PATHOMORPHOLOGICAL RATIONALE FOR REHABILITATION THERAPY AFTER ECTOPIC PREGNANCY

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Abstract. The development of critical conditions in patients with ectopic pregnancy is directly related to defects in the provision of medical care: errors in the diagnosis, and subsequently in the formulation of the final clinical diagnosis, transportation, operating room setup time, unpreparedness for high-quality infusion therapy, and insufficient qualifications of specialists.
Keywords: ultrasound, ovarian pregnancy, ectopic pregnancy, gynecological emergencies.

Relevance. Ectopic pregnancy is considered an unrecorded reproductive loss, but it remains a major problem in reproductive medicine, impacting subsequent fertility, the development of pelvic adhesions, secondary tuboperitoneal infertility, and recurrent ectopic pregnancies.Ectopic pregnancy accounts for 0.5-12.0% of gynecological diseases [1,6, 9,10,11,12], and is a common cause of pelvic genital surgery, although it varies from 8.8% to 55.0% across gynecological hospitals [1,16,17]. In the general population, the incidence of ectopic pregnancy reaches 1.4-2.0% of all pregnancies [8,13,14,15], increasing to 3-5% in assisted reproductive technology programs [2,18,19] . On the one hand, this pathology poses a threat to a woman's life due to the rapid development of the clinical picture, requiring emergency intervention. On the other hand, complications can affect not only fertility but also quality of life.
In this regard, the WHO's "10 Facts on Maternal Health" are of particular interest. Point six states that most maternal deaths can be prevented through skilled obstetric care and access to emergency obstetric care. Point ten indicates that the main barrier to progress in improving maternal health is the lack of skilled care [5, 10, 12, 13].
Morphological studies reliably indicate the inflammatory genesis of tubal pathology. Discussions determine laparotomic or laparoscopic tactics of surgical treatment, options for conservative therapy. However, the results of pregnancy onset are low, despite the fact that microsurgical operative technique allows in 80-97% of cases to restore the anatomical patency of the fallopian tubes [1,2,3,4,5]. It can be assumed that this is due to underestimation of the state of the systems of the whole organism, their adequate rehabilitation after surgical trauma and blood loss.

The aim of the study was to substantiate rehabilitation measures after tubal pregnancy based on morphofunctional changes in the pituitary-ovarian system and adrenal glands.
Material and Method. The study involved patients with the most common tubal localization of the fertilized egg. To conduct the main stages of the work, 233 hospital records of patients with tubal pregnancy were selected by random sampling. The criteria for forming the main groups were the severity of the condition at the time of admission to the hospital, as well as the outcome of the disease. Group 1 included 184 patients with various pathogenetic variants of tubal pregnancy, who underwent surgical interventions (tubectomy and tubotomy) with the volume of blood loss not exceeding 500 ml. Group II was represented by 49 "near miss" patients (according to WHO criteria) with massive blood loss (more than 1500 ml) resulting from a rupture of the fallopian tube. Patients of group 1 were divided into clinical subgroups: Subgroup 1 (n=68) - women with progressive tubal pregnancy; Subgroup 2 (n=56) included patients with tubal abortion; Subgroup 3 (n=60) included patients with tubal rupture.
For the prospective study, subgroups 4 (n=19) were identified from Group 1 and 5 (n=15) from Group 2. Subgroups were formed based on a tubectomy performed 4-6 months previously due to tubal rupture during VB and blood loss of no more than 500 ml in Subgroup 4 and over 1500 ml in Subgroup 5. The study was conducted in three stages. In the first stage, the anamnestic, clinical, and organizational aspects of each case in the studied subgroups were comparatively analyzed. During hospitalization, the timeliness of examination and diagnosis, the duration of the preoperative period, access options and the extent of the surgeries performed, the course of the postoperative period, the results of histological examinations of the removed fallopian tubes, and the physician's recommendations for patients during the postoperative period, determining the scope and focus of rehabilitation measures, were assessed.
During the second phase of the study, Groups II and III analyzed the factors leading to a fatal outcome in cases of maternal death and the high risk of death in women who had "nearly died." The principles of compiling final clinical (FCD) and pathological diagnoses (PAD) were studied, as well as the autopsy results of maternal deaths, which included characteristics of morphological changes in the anterior pituitary gland and adrenal glands during bleeding associated with the termination of a tubal pregnancy. The prospective (third) stage of the study consisted of a clinical analysis of two subgroups of patients with tubal rupture after tubectomy, but with different blood loss: less than 500 and more than 1500 ml.
Ultrasound and Doppler studies were performed on an Acuson 128 XP/10 system using abdominal and transvaginal transducers with frequencies of 4 and 7 MHz. Histological

examination of autopsy sections stained with hematoxylin and eosin was performed using a Bimam P-11 binocular microscope. Additional techniques were used when necessary: van Gieson, Mallory, Weigert, Masson, and Foote. All anatomical sections of the fallopian tubes were subjected to morphological examination. The specimens were fixed in 10% buffered neutral formalin and embedded in paraffin. Histological sections (5 μm thick) were stained with hematoxylin and eosin, picrofuchsin, and van Gieson (to assess sclerosis), azan (to detect fibrinoid), Picro-Mallory III (to determine the age of fibrin in a thrombus), and Weigert (to detect elastic fibers).

For morphometric studies of the anterior pituitary gland, the volumes of the following morphological components were determined using a stereometric grid: basophilic endocrinocytes (BE), hypertrophied BE, normal acidophilic endocrinocytes (AE), hypertrophied AE, necrotic cells, edema fluid, extravasates, microvascular thrombosis, and microcysts.

Results and discussion. A retrospective analysis of the medical records of patients in Group I with various pathogenetic variants of tubal pregnancy confirmed the development of classic clinical symptoms in patients of all studied subgroups. Initial visits to the antenatal clinic upon the appearance of early signs of the disease were significantly higher ($p < 0.05$) in patients with progressive tubal pregnancy—subgroup 1 (46 of 68, 67.65%)—compared to subgroups 2 (27 of 56, 48.21%) and 3 (21 of 60, 35.00%). They were significantly more likely to be hospitalized by referral from the antenatal clinic. In subgroups 2 and 3, patients (29 women, 51.78%) and 39 women, 65.00%, respectively, were primarily transported to the hospital by ambulance or admitted independently.

Women's low awareness of their own health issues and their late presentation for care, which exacerbated the development of pathology, were noteworthy. The time from the onset of the first symptoms to seeking medical care in all subgroups was up to 7 days (average 5.81 ± 0.93 days). Moreover, in cases of initial visits to the antenatal clinic, referral and hospitalization occurred within 24 hours. Paradoxically, in women with ruptured tubal pregnancies (subgroups 2 and 3), despite more pronounced clinical symptoms compared to those with the progressive form of the disease, delayed hospitalization was more common than in subgroup 1.

Upon hospitalization of patients in the gynecological hospital, the preliminary diagnosis of "ectopic pregnancy" was encountered with the highest frequency in the subgroups with tubal abortion and tubal rupture: 96.43% in the 2nd subgroup and 98.33% in the 3rd. In cases of progressive tubal pregnancy, this diagnosis was made in 79.41% of patients. The time period from the moment of hospitalization to the

operation, required for examination of patients, clarification of the diagnosis, preoperative preparation, was significantly lower in the 2nd and 3rd subgroups with termination of tubal pregnancy (42.14 ± 9.27 and 32.41 ± 11.36), compared to the progressive form (258.32 ± 24.12) ($p < 0.01$). This was facilitated by the characteristic clinical picture of hemoperitoneum, confirmed by additional diagnostic methods, the deterioration of the patients' general condition, and complaints pathognomonic of this disease.

Determining the gestational age of tubal pregnancy based on the date of the last menstrual period revealed significant differences in the compared subgroups. In groups 2 and 3 (patients with a terminated pregnancy), tubal pregnancy was observed to prolong from 4 to 7 weeks, while its development without termination did not exceed 28 days from the beginning of the cycle.

According to our data, the social status of the patients included in the study did not significantly differ. Most patients were married and had permanent employment. There were no significant differences in blood type or Rh factor among the patients studied. Menstrual histories were comparable across all subgroups. The first experience of sexual intercourse between the ages of 14 and 16 years was observed in each of the studied subgroups of patients, but was more often observed in cases of tubal rupture-type abortion (70.0%). Early sexual debut was noted in almost every second woman with a tubal abortion (44.6%), and in every third (35.9%) with a progressive form of tubal pregnancy. In the structure of gynecological diseases of patients whose reproductive history was burdened by early sexual debut, artificial abortions, low intergenerational interval, adverse pregnancy outcomes in early stages, inadequate contraception, inflammatory processes of the genital organs prevailed (65.51%; 39.62% and 53.97% in the subgroups, respectively). A history of urogenital infections was observed in a comparable proportion of patients and did not differ significantly across subgroups (62.5%, 52.6%, and 60.0%, respectively, across subgroups). Most frequently, pregnancy developed in the ampullary part of the fallopian tube (56.0%). In every third case, ectopia of the ovum occurred in the isthmic section (31.0%), and less frequently in the interstitial section (13.0%). Adhesions of stage 1 and 2 were more frequently observed in patients with progressive tubal pregnancy — 71.42%, while in the subgroups with tubal abortion and fallopian tube rupture, they occurred only in 28.57% of cases.

The analysis showed the advantages of the laparoscopic approach compared to the laparotomy, consisting of a shorter surgical time (59.18 ± 7.41 minutes versus 94.31 ± 8.32) and hospital stay (7.81 ± 0.47 days versus 9.14 ± 0.12), a low incidence of

postoperative complications: anemia, leukocytosis, and hyperthermia (4.12% ± 0.52; 8.19 ± 0.84 and 11.24 ± 1.11 versus 8.21 ± 0.74; 11.16 ± 0.43 and 16.31 ± 1.07, respectively).

Autopsy material was studied to identify changes in the systems and organs in cases of MC during tubal pregnancy. All of them were characterized by ischemic events, vascular thrombosis, and hemorrhages of varying intensity, characteristic of massive blood loss syndrome. Of particular interest were the morphometric data characterizing anterior pituitary lesions depending on the volume of blood loss. Thus, with blood loss volumes not exceeding 2000 ml, signs of hypertrophy of basophilic endocrinocytes (BE) and, to a lesser extent, acidophilic endocrinocytes (AE) were detected, with minor amounts of necrosis, stromal edema, extravasations, and other changes.

The percentage of hypertrophied basophilic cells in the anterior pituitary glands of patients who died from greater blood loss (2200-3000 ml) was almost twice as high.

Conclusion. The development of critical conditions in patients with ectopic pregnancies is directly related to iatrogenic factors: deficiencies in the initial diagnosis, and subsequently in the final clinical diagnosis, transportation, operating room setup time, unpreparedness for high-quality infusion therapy, and insufficient specialist qualifications. A significantly higher incidence of these conditions is observed in cases of maternal death.

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