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CLINICAL MEANING OF RAPID GROWTH HYSTEROMYOMA, APPROACHES TO THE DIAGNOSTICS

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Introduction

Hysteromyoma is known as one of the leading points in the structure of gynecological morbidity rate in Russia; recently the growth of hysteromyoma incidence has been marked in women of reproductive age, as well as the tendency to the rejuvenation of sick women contingent [11, 18, 21]. The actuality of growing morbidity rate in women of reproductive age is considered because of preservation or restoration of reproductive function and in connection with frequent combination of hysteromyoma with pregnancy and hyperplastic processes of endometrium [10, 12, 24].

In modern literature two causes of rapidly growing hysteromyoma have been marked out: *true*, which is connected with activation of proliferative processes of myometrium, and *false*, which appears as a result of inflammation and edema of nodes [3, 11]. Thus, rapidly growing hysteromyoma demands the increased oncological suspicion because of the possibility of its combination with hyperplastic processes of endometrium, precancer and cancer of endometrium, ovary tumors and transformation to leiomyosarcoma [1, 16]. The performance of nonadequate operation in such cases significantly impairs the prognosis for a patient [1, 12, 16].

Timely and correct clinical assessment of various types of rapidly growing hysteromyoma often helps to specify the diagnosis and to determine the adequate treatment of such patients. That is why it is actual to search the criteria allowing to objectivize exactly the diagnosis of rapidly growing hysteromyoma in combination with endometrium pathology.

Methods of the investigation

For the achievements of the aim we have analyzed clinico-laboratory data of 978 women at the age of 24-56. The control group consisted of 268 (27,4%) patients without tumors of reproductive organs. All the rest were divided into two groups: the first one consisted of 478 (48,8%) patients with slowly growing hysteromyoma; the second group included 232 (23,7%) patients with rapidly growing hysteromyoma

(the increase of uterus sizes was as ≥ 4 weeks of pregnancy during a year).

All the patients had ultrasound examination of mammary glands and organs of pelvis minor (with transvaginal detector), along with traditional clinico-laboratory examination; according to showings some of them had mammography, cytologic examination of material from ecto- and endocervix, aspirate from the uterus cavity and hysteroscopy.

In addition to the listed above methods we worked out and used the specifying method of diagnostics of rapidly growing hysteromyoma. This method is based on the comparative estimating of uterus volume and making structural analysis of endometrial washes or menstrual discharges which flow from the organ with tumor.

The estimating in these biological fluids the final and interstitial products of peroxide lipid oxidation (malon dialdehyde in particular, which has the property of cellular toxin) reflected the level of free radical processes. The detection of malon dialdehyde was carrying out according to the technique of J.A.Stroev and J.G.Makarov (1986).

Recently the method of structural analysis (wedge-shaped dehydration) of biological fluids has been widely spread in clinical medicine; it is based on the extraction of information of overmolecular level in phase of transformation of biological fluid into solid condition [14, 19, 20].

For carrying out the morphostructural analysis 0,2 ml of supernatant of endometrial wash or menstrual discharge was put on the glass. The drop was dried at room temperature, at relative air humidity 60-70% and at minimal mobility of air during 18-24 hours. The studying of structure forming elements of the dehydrated drop (facii) and their photographs was carried out with magnifying from x10 till x160, with stereomicroscope Mz-12 (Leica) and colour digital camera "Pixera" (USA). Morphometrical showings of facii of endometrial wash were assessed with the programme Image Tool.

The size of uterus with hysteromyoma is one of the basic parameters in diagnostics and treatment. Its assessment according to weeks of pregnancy in the process of dispensary observation can be understood by physicians rather subjectively, this makes difficult to diagnose rapidly growing hysteromyoma.

For the objectification of uterus size and rate of growth of hysteromyoma the ultrasound showings were undergone the mathematical processing with the formula offered by A.N. Strizhakov et al.(2000) and J.M. Vikhliajeva (2004). The formula of drawn out ellipsoid was taken as a basis of calculation of uterus volume:

$V_0=5236*A*B*C$; A – the length of the uterus, B- its anteroposterior size, C – its width.

Because of hysteromyoma nodes the calculation of uterus volume was carried out according to the modified formula (the volume of separate hystero-

myoma nodes of any localization was added to the volume (V_0). Each hysteromyoma node was considered as a sphere, the maximal diameter of which was also assessed in ultrasound examination:

$V_i = 0,5236 (D_i)^3$, where V_i is the volume of 1, 2, 3 nodes etc.

$$V = V_0 + V_1 + V_2 + V_3 \text{ etc.}$$

For the assessment of power of statistical interconnection between the investigated showings (V – uterus volume; V_i – hysteromyoma nodes) the correlation-regressive analysis was carried out and the coefficient of determination was defined.

The showings of malon dialdehyde content and morphostructural features of endometrial washes or menstrual discharges were compared with the results of echographic examination of uterus sizes, cytological analysis of aspirates from uterus cavity and pathohistological results of endometrial cytologic brushings.

The results of the investigation and their discussion

The analysis of questionnaires showed that 80 (34,5%) of women with rapidly growing hysteromyoma complained of menometrorrhagia, 75 (32,3%) complained of pelvis pain, 12 (5,2%) had functional disturbance of adjacent organs, 45 (19,4%) had combination of symptoms, 20 (8,6%) didn't complain of anything. 232 (48,5%) women with slowly growing hysteromyoma complained of menometrorrhagia, 101 (21,1%) had pelvis pain, 77 (16,1%) had combination of symptoms, 8 (1,6%) had functional disturbance of adjacent organs, 60 (12,2%) had no complaints.

The duration of the disease for 5 years was marked in 58,4 % women with slowly growing hysteromyoma and in 75,9 % with its rapid growth ($p < 0,01$) All the rest patients in both groups had the duration of the disease more than 6 years. The uterus sizes (according to pregnancy weeks) were normal in the control group; $7,8 \pm 0,73$ in women with slowly growing hysteromyoma, $13,7 \pm 1,14$ in women with rapid growth ($p < 0,01$). Operations in women with rapid hysteromyoma growth were performed in 97,8% of cases, in women with its slow growth in 74,9 %; all the rest had conservative therapy.

In addition the analysis of the number of nodes and the peculiarities of their localization was carried out. Submucous nodes were registered equally in both groups ($p \geq 0,05$). Multiple hysteromyoma nodes were two times more often in women with rapid growth – 84 (36,2%) in comparison with the group with slow growth – 81 (16,9 % $\pm 1,7$ %, $p < 0,01$).

The preferential localization of nodes among the patients of both groups were the fundus and the body of uterus: in 88, $1 \pm 1,48\%$ with slow growth and in $74,6 \pm 2,8$ with rapid growth. The localization of nodes in the area of uterus ribs was marked more often in women with rapid hysteromyoma growth ($p < 0,05$). In patients with slow growth the average size of

the biggest node was $3,5 \pm 0,12$ cm, and in the group with rapid growth it was $6,9 \pm 0,22$ ($p < 0,001$).

The important factor which defined the treatment of women having hysteromyoma is the condition of endometrium. In 61 (26,3%) patients with rapidly growing nodes the structure of endometrium was normal, in 127 (54,7%) women the glandular hyperplasia was revealed, 3 (1,29%) had atypical hyperplasia, in 41 (17,6%) women the endometrium was diagnosed. Besides, 1 patient (0,4%) had carcinosarcoma, 5 patients ($2,2 \pm 0,95\%$) had proliferated hysteromyoma, 37 patients ($15,9 \pm 2,4\%$) had combination of hysteromyoma with adenomyosis, and 11 patients (47,8%) had hysteromyoma with ovary tumors.

In patients having slowly growing hysteromyoma normal endometrium structure was revealed in 231 (48,3%) cases, glandular hyperplasia was diagnosed in 79 (16,5%), atypical hyperplasia in 4 (0,8%) cases, 87 (18,2%) patients had endometritis. It is important to note that 23 (4,8%) cases of endometrium cancer were revealed in patients of this group.

The duration of hysteromyoma in patients with cancer fluctuated from 6 to 27 years, it was $15,5 \pm 0,25$ years, in average. The frequency of revealing carcinosarcoma and ovary tumors in this group corresponded to the frequency of their revealing in patients having rapidly growing hysteromyoma: 3 (0,6%) and 213 (44,6%) cases. The frequency of proliferated hysteromyoma and adenomyosis in patients with slowly growing hysteromyoma was less: 1 ($0,2 \pm 0,08\%$) and 50 ($10,5 \pm 1,6\%$) cases ($p < 0,05$).

The received data allow to consider hysteromyoma as one of the main risk factors of tumors of reproductive organs (multiple primary tumors among them).

Nowadays, a lot of factors have been gathered which show the excessive activation of peroxide lipid oxidation and activity changing of antioxidant protection enzymes in some pathologic processes [6, 7, 9, 13]. The activation of peroxide lipid oxidation is considered as a mechanism of cellular pathology development and the reason of many cardiovascular, oncological, autoimmune diseases. The most aggressive are final and intermediate products of peroxide lipid oxidation, malon dialdehyde in particular. It is possible that the increasing in number of oxidated proteins change cell functions, especially the receptor apparatus of membranes. The damage of antioxidant protection and the growth of peroxide lipid oxidation products leads to the changes in genetic apparatus and the disturbance in regulation of apoptosis and to the decreasing of cell activity limits [13]. The accumulation of malon dialdehyde changes the receptor apparatus of the organ and promotes the intensification of pathologic process in tissues in connection with the loss of their sensitivity to humoral influence [15]. In rapidly growing hysteromyoma nodes biochemical changes take place: the aerobic and anaerobic rate glycolysis is increased [16]. It is possible that the development of

hyperplastic endometriosis arises due to intensification of peroxide lipid oxidation reactions, which are evident in the increasing of lipid peroxidation products level [2, 22].

The determination of malon dialdehyde was carried out in blood serum and menstrual discharges, and in these biological liquids the received results were the most evident.

Table 1. Uterus volume and malon dialdehyde level in rapid and slow growing of hysteryomyoma.

The investigated groups	Uterus volume (cm ³), M±m	Malon dialdehyde, peripheral blood (nmol), M±m	Malon dialdehyde, endometrial washes (nmol), M±m	Malon dialdehyde, menstrual discharges, (nmol), M±m
Control (n= 268)	50,5 ± 1,0	0,71 ± 0,02	0,37 ± 0,01	0,62 ± 0,07
Slowly growing hysteryomyoma (n = 478)	243,7± 21,32 ²	0,85±0,04	0,49±0,06 ¹	1,59±0,04 ²
Rapidly growing hysteryomyoma, true growth (n=191)	1636,0 ± 79,6 ^{3,6}	1,74± 0,07 ^{3,6}	2,6± 0,05 ^{3,4}	2,81± 0,08 ^{3,6}
Rapidly growing hysteryomyoma, false growth (n=41)	826,0± 21,2 ^{3,6}	1,31± 0,07 ^{2,5}	1,45± 0,05 ^{3,4}	1,61± 0,07 ^{2,5}

The differences are true:

¹p<0,05, ²p<0,01, ³p<0,001 – in comparison with the control group; ⁴p<0,05, ⁵p<0,01, ⁶p<0,001 – between the showings in the subgroups.

The table shows that the uterus volume in patients from the control group didn't differ from the normal meanings. The coefficient of determination, calculated between the volume of hysteryomyoma nodes and the uterus volume was 0,77 with slow growth and 0,65 with true rapid growth of hysteryomyoma, this fact reveals the presence of strong and middle connection between the investigated parameters.

In the assessment of growth rate due to the received data for slowly growing hysteryomyoma the average increasing of the organ during a year didn't exceed 21,3 % (p < 0,05). In this given case the critical level of meaning (p) was defined concerning patients with slowly growing hysteryomyoma. Along with the increasing in number and diameter of hysteryomyoma nodes and uterus size the level of malon dialdehyde in endometrial washes or menstrual discharges also increased.

In patients with preserver menstrual cycle the determination of malon dialdehyde was carried out both in the stage of proliferation and secretion. From 231 women with slow hysteryomyoma growth (having normal structure of endometrium), 131 (56,7%) patients were observed, and in the phase of secretion 100 (43,7%) patients were observed. Showing of malon dialdehyde in the phase of proliferation was 0,5 ± 0,02 nmol, in the phase of secretion – 0,6 ± 0,02 nmol (p > 0,05).

Thus, the showings of malon dialdehyde received both in the phase of proliferation and in the

phase of secretion in women with hysteryomyoma having normal structure of endometrium had small differences and didn't depend on the phase of menstrual cycle.

The most demonstrative was the dynamics of malon dialdehyde content in endometrial washes according to the increasing of endometrium pathology. Patients having hysteryomyoma with normal structure of endometrium the investigated showing was 0,4 ± 0,05 nmol, and patients having hysteryomyoma in combination with hyperplastic endometrium processes it was 1,7 ± 0,23 nmol (p < 0,01). Even more significant increasing was marked in patients having rapidly growing hysteryomyoma in combination with atypical hyperplasia, the meanings were 3,0 ± 0,85 nmol (p < 0,05).

In patients having hysteryomyoma with endometrium cancer the level of malon dialdehyde was variable, it depended on the depth of invasias and differentiation of tumor. On the first and second stage of the disease (T1-2NoMo, G1) the level of malon dialdehyde in endometrium washes was 0,61 ± 0,21 nmol, with T1-2 and G2 the maximum meaning of malon dialdehyde was 1,11 ± 0,3 nmol (p < 0,01). In patients having the third stage of the disease (T1-3, Nx-1, Mo G3) the meaning was 3,02 ± 0,15 nmol (p < 0,001).

The analysis of structure forming elements which were revealed by the method of wedge-shaped dehydration of endometrial washes allowed to determine 3 types of facii, characterizing the condition of endometrium. The radial type, forming the so-called

“separate parts”, was always registered in women of control group (during both phases of menstrual cycle) and in 48,4 % cases in patients having hysteromyoma with normal structure of endometrium. The combined type was found in patient having hysteromyoma in combination with hyperplastic endometrium processes, the radiallyity was preserved, but a number of three ray fissures appeared; and then the three ray type appeared, which was specific for women with atypical hyperplasia and endometrium cancer. In the investigated material of women with endometrium cancer on the whole area of facii of endometrial washes the net of three ray fissures appeared.

Thus, pathognomonic sign of the increasing of endometrium pathology (in patients with rapidly growing hysteromyoma among them) is the increasing of specific proportion of area of three ray fissures (Str) and the decreasing of radiallyity area (Srad).

Thus, in patients of control group Str was $0,4 \pm 0,06$ mm², in patients having hysteromyoma with normal endometrium structure it was $1,1 \pm 0,08$ mm², and in patients having glandular hyperplasia and atypical hyperplasia of endometrium it was $2,1 \pm 0,11$ mm² and $3,2 \pm 0,58$ mm². This showing was maximal in patients having hysteromyoma in combination with endometrium cancer $6,7 \pm 0,6$ mm² ($p < 0,05$).

To determine the strength of interconnection between Srad and Str the tetrachoric Pirson coefficient was calculated, which was increased with the increasing of pathology of myoendometrium from 0,3 in the control group to 0,8 in patient having endometrium cancer.

The presented diagnostic approach providing nontraumatic method of taking material allows to get the information of tumor growth and endometrium condition in out-patient clinic with small amount of biological fluid (with minimal financial expenditures and in short terms). It helps to make the proper plan of treatment. Another important characteristics of this approach is the possibility of simultaneous carrying out of cytological biochemical and crystallographic methods of research which increases the exactness of diagnostics. It should be noted, that the given parameters must be assessed regularly due to normative documents; only this approach allows to make conclusions about slow or rapid growth of hysteromyoma.

The results of the investigation are the patent for the invention (Russian Federation) №2290639, given 27.12.2006. “Method of the evaluation of endometrium condition in female genitals neoplasms”, and the positive reply for the patent №2007106294 (006840) given 19.01.2008 “Method of the diagnostics of rapidly growing hysteromyoma”.

Conclusions:

1) Rapidly growing hysteromyoma is the disease which decreases reproductive possibilities of women; it is a risk factor of multiple primary tumors (hyperplastic processes of endometrium and endo-

metrium cancer among them) of hormonodependent organs.

2) Mathematical analysis of uterus sizes received in ultrasound examination allows to specify the rate of hysteromyoma growth. In average annual increase of uterus volume not exceeding 12,5 % the slow tumor growth takes place; in the increase of uterus volume to 14,9% there is a possibility of false hysteromyoma growth; in average annual increase of volume more than 21,3 % we should consider true rapid hysteromyoma growth.

3) The level of malon dialdehyde in endometrial washes or menstrual discharges correlates also with the degree of hyperplastic processes; the evaluation of this showing increases the effectiveness of the diagnostics.

4) For the more exact evaluation of endometrium in patients with hysteromyoma the traditional cytologic investigation of aspirate from the uterus volume should be supplemented with the structural analysis of facii of endometrial wash (or menstrual discharge) which reveals pathognomonic signs of the increasing endometrium pathology, the increasing of area of three ray fissures on the surface of facii in particular.

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THE TOPICAL AND TEMPORAL CHANGES IN QUANTITATIVE ELECTROENCEPHALOGRAPHY OF HIGH QUALIFICATION ATHLETES OF DIFFERENT SPECIALIZATIONS DURING ONE YEAR TRAINING PROCESS

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The Sports Council (London) on behalf of the Open Section of the British Association of Sports Sciences commissioned a review to provide information pertinent to the formulation of a strategy that would guide fundamental sports science research in the UK and propose directions for future research. The four topics were peaking, talent identification, adherence and injuries (Burwitz L. et al., 1994). Neurobiofeedback has used since 1967 with the aim to treat some illness and with the aim to achieve the peak performance in athletes (Angelakis E. et al., 2007).

The relation between humane performance and they functional condition described as parabolic curve and carried in practice the notion of optimum functional condition. However, in spite of conspicuity of practical value of the problem of the functional condition, methods of its diagnostics and optimization remain it is not enough studied (Danilova N.N., 2003). With reference to the training process of the elite athletes there is very small number of the studies intercoupling the functional condition and electrical activities of the cerebrum, executed by method visual-logical description of electroencephalogram (EEG). Study of the quantitative factors of electroencephalogram (QEEG) will allow to get elaborating dates about relationship of QEEG with functional condition of athlete and to get new predictors to the athlete's capacity.

The purpose of this investigation was to obtain the additional dates about QEEG of high qualification athletes during the large circle of there training and competition process.

The organization and the methods of investigation

The number of athletes have took participate in the study were 81. Athletic specialization was ski racing at 17 participant, biathletes were 6, hockey were 24, volleyball were 14, football were 10, box were 4, fight were 4, swimming was 1 and billiards was 1. The sportive qualifications of participants were following: the master of sport of international class – 3; the master of sport – 12; the candidate master of sport – 34; first category – 32. The participant's age was $20 \pm 1,7$ years. Male persons were 57 and female persons were 24. The survey at starting-up period was performed at