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CASE REPORT

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Incidental choriocarcinoma confined to a near-term placenta

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Abstract A large solitary choriocarcinoma was found incidentally in a placenta from a 36-week gestation following caesarean section performed because of intrauterine fetal distress. Macroscopically, there appeared to be a large old infarct in the centre of the placenta proper. Microscopically, there was extensive central necrosis with a rim of viable trophoblastic tumour that had the typical morphology of choriocarcinoma. Although the tumour was floating within maternal blood and was also detected in direct contact with fetal vessels, no metastatic disease was reported in the subsequent $1^1/_2$ years either in the mother or in the child. Placental infarcts are often not examined histologically, and an intraplacental tumour may thus be missed. Central friability and an unusual colour should alert the pathologist and lead to histological clarification. The management of an incidentally discovered intraplacental choriocarcinoma should be an expectant one, consisting of extensive workup for any evidence of metastases and serial β-HCG measurements in both mother and child.

Key words Choriocarcinoma · Placenta · Infarct

Introduction

A normal pregnancy is the precursor of approximately 22.5% of cases of gestational trophoblastic disease (GTD) [8]. The detection of a choriocarcinoma in an otherwise normal placenta has rarely been reported, however [2–6, 9, 11].

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Clinical history

A 30-year-old primagravida at 36 weeks of gestation presented with intrauterine growth retardation (IUGR) of about 4 weeks on routine clinical check-up. She underwent caesarean section because of intrauterine fetal distress. Neither child nor mother showed any abnormalities. The placenta was examined in an attempt to find an explanation for the IUGR, and a choriocarcinoma confined to the placenta proper was found.

The mother and the neonate were then examined very intensely for metastases. No evidence of choriocarcinoma was found in the mother or the child. β-HCG levels were within normal limits and the postpartum decline was comparable to that in the average non-compromised post-gravid woman. Prophylactic chemotherapy was considered but not given because of the absence of metastatic disease, and a wait-and-see policy was adopted.

Mother and child have been well since the birth. Today, 18 months after the event, the mother is pregnant again.

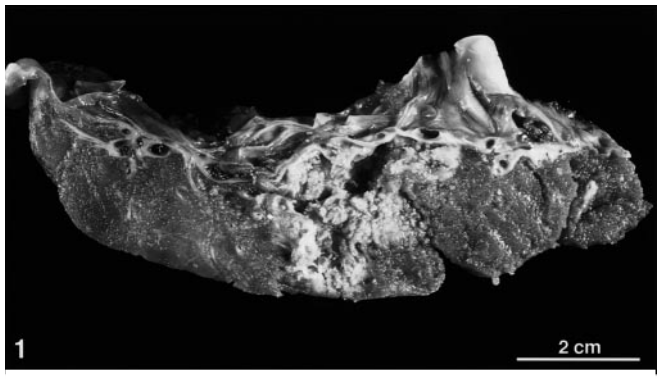
Materials and methods

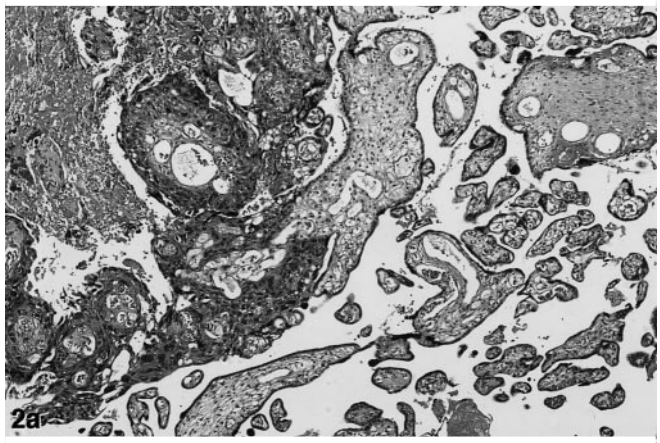
The formalin-fixed placenta and the membranes were routinely examined with inspection of the colour of the amnion and measurement of the placental weight and diameter and the length of the umbilical cord. The placenta was cut in 5-mm-thick slices, and representative samples were taken for microscopic examination. In haematoxylin and eosin stains, viable tumour was identified surrounding a necrotic centre. Additional immunohistochemical studies were performed on tissue from these blocks.

Tissue sections were incubated with antibodies against the β-chain of human chorionic gonadotropin (β-HCG; Biomedicals, BMA, Basel, Switzerland; dilution 1:200), human placental lactogen (HPL; DAKO, Copenhagen, Denmark; 1:400), placental-like alkaline phosphatase (PLAP; DAKO; 1:30), broad-spectrum cytokeratin (Pan-CK; BMA; 1:250), MiB-1/Ki67 (Milan Analytica, LaRoche, Switzerland; 1:10), collagen type IV (collagen IV 22; BMA; 1:25), and CD 31 endothelial cell (DAKO; 1:10). Visualization was performed using the peroxidase-labelled avidin–biotin technique (DAB Detection Kit; Ventana, Tucson, Ariz., USA). Negative and appropriate positive controls were run concurrently for each antibody tested.

Pathological findings

On gross examination, the placenta weighed 366 g and showed an oval configuration (16.5×15×2.5 cm).





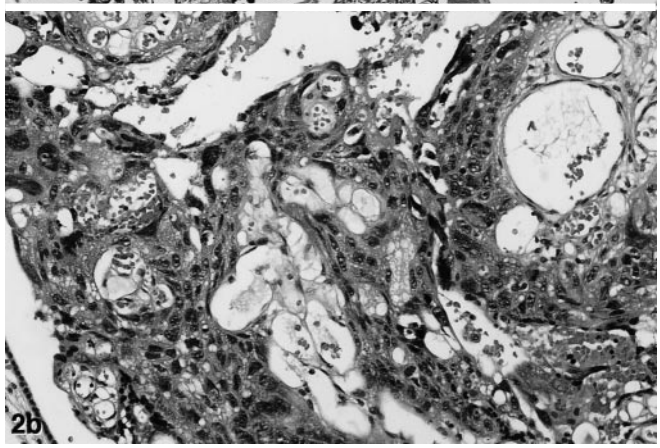


Fig. 1 Macroscopic view of the placenta with umbilical cord insertion: the cut surface shows a solitary yellow-tan area 3 cm in diameter, which is very friable in the centre

Fig. 2 **a** Histologically three zones can be distinguished (*left* to *right*): necrotic area, anaplastic cyto- and syncytiotrophoblast, and adjacent uninvolved mature villi. **b** Higher magnification of the lesion in **a**, showing the invasion of the villus stroma and the close proximity of the neoplastic cells and fetal villus vessels. There is no intravascular spread

The basal surface was complete, with regular distribution of maternal cotyledons. The 16-cm-long umbilical cord displayed three vessels on cross section and was centrally inserted. The placental membranes were normal.

When the placental parenchyma was cut a centrally located, yellow-tan, friable, and sharply circumscribed lesion measuring 3 cm in diameter was revealed (Fig. 1). Macroscopically it was interpreted as an old infarct.

Histologically the lesion showed the typical biphasic pattern of a choriocarcinoma embedded in an otherwise almost mature placenta. Three zones could be distinguished: a surrounding regularly dividing villous tree, an atypical cyto- and syncytiotrophoblast, and a central zone of necrosis (Fig. 2a). The viable rim of trophoblastic proliferation showed cytological pleomorphism of both the cytotrophoblast and the syncytiotrophoblast, with variation in nuclear size, increased nuclear-cytoplasmic ratio, and formation of anaplastic cells. The fibrous core of the adjacent villi was invaded by this malignant epithelial neoplasm (Fig. 2b). Examination of several specimens taken from sites at some distance from the lesion revealed no evidence of additional vascular spread. The neoplasm was restricted to the placenta proper, not having infiltrated the maternal basal plate.

Additional immunohistochemical studies confirmed the obvious trophoblastic origin of the neoplastic cells. The malignant syncytiotrophoblast was immunoreactive for Pan-CK, β-HCG, HPL, and PLAP. This reactivity was stronger than in the adjacent normal villi. Mitotic activity, as evidenced by MIB-1 immunoreactivity, was almost restricted to the cytotrophoblast, being most intense in the malignant component. Antibodies against collagen type IV and against CD31, both delineating the vascular wall, showed close apposition of tumour cells to fetal vessels but no frank invasion into the lumina.

Discussion

There are few case reports of intraplacental choriocarcinoma [2–6, 9, 11]. Those that have been reported can be divided into two major groups, according to the presence or absence of metastatic disease. Maternal metastases, primarily located in the lung and the brain, have caused death in over half of the cases [2, 3]. Evidence of maternal metastatic disease has been the most frequent indication for intense examination of the placenta for a primary tumour site, but in one case it was the presence of intraplacental choriocarcinoma that led to the identification of pulmonary metastases in the mother [9].

In five other cases and in this one, a choriocarcinoma confined to the placenta proper was found incidentally [4–6, 11]. The indication for examination of the placenta was fetal-maternal haemorrhage in two of the five cases, leading to fetal hydrops and intrauterine fetal death in one [5, 11]. In another, it was stillbirth [6]. In each of the remaining two cases a choriocarcinoma was found on ‘‘routine’’ examination of a third-trimester placenta [4, 6]. Further studies revealed no metastases in the mother or in the child.

The term ‘‘choriocarcinoma in situ’’, meaning a choriocarcinoma limited to the placenta without any evidence of metastatic disease, is sometimes used for this neoplasm [7]. We do not think this term is sensible, since it might suggest that the tumour is not capable of metas-

tasis at that stage. This is not appropriate, as consideration of the reports on metastatic choriocarcinomas occurring after term pregnancies will show [1].

In agreement with the other case reports, we found no vascular invasion on histological examination, but did find, for the first time, invasion of the villus stroma (Fig. 2b). However, there must have been some sort of villus vascular invasion in view of the reports of concurrent choriocarcinoma in both mother and fetus [12].

Other reports describe the lesion as ''limited to a single villus'' ranging up to 50 mm in diameter [3]. Those visible to the naked eye (most of them greater than 10 mm) were described as being red to grey-yellow with an extensive central friable area of necrosis. The macroscopic diagnosis was early or chronic infarct in all these cases. With the recently published guidelines for examination of the placenta developed by the Placental Pathology Guideline Development Task Force of the College of American Pathologists [10], most of these neoplasms probably would not have been detected for two reasons. The recommended sectioning of the placenta at approximately 1- to 2-cm intervals is likely to miss neoplastic areas less than 1 cm in diameter. (We agree with Vogel [13], who recommends an interval of about 5 mm). Secondly, the statement that ''isolated or very occasional small infarcts or thrombi, which have been clearly identified and described grossly, need not to be sectioned'' is in accordance with the general custom in placental pathology. With this strategy, visible lesions that might be trophoblastic neoplasms will be missed, but it is neither advisable nor practicable to section every apparent placental alteration. In our case the lesion would not have been overlooked on routine examination, but it might not have been sectioned. However, the friability and the yellow-tan discoloration of the lesion differentiate it from the typical morphology of an infarct and should raise some doubt in the mind of the pathologist. We recommend sampling lesions that have an atypical presentation, especially a central friable zone.

What does the diagnosis of an incidental intraplacental choriocarcinoma mean for the patient and the clinician? It is obvious that both mother and child should be checked for metastases, using imaging studies and serial β-HCG measurements. If there is no evidence of metastasis we agree with Duleba et al. that an expectant management should be recommended rather than prophylactic chemotherapy [5].

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