atypical cells, she was diagnosed to have choriocarcinoma with possible pulmonary metastasis (stage IIIC FIGO and with 17 points in the World Health Organisation [WHO] classification scale). Therapy was started with six chemotherapy cycles, following the protocol with etoposide-metotrexate-actinomycin/cisplatin-etoposide (EMA-CE). Beta-HCG was undetectable, and the pulmonary lesions disappeared. In a second stage, hysterectomy and bilateral anexectomy were performed, with no complications.

Two months later, she was re-admitted for right hand paresis and the laboratory tests showed a beta-HCG level of 822 mIU/L. On CT and magnetic resonance (MR) imaging of the brain, left frontoparietal metastasis measuring 18 mm in size was seen, with marginal bleeding and surrounding oedema (Fig. 2). Given the recurrence of the trophoblastic tumour, the metastasis was resected, followed by administration of a triple polychemotherapy cycle, with the bleomycin-etoposide and cisplatin (BEP) regimen. The neurological clinical signs disappeared, as well as the beta-HCG, and she has been asymptomatic since then. The patient was currently regularly monitored in the outpatient clinic, without further detection of beta-HCG elevation or new symptoms over the past 16 months.

DISCUSSION

Trophoblastic disease includes a number of conditions: hydatiform mole that is a hydropic degeneration of chorionic vellosities, the invasive mole with the ability for local invasion, and choriocarcinoma that is anaplastic cuboid cytrophoblast epithelium and syncitiotrophoblast. The latter manifests as a necrotised mass, bleeding greatly inside the uterus, with high local aggressiveness and distant spread through blood. The risk of developing choriocarcinoma is exceptional before 20 years of age and increases significantly from 40 years onwards.[1] The diagnosis of this disease is more common in Asian countries, with an incidence

rate of one per every 2,000 pregnancies. The reviewed databases only include 150 cases of choriocarcinoma that show brain and pulmonary metastasis.[1-4]

Approximately 30% of the patients with choriocarcinoma show metastasis on diagnosis. In our case, it had spread to the lung and brain, which occurs in 50% and 10% of the cases, respectively. Other less common locations are the vagina (30%), liver and kidney.[5] In the series reviewed, it was preceded by a hydatiform mole in 60% of the cases, by previous miscarriages in 23%, primary in 5% and after full-term pregnancy in 10% of the cases.[4] Our patient started with clinical signs of intermittent vaginal bleeding several months after labour, but was not diagnosed until 12 months later. The diagnosis requires consistent clinical signs, beta-HCG levels produced by the syncytiotrophoblast and pathology with the presence of cyto- and syncitiotrophoblasts. Beta-HCG is necessary for the diagnosis, and is also useful for the follow-up in the detection of recurrence and as prognostic marker.

There are different scales that allow for staging the tumour, as it is necessary to establish its extension, and this will allow for establishing the diagnosis and choice of the most appropriate approach for the case. The WHO scale suggests that patients with scores over eight are considered a special high risk, and recommends starting therapy as soon as possible without ruling out the use of additional therapies such as surgery and radiation therapy.[6] Our patient had scored 17 points on this scale. The FIGO classification and TNM classification of the AJCC are other valuable classification scales (Table I).[7,8] A mitotic index over six, distant metastasis, endometrial invasion and diagnosis two years after childbirth are poor prognostic factors in the disease.[3,4]

The treatment of choriocarcinoma consists of polychemotherapy, including regimens that have generally shown to be beneficial with acceptable cure rates and low recurrences. Treatment with the EMA-CO regimen (etoposide, methotrexate, actinomycin/ cisplatin-vincristin) in a study performed by Bolis et al showed a 32-month survival of 88%, in patients at a high risk.[9] Swisher et al reported 28% complete remissions in their study.[10] The EMA-CE regimen is more potent than the abovementioned, and is considered to be a better option in case of disease with metastasis or recurrences.[11,12] Other options are BEP regimens and VIP (vimblastin, iphosphamide, cisplatin) that are considered as second-line options in cases of recurrence of disease progression.[13] Our patient received the EMA-CE regimen and BEP for recurrence.

The case of adjuvant radiation therapy is still controversial; some authors recommend holocranial irradiation with 30-40 Gy concomitantly with chemotherapy in the case of brain metastasis.[14,15] In a study of 78 patients with choriocarcinoma and brain metastasis, a survival of 50% in the group treated with radiation therapy and chemotherapy, vs. 24% in those receiving chemotherapy alone and 0% in those receiving no therapy. Surgery is considered a second option in patients with local, chemotherapy-resistant metastasis and in recurrences.[15] In summary, an uncommon case of choriocarcinoma is reported in a patient where the respiratory symptoms of the condition delayed the diagnosis, as the context of the clinical history made probable the possibility for other respiratory conditions. The appearance of brain metastasis despite optimum treatment is another distinct characteristic of the case.

REFERENCES

1. Shih IM, Kurman RJ. Placental site trophoblastic tumor-past as prologue. Gynecol Oncol 2001; 82:413-4.
2. Gillespie AM, Liyim D, Goepel JR, Coleman RE, Hancock BW. Placental site trophoblastic tumour: a rare but potentially curable cancer. Br J Cancer 2000; 82:1186-90.
3. Su YN, Cheng WF, Chen CA, et al. Pregnancy with primary tubal placental site trophoblastic tumor- a case report and literature rewiew. Gynecol Oncol 1999; 73:322-5.
4. Lathrop JC, Lauchlan S, Nayak R, et al. Clinical characteristics of placental site trophoblastic tumor (PSTT). Gynecol Oncol 1988; 31:32-42.
5. Small W Jr, Lurain JR, Shetty RM, et al. Gestational trophoblastic disease metastatic to the brain. Radiology 1996; 200:277-80.
6. Dubuc-Lissoir J, Sweizig S, Schlaerth JB, et al. Metastatic gestational trophoblastic disease: a comparison of prognostic classification system. Gynecol Oncol 1992; 45:40-5.
7. Ngan HYS, Benedet JL, Jones III HW, Bender HG, Pecorelli S. FIGO Staging and risk factor scoring for trophoblastic neoplasia. Int J Gynecol Obstet 2002; 77:285-7.
8. Kohorn EI. The trophoblastic tower of Babel classifications systems for metastatic gestational trophoblastic neoplasia. Gynecol Oncol 1995; 56:280-8.
9. Bolis G, Bonazzi C, Landoni F, et al. EMA/CO regimen in hich-risk gestational trophoblastic tumor (GTT). Gynecol Oncol 1988; 31:439-44.
10. Swisher E, Drescher CW. Metastatic palcental site trophoblastic tumor: long-term remission in a patient treated with EMA/CO chemotherapy. Gynecol Oncol 1998; 68:62-5.
11. Papadopoulos AJ, Foskett M, Seckl MJ, et al. Twenty-five years´ clinical experience with placental site trophoblastic tumors. J Reprod Med 2002; 47:460-4.
12. Newlands ES, Bower M, Fisher RA, Paradimas FJ. Management of placental site trophoblastic tumors. J Reprod Med 1998; 43:53-9.
13. Ajithkumar TV, Abraham EK, Rejnishkumar R, Minimote AL. Placental site trophoblastic tumor. Obstet Gynecol Surv 2003; 58:484-8.
14. Lurain JR and Brewer JI. Treatement of high risk gestational trophoblastic disease with methotrexate, actinomycin D and cyclophosphamide chemotherapy. Obstet Gynecol 1985; 65:830-6.
15. Rustin GJ, Newlands ES, Begent RH, Bagshawe KD, Weekly alternatin etoposide, methotrexate and actinomycin D and cyclophosphamide chemotherapy for the treatment of CNS metastases of choriocarcinoma. J Clin Oncol 1989; 7:900-4.