Hydatidiform mole metastasizing to the lung

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Pulmonary lesions developed in three patients with an invasive hydatidiform mole. At open thoracotomy the nodules were found to contain molar tissue. Therapy with twice-weekly methotrexate induced complete clinical and biologic remission of the disease in all three patients.

Des lésions pulmonaires sont apparentes chez trois patientes atteintes d'une môle hydatidiforme envahissante. Il a été découvert à la thoracotomie que les nodules contenaient du tissu molaire. Le traitement, consistant en l'administration de méthotrexate deux fois par semaine, a entraîné une rémission clinique et biologique complète de la maladie chez les trois patientes.

Evidence of nonchoriocarcinomatous, villus-containing pulmonary metastases from a hydatidiform or invasive mole has been documented occasionally.1,2 The frequency of this complication can only be estimated, however, because patients with pulmonary metastases from a hydatidiform mole are usually treated without histologic verification of the pulmonary lesions.

In this communication we report three cases in which pulmonary lesions that proved to be composed of benign villous tissue developed after a molar pregnancy.

Case reports

Patient 1

A 17-year-old white woman was admitted to hospital in shock with massive uterine bleeding. Her uterus was enlarged to 3 cm above the umbilicus. While receiving blood transfusions she spontaneously passed 1500 g of histologically typical hydatidiform mole. Tissue from a curettage showed necrotic hydatidiform mole and decidua. A chest radiograph was normal. The patient recovered uneventfully and was discharged. Human chorionic gonadotropin (HCG) was not assayed in the urine.

Five months later a pre-employment chest radiograph showed several round pulmonary lesions and the patient was referred to the University of Alberta Hos-

pital for further investigation. At this time she was asymptomatic; normal menstrual periods had recurred 2 months after her previous admission. The uterus was soft and enlarged to a size consistent with a 7- to 8-week pregnancy; there were no other abnormal physical findings.

Routine hematologic and biochemical studies yielded results within normal limits. The patient’s blood group was A and her husband’s, B. Her HLA antigen profile was [2]8,12 for the two subloci; that of the husband was [1]8. Chest radiography confirmed the presence of four pulmonary lesions, the largest measuring 4 x 3 cm. Pelvic arteriography showed an increase in blood flow to the uterus, with an arteriovenous malformation involving the entire organ and extending outside its wall on both sides. Liver and brain scans were normal. The 24-hour urine HCG titre was 164 000 IU.

Open thoracotomy was performed with wedge resection of two subpleural nodules. Histologic examination of the nodules showed extensive hemorrhage with several degenerating villi covered by trophoblastic cells (Fig. 1), and a dense chronic inflammatory infiltrate and reactive fibrosis in the surrounding lung parenchyma.

Treatment with methotrexate, 20 mg/m² orally twice weekly, was continued for approximately 13 months. After 6 weeks of treatment a 24-hour urine HCG titre was 21 000 IU. Thereafter, the serum concentration of lutetotropic hormone (LH), immunologically crossreacting with HCG, was periodically determined by the radioimmunoassay technique described by Schalch and colleagues.3 After 5 months of treatment a pelvic examination yielded normal findings.

Although a pulmonary lesion remained visible after 1 year of continuous methotrexate treatment, therapy was discontinued because the serum LH values had been normal for 6 months. It was assumed that the lesion was inactive. At the time of this report the patient was in complete clinical remission, with a normal chest radiograph and normal serum LH values.

Patient 2

A 31-year-old East Indian woman presented with uterine bleeding. Her last regular menstrual period had occurred 6 months before, but two episodes of hemoptysis had occurred 2 months later and moderate uterine bleeding 1 month after that. Her uterus was soft and enlarged to 4 cm above the normal level. The patient’s areas were palpable and the fetal heart was not heard. There were no other abnormal physical findings. Shortly after admission she spontaneously passed 700 g of tissue histologically typical of hydatidiform mole and showing focal hyperplastic trophoblast.

Routine hematologic and biochemical studies yielded results within normal limits. The patient’s blood group was A and her husband’s, O. Her HLA antigen profile was [W29(T,63) and W32(T,59)]5 for the subloci; her husband’s profile was [28 and W32(T,59)]7 and [T,50(W5,1)1. Pregnancy tests with the Wellcome Pre-purex HCG were positive at a dilution of 1:64, equivalent to 192 000 IU/l of HCG. Multiple bilateral round lesions 1 to 2 cm in size were seen on the chest radiograph. A pelvic arteriogram was similar to that of Patient 1. Liver and brain scans were normal. At open thoracotomy, tissue was obtained by wedge resection of the subpleural lesion—a hemorrhagic nodule containing villi with slightly hyperplastic trophoblast (Fig. 2). Adjacent lung tissue was densely infiltrated by monocellular and fibrous tissue.

After 1 month of parenteral therapy with methotrexate, 20 mg/m² twice weekly, the uterus was still enlarged, but no villi or trophoblastic tissue was found by curettage; the chest radiograph still showed bilateral pulmonary lesions. Two months later, physical findings, chest radiograph and serum LH values were normal, and they remained so on subsequent follow-up. Methotrexate therapy was discontinued 3 months later.

Patient 3

A 33-year-old white woman presented with abnormal uterine bleeding, nausea and malaise. Her uterus was enlarged to

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FIG. 1—Patient 1. Degenerating molar villus in pulmonary subpleural nodule. Adjacent lung tissue is fibrotic and infiltrated by inflammatory cells (hematoxylin and eosin [H–E]; x1000).
about twice the normal size but no other physical abnormalities were found. Routine hematologic and biochemical studies yielded results within normal limits. The patient's blood group was O and her husband's, A. A pregnancy test was positive and the 24-hour urine HCG titre was 121 000 IU.

One month later uterine bleeding occurred and the patient expelled tissue histologically typical of hydatidiform mole. Despite suction and curettage uterine bleeding persisted and after 1 week an emergency hysterectomy was performed because of perforation of the uterus. Histologic examination of the uterus showed an invasive mole with few villi but severe trophoblastic proliferation (Fig. 3). At that time and 1 month later the chest radiographs were normal. However, 1 month later, bilateral round pulmonary lesions were observed and an open thoracotomy with resection of a pulmonary mass was carried out. The nodule was histologically similar to that of patients 1 and 2. Twice-weekly methotrexate therapy was begun the day the thoracotomy was performed. At the time of this report she was in complete clinical and biologic remission.

Discussion

Histologic detection of neoplastic cytotrophoblast and syncytiotrophoblast without an intrinsic stroma is diagnostic of choriocarcinoma, whereas the finding in the uterus of a villous structure with stroma indicates benign disease. Attempts at precise histologic classification and grading have failed, however, to predict the metastatic or malignant potential of molar tissue. Indeed, pulmonary metastasis may occur whether the diagnosis from uterine tissue is hydatidiform mole, invasive mole or choriocarcinoma. These trophoblastic neoplasms are now viewed as representing a biologic continuum, each being capable of merging into the more aggressive or malignant forms. HCG is a more reliable marker of biologic behaviour of a mole since it reflects viable trophoblast.

The incidence of pulmonary metastasis, as evidenced by chest radiography, following molar pregnancy varies between 3.9 and 13.4% . Histologic verification of the nature of the pulmonary lesions has rarely been obtained. In a review of the English literature Meyer in 1966 was able to find only seven proven cases of nonchoriocarcinomatous lung metastases and added one personal observation. Four other documented cases have been reported recently.

In the three cases presented in this communication lung biopsy showed villi and trophoblastic tissue, from which the diagnosis of metastasizing mole was made. Chemotherapy with methotrexate cured all three patients.

As in our first case, a pulmonary lesion may still be visible on the chest radiograph long after the HCG or LH titre becomes normal, which indicates that the residual tissue was, in all likelihood, functionally inactive. Thus, HCG titres are a more accurate reflection of therapeutic efficacy than regression of the lung tumours, and remain the major factor on which the decision to discontinue therapy should be based.

We are indebted to Drs. T. Groves, J. McAllister and D. Asp from the Calgary General Hospital for permitting us to include patient 3 in our study.

References


Present trends in tuberculosis control

Although mass radiographic screening has traditionally been used in the control of tuberculosis, unselective mass radiography fails to detect new sources of infection in a community. Most epidemiologically dangerous cases of tuberculosis are detected not through screening but through the development of symptoms. This, as Toman (WHO Chron 30: 51, 1976) indicates, is not a new observation, but, together with the decline of the tuberculosis problem in industrial countries and the necessary reappraisal of the specialty of tuberculosis medicine, it does mean that time-honoured measures in tuberculosis control must change. The emphasis now has moved to selective mass radiography of persons considered to be at high risk (with radiographic abnormalities of unknown cause or previous active but inadequately treated tuberculosis) and to selective case-finding.

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