DNA polymorphism analysis of a pure non-gestational choriocarcinoma of the ovary: case report

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Summary

A 45-year-old nulligravida woman died from carcinoma peritonitis with choriocarcinoma arising in the ovary. This tumor was resistant to chemotherapy after debulking surgery. DNA polymorphism analysis was useful in proving the choriocarcinoma to be non-gestational carcinoma. In this paper, the clinical course and DNA polymorphism findings are mainly discussed.

Key-words: Ovary; Choriocarcinoma; Non-gestational origin; DNA polymorphism analysis.

Introduction

Ovarian choriocarcinoma usually appears as a component of a mixed germ cell tumor and a pure choriocarcinoma shows highly malignant behavior. A pure ovarian choriocarcinoma is rare and is more likely to be a gestational choriocarcinoma which has metastasized from a choriocarcinoma resulting from a uterine or tubal pregnancy, or has arisen from an ovarian pregnancy. It is difficult to differentiate a pure ovarian carcinoma with a non-gestational origin from a gestational one using histopathological investigations.

We previously reported DNA polymorphism analysis to be useful in determining the modes of origin in trophoblastic disease [1, 2]. In the present study, we proved that the tumor of this case was a primary non-gestational choriocarcinoma arising from the ovary. The patient expired due to carcinoma peritonitis as the tumor was resistant to chemotherapy after debulking surgery.

Case Report

A 45-year-old nulligravida woman was admitted to Fukuoka City Hospital in Japan in March 1997 with a painful abdominal mass. During an exploratory operation at Fukuoka City Hospital on April 7th, she was diagnosed as hairng ovarian cancer with carcinoma peritonitis. Biopsy specimens from the affected right ovary were diagnosed as choriocarcinoma. She was thereafter transferred to Kyushu University Hospital to undergo further treatment on April 25th. At admission to our ward, a chest X-ray showed bilateral multiple lung metastatic lesions. A CT scan revealed multiple masses in the liver and a solid mass measuring 16x9 cm in diameter in the pelvis. A brain CT showed no evidence of metastasis.

The serum ß-hCG and hCG-CTP values at the time of admission to our ward increased to 1,800 ng/ml (normal limit: 0.2 ng/ml, and 27,000 IU/ml (normal limit: 0.5 IU/ml) respectively, while the value of the serum α-fetoprotein ranged within the normal limits (10 ng/ml).

Revised manuscript accepted for publication November 2, 1999

EMA therapy (etoposide: 200 mg/m^2, methotrexate: 300 mg/m^2, actinomycin D: 1.0 mg/body) was initiated on April 28th. Thereafter, a second debulking surgery was performed on May 19th. After removing any severe adhesion in the pelvic cavity, 50% of the primary tumor mass was removed with the invaded jejunum.

While the EMA/CO (etoposide: 200 mg/m^2, methotrexate: 300 mg/m^2, actinomycin D: 1.0 mg/body, endoxan: 600 mg/m^2, vincristine: 1.0 mg/m^2) regimen for postoperative chemotherapy was followed by a carboplatin/etoposide regimen (carboplatin: 200 mg/m^2, etoposide: 200 mg/m^2), all four chemotherapeutic courses had no effect at all on her disease progression and she died of respiratory failure due to multiple lung metastases on September 9th, 1997.

On about 50 histological specimens obtained at the second debulking surgery, no neoplastic germ cell elements, except for choriocarcinoma, could be detected. In addition, 80 specimens from the other organs (e.g. lung, liver, peritoneum) obtained at the autopsy showed the same findings as the above specimens and no specimens showed any features suggesting other germ cell components. As a result, a histopathological diagnosis of ovarian choriocarcinoma was finally made.

In order to confirm the origin of the tumor, DNA polymorphism analyses of the tumor, the patient and her partner were thus performed. DNAs were extracted from the tumor tissue and heparinized blood from the patient and her partner by sodium dodecyl sulfate-proteinase K and phenol/chloroform treatment. Polymerase chain reaction (PCR) amplification was done to amplify the ten targeted regions. The DNAs were digested with appropriate restriction endonucleases, separated by agarose gel electrophoresis, and then transferred to nylon membranes (Hybond-N$^+$; Amersham) to display polymorphisms. All probes were obtained from the Japanese Cancer Research Resources Bank (JCRB) and were described in Human Gene Mapping 11 [3]. All restriction fragment length polymorphism (RFLP) patterns obtained in the present study were compatible with this information.

Table 1 shows the results of this analysis; the tumor possessed genomic DNA allele(s) common to the patient (D1S80, D2S44, D13S1 and D10S5 loci). However, the tumor did not possess any alleles which were clearly common to her partner

Table 1. — *DNA polymorphism analyses of the tumor, the patient and her partner.*

Location	Locus	Primer	Detection	T	PA	P
1p36-25	D1S80	MCT118	PCR-VNTR	b/–	b/–	a/–
2p24-23	ApoB	3-beta	PCR-VNTR	a/c	a/c	a/b
12q13	D17S30	DYZ22	PCR-VNTR	a/–	a/–	a/b
17p13.3	Col2A1	Col2A1	PCR-VNTR	a/b	a/b	a/b
1p31-pter	D1S57	YNZ2	Southern	a/b	a/b	b/–
2p	D2S44	YNZ24	Southern	c/d	c/d	a/b
8p23	D8S7	SW50	Southern	a/b	a/b	a/b
13q12-213	D13S1	7F12	Southern	b/d	b/d	a/c
17p13.8	D10S5	YNZ22	Southern	c/d	c/d	a/b
18q21.3-ter	D18S5	OS-4	Southern	a/–	a/–	a/b

Abbreviations: T, tumor DNA; PA, patient's DNA; p, partner's DNA.
Underlined data: indicate the loss of a partner's band.

in these loci. The choriocarcinoma in this case was thus considered to be non-gestational carcinoma.

Based on these findings, this tumor was diagnosed as a pure non-gestational choriocarcinoma which arose in the right ovary.

Discussion

Choriocarcinoma of the ovary originates in two different ways: (1) gestational choriocarcinoma, (2) non-gestational choriocarcinoma. The first tumor may be divided into two groups: a primary gestational choriocarcinoma associated with ovarian pregnancy or a metastatic choriocarcinoma from a primary gestational choriocarcinoma arising in other parts of the genital tract, mainly the uterus. The second tumor is rare and is usually admixed with other neoplastic germ cell elements which lead to a diagnosis of non-gestational choriocarcinoma. A pure choriocarcinoma of germ cell origin is rarer than an admixed one and there have so far been only a few reports regarding such tumors [4, 5].

In the present case, histopathological examination proved that the tumor was choriocarcinoma, while it remains to be clarified as to whether or not this tumor arose from a gestational or non-gestational origin. It is considered to be important to ascertain the origin of the tumor in order to select the most appropriate treatment and make an accurate prognosis.

We previously reported on RFLP analyses in order to identify the genetic origin of trophoblastic diseases [1, 2]. In these studies we described how DNA polymorphism analyses were helpful in determining the modes of origin in malignant trophoblastic diseases. Based on this information, we amplified 10 genomic DNA alleles from each tumor sample and the peripheral leukocytes from the patient and her partner in order to analyze the RFLP pattern. In the present case, four RFLPs (i.e., D1S80, D2S44, D13S1, D10S5) showed a loss of the partner's allele. This finding suggests that the tumor inherited only the patient's alleles and the tumor was thus considered to originate from the neoplastic germ cell elements of the patient.

To clarify whether or not the tumor arose from a gestational or non-gestational origin is important in order to select the most appropriate treatment and make an accurate prognosis. In conclusion, RFLP analyses, such as those used in the present case, are relatively simple to perform and are thus considered to be useful in determining the genetic origin of the tumor.

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