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PROGNOSIS OF GESTATIONAL CHORIOCARCINOMA – 8 -YEAR EXPERIENCE

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Choriocarcinoma is a highly malignant tumour which originates from the developing trophoblastic tissue, most commonly following molar pregnancy. It is a potentially fatal disease, but current management protocols have changed the prognosis as highly favourable.

The aim of the study was to analyze the ways of establishing the diagnosis, methods and results of treatment of choriocarcinoma in our institute.

The study was conducted as a retrospective analysis of the eight-year period, from 2000 to 2008. The obtained data were collected from medical charts with choriocarcinoma treated in our institute.

In the eight-year period, eight cases of choriocarcinoma were registered. In one (12.5%) case choriocarcinoma developed after molar pregnancy, whereas in six (75%) cases the antecedent pregnancy resulted in a spontaneous abortion. In one patient the diagnosis was made after hysterectomy. Particular chemotherapeutic protocol was introduced to each patient. All patient survived.

Prognosis of gestational choriocarcinoma is favourable provided the appropriate therapy is administered early in the course of disease. Provision of free medical care should be considered for these patients to save their lives. *Acta Medica Medianae 2012;51(2):11-14.*

Key words: *choriocarcinoma, treatment, chemotherapy*

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Introduction

Gestational choriocarcinoma is a relatively rare and highly malignant variant of gestational trophoblastic disease. Although choriocarcinoma might be preceded by any gestational event, hydatidiform mole is the most common precursor (1). It is a potentially fatal disease, but availability of different diagnostic aids like radiology, serum human chorionic gonadotrophin (HCG) and unique sensitivity of tumour to chemotherapy has turned the prognosis highly favourable. It is one of the rare human malignancies that are highly curable even with wide spread metastasis. Prognosis of gestational choriocarcinoma largely depends upon early diagnosis of the disease, comprehensive meta-static workup, selection of appropriate regimen of chemotherapy from outset and carefully planned follow up (2).

Throughout the world, the incidence rates for choriocarcinoma differ widely. In Europe and North America, choriocarcinomas are reported to affect one in every 30.000-40.000 pregnancies, and one in 40 molar pregnancies, whereas in Southeast Asia, rates as high as one in every 500-3000 pregnancies have been reported (3). These regional variations have been reported with many speculative factors as ethnic origin, blood group, age, parity, diet and nutrition, contraception, socio-economic status, immunologic factors and genetic constitution (4).

The aim of the paper was to analyze the ways of establishing the diagnosis, methods and results of treatment of choriocarcinoma in our institute.

The study was conducted as a retrospective analysis of the eight-year period, from January 2000 to October 2008, involving all patients with gestational choriocarcinoma presenting to the Institute of Gynaecology and Obstetrics, Clinical Centre of Serbia. On admission, a detailed history was obtained from each patient and thorough clinical examination was performed including general, systemic and pelvic examinations. Diagnosis of choriocarcinoma was mainly based on clinical course of the disease (history, abnormal vaginal bleeding, adnexal masses) and elevated levels of serum b-HCG. Evaluation of metastatic disease was done by thorough clinical examination and set of investigations including chest radio-graphy and ultrasound scan of abdomen and pelvis. There was no need for computed tomography. Patients were assigned low, medium and high risk groups according to the prognostic scoring system suggested by WHO in 1983 (Table 1).

Table 1. WHO Scoring System based on prognostic factors

Prognostic Factors	Score			
	0	1	2	4
Age (years)	<39	>39		
Antecedent Pregnancy	Hydatidiform Mole	Abortion	Term	—
Interval*	4	4–6	7–12	12
hCG (IU/l)	$<10^3$	10^3–10^4	10^4–10^5	$>10^5$
Largest tumour including uterine tumours	—	3–5 Cm	>5 Cm	—
Site of metastases	—	Spleen Kidney	GIT, Liver	Brain
Number of metastases identified	—	1–4	4–8	>8
Prior Chemo therapy	—	—	Single Drug	Two or more

The total score for a patient is obtained by adding the individual score for each prognostic factor
Total score: ≤4=low, 5–7= middle risk, ≥8= high risk
*time interval (months) between end of antecedent pregnancy and start of chemotherapy

Patients were managed in consultation with board for gestational trophoblastic disease. All patients were put on particular chemotherapeutic protocol according to risk score and prognostic factors. These protocols include Methotrexate (MTX), multiagens regime that consists of Metotrexate, Aktinomicina-D and Ciklofosfamid (MAC), and EMA-CO protocol (composed of: Etopozyd, Metotrexate with folic acid, Aktinomycina-D, Cyklofosfamida and Vincristin). Therapy was monitored by serum concentration of b-HCG, which was estimated fortnightly. Chemotherapy was given cyclically until complete remission was attained. Patients were vigilantly observed for adverse effects of chemotherapy (vomiting, diarrhoea, liver function, bone marrow depression and alopecia) and supportive treatment was given. Radiotherapy was used only to treat the complications like vaginal haemorrhage.

Results

During the eight-year period there were eight patients suffering from choriocarcinoma. Epidemiological features are given in Table 2. All patients survived.

Table 3 shows the applied chemotherapeutic protocol for each patient.

Discussion

Out of eight patients, seven were multiparous and in only one patient the first pregnancy resulted in choriocarcinoma. Spontaneous abortion preceded choriocarcinoma in five patients (62.5%), while in two patients it was vaginal bleeding. Antecedent pregnancy was hydatidiform mole in one patient (12.5%). In the oldest patient in this group (48 years old, with the history of two term deliveries and seven spontaneuos abortions), choriocarcinoma was diagnosed after complete hysterectomy.

Table 2. Baseline characteristic of patients with choriocarcinoma

Age (years)	Antecedent pregnancy and chemotherapy (months)	Risk category	Metastases
48	13	middle	lung
27	6	high	no
29	5	high	lung
27	8	high	no
30	9	middle	lung
32	4	low	no
18	6	high	no
29	5	middle	no

Table 3. Chemotherapeutic protocol

Age (years)	Protocol	Number of cycles of chemotherapy	Complications of chemotherapy
48	MTX, MAC	3	nausea, vomiting
27	MAC	1	nausea, vomiting
29	EMACO, MAC	2	rash, nausea, vomiting
27	EMACO, MTX, MAC	3	vomiting, nausea, alopecia
30	EMACO, MAC	1	nausea, vomiting
32	MTX	1	nausea, vomiting
18	MTX	3	fever, rash, vomiting, nausea
29	MAC	1	nausea

Also, she had lung metastases and the longest period from the end of antecedent pregnancy and onset of chemotherapy (13 months). Knowledge of antecedent pregnancy is important because prognosis depends upon it. Gestational trophoblastic disease most commonly follows molar pregnancy and may also occur following normal or ectopic pregnancies and spontaneous or therapeutic abortion (5). The incidence of choriocarcinoma after complete hydatiform mole is about 1000 times greater than after a normal pregnancy (6). Choriocarcinoma is suspected when there is persistent or irregular uterine haemorrhage, following abortion or hydatiform mole. Rapid growth and haemorrhage make the tumor a medical emergency.

Majority of cases of choriocarcinoma occur in women aged less than 35 years of age (7). In our researh, the mean age was 30 years – the youngest was 18, the oldest 48 years old. Histerectomy was performed in only one patient, after which choriocarcinoma was diagnosed.

Patients were categorized in three groups as low, medium and high risk. The largest number (50%) belonged to group with a high risk score, than middle (37.5%) and one patient had low risk score.

The b-HCG level was estimated prior to and during chemotherapy. On admission, levels of b-HCG varied from 918 to 190000 IU/L. Average time of falling in b-HCG level after chemotherapy was 68 days.

Time interval between end of antecedent pregnancy and onset of chemotherapy was recorded. It varied from 4 to 13 months, on average 7 months. Time interval is a crucial factor influencing the prognosis. If it is shorter and chemotherapy starts sooner, the prognosis is better.

As trophoblastic tissue has a tendency for hematogenous dissemination, the lungs and their vascular system are usually involved by pulmonary metastasis (85% in related choriocarcinoma), tumor emboli with or without lung infarct. Other organs where metastasis may occur are the CNS, uterus, vagina, liver, and spleen (8). Pulmonary metastasis in GTD usually has a good prognosis compared to brain metastasis. The mortality rate of patients with pulmonary metastasis was found to be 8%. These metastases tend to disappear rapidly in response to drugs, radiotherapy, or surgery (9). In our research, lung metastases were present in three patients. They responded well to chemotherapy.

Chemotherapy was administered to all patients. Radiotherapy was not used as a primary treatment, but it was given to two patients who developed massive vaginal haemorrhage. No patient was treated with surgical resection. The number of cycles of chemotherapy did not exceed three cycles.

All the patients had nausea and vomiting, one developed alopecia, two patients had rash and one had fever. No one had bone marrow depression. No other adverse effects were seen.

It is apparent from the above study that all patients with choriocarcinoma are potentially curable provided that the appropriate therapy is given early enough in the course of the disease. In our study 100% patients attained complete remission and they survived without any morbidity during the two-year follow up period. There were no patients who did not respond to chemotherapy.

Conclusion

As a result of modern diagnostic and therapeutic techniques, nearly 100 percent of patients with GTD can be cured of a disease that recently had a high death rate. To achieve this, skillful mixing of chemotherapy, surgery, and irradiation, as well as supportive therapy, are necessary. Complete remission can be obtained in majority of patients by administration of appropriate chemotherapy from the outset. Prognosis depends upon early diagnosis and management. Understanding and utilizing the HCG assay to monitor disease status is vital, because a rapid diagnosis and treatment may change dramatically their survival. With this approach, essentially all of these patients should survive, many to have successful future pregnancies. According to presented data, we can conclude that chemotherapeutic treatment is very efficient in the treatment of choriocarcinoma.

Continued awareness and education is required, so that choriocarcinoma developing after molar or non-molar pregnancy is detected as early as possible, thereby reducing the choriocarcinoma mortality rate.

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PROGNOZA GESTACIJSKOG HORIOKARCINOMA – OSMOGODIŠNJE ISKUSTVO

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Horiokarcinom predstavlja maligni tumor trofoblastnog tkiva. Najčešće nastaje nakon molarne trudnoće. Nekada je horiokarcinom bio fatalno oboljenje, a danas je najbolje lečeni ginekološki malignitet zahvaljujući savremenim protokolima.

Cilj rada bio je analiziranje načina postavljanja dijagnoze, metoda i rezultate lečenja horiokarcinoma u Institutu za ginekologiju i akušerstvo. Urađena je retrospektivna analiza svih bolesnica obolelih od horiokarcinoma u osmogodišnjem periodu (2000.-2008.).

U periodu praćenja registrovano je ukupno 8 žena obolelih od horiokarcinoma. Kod jedne bolesnice (12,5% slučajeva) horiokarcinom se razvio nakon molarne trudnoće, dok je kod 6 (75%) slučajeva prethodio spontani abortus. Kod jedne bolesnice dijagnoza je postavljena nakon histerektomije. Sve bolesnice su uspešno izlečene, nije bilo smrtnih ishoda.

Ukoliko se dijagnoza i lečenje postavi i započne u ranijem stadijumu bolesti, može se očekivati povoljan ishod. *Acta Medica Medianae 2012;51(2):11-14.*

***Ključne reči**: horiokarcinom, lečenje, hemoterapija*