

Case Report

Identification of causative pregnancy of gestational trophoblastic neoplasia diagnosed during pregnancy by short tandem repeat analysis



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ARTICLE INFO

Article history:

Received 8 January 2014

Accepted 8 April 2014

Available online 18 April 2014

Keywords:

DNA analysis

Intra-placental choriocarcinoma

Placental site trophoblastic tumor

Pregnancy

Short tandem repeat

Introduction

Gestational trophoblastic neoplasias (GTNs) are tumors that arise from trophoblasts such as invasive mole, choriocarcinoma, placental site trophoblastic tumor (PSTT) and epithelioid trophoblastic tumor (Lurain, 2011). Invasive mole is a pre-malignant disease which occurs in 10–20% cases of hydatidiform mole. Choriocarcinoma and PSTT are malignant tumors which arise from the trophoblasts of any kind of pregnancy, including hydatidiform mole. It has been shown that the causative pregnancy of GTNs is not necessarily the immediately antecedent pregnancy using DNA analysis (Fisher et al., 1995).

GTNs which are detected during pregnancy are very rare and most of them are intraplacental choriocarcinomas. Although the causative pregnancy of GTN during pregnancy may be a concurrent pregnancy or a previous pregnancy, as an extensive examination of the literature shows that there is only one study which demonstrates that the origin of intraplacental choriocarcinoma was a concurrent pregnancy (Kanehira et al., 2013). In this paper the patients presented with PSTT and intraplacental choriocarcinoma, which were diagnosed pathologically in the 11th and 38th gestational weeks, respectively. To identify

the causative pregnancies, DNA analysis for 15 short tandem repeats (STRs) was performed using a commercially released kit.

Cases

Case 1 is a 37-year-old Japanese woman, gravida 8, para 6, who visited a local hospital because she found that she had become pregnant. Her last pregnancy ended in normal delivery at term and she had been having regular menstrual periods for two years. Pelvic ultrasonography detected a myoma (72 × 68 × 58 mm) and a normal sized fetus in a gestational sac. A hysterectomy was performed at the 11th week because the patient and her husband hoped for an artificial abortion and the myoma caused anemia. There was a 17 mm tumor in the myometrium next to the myoma macroscopically. Histological examination demonstrated that the tumor was composed of intermediate trophoblastic cells which invaded the myometrium in a sheet-like structure (Fig. 1B). The cells were positive for human placental lactogen (hPL) and weakly positive for hCG (Fig. 1C–D). Focal necrosis and extensive vascular invasion were seen in the myometrium. One mitotic figure per 10 high-power fields was observed. Diagnosis of PSTT was strongly considered. All villi and trophoblasts in anchoring villi were normal (Fig. 1A). Serum hCG and hPL levels were 101.4 mIU/ml and less than 0.07 µg/ml on the 14th postoperative day, and decreased with time after surgery. There has not been any clinical evidence of recurrence for over 18 months.

Case 2 concerns a 31-year-old Japanese woman, gravida 6, para 3, who became pregnant naturally. Her last pregnancy ended in spontaneous abortion and she had been having regular menstrual periods for a year. She had an ultrasound examination once or twice a month. Melena started at the 35th week which caused severe anemia. An emergency Cesarean section was performed at the 38th week and a tumor was found in the jejunum. Pathological examination showed that a small part of the placenta and the tumor of the jejunum consisted of malignant trophoblasts like syncytiotrophoblasts, cytotrophoblasts and intermediate trophoblasts. Necrosis and hemorrhage were found more in the jejunal tumor than in the placenta (Fig. 1E–F). These cells were positive for hCG strongly and the pathological diagnosis was made as choriocarcinoma. MRI, CT scans and colonoscopy showed that choriocarcinoma had spread to the brain, the lung, the liver, the ileum and the colon, as well as the myometrium. The patient had chemotherapy with MEA

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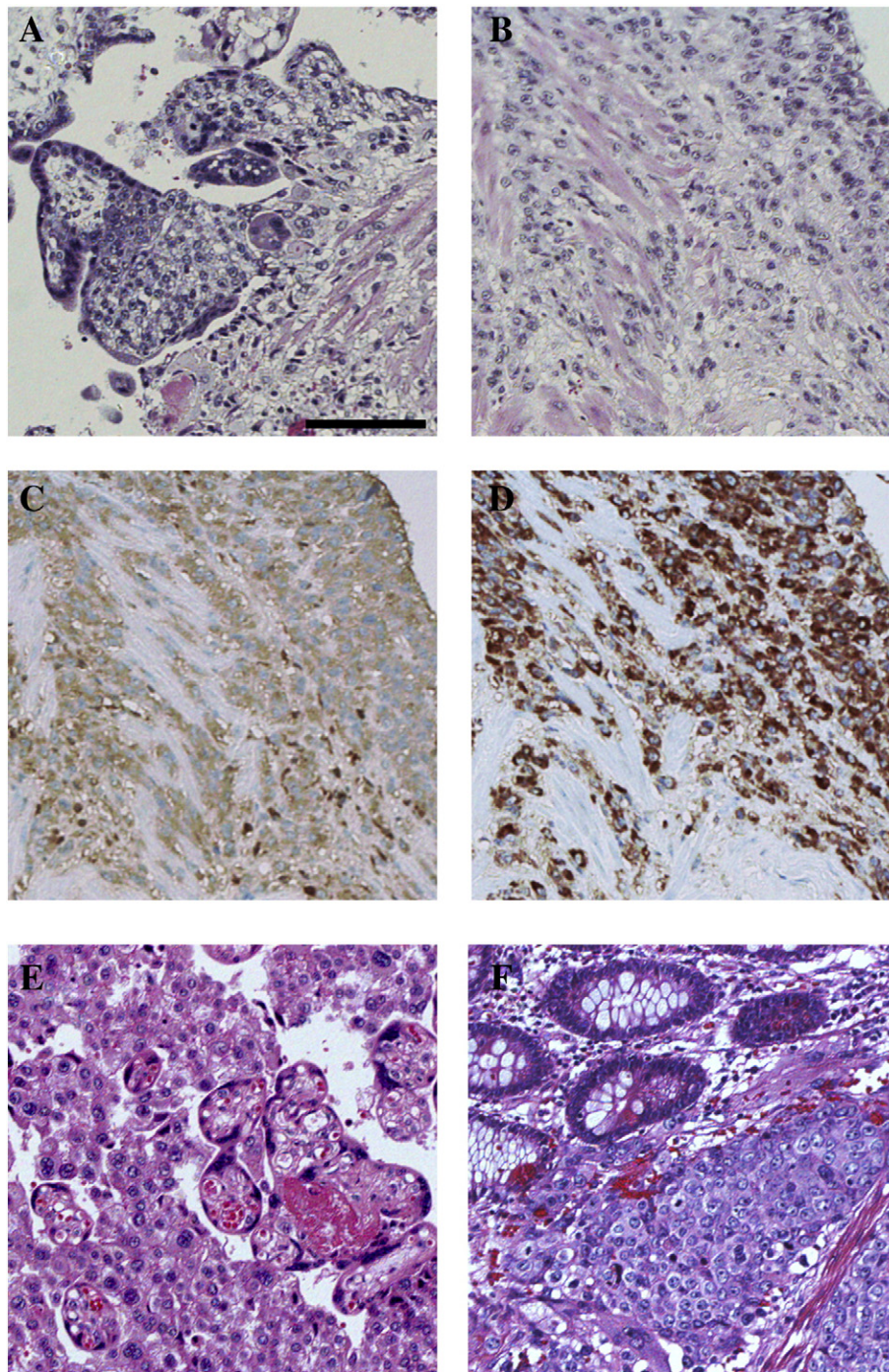


Fig. 1. Histological features of PSTT during pregnancy (A–D) and intraplacental choriocarcinoma (E–F). (A) Intermediate trophoblasts invading from anchoring villi into the myometrium were of normal appearance (H&E). (B) The tumor was composed of intermediate trophoblastic cells with atypia and myometrium invasion (H&E). Cells were positive for (C) hCG and (D) human placental lactogen in immunohistochemistry. (E) Choriocarcinoma in the placenta and (F) in the jejunum showed avillous trophoblastic proliferation and atypia (H&E). $\times 100$ magnification, scale bar = 100 μm .

therapy (methotrexate, etoposide and actinomycin-D) and whole brain radiation. The patient achieved remission after seven cycles of chemotherapy, received four additional cycles for consolidation, and has been in remission for 18 months.

To identify the causative pregnancies of the two cases, STR analysis was performed. This study was approved by the ethics committee of Nagoya University Graduate School of Medicine. Informed consent was obtained from the patients and their partners. Genomic DNA was extracted from parental oral cells and microdissected tissue of villi and

GTNs from paraffin sections. DNA was amplified with 15 STR markers and a gender-determination marker. The villous and PSTT allotypes showed a complete match in all 16 loci analyzed (S1). These results suggest that PSTT arose from the concurrent pregnancy. In case 2, the results of STR analysis in 14 loci were informative (Table 1). The results of the choriocarcinoma in the placenta and the jejunum were the same as the results of the villi in nine loci but different in five loci. These results suggest that choriocarcinoma originated not from the concurrent pregnancy, but from one of the previous pregnancies.

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