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Lesson of the week

Unusual case of choriocarcinoma occurring 12 months after delivery

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Choriocarcinoma should be considered in women of childbearing age with acute haemorrhage occurring even years after a normal birth

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Choriocarcinoma is a malignant tumour that arises from trophoblastic epithelium; it has an incidence of 0.05 to 0.23 per 1000 live births.¹ The most important risk factor, a history of hydatidiform mole, is present in only half of cases, and many cases occur after a normal full term pregnancy.² We report the case of a young woman with choriocarcinoma who presented with an intraperitoneal haemorrhage from splenic metastases. She also developed multiple pulmonary tumour emboli and haemorrhage from tumour infiltration. She is the first patient in the United Kingdom, so far as we are aware, to survive ventilation for this disease.

Case report

Twelve months before she presented with choriocarcinoma this 32 year old woman had given birth by normal vaginal delivery to a boy, the second of two children. At both 3 and 6 months before presentation she had had two transient ischaemic episodes (attributed to protein S deficiency) affecting the right middle cerebral artery. Shortly after beginning warfarin treatment for these attacks she had a left parieto-occipital haematoma; it was evacuated but she was left with right hemiparesis and she developed epilepsy after surgery. The bone flap was not replaced.

Two months after surgery she was admitted to hospital after several days of upper abdominal discomfort and nausea. She was mildly tachycardic, normotensive, and tachypnoeic. She had a diffusely tender abdomen and smooth hepatomegaly of 4 cm. Laboratory analysis showed modest neutrophilia, slightly raised serum urea, γ -glutamyl transaminase, and alkaline phosphatase concentrations. Within hours she became anaemic and went into shock. She subsequently needed a blood transfusion. She had no external blood loss, and upper gastrointestinal endoscopy gave normal results.

The next day abdominal ultrasonography and aspiration identified free intraperitoneal blood, numer-

ous focal liver lesions, and a subcapsular splenic haematoma. A pelvic ultrasound scan was normal. Angiography showed the liver lesions to be vascular, and a vascular pelvic lesion was thought to be either the normal uterus or an ovarian tumour. The next day multiple focal masses in the lungs that had not been seen in a chest x ray film and another mass in the right kidney were identified on computed tomography. The splenic lesion was confirmed as the source of continuing haemorrhage. Vascular metastases from an

Fig 1 Computed tomogram showing extracranial extrusion of right cerebral hemisphere as result of cerebral oedema. Extrusion is through site of evacuation of previous intracranial haematoma, which was not covered with bone flap after surgery

Fig 2 Serum concentrations of human chorionic gonadotrophin during drug treatment in patient with gestational choriocarcinoma. Doses were adjusted to account for grossly deranged liver function (EP=etoposide, cisplatin; ACE=dactinomycin, cyclophosphamide, etoposide)

undetermined primary or multiple haemangioma were considered the likely diagnosis, and she was transferred to the regional liver unit for further tests.

Biopsy of the liver guided by ultrasonography was initially unsuccessful. She developed haemoptysis and sudden opacity of the right lung in a chest x ray film. Bronchoscopy showed multiple bleeding lesions in the main bronchi. The diagnosis of choriocarcinoma was confirmed on biopsy of the liver guided by computed tomography and by serum concentrations of β human chorionic gonadotrophin of 20 000 IU/l. The patient was transferred to London for treatment.

By the time of transfer she had developed respiratory failure as a result of extensive pulmonary infiltration by the tumour, pulmonary oedema, and pleural effusion. She also had ascites and grossly abnormal hepatic function. Once respiratory function was stabilised, chemotherapy was started with reduced doses of etoposide and cisplatin to minimise the risk of the acute tumour lysis syndrome. Within a few days, however, her respiratory function had deteriorated as a result of tumour embolisation and pulmonary infarction and she required admission to the intensive care unit for ventilation by continuous positive airways pressure. By then she was grossly jaundiced as a result of both deteriorating hepatic function and intravascular haemolysis from coagulopathy. After two courses of etoposide and cisplatin her respiratory and hepatic functions began to improve. However, her coagulopathy proved difficult to control, and she developed extensive intrapulmonary haemorrhaging, which necessitated intubation and ventilation. While she was being ventilated she developed gross cerebral oedema, which would have proved fatal were it not for the expansion afforded by the absent bone flap (fig 1). Her stay in the intensive care unit was further complicated by the adult respiratory distress syndrome, Gram negative septicaemia, and pseudomembranous colitis. After six weeks and four courses of chemotherapy her coagulopathy had resolved, and her respiratory and

liver functions were improving sufficiently to permit extubation and transfer to the ward.

She began treatment with dactinomycin, cyclophosphamide, and etoposide alternating with etoposide and cisplatin every two weeks. The chemotherapy regimen was selected to avoid the potential hepatotoxicity of methotrexate, which is difficult to administer in cases of gross ascites because it is excreted renally. Serum concentrations of human chorionic gonadotrophin returned to normal after three cycles (fig 2). The patient had another pulmonary embolism, for which she was treated with low molecular weight heparin. She also developed transient cranial diabetes insipidus. Renal tubular dysfunction induced by the cisplatin caused persisting hypomagnesaemia which led to problems in controlling her epilepsy. Additionally, malabsorption compounded her electrolyte disturbances and her weight dropped to 44 kg. She gradually improved, though persisting hepatic dysfunction and ascites (probably due to portal hypertension from scarring around previous hepatic metastases) remained a problem.

Review of the results of coagulation studies from the time of her transient ischaemic attacks showed a modest reduction in both protein S and factor VII concentrations which could be explained by early liver dysfunction. More recent testing for thrombophilia showed normal results.

More than a year after diagnosis computed tomography showed persisting large intrahepatic cysts, at least one of which later ruptured intraperitoneally (fig 3). Her liver function has since improved considerably, and she has now returned to normal activity. Concentrations of human chorionic gonadotrophin remain below detection thresholds, which indicates continuing remission.

Discussion

This case illustrates the need for prompt diagnosis and awareness of the protean manifestations of choriocarcinoma. Choriocarcinoma may form brain emboli, which cause cerebral ischaemia⁵ and possibly intracere-

Fig 3 Computed tomogram of abdomen more than one year after diagnosis of choriocarcinoma. Darker areas show multiple large, intrahepatic, fluid filled cysts at site of previous hepatic metastases

ebral haemorrhage, especially in patients who are not taking anticoagulants. Unfortunately, the clot that had been evacuated from our patient was not available for retrospective histological examination. Her neurological problems, however, were probably the early signs of disseminated malignancy that went unrecognised rather than an independent disease process. We believe that the transient ischaemic attacks were caused by cerebral tumour emboli; computed tomography gave negative results, and the coagulation disturbance was minimal at that stage. The massive haemorrhage that occurred later could have been caused by a combination of cerebral metastasis and a deficiency in vitamin K dependent factors that was aggravated by treatment with warfarin.

The primary symptoms of choriocarcinoma are gynaecological in only 50% to 60% of postpartum cases; the most common symptoms are dyspnoea, neurological symptoms, and abdominal pain.³ The delay between birth and presentation may exceed that in our case: intervals of several years have been recorded.³ Choriocarcinoma metastasises readily—especially to lung, brain, and liver—and it can present with widely disseminated disease. The metastases are highly vascular, and cerebral and intestinal haemorrhage are recognised presentations, though splenic bleeding has been reported only rarely.^{6,7} Haemorrhage may be massive and life threatening, making early tumour diagnosis and vigorous support critical. Diagnosis is ideally on the basis of raised concentrations of human chorionic gonadotrophin and appropriate histology (to exclude other tumours that produce human chorionic gonadotrophin, such as those of the lung and stomach). Adequate tissue may

be difficult to obtain, so diagnosis may have to be on the basis of an appropriate clinical setting and high concentrations of human chorionic gonadotrophin. Serial testing of serum concentrations is essential in monitoring treatment and confirming remission. Monitoring of human chorionic gonadotrophin concentrations should be continued for life as late recurrences may occur.

Choriocarcinoma should be considered in any woman of reproductive age with widespread vascular lesions, metastases of unknown origin, or cerebral or intra-abdominal haemorrhage. Serum concentrations of human chorionic gonadotrophin should be measured in all such patients.⁴ Cure rates are high with chemotherapy even in widely disseminated disease, but treatment of choriocarcinoma after a live birth is associated with higher mortality. Eliminating the disease becomes more difficult as the time between pregnancy and the onset of treatment increases.²

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When I use a word...

Spurious words

Lexicographers don't always get it right. James Boswell tells how a woman challenged Samuel Johnson to explain why, in his dictionary of 1755, he had defined "pastern" as "the knee of a horse." [Johnson amended this error in the subsequent abridged version of 1756, in which pastern is correctly defined as "that part of the leg of a horse between the joint next the foot and the hoof."] Johnson's reply was typically robust: "Ignorance, madam, pure ignorance."

Among the almost 300 000 entries in the second edition of the *Oxford English Dictionary* a tiny minority (fewer than 400) are distinguished by being completely enclosed in square brackets. These rarities are spurious words, which James Murray originally included in the first edition to correct errors that had been perpetrated in other dictionaries—a sort of one-upmanship on the editor's part. Most of these spurious words arose through misprints or through the errors or misreadings of copyists or translators. For example, exidemic for epidemic, owing to the similarity between x and p in early handwriting.

Some, however, have interesting stories. For instance, dentize, defined as "to cut new teeth," was a misreading of "dentire" in *Sylvia* (1626), in which Francis Bacon recounted how "They tell a tale of the old Countesse of Desmond, who lived till she was seven-score yeares old, that she did Dentire, twice, or thrice; Casting her old Teeth, and others Comming in their Place." An unlikely tale? Well, the term "third dentition" has been used to

describe the eruption of teeth after the loss of all permanent teeth. Ooë (*Okajimas Fol Anat Jap* 1969;46:243-51) referred to some reported cases (attributed, however, to delayed eruption of supernumerary teeth) and also described a histological structure that he proposed was the precursor of a potential third dentition in man. Still, "third dentition" is more commonly used to describe false teeth.

A well known example in modern times of a spurious scientific word is "dord," defined in *Webster's New International Dictionary* as "density." The error was explained by the editor of *Webster's Third New International*, Philip Gove, in an article in *American Speech* (1954;29:136-8). An expert had sent the publishers a definition slip bearing the words "D or d, cont/density." "Cont," short for continued, meant that this would be one in a series of entries for the abbreviation "D," but it was misinterpreted to mean that the "D or d" should be read as a continuous string. And so "dord" was created. Gove thought it a pity that it was spurious, "for why shouldn't dord mean density?"

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We welcome articles up to 600 words on topics such as *A memorable patient*, *A paper that changed my practice*, *My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk.