Gestational Choriocarcinoma with Brain Metastases : A Clinical Analysis

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Abstract : *This report reviews the clinical features of 14 choriocarcinoma patients with brain metastases treated from 1986 to 1990 at the University of Texas MD Anderson Cancer Center. The incidence is 5.3% of 264 gestational trophoblastic tumor patients. Brain metastases occurred after term delivery, abortion and hydatidiform mole in 9, 3, and 2 patients respectively. The group of term deliveries had a longer interval than the other two groups. Seven patients (50%) presented with neurological signs or symptoms, only one patient was asymptomatic. Five patients developed brain metastases during or after treatment with first line drugs. Abnormal serum : cerebrospinal fluid hCG ratio (less than 60 : 1) were found in only 3 patients (21%). Thirteen of 14 patients (93%) had accompanying pulmonary metastases. Brain metastases occurred equally in both cerebral hemispheres. The average modified WHO score was 15.2 (range 7-22). (Thai J Obstet Gynaecol 1991;3:31-37.)*

Key words : gestational choriocarcinoma, brain metastases

Gestational choriocarcinoma is a malignancy of the human placenta with the potential for rapid growth and widespread dissemination via hematogenous route, attributable to the erosive property of trophoblastic cells to invade adjacent tissues such as myometrium and blood vessels. Approximately one half of the cases were preceded by hydatidiform mole, with 25% following abortion, 22.5% following normal pregnancy, and 2.5% following ectopic pregnancy[1]. The incidence of gestational choriocarcinoma patients presenting with cerebral metastases not only varies between centers and geographic origins but also depends upon the surveillance and referral systems. These account for the incidence ranging between 7-28% with the higher ones in centers from the oriental countries[2-7]. The purpose of the current report is to analyze the clinical features of 14 patients with brain metastases of choriocarcinoma who were treated at the

University of Texas MD Anderson Cancer Center between February 1986 and July 1990.

Materials and Methods

A review was made of the medical records for all patients diagnosed as having choriocarcinoma with brain metastases to determine their age, parity, antecedent pregnancy, time interval from antecedent pregnancy to start of chemotherapy, pregnancy, presenting symptoms, initial urinary or serum hCG levels before treatment, prior chemotherapy, size, and sites of brain and other metastases. For assigning a score according to the World Health Organization (WHO) criteria[8], each chart was reviewed based on the prognostic factors except the information on ABO blood group which was not available in all cases. Hematologic profiles, chemical surveys, liver function test, urinalysis, and chest films were obtained in all patients at the time of initial examination. Radionuclide scan of the brain was used to identify cerebral metastases in most patients, but recently, computerized tomography (CT) and occasionally, magnetic resonance imaging (MRI) have been utilized for precise localization of the cerebral lesions. Other diagnostic radiologic tests were performed according to judgement of the attending physicians. Lumbar puncture with cerebrospinal fluid (CSF) examination for cytology, biochemistry and hCG measurement was usually employed unless there was evidence of increased intracranial pressure.

Results

The 14 patients of gestational choriocarcinoma with brain metastases constituted 5.3% of the total 264 patients with gestational trophoblastic tumor (GTT) and 20.5% of the total 68 patients with metastatic GTT treated in this institute during the study period. The characteristics and clinical profiles of the patients are listed in Table 1. The WHO score based on prognostic factors, excluding ABO blood group, is also assigned for each patient.

The ages ranged from 18 to 45 years (average = 30 years). The antecedent pregnancies included 9 term deliveries, 3 abortions, and 2 hydatidiform moles. The time between end of antecedent pregnancy and start of chemotherapy ranged from 6 months to 9 years (average = 30.8 months). The average interval was 35.5, 26.0 and 17.0 months in the groups of term deliveries, abortions and hydatidiform mole respectively. Seven patients presented with neurological sings or symptoms, most common were the signs of increased intracranial pressure such as severe headache, nausea, vomiting and impairment of consciousness or focal neurological signs caused by intracerebral lesions. Three patients presented with abnormal vaginal bleeding, all of them developed brain metastases while on treatment. One patient (KPC) was initially asymptomatic, but discovered lung nodule on

Table 1 Patient characteristics

Patients/ Year of admission	Age	History of pregnancy	Antecedent pregnancy	Interval[1]	Presenting symptoms	hCG[2] (mIU/ml)	Prior chemotherapy	WHO score[3]
LFT/1968	18	0010	Mole	10 mo	headache	+preg test	-	7
CTM/1972	37	6006	Term	9 mo	headache	-24 hr urine	-	11
KAD/1972	23	1001	Term	3 yr	lt. hemi-paresis	250	++	18
VAP/1972	23	0010	Mole	2 yr	chest pain	450,000*	++	16
MJH/1974	30	3003	Term	6 mo	Vg bleed & hemop[4]	850,000	++	20
JFR/1974	45	3003	Term	9 yr	Vg bleed & hemop[4]	180,000	-	21
GD/1975	31	5005	Term	5 yr	Vg bleed	150,000	++	22
PMG/1976	22	2002	Term	10 mo	seizure	14,000	-	15
TKT/1981	21	0010	Abortion	2 yr	headache	8,746*	-	12
RUN/1981	38	2002	Term	1 yr	lower GI bleed	739,200*	-	14
RDJ/1981	28	1021	Abortion	4 yr	Vg bleed	217	++	14
MLS/1982	38	6061	Term	6 yr	dizziness & diplopia	47,500	-	15
KPC/1988	22	1021	Abortion	6 mo	no symptom	1,048,800	-	12
SKS/1990	21	2002	Term	7 mo	coma	1,268,000	-	16

1 Time between end of antecedent pregnancy and start of chemogherapy
2 Initial serum hCG level before treatment; ++ = 2 or more drugs prior chemotherapy
3 World Health Organization scoring system based on prognostic factors
4 Vaginal bleeding & hemoptysis
* = Serum hCG: cerebrospinal fluid hCG ratio <60:1

routine preoperative chest film for cholecystectomy.

Levels of serum hCG were found to be over 40,000 mIU/ml in 8 patients, surprisingly, brain metastases could occur even in 2 patients (KAD and RDJ) whose serum hCG levels were extremely low. Only 3 patients had abnormal serum : CSF of hCG concentration (less than 60:1) and one (VAP) occurred before identification of the cerebral lesions. All cytologic studies were negative for malignant cells.

Five patients had received 2 or more chemotherapeutic agents prior to the start of treatment, four of them developed brain metastases later. The average WHO score for all patients was 15.2 (range 7-22).

Sites of metastases are shown in Table 2. Cerebral metastases were likely to occcur equally in both hemispheres, more common at the parietal lobes (5 patients). The other sites were found in equal number of three. Thir-

Table 2 Sites of metastases

Patients	Site of cerebral lesions	Lung	Liver	Others
LFT	Brain stem	-	-	-
CTM	Lt. occipital	+	-	Pelvis, rt. ureter, Scalp, breast
KAD	Rt. parietal	+	-	-
VAP	Brain stem	+	-	-
MJH	Lt. frontal	+	-	-
JFR	Rt. & Lt. occipital	+	-	Pelvis
GD	Rt. parietal	+	-	-
PMG	Lt. parietal	+	+	Spleen, retroperitoneal lymph nodes
TKT	Lt. parietal & Rt. cerebellum	+	-	-
RUN	Rt & Lt cerebellum	+	+	Rt. kidney, adrenal gland, colon, retroperitoneal lymph nodes
RDJ	Brain stem	+	-	-
MLS	Lt. parietal	+	+	Small bowel (jejunum & ileum)
KPC	Rt. frontal	+	-	Rt. kidney
SKS	Rt. frontal	+	+	Rt. kidney, spleen

teen of fourteen patients(93%) were accompanied by pulmonary metastases. Furthermore, there were 7 patients in whom metastases were identified elsewhere, such as liver (4), kidney (3), spleen (2), pelvis (2), retroperitoneal lymph nodes (2), ureter, adrenal gland, scalp, breast, colon and small bowel.

Discussion

In the most recent years, several reports concerning brain metastases of choriocarcinoma from many cancer centers have been presented through various journals amidst, controversial points of view about prevention and early diagnosis, either prophylactic intrathecal methotrexate or serum : CSF hCG ratio, even the classification and staging system.

In our instiute, various diagnostic procedures and therapeutic regimens have been utilized according to the patient's conditions and advancement of medical care. The total number of patients is small, however, we have learned some interesting and valuable points from them. The incidence of choriocarcinoma patients with brain metastases is only 5.3% of total patients diagnosed GTT, which is less than those reported from other institutes[1,9-11]. Fifty per cent of our

patients were referred from elsewhere.

All but one patient (93%) were associated with pulmonary metastases. Reports from other series revealed that 92-100% of choriocarcinoma with brain metastases were preceded by pulmonary metastases[3,4,6,9,10,12,13]. In fact, metastatic pathway of choriocarcinoma to the central nervous system is likely to originate from pulmonary deposits, but some patients may present without any evidence of pulmonary lesions. This finding, however, depends upon sensitivity of pulmonary investigation. Occult pulmonary metastases are frequently identified on CT scanning of the lungs in patients with normal chest radiograph. Approximately 40% of nonmetastatic GTT patients had pulmonary micrometastases detected by CT scanning which were not found by routine chest x-ray[14]. As a result, it would be reasonable to consider screening all patients diagnosed GTT for occult metastases with CT scanning of the lungs.

We found abnormal serum : CSF hCG ratio (<60) in only 3 of our patients. Bagshawe and Harland[3] originally reported that 29 of 33 patients with brain metastases had positive results before any other clinical signs became abnormal[3]. However, Goldstein and Berkowitz[11] had found both false positive and false negative results from their investigation. They concluded that unless corroborated by clinical or radiographic data, or both, a single abnormal serum : CSF hCG ratio is insufficient to diagnose brain involvement. Weed and Hammond[15] suggested that its potential usefulness may be in the asymptomatic patients who have lung metastases, normal brain scans, and persistently elevated hCG titers. We think that it may benefit some cases of negative brain imaging procedures and should be used supplementary to other investigations. Positive results should arouse the suspicion of cerebral involvement. Every effort, utilizing highly sensitive methods, must be made to rule out or detect early cerebral metastases. Although CT scanning is documented to be more sensitive than the isotope scan in detecting cerebral metastases (95% vs 71%), it may be, however, initially negative in patients with asymptomatic metastases[3]. Currently, MRI, the most recent noninvasive diagnostic innovation has been reported to be more sensitive than CT scanning in detecting small metastatic foci[16,18]. In the future, MRI may replace CT scan for brain imaging and play a significant role in detecting occult cerebral metastases.

GTT patients with brain metastases are classified as a high-risk group according to Hammond clinical classification system and are also in stage IV when classified by anatomic staging system of FIGO Cancer Committee[19]. We categorized the patients based on WHO prognostic scoring system and found that all 14 patients fell into the high-risk group if ABO blood group was not considered. Analyzing the experience at the New England Trophoblastic Disease Center, DuBeshter et al[20] found that the

WHO scoring system was more effective than traditional criteria in predicting which patients required intensive combination chemotherapy initially. The WHO score seems to be a very important factor predictor of treatment outcome[8,21,22].

For early detection of brain metastases, all patients diagnosed persistent GTT should be categorized according to WHO prognostic score to identify high-risk group and undergo through metastatic work up. Any low-risk patients, patients with pulmonary metastases and all high-risk patients should receive careful metastatic search for brain involvement by highly sensitive methods including CT scanning or MRI. Supplemental serum : CSF hCG measurement may be individually considered in case of negative metastatic work-up.

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