CLINICAL AND DIAGNOSTIC PARALLELS,
THERAPEUTICAL STRATEGIES IN BENIGN
OVARIAN TUMOR-LIKE FORMATIONS

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Abstract: This paper deals with study of the characteristics of clinical course of benign ovarian tumor formations in women of reproductive age, depending on the fertility and the choice of treatment strategy. Functional ovarian cysts in 60.45% of cases were diagnosed in parous patients, in 39.55% - in nulliparous women, in 5.22% - in women with infertility. Corpus luteum cysts in 36.96% of cases occurred in nulliparous patients, whereas follicular cysts were more common for parous women (28.4%) and infertile patients (28.57%). The clinical picture of ovarian retention formations to 56.72% of cases manifested by the pain syndrome in all patients, regardless of parity, whereas cycle disorders were more specific for parous patients (37.04%). In 14.29% of patients with infertility ovarian tumor formations were asymptomatic. In nulliparous patients inflammation of the uterine appendages was diagnosed significantly more often than in parous women. Increasing of the frequency of the myometrium pathology in the group of parous patients was significantly more often than in nulliparous women. Lack of individualization of the diagnostic algorithm, low commitment to hormonal, immunomodulatory therapy, use of standard antibiotic regimens led to ineffective treatment measures and to the formation of antibiotic resistance and the development of the process relapse.

Keywords: ovarian tumor-like formations, reproductive age, parous women, nulliparous women, sterility, ultrasound.

Introduction

The problem of the management of patients with benign ovarian tumor formations remains actual in gynecological practice. Originally medical tactics is determined by the characteristics of the clinical picture of the disease as well as previous treatment (Bondarenko, Ivashhenko and Svechnikova, 2004) and tumor markers, although the last, as shown by recent studies (Podzolkova et al., 2011), are not always informative. Nowadays in therapeutic arsenal of gynecologist there are modern hormonal contraceptives, the use of which is no longer limited by the contraceptive effect, and various forms of progesteron drugs, agonists of gonadotropin-releasing hormone (Podzolkova, 2009; Prilepskaya, 2009; Savel’eva and Gorodniceva, 2005; Serov and. Cvetaeva, 2009; Serebrennikova and Kuznecova, 2010). Treatment regimens of ovarian tumor formations are complemented by the active use of antibiotics, nonsteroidal anti-inflammatory drugs, immunomodulators, systemic enzyme therapy drugs (Tarasov, V., 2007; Romanov, 2000). The expansion of the classes of drugs recommended for the treatment of benign ovarian pathology, as well as the widespread introduction into clinical practice laparoscopic techniques largely simplify the problem of choice of treatment of tumor like formations of ovaries, but, unfortunately, not always reduce the percentage of disease recurrence. According to some researchers relapsing course of ovary tumors often reaches 40 - 50% (Rybalko, 2011; Vovk, and Kondratjuk, 2006; Rybalka, A. and Egorova, Ja., 2010). Such a high rate of relapse leads to restriction of drugs re-use and the expansion of indications for a surgical treatment. All this reduces the reproductive potential of women, which is especially important for nulliparous women and women with infertility.

The aim of the study was to conduct a retrospective evaluation of the effectiveness of treatment of ovarian tumor formation in women of reproductive age based on parity.

Method

A retrospective analysis of 3555 case histories of patients who were hospitalized in the Gynecological Department of the Municipal Clinical Hospital №7 Zaporozhye (Ukraine) for the period from 2009 - 2014. For a thorough analysis of the features of choice of medical tactics in benign ovarian tumor formations 134 case histories of patients with functional ovarian cysts have been selected by the method of blind randomization. All the patients underwent clinical examination,
transvaginal ultrasound of the pelvic organs. The data were processed using the statistical software package STATISTICA (StatSoft Statistica v.6.0).

Results

Investigated group consisted of 134 patients of reproductive age from 18 to 49 years (average 34,83 ± 0,82 years old). In accordance with the implementation of reproductive function they were divided into 3 groups: I group - women having born (81 patients - 60,45%); II group -nulliparous (53 - 39,55 %); III group - patients with infertility (7 persons - 5,22 %).

It was established that only 35 women had previously used various methods of contraception: 27 – barrier methods, 6 - hormonal, in 2 cases - intrauterine system "Mirena".

On admission to the hospital the leading place in the structure of complaints held pain syndrome - in 76 patients (56,72 %). The pain was aching, drawing the character of varying intensity, often radiating to the lumbar region, hip. The clinics of "acute" abdomen wasn't observed. In the I group the pain occurred in 37 women (45,67 %), in the II group -in 33 (71,74 %).

The second complaint rate were various disorders of the menstrual cycle – (37 cases – 27,61 %). Thus, bleeding was observed in 65,96 % of patients, amenorrhea - in 34,04 %. Intermenstrual bleeding had a history in 19 patients (51,35 %). In the I group menstrual disorders were observed in 30 cases (37,04 %), in the II group - in 7 (15,22 %).

Of the total number of surveyed in 14 patients (10,43 %) the pain syndrome was accompanied by various disorders of the menstrual cycle. Thus, in group I there was a combination of several complaints in 9 patients (11,11%), in the II group - in 4 (8,7 %).

The frequency of asymptomatic course of the disease as a whole was in 6,36 % of cases.

We noted that in the group of patients with infertility (III group) in 85,71 % of cases there was observed clinical manifestation of tumor formation. So, in 6 patients (85,71 %) there was a pain syndrome. In 1 case (14,29 %) the disease had asymptomatic course.

The obtained data are presented in Table 1.

<table>
<thead>
<tr>
<th>Clinical symptoms</th>
<th>I group N=81</th>
<th>II group N=46</th>
<th>III group N=7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain syndrome</td>
<td>37* (χ²=8,0) 45,67</td>
<td>33 71,74</td>
<td>6** (χ²=4,1) 85,71</td>
</tr>
<tr>
<td>Menstrual cycle disorders</td>
<td>30** (χ²=6,8) 37,04</td>
<td>7 15,22</td>
<td>0** (χ²=3,9) 0</td>
</tr>
<tr>
<td>Combination of several complaints</td>
<td>9 11,11</td>
<td>4 8,7</td>
<td>0 0</td>
</tr>
<tr>
<td>Asymptomatic course</td>
<td>4 4,94</td>
<td>2 4,35</td>
<td>1 14,29</td>
</tr>
</tbody>
</table>

Note: * - The difference between the rates of the I and the II groups is statistically significant, P <0,05;
** - the difference between the rates of the I and the III groups is statistically significant, P <0,05;
*** - the difference between the rates of the II and the III groups is statistically significant, P <0,05.

Thus, such symptom as the pain in the clinic of ovarian tumor formation was observed significantly more frequently in the group of nulliparous women (II group), and cycle disorders were significantly more frequent in patients with previously implemented reproductive function (I group). Almost in 15 % of cases of infertility ovarian tumor formation had no clinical manifestations, but rather, was diagnosed by chance during clinical examination or passing ultrasound examination. No significant statistical differences between the indices of the patients of the I and the III groups have been identified, although they were clinically significant.

When collecting history in patients with benign ovarian tumor formations it was found that in 30,08 % admitted to the hospital ovarian pathology was diagnosed as an independent nosological unit. 69,92 % of cases noted its combination with gynecological diseases. 34 patients (25,37 %) had
recurrent course of the disease. No doubt is the fact of infectious agent influence on the occurrence of abnormalities in the reproductive system. Given the low percentage of coverage of the patients of the study group by barrier methods of contraception (20,15%), special attention was paid to the frequency of the transferred inflammatory diseases. Thus, according to several studies (Kulakov, 2005; Vovk, et al., 2013) 60 % of ovarian cysts occur on the background of inflammatory processes, in 21,53% of patients there is a hyperproliferative pathology of myo- and endometrium.

24 patients in the I group (29,63 %) had a history of chronic salpingooophorites, in the II group - 26 patients (56,52 %) in the III - 3 (42,86 %). Thus, the medical history of chronic inflammation of the uterus and its appendages in the group of nulliparous patients in 1,9 times was more common than in women given birth. In patients with infertility incidence of inflammation observed in 3,2 times more likely than in having born women.

On admission to the hospital, all patients were held sonological examination. The results of ultrasound picture are presented in Table 2.

The results of sonological examination of the pelvic organs

<table>
<thead>
<tr>
<th>Gynecological pathology</th>
<th>I group (N=81)</th>
<th>II group N=46</th>
<th>III group N=7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abs. amount</td>
<td>%</td>
<td>Abs. amount</td>
</tr>
<tr>
<td>Salpingoophorites</td>
<td>18*(χ²=7,9)</td>
<td>22,22</td>
<td>22</td>
</tr>
<tr>
<td>Myoma</td>
<td>34*(χ²=8,7)</td>
<td>41,98</td>
<td>8****(χ²=14,6)</td>
</tr>
<tr>
<td>Endometrium pathology</td>
<td>28*(χ²=9,3)</td>
<td>34,57</td>
<td>5</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>10</td>
<td>12,35</td>
<td>2</td>
</tr>
</tbody>
</table>

Note:* - The difference between the rates of the I and the II groups is statistically significant, P <0,05; ** - the difference between the rates of the I and the III groups is statistically significant, P <0,05; *** - the difference between the rates of the II and the III groups is statistically significant, P <0,05.

Therefore, in nulliparous patients with cysts (II group) during ultrasound examination inflammation of the uterine appendages was diagnosed significantly more often than in parous women (I group), indicating probably a primary infectious genesis of cysts. Increasing of the frequency of the myometrium pathology in the group of patients with previously sold generative function (I group) was significantly more often than in nulliparous group (II group), and evidenced of hormonal disorders. The high frequency of endometrial pathology, which had hormonal and infectious aspects of occurrence (Vdovichenko and Gopchuk, 2012), was common both for the I and the II groups of patients. Such a high incidence of concomitant gynecological pathology coincided with published data, according to which the incidence of endometrial hyperplasia wass 25-89 %, uterine fibroids - 23-53 % (Davydov, 2007; Serebrennikova, 2010).

Analyzing the data of patients with infertility (III group), it has been identified a significant increase of the frequency of inflammatory diseases of the ovaries, and uterine fibroids compared with parous women (I group). The uterine fibroids rate was significantly higher in the group with infertility (III group) than in nulliparous group (II group), but the incidence of inflammatory diseases in these groups did not differ significantly.

The frequency of endometrial pathology incidence was significantly higher in the I group of patients compared to the II and the III groups. The frequency of endometrial pathology among the patients of the II and the III groups did not differ significantly.

Thus, on the basis of clinical features and ultrasound diagnostics it could be suggested that in patients with previously implemented of the reproductive function tumor-like formations of ovaries occur against the background of hormonal disorders, although the inflammatory factor was also important. In nulliparous patients genesis of cysts, probably had a primary infectious nature. While infertility had a combination of infection and hormonal factors.

Carrying out of ultrasound examination allowed to determine the nature of tumor formations in 40,3 % of cases. Thus, in general, the corpus luteum cysts were detected in 26 patients (19,4 %),
follicular cysts - in 28 (20.9 %). The diagnosis of ovarian tumor-like formation was put in 80 patients (59.7 %).

Table 3 presents data on groups.

### Table 3

<table>
<thead>
<tr>
<th>The nature of tumor-like formation of the ovary</th>
<th>I group (N=81)</th>
<th>II group N=46</th>
<th>III group N=7</th>
</tr>
</thead>
<tbody>
<tr>
<td>The corpus luteum cysts</td>
<td>8</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>Follicular cysts</td>
<td>23</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Ovarian tumor-like formation</td>
<td>50</td>
<td>26</td>
<td>4</td>
</tr>
</tbody>
</table>

#### Discussion

The data obtained allows the practitioner to carry out a differentiated treatment of tumor formation only in 40.3 % of cases, 59.7 % of patients receive a conventional treatment regimen.

Thus, when choosing a treatment strategy it is important to take into account the associated gynecological background and the nature of tumor formation. The findings suggest about differences of ethiopathogenesis occurrence of tumor-like formations of ovaries in women with various embodiments of the reproductive function.

It is known that many diseases of the reproductive system, and in particular, tumor-like formations of ovaries occur against the background of vaginal dysbiosis (Alieva, 2015). Many researchers have noted a connection between the implementation of the pathogenic effect of commensal microorganisms and reduction of local immunity (Shapoval and Voroncova, 2015; Tarkovskij, 2015). Microecosystem of vagina to some degree can be suggested as a marker of immune system wellbeing.

Therefore microscopy smears from the vagina in women with ovarian tumor-like formations was included to the general standard of clinical methods of examination. The data showed that 33 patients in the I group (40,74 %) had vaginal dysbiosis phenomenon in the form of colonization of coccus, coccobacillus. In the II group dysbiosis was detected in 22 patients (47,83 %) and in the III group – in 3 (42,86 %). Thus, 40 % of patients with retention ovarian cysts determined phenomenon of dysbiosis, often subclinical. Microscopic examination of the genital tract microflora suggested a decrease in tensions of immunological processes in the body that can later lead to chronic relapse and the emergence process. In order to achieve improved treatment outcomes by assigning selective antimicrobial drugs routine microscopy should be supplemented by culture methods to study the definition of bacterial sensitivity to antibiotics.

After completing general clinical and ultrasound examination all the patients were signed a course of treatment. 35 patients (26,11 %) of the total number of women in relation to endometrial pathology diagnosed echographically were conducted fractional treatment and diagnostic curettage of the uterus. in 4 cases (2,99 %) hysteroscopy was carried out. Puncture of tumor formation was performed in 6 patients (4,48 %). Surgical treatment was performed in 11 patients (8,21 %): in 2 cases - resection of the ovary (18,18 %) and in 81,82% (9 patients) the advantage of cystectomy was given. 123 patients (91,79 %) received a standard course of antikinflammatory therapy, comprising a broad-spectrum antibiotics, and nonsteroidal anti-inflammatory drugs. Immunomodulatory therapy was prescribed in 4 patients (3,25 %). Hormone therapy was administered in 7 cases (5,22 %) at the stage of the hospital in % of cases. The average duration of treatment in the hospital was 12,52 ± 0,51 days.

It should be noted that the choice of treatment strategy was implemented in accordance with generally accepted standards, without the individualization of reproductive potential implementation. If the correction of pain was performed in all patients with non-steroidal anti-inflammatory drugs, the menstrual cycle disorders, more typical for patients who gave birth, were not purposefully adjusted. The group of infertile patients who had asymptomatic course of disease (15 %) was also underestimated. Standard therapy and not always well-founded surgery in this group of patients often leads to chronic relapse and the development of process.

Standardization of anti-inflammatory regimens excluding etiology before suffering an inflammatory process leads to primary ineffectiveness of the treatment, as well as the development of
resistance of microorganisms to antibiotics, which is especially important in previously nulliparous patients and patients with infertility, who often face subacute endometritis and related disorders of steroid hormones receptions in ovarian tissue and endometrium. Correction of concomitant vagina dysbiosis was only carried out in 15% of cases by broad-spectrum drugs because of the lack of microbiological culture research. It is known that microorganisms of the genital tract mucosa, including commensals, are able to form biofilms (Shah, Spoering, and Lewis, 2004; Trautner, and Darouiche, 2004; Sandoe, 2006; Temke, 2006), which can lead to a lack of positive effect of the therapy, the development process of relapse under certain conditions.

Low adherence to hormone therapy retention ovarian cysts and its standardization without regard to the nature of tumor formations, leads to ineffective treatment strategy, the emergence of the recurrence of the process and therefore reduce reproductive potential.

A number of scientific studies (Shapoval and Voroncova, 2015) shows a different focus units of immunity in women with tumor-like formations of ovaries, depending on the implementation of their reproductive function, both the immunodeficiency states, and to autoimmune reactions. In this paper, attention is drawn to the low percentage of use of immunotherapy, which was carried out without prior immunogram.

Lack of individualization of the diagnostic algorithm in patients with tumor-like formations, low commitment to hormonal, immunomodulatory therapy, as well as the use of standard antibiotic regimens lead to ineffective treatment measures, as well as to the formation of antibiotic resistance and the development of the process relapse.

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