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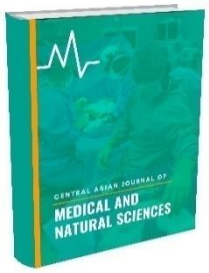

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Ovarian Apoplexy and its Impact on Reproductive Health

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Abstract: Ovarian apoplexy is a disease of women of reproductive age, which accounts for 0.5-2.5% of the causes of intra-abdominal bleeding. The disease has a sharp upward trend from 1997 to 2009. From 3 to 17%. According to various authors, the incidence of ovarian resection as an operation that injures the organ in apoplexy reaches 59% . Relapses of this disease were noted in 21.6–69.0% of cases.

Key words: trophoblast, hyperstimulation, hyperandrogenism.

Despite the fact that the urgent pathology under study cannot be classified as rare, there are a limited number of reports in the current literature regarding its etiopathogenetic aspects. It is known that the above ovarian pathology is genetically determined, in particular, by the GPIIIa gene nosological unit. According to K. Aalto-Setala, the presence of the PL-AII allele leads to a high risk of thrombosis of the coronary vessels, and studies by S. R. Steinhubl, D. J. Moliterno demonstrate an association between the carriage of the PL-AII allele and increased adhesion and aggregation of platelets in arterial vessels [22, 23] . Particular attention is paid to the PL-AII allele, the presence of which leads to implantation disorders in the form of insufficient invasion of the trophoblast by the surface layers. In the studied ovarian pathology, an increase in the frequency of carriage of the PL-AII allele contributes to the violation of the integrity of the ovarian tissue due to weak intercellular contacts in it and increased thrombus formation in small ovarian vessels, resulting in hemorrhage [17]. Most scientists agree that sexual intercourse, excessive physical activity and stress are the main provoking factors of this urgent condition [1, 9, 10, 14, 15, 16, 18, 19]. However, they cannot be the direct cause of hemorrhage in the ovary. Acting against the background of hormonal imbalance in the presence of ovarian anatomical changes in the form of a cystic corpus luteum, a multifollicular structure, a persistent follicle, and in the presence of sclerotically altered vessels, provoking factors lead to an increase in pressure in the vessels due to blood filling of the pelvic organs and cause a violation of their integrity [15]. Hormonal imbalance in the genesis of ovarian apoplexy, according to A. S. Gasparov, A. E. Ter-Ovakimyan, is due to a stress factor leading to hypercortisolism and hyperprolactinemia. Hyperproduction of these hormones is the cause of the multifollicular type of ovarian structure, followed by the implementation of ovarian apoplexy. These disorders underlie

endogenous ovarian hyperstimulation. Detected hyperprolactinemia indicates a deficiency of dopaminergic activity of the basal hypothalamus as a pathogenetic factor in ovarian rupture. In patients with ovarian apoplexy, a significant increase in cortisol and DHEA, apparently, indicates an adrenal genesis of hyperandrogenism [17]. In addition, a fairly high frequency of abdominal surgical interventions in their history is evidence of an already existing adhesive process in the abdominal cavity. New data on the state of the immune system in terms of the pathogenesis of the studied nosology were obtained by A. S. Gasparov, A. E. Ter-Ovakimyan. Determination of embryo-specific antibodies as a marker of the state of the immune system made it possible to distinguish two conditions in ovarian apoplexy: hyperreactivity in primary acute ovarian pathology and absolute hyporeactivity in its reappearance [1, 17,22,23]. Unrealized childbearing function in women with ovarian apoplexy is due to the high incidence of artificial abortion in this group of patients [1, 17]. Termination of pregnancy against the background of existing hormonal disorders and inflammatory changes in the ovaries with unfulfilled reproductive function leads to pathological changes in the woman's homeostasis [4, 13,20,21]. Some changes have been made to the classification of ovarian apoplexy over the past decade. For a long time it was customary to distinguish pain, anemic (hemorrhagic) and mixed form of ovarian apoplexy depending on the clinical form. Since varying degrees of bleeding are observed in all cases of ovarian apoplexy, the division into the above forms is not entirely legitimate. In this regard, in modern literature, the hemorrhagic form of this urgent pathology has also been classified according to the amount of blood loss into mild (blood loss 100–150 ml), moderate (blood loss 150–500 ml) and severe (more than 500 ml) ovarian apoplexy [7, 12,24] . However, the opinions of various scientists differ on the choice of tactics for managing patients depending on the amount of blood loss. The most debatable issues are the method of surgical intervention and indications for conservative treatment. L. V. Adamyan, A. S. Gasparov believe that laparoscopy is the main treatment method for any form of ovarian apoplexy, since it allows preventing adhesions in the pelvic organs, recurrence of the disease and pathology in the reproductive system [1,25,26]. Another point of view is shared by O. S. Elibekova, who believes that conservative treatment of ovarian apoplexy is also possible with a mild form with blood loss up to 150 ml. However, in this group, the risk of developing adhesions of the III—IV degree increases by 3.5 times, endometriosis of the pelvic organs - by 1.4 times [21]. According to S. V. Shtyrov, only the presence of massive blood loss and hemorrhagic shock can be an absolute contraindication to laparoscopy in the studied urgent pathology [20,27,28]. The problem of preserving the reproductive function of women after surgical treatment of ovarian apoplexy has gained increasing social and medical significance over the past few years. This is due to the steady increase in the number of patients under outpatient supervision after ovarian surgery and the high percentage of reproductive health disorders in this group, which largely determines the deterioration in the quality of life, especially at a young age. The issues of the impact of surgery on the reproductive potential of women after ovarian apoplexy are widely discussed. So, E. A. Kalinina believes that any surgical intervention on the ovaries leads to a decrease in a woman's fertility not only in natural cycles, but also during the IVF procedure. Thus, 10% of patients after wedge resection of the ovaries with the ovarian form of polycystic ovary syndrome (PCOS) do not respond to stimulation of superovulation, which is associated with a decrease in ovarian volume, as well as depletion of the follicular apparatus [4,29]. However, according to K. V. Krasnopolskaya, resection of the ovaries does not always affect their functional reserve and is mainly determined by the nature of the previous pathological changes in them, and not by the actual surgical intervention. She found that pre-existing endometriotic and inflammatory changes in the ovaries have the most negative impact on fertility. In addition, the author notes that as a result of surgery on the ovary / ovaries, coupled with the initially existing pathological process, an acquired disorder is formed in the vascular bed of the ovaries, which leads to a redistribution of circulating gonadotropins due to a

weakening of the microcirculation around the dominant follicles, which predetermines a weak response to stimulation of superovulation as part of the IVF program [54,32,33,34]. O. S. Elibekova believes that the frequency of ovulatory cycles after surgical treatment for acute gynecological diseases depends not so much on access as on the volume of surgical intervention [14,30,31]. Currently, in the available medical literature, we have come across a few works on the effect of ovarian apoplexy and both conservative and surgical treatment on women's fertility, as well as the course of pregnancy and childbirth [1]. However, any surgical intervention on the ovaries leads to problems in the performance of female reproductive function, not only in natural cycles, but also when applying the in vitro fertilization procedure [4]. As a result of surgical treatment of the studied ovarian pathology, a change in the concentration of gonadotropic hormones occurs due to the deterioration of microcirculatory circulation around the dominant follicle, which is caused by an initially existing pathological process and an acquired disorder in the ovarian vascular pool [4, 6,35,36]. As a result of these processes, it is legitimate to expect ovarian dysfunction. So, according to N. G. Litvintseva, in the late postoperative period, there is a high frequency of anovulatory cycles with the formation of follicular cysts or luteinization of unovulated follicles with the development of relapses of ovarian apoplexy. A morphological study of the ovarian tissue confirmed the results obtained by the researcher on the presence of a luteinized non-ovulated follicle in this pathology [9,37,39]. N.V. Sodnomova also pointed out the predominance of anovulatory menstrual cycles: hormonal imbalance by the type of hyperestrogen anovulation in patients with hemorrhagic form of ovarian apoplexy and ovarian dysfunction - with a painful form. In addition, highly resistant blood flow in the previously affected ovary, minor functional manifestations of encephalopathy, and hemodynamic disturbances in the form of increased cerebral perfusion were determined [15]. The results of the work of A. E. Ter-Ovakimyan indicate that one of the main gynecological disorders detected in patients after suffering ovarian apoplexy is a decrease in the functional activity of the corpus luteum - insufficiency of the luteal phase. For patients who have undergone ovarian apoplexy, the author recommends that reproductive function be realized up to 2 years after surgical treatment, since over 2 years there is a sharp decrease in the likelihood of childbearing, which may serve as a reason for turning to in vitro fertilization [17,43,39]. The study of the prevalence of infertility among operated patients showed its significant increase. Problems in the performance of reproductive function were diagnosed in every tenth woman, which is 4 times more often when compared with the same indicator before surgery. It is noteworthy that a low percentage of uterine pregnancy was observed among patients after a conservative method of treatment, in contrast to patients after surgery [21]. There are few data on the structure of complications during pregnancy and childbirth in patients with ovarian apoplexy in history. According to some authors, complications in the early stages of gestation predominate in pregnant women of this group, mainly in the form of spontaneous abortion and non-developing pregnancy. At the same time, the frequency of complications in late gestation and in childbirth was comparable to the average population [17,40,41,42]. According to our data (Zharkin N.A., Kravchenko T.G., 2014), ovarian apoplexy significantly more often leads to miscarriage, preeclampsia, premature rupture of amniotic fluid, rapid delivery and hypotonic bleeding in the early postpartum period. So, based on a retrospective analysis of a continuous sample of 6635 birth histories, the frequency of occurrence in the population of puerperas with a history of ovarian apoplexy was 0.94%. It was found that the main complication in the first trimester was reproductive losses, mainly in the form of non-developing pregnancy (OR = 2.66). In the early stages of gestation, the threat of interruption in the main group also occurred 3 times more often than in the control group (OR = 4.86). The development of preeclampsia in pregnant women with a history of ovarian apoplexy occurred 2 times more often than in the group without the studied nosology (OR = 2.52). In puerperas with a history of apoplexy, blood loss in the postpartum period was significantly higher than in the control group — 380 ml versus 280

ml ($p < 0.05$). In addition, 8.5 times more often hypotonic bleeding in the early postpartum period occurred in women with a history of ovarian apoplexy [3]. The main principles of managing patients after ovarian apoplexy are measures aimed at preventing the adhesive process and temporarily suppressing ovulation by prescribing combined oral contraceptives. In the early postoperative period, various methods of physiotherapy are recommended: magnetotherapy, quantum therapy, electrophoresis with longidase, zinc, ozone therapy [10, 15, 16, 17, 18]. In the late postoperative period, there are widespread recommendations for prescribing combined oral contraceptives (COCs) to prevent recurrence of ovarian apoplexy [5, 11, 15, 16, 17, 21]. At the same time, according to M. M. Chertovskikh, taking COCs does not affect the recurrence of the disease, but only gives a temporary clinical effect. When the ovulatory cycle is restored, relapses of ovarian apoplexy may occur again [19,43,44,3]. In accordance with this, O. M. Sirota recommends a differentiated approach when prescribing hormonal therapy, taking into account thrombophilic changes in the hemostasis system in the acute period of ovarian apoplexy [14]. So, based on a retrospective analysis of a continuous sample of 6635 birth histories, the frequency of occurrence in the population of puerperas with a history of ovarian apoplexy was 0.94%. It was found that the main complication in the first trimester was reproductive losses, mainly in the form of non-developing pregnancy (OR = 2.66). In the early stages of gestation, the threat of interruption in the main group also occurred 3 times more often than in the control group (OR = 4.86). The development of preeclampsia in pregnant women with a history of ovarian apoplexy occurred 2 times more often than in the group without the studied nosology (OR = 2.52). In puerperas with a history of apoplexy, blood loss in the postpartum period was significantly higher than in the control group — 380 ml versus 280 ml ($p < 0.05$). In addition, 8.5 times more often hypotonic bleeding in the early postpartum period occurred in women with a history of ovarian apoplexy [3,45,46,47]. The main principles of managing patients after ovarian apoplexy are measures aimed at preventing the adhesive process and temporarily suppressing ovulation by prescribing combined oral contraceptives. In the early postoperative period, various methods of physiotherapy are recommended: magnetotherapy, quantum therapy, electrophoresis with longidase, zinc, ozone therapy [10, 15, 16, 17, 18]. In the late postoperative period, there are widespread recommendations for prescribing combined oral contraceptives (COCs) to prevent recurrence of ovarian apoplexy [5, 11, 15, 16, 17, 21]. At the same time, according to M. M. Chertovskikh, taking COCs does not affect the recurrence of the disease, but only gives a temporary clinical effect. When the ovulatory cycle is restored, relapses of ovarian apoplexy may occur again [19,48.49]. In accordance with this, O. M. Sirota recommends a differentiated approach when prescribing hormonal therapy, taking into account thrombophilic changes in the hemostasis system in the acute period of ovarian apoplexy [14]. Pregnancy occurred in 40% of women out of 52% planning pregnancy after rehabilitation. At the same time, the authors noted in patients the presence of such complications of pregnancy as the threat of abortion, early toxicosis, mild to moderate gestational anemia [18,50,51]. Given the data on the inflammatory process as one of the etiopathogenetic factors of ovarian apoplexy, in modern literature it is considered necessary etiotropic antibiotic therapy with subsequent correction of the vaginal microbiocenosis as one of the stages of postoperative rehabilitation [16, 19, 52]. The conducted studies prove the dependence of the severity of ovulation diseases on the degree of infection of the genitourinary tract. According to some authors, surgical debridement of the abdominal cavity with subsequent elimination of the infectious agent and elimination of foci of infection can contribute to the implementation of reproductive function in 75% of patients [16]. An analysis of modern scientific data has shown the fragmentation of the existing rehabilitation schemes and the absence of a comprehensive system for restoring reproductive function from the acute period of ovarian apoplexy to the period of preconception preparation that affects all pathogenetic links, including the hemostasis system. Thus, the increase in the incidence of ovarian apoplexy over the past decades has updated the

study of this pathology. This contributed to a change in scientific views on the etiopathogenesis, classification and management of women with ovarian apoplexy. However, the uncertainty and controversy of many aspects of diagnosis, treatment and rehabilitation make modern scientific research in this direction urgent. An important point in the choice of tactics for the treatment of patients with ovarian apoplexy is the assessment of long-term results of treatment and the quality of life of patients who underwent surgical treatment for this reason. The solution of these problems will allow to preserve the reproductive function of a woman to the maximum, which is the main task of a surgeon who is faced with the problem of an acute abdomen in gynecological practice.

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