

## **Clinical features of gestational trophoblastic neoplasia after hydatidiform mole in women of different age groups**

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**Summary.** We describe the clinical features of gestational trophoblastic neoplasia after hydatidiform mole in women of different age groups

**Key words:** hydatidiform mole, gestational trophoblastic neoplasia, clinical features

Trophoblastic pregnancy disease is a complex phenomenon which includes the group of benignant and malignant trophoblastic neoplasms. It is a rare disease (1–2.5% among malignant neoplasms of female reproductive organs) predominantly developing in women of child-bearing age [1].

The most often occurrences in the clinical practice are represented by the complete and partial hydatidiform mole [2,3]. These benignant tumors may initiate all the currently known gestational trophoblastic neoplasia (GTN): pregnancy related choriocarcinoma, placental site trophoblastic tumor and epithelioid trophoblastic tumor [4-7].

Nowadays the scientists discuss the clinical, diagnostics and treatment peculiarities of cancerous trophoblastoma in teenager and adult women [8-10].

The goal of this study is to analyze the clinical peculiarities of cancerous trophoblastoma initiated by hydatidiform mole in women of various age groups

### **Materials and Methods**

186 women suffering from cancerous trophoblastoma initiated by hydatidiform mole were examined and treated. These women received ad-hoc treatment at oncogynecology research and development department from 1999 through 2012. 25 of those examined (13.4%) were teenager women and 161 (86.6%) – the women 20 y.o. plus (figure 1).

The teenager patients' age ranged from 16 to 19 years old, which in average constituted  $18.0 \pm 1$  years old. Subject to the peculiarities of cancerous

trophoblastoma behavior in women 40 years old and elder (1 score according to FIGO- WHO forecasting scale), the adult women were subdivided into two groups: the medium age group 20 to 40 y.o. and the senior age group  $\geq 40$  y.o. The average age of the medium age group patients constituted  $27 \pm 5$  years. The most of the medium age group patients (63.7%) were 20-27 years old. The senior age groups patients were 40 to 55 years old, which in average constituted  $46 \pm 4$  years old. It should be mentioned that four women of the senior age group (10.8%) were over 50 y.o. Starting from 50 y.o. women face the highest relative risk of full hydatidiform mole development (RR 519) [11]. Such a high risk is caused by the combination of relatively small quantity of spontaneous pregnancies and increased number of anomalous ovocytes. Today the literature describes certain cases of hydatidiform mole and GTN after hydatidiform mole in women over 50 y.o. [12,13]. The age differences between the three researched groups are statistically significant.

The patients of the researched groups were staged according to FIGO-WHO (2002) anatomic classification (Table 1).

The data given in the table shows that in the most of the examined women the disease was diagnosed at its stage I.

All the patients before the treatment start were included to the group of low risk methotrexate resistance (individual number of scores according to FIGO-WHO forecasting scale  $\leq 6$ ) [2], therefore the comparative analysis is applicable.

In order to study dependence of the neoplastic process proliferation and the tumor's morphological variant on the age of a patient with GTN after hydatidiform mole, the logistic regression was used under the method described in the paper [14]. The method implies prediction of certain event occurrence probability against the values of various attributes.

## **Results and Discussion**

The completed study allowed highlighting the following clinical peculiarities of GTN after hydatidiform mole in women of various age groups.

The complete hydatidiform mole initiated development of GTN in women of all age groups: in 92.0% case in teenagers, in 87.9% in the medium age group and in 83.8% in the senior age group ( $p > 0.05$ ).

One of the risk factors of hydatidiform mole neoplastic transformation is represented by theca-lutein ovarian cysts with diameter of over 6 cm (Table 2).

The data given in the table shows that out of the 186 examined women the theca-lutein cysts with diameter of over 6 cm were diagnosed in 61 patient (32.8%): 1 patient of teenager group and 60 women of the medium age group. The sonograms showed that the ovaries looked like multichamber formations with multiple anechoic inclusions and thin even links and isolated vessels in the cysts' walls. The cysts' walls ranged from 6 to 16 cm, which in average constituted  $11.3 \pm 0.8$  cm in diameter. Thus, the ovarian cysts were the most often ( $p < 0.05$ ) diagnosed in women of the medium age group.

The major currently applied criterion of diagnosing GTN after removal of hydatidiform mole is the chorionic gonadotropic hormone (hCG) level in blood serum. The hCG baseline level constituted  $37357 \pm 132.8$  mIU/L in the teenager group,  $16499 \pm 85.4$  mIU/L in the medium age group and  $13297 \pm 75.4$  mIU/L in the senior age group. Thus, the higher hCG baseline level in blood serum was diagnosed in women of the teenager age group ( $p < 0.05$ ).

In the same age group, even at stage I of the disease the tumoral nodes in myometrium of over 5 cm in diameter (fig. 2-4) were identified the most often (2 scores according to FIGO-WHO forecasting scale) (table 3).

The completed research showed existence of the positive correlative link between hCG level in blood serum and the tumoral node's size, the correlation ratio is  $r = 0.88 \pm 0.09$ ,  $p < 0.05$ . Therefore, the tumoral node's size in myometrium reflects activity of the tumoral process.

The tumoral nodes were located submucously in 27.9% cases and caused bloody issues from the genital tracts with various intensity. Anemia, as a result of bleeding was identified more often ( $p < 0.05$ ) in women of the teenager age group - in 30% cases.

The examined groups showed the following morphological variants of GTN after hydatidiform mole: 1) hydatidiform mole (the malignant tumor was diagnosed according to the criteria of the FIGO-WHO 2002 against the hCG level and the results of ray-stretching method examination); 2) invasive hydatidiform mole; 3) choriocarcinoma.

According to the results of the completed regression analysis the researches identified statistically significant ( $p < 0.05$ ) increase of invasive hydatidiform mole and choriocarcinoma probability every four years of the age increase by 58.9% and 49.6%, respectively, in patients with GTN after hydatidiform mole (figure 6).

The obtained results mathematically substantiate expedience of the combined method of treating the patients of the low risk level 40 years old and elder with tumoral nodes in uterus, and prove expedience of revising the algorithm of following up the patients with metastatic hydatidiform mole in women of this age group.

1 case of synchronous cancer was recorded in each age group: the medium and the senior age group - cervical cancer, the teenager age group - marginal serosal-papilliferous ovarian cyst.

Thus, there are no proven differences in the nature of tumor initiating development of gestational trophoblastic neoplasia in teenager and adult women. However in the teenager age group, even at stage I of the disease the tumor nodes in myometrium of over 5 cm in diameter with high hormonal activity were identified the most often (hCG level was higher), bloody issues from the genital tracts with various intensity, and anemia as a result.

In 87.5% of cases subject to strict compliance with the algorithm of following up the patients after removal of hydatidiform mole, the gestational trophoblastic neoplasia may be diagnosed at the preclinical stage even with the patients suffering from high risk hydatidiform mole [15]. Such treatment is technically easy, economically feasible and results in a prompt clinical effect, without affecting the patient's life quality. As a rule, late diagnosing gestational

trophoblastic neoplasia in teenagers results from incompliance with the rules for monitoring the hCG by the patients.

The results obtained upon completion of the study concerning somewhat more aggressive progress of gestational trophoblastic neoplasia in teenagers show the necessity of health educating teenagers of our country, especially in Sumy, Odesa, Dnipropetrovsk and Zhytomyr regions, which face a high level of hydatidiform mole incidents among teenagers, in order to prevent development of disseminated forms of gestational trophoblastic neoplasia.

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