

# Choriocarcinoma with lung metastases during pregnancy with successful delivery and outcome after chemotherapy

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## Abstract

**A patient with an intrauterine pregnancy of 27 weeks had a coexisting pulmonary metastatic choriocarcinoma. On the chest radiograph the lung metastases appeared as pulmonary infiltrates, simulating atypical pneumonia. Serum human chorionic gonadotrophin levels were normal for gestational age. Treatment with methotrexate was successful. This is the first reported case of choriocarcinoma in a woman with a pregnancy of less than 35 weeks in which both mother and child survived. The case emphasises the need to consider choriocarcinoma in any pregnant woman who presents with haemoptysis and pulmonary nodules or infiltrates.**

Choriocarcinoma associated with a viable pregnancy is extremely rare. Metastases may be fatal before the diagnosis of choriocarcinoma is even suspected.<sup>1</sup> We describe a normal pregnancy coexisting with a metastatic choriocarcinoma of the lungs. Serum human chorionic gonadotrophin levels were normal for the period of gestation and the chest radiograph appearance suggested an inflammatory process rather than malignancy. Timely diagnosis of the disease is important for successful treatment and aggressive diagnostic procedures may therefore be warranted.

## Case report

A 36 year old woman with a 27 week pregnancy was admitted complaining of dyspnoea and haemoptysis in May 1987. During 1974-84 she had had seven term pregnancies and two spontaneous abortions. In July 1985 and March 1986 she had had further spontaneous abortions, both after 18 weeks' amenorrhoea. Her periods were then normal until October 1986, when she once again became pregnant. In December 1986 she had an episode of cough and production of green sputum. From the 13th to the 17th week of pregnancy painless

vaginal bleeding occurred. In March 1987 she became progressively more dyspnoeic and she consulted her physician when she developed haemoptysis. On admission she was breathless but not cyanosed, and had bilateral basal inspiratory crackles. There were no signs of infection. Arterial blood gas values were: pH 7.45, carbon dioxide tension 3.7 kPa, oxygen tension 10.6 kPa, oxygen saturation 96%. The size of the uterus was appropriate for 28 weeks' gestation. The serum human chorionic gonadotrophin level was 19 250 U/l (Abbott enzyme immunoassay), which was normal for the gestational age (range 5000-50 000 U/l). Chest radiography showed bilateral fluffy, fairly confluent densities simulating pneumonia. Ultrasound examination showed a normal placenta; no pathological abdominal mass was detected. Bronchoscopic inspection showed an oedematous mucosa with traces of blood. Cytological examination of secretions obtained during bronchoscopy suggested malignancy. Open lung biopsy was performed on the fourth day after admission despite her rapidly worsening condition and radiological progression of the alveolar infiltrates (fig 1).

Histological examination showed a high grade malignant tumour with necrotic areas and haemorrhage. The tumour was arranged in solid masses with papillary formations and consisted essentially of two distinctive cell types, one type compatible with syncytiotrophoblasts and another with cytotrophoblasts. Many cells proved to be positive for human chorionic gonadotrophin.

The patient was treated with intravenous methotrexate (fig 2a). Several hours later she had severe bilateral pleuritic pain, which could be suppressed only by high doses of morphine. Treatment was continued according to the protocol of the New England Trophoblastic Disease Center for low risk gestational trophoblastic neoplasms<sup>2</sup>—that is, methotrexate 1 mg/kg intramuscularly every other day for four doses and leucovorin 15 mg orally 30 hours after each dose of methotrexate. The courses are given every other week and are repeated twice after the serum human chorionic gonadotrophin levels have become normal. During treatment the serum human chorionic gonadotrophin levels fell to a plateau at 7000 U/l, which is low for the gestational age. Production of  $\beta$  subunits, measured by the IRE-Medgenix radioimmunoassay (normal < 1  $\mu$ g/l, range for gestational age 7-45  $\mu$ g/l), was disproportionately reduced, with a decline in serum  $\beta$  human chorionic gonadotrophin levels of 87%; but intact human chorionic gonadotrophin as measured by Hybritech assay (normal < 25 U/l, range for gestational age 6000-48 000 U/l) decreased also (fig 2b).

After the fourth course of methotrexate the cervix was ripened with local prostaglandin E<sub>2</sub> and labour was induced at 34 weeks. A healthy boy of 2000 g was born. Histological examination of the placenta showed no malignancy. Postpartum serum human chorionic gonadotrophin levels fell to normal (< 5 U/l) according to a log linear pattern (fig 2a). The chest radiograph became normal. Two years after

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Figure 1 Posteroanterior chest radiograph showing disseminated irregular, fluffy densities, mostly confluent, simulating pneumonia with fading of the heart figure and right diaphragm. There are no signs of cardiac failure, and no mediastinal or hilar masses are seen.



delivery mother and son are in good health and do not show any evidence of disease.

### Discussion

Choriocarcinoma is a relatively uncommon tumour and its occurrence during pregnancy is even more rare. Kuhn *et al*<sup>3</sup> found 28 published cases and added two of their own. The most common symptom is vaginal bleeding. A third of patients present with signs of metastases. Metastases occur frequently in the lungs (80%) and less often in the vagina (30%), pelvis (20%), and brain (10%).<sup>4</sup> Primary choriocarcinoma of the lung<sup>5</sup> and metastatic endobronchial tumour with bronchial obstruction and pleural effusion<sup>6</sup> have been described. There are three main types of pulmonary choriocarcinoma, all caused by haematogenous metastases.<sup>7,8</sup> Firstly, in 65–95% of cases

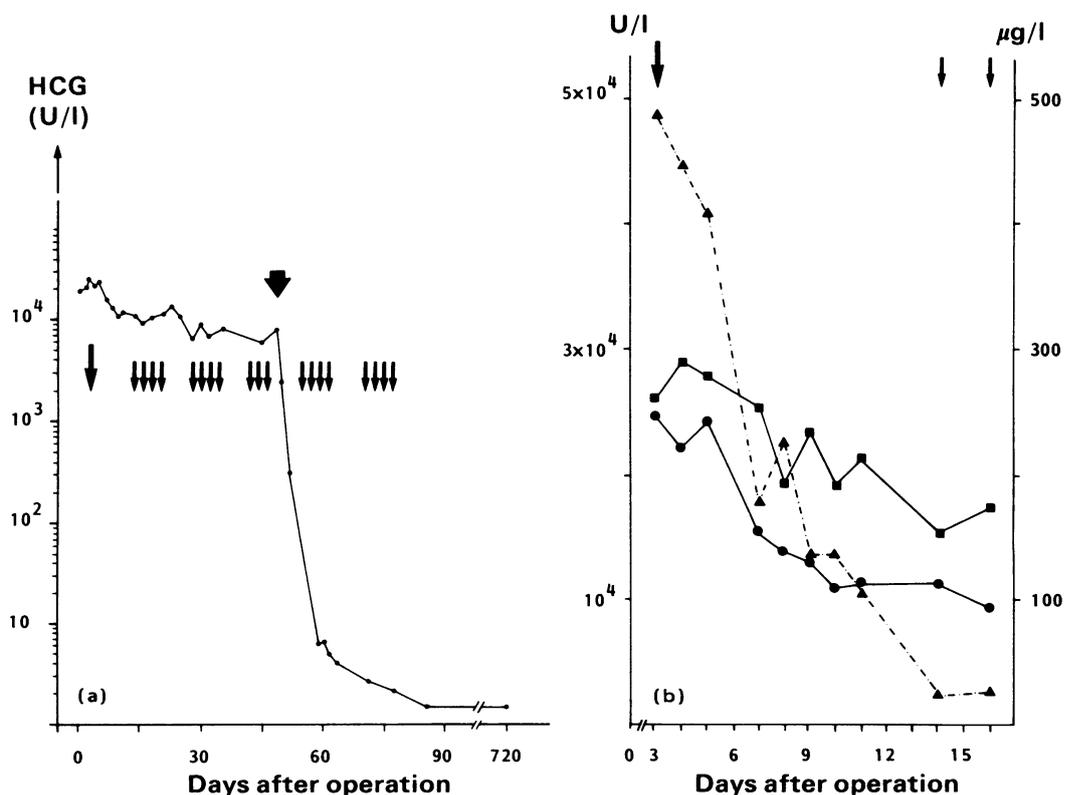
patients have well defined, round nodular lesions; usually less than 10 are present, and solitary nodules have been described. The nodules may cavitate. Secondly, in 5–15% of cases the radiological appearances have a miliary or alveolar pattern with indefinite borders simulating an inflammatory process. Progression of this type of lesion may be remarkably rapid, as in our patient. Thirdly, embolisation of the pulmonary artery by tumour metastases may cause infarction and pulmonary hypertension; although an incidence of 25% has been reported,<sup>8</sup> current experience suggests a figure of less than 1%.<sup>7</sup> These patients show no typical radiological appearance, though variable amounts of pulmonary shadowing and evidence of loss of lung volume may occur.

In choriocarcinoma serum human chorionic gonadotrophin levels are usually raised. This is not invariable, however—particularly in tumours that occur a long time after pregnancy. In the case of choriocarcinoma coexisting with pregnancy, where serum human chorionic gonadotrophin levels have been reported, they have been substantially raised except in one case, where levels were near normal.<sup>9</sup>

In our case histological examination of the lung biopsy specimen showed a tumour densely populated by cells containing human chorionic gonadotrophin. The serum human chorionic gonadotrophin levels were in accordance with the patient's gestational age, suggesting that the tumour mass was small; in that case the extensive lesions on the chest radiograph may represent haemorrhage, or else a tumour secreting little or no human chorionic gonadotrophin.

Treatment with methotrexate evoked a strong reaction, with chest pain probably

Figure 2 (a) Time course of change in serum human chorionic gonadotrophin as shown by the Abbott enzyme immunoassay (Abbott). ↓ 200 mg methotrexate, intravenous bolus injection; ↓ 75 mg intramuscular methotrexate. After delivery (↓) the values became normal. (b) Time course of serum human chorionic gonadotrophin after a single bolus injection of methotrexate (↓) on the third postoperative day, measured by different methods. The enzyme immunoassay from Abbott (●—●) measures intact HCG and β HCG subunits; the Hybritech enzyme immunoassay (Hybritech Europe, Liège, Belgium: ■—■) measures only intact human chorionic gonadotrophin, whereas the IRE-Medgenix radioimmunoassay (IRE-Medgenix, Fleurus, Belgium ▲—▲) measures predominantly β subunits with about 10% cross reactivity with intact human chorionic gonadotrophin.



caused by tumour necrosis and pleural irritation. The human chorionic gonadotrophin produced during the plateau phase (fig 2a) is probably derived from the normal placenta. The titre of  $\beta$  subunits, which are likely to be produced by the tumour, showed a disproportionately rapid decline, suggesting that this was due to tumour necrosis (fig 2b). The decrease of intact human chorionic gonadotrophin titres may be attributed to killing of tumour cells and perhaps to a negative effect of methotrexate on placental function, resulting in serum human chorionic gonadotrophin levels that were low for gestational age. Although the patient had a period of vaginal bleeding, histological examination of the placenta did not show any malignancy. This might be the result of chemotherapy, though ultrasound examination before treatment did not show any placental tumour. Spontaneous regression of primary choriocarcinoma has been reported, even when extensive dissemination was present.<sup>10</sup>

To our knowledge, only five cases of gestational choriocarcinoma coexisting with intrauterine pregnancy have been described in which both mother and child survived.<sup>11</sup> These cases occurred in pregnancies of 35 weeks or more, in which survival of the fetus could be expected. In our patient a choriocarcinoma was diagnosed at 27 weeks. After an aggressive diagnostic procedure adequate treatment was given and mother and child survived without evidence of disease or major toxicity.

Our case confirms that choriocarcinoma may

occur in an otherwise normal pregnancy. Pulmonary metastases may present as alveolar infiltrates. Choriocarcinoma should therefore be considered even when a primary tumour is not detectable and when serum human chorionic gonadotrophin levels are normal. Histological confirmation is essential for proper management.

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