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CERTAIN ASPECTS OF THE DIAGNOSIS OF POLYCYSTIC OVARY SYNDROME IN FERTILE WOMEN.

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Abstract:

Current diagnostic criteria for polycystic ovary syndrome (PCOS) are reviewed with emphasis on stratification of subtypes based on metabolic features. Then, from the identified subtype, treatment options are reviewed according to the management goal: relief of hyperandrogenemia symptoms, menstrual regulation and fertility restoration. The diagnostic features of SPCJ, including ultrasonographic features, are relevant to the diagnosis. It is believed that future studies should focus on the health outcomes of postmenopausal women with PCOS.

Keywords: polycystic ovary syndrome, ultrasound diagnostic criteria

Polycystic ovary syndrome (PCOS) is a genetic and epigenetic endocrine disorder. At the same time, there is a view that PCOS is a multifactorial systemic inflammatory steroid dysregulation, an autoimmune disease that manifests largely due to an inappropriate lifestyle. The clinical manifestations of this syndrome depend on the age and period of a woman's life, and diagnostic and therapeutic measures have their own specificities. This is due to the fact that CJS manifests itself with a complex of reproductive, metabolic and psychological features. Due to reproductive disorders, the syndrome is accompanied by infertility; endocrine disorders are associated with disturbances of carbohydrate metabolism, clinically manifested by type 2 diabetes mellitus (DM).

Hyperandrogenic dermatopathy is expressed as acne, hair growth, alopecia. In older age, cardiovascular diseases and hyperplastic processes of the endometrium are observed. Psychological disorders in the form of depressive states, anxiety disorders, sudden mood changes may accompany the syndrome throughout the reproductive period of a woman's life. In the late reproductive period, malignant diseases may develop, which is largely due to the presence of obesity in a number of patients with PCOS .

Currently there is no uniform understanding of the pathogenesis and aetiology of CJD. At the same time, the pathogenesis of the syndrome is characterised by changes in various parts of the neuroendocrine system, and disturbances occurring in these parts may be the trigger for the development of severe symptoms of the disease. These changes may originate at any level of the hypothalamic-pituitary-ovarian system, as well as in the adrenal glands and peripheral insulin-dependent tissues.

The prevalence of CJD is 8-21% . CJD is a widespread disease, which is the most common endocrine-metabolic disorder in women of reproductive age.

In the International Classification of Diseases, 10th Revision, PCOS is classified under the code for ovarian dysfunction (E28): E28.2 - Polycystic ovary syndrome. The European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine define the criteria for PCOS: oligoabortion, hyperandrogenemia (clinically or biochemically manifested), polycystic ovarian morphology on ultrasonography. If two of the three main criteria are present, a specific type (phenotype) of PCOS is defined. Clinicians should clearly identify a patient's phenotype when making a diagnosis of PCOS.

Despite the current view that CJD may be a complex polygenic disease with strong epigenetic and environmental influences, including diet and lifestyle factors, the syndrome is often associated with abdominal obesity, insulin resistance, obesity, metabolic disorders and cardiovascular risk factors.

Although numerous studies have focused on PCOS, the underlying pathophysiological mechanisms of the disease remain unclear. The perception is that mitochondria play a key role in energy production and mitochondrial dysfunction at the cellular level can affect systemic metabolic balance. The recent widespread recognition of functional mitochondrial abnormalities as a correlating factor in numerous diseases has led to the suggestion that abnormal mitochondrial metabolic markers are associated with PCOS. Studies in recent years have confirmed that increased oxidative stress is associated with the progression and associated complications of PCOS, and have also shown an association between other mitochondrial dysfunctions and PCOS.

The diagnosis of PCOS is based on the results of clinical manifestations: hyperandrogenic

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dermatopathy, laboratory data suggestive of hyperandrogenemia, anamnestic evaluation of menstrual and ovulatory periods, as well as the morphological structure of the ovaries, which is determined by ultrasound. The various approaches to diagnosing the syndrome may differ slightly depending on the age period of a woman's life. In young adolescent girls, CJD may be suspected in the presence of clinical signs of hyperandrogenemia and menstrual abnormalities, with little or no consideration of ultrasonographic criteria. In general, PCOS poses a particular diagnostic challenge in adolescents because physiological changes during puberty may present a similar phenotype. Thus, the application of adult criteria leads to overdiagnosis of PCOS in adolescents.

Other authors believe that the diagnosis and treatment of CBC is straightforward, requiring only the judicious application of several well-standardized diagnostic methods and appropriate therapeutic approaches for hyperandrogenism, the consequences of ovarian dysfunction and associated metabolic disorders. The diagnostic criteria for the comorbidities of GDM, which may occur more frequently than in the general population and may also be a consequence of the syndrome, should be particularly well known. Women with MS are at increased risk of glucose intolerance and type 2 DM. Hepatic steatosis and metabolic syndrome, hypertension, dyslipidemia, vascular thrombosis, cerebrovascular disorders, risk of arterial hypertension; infertility and obstetric complications; atypia or endometrial carcinoma and possibly ovarian malignancies; mood disorders and psychosexual disorders. It is also important to consider different phenotypes separately when determining management, as they may require different treatments with different outcomes.

Traditionally, the evaluation of patients suspected of having CTC includes a careful detailed history and physical examination, evaluation for hyperthyroidism, ovarian ultrasound and hormonal tests to confirm hyperandrogenism and oligoimmunoreactivity, as appropriate, and to exclude similar or mimicking disorders (9). Based on the relatively small number of studies conducted so far, an increased prevalence of various psychiatric disorders may be observed in women with PCOS. These include depression, generalized anxiety disorder, personality disorders, social phobia, obsessive-compulsive disorder, attention deficit hyperactivity disorder and eating disorders. Bipolar affective disorder, schizophrenia and other psychotic disorders are also more common in patients with PTSD than in the general population. The higher prevalence of psychiatric disorders in CJD patients, particularly depressive and anxiety disorders, may be due to both hyperandrogenemia and the resulting somatic symptoms.

When a general examination is performed and symptoms of hyperandrogenic dermatopathy (acne, significant facial hair or, conversely, hair loss) are detected, a hair number is calculated to assess the level of hair loss using the modified Ferriman-Gallwey scale. Excessive hair loss is more common in the classic syndrome phenotype and occurs in 75% of patients. Hairiness is usually indicated by an elevated score (above 4) on the scale, but racial characteristics of body hairiness should be taken into account. The severity of hair loss in CJD is not always associated with an increase in serum androgen levels. Greater hair loss is sometimes identified with a small increase in androgen levels, while a significant increase in markers is not always accompanied by significant loss of body hair. The lack of correlation between hormonal markers and the degree of hair loss is due to the different individual sensitivity of target tissues to hormones.

If there are complaints of acne and significant hair loss, a dermatologist should be consulted to determine the cause of hyperandrogenic dermatopathy. At the same time, there are no validated scales for determining the severity level of acne; the existing Ludwig scale is used to determine the severity level of baldness in the scalp area. The occurrence of acne and alopecia are not reliable indicators of elevated serum androgens. In adolescent girls, only severe acne is considered a reliable symptom of hyperandrogenemia.
General examination of patients may reveal black acanthosis, which is one of the clinical signs of insulin resistance (IR) in patients with PCOS. The signs of black acanthosis are papillary and pigmented dystrophic skin lesions in the form of small localized areas of dark brown hyperpigmentation in the folds, most commonly located in the neck region, often in the axillae and groin. Histological examination of these areas reveals hyperkeratosis or papillomatosis.
Patients with a presumptive diagnosis of PCOS should have their height and body weight measured and body mass index (BMI) calculated to identify overweight or obesity.

Increased BMI in CJD is more common than in the general population, which significantly increases the risk of type 2 diabetes by 4-fold. Obesity in CJD is an additional risk factor for cardiovascular disease, as well as a factor leading to an increased risk of endometrial cancer (occurring many times more frequently than in women without CJD). Obesity is also an aggravating factor in the development of depressive and anxiety states; a factor affecting fertility and the adequate

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effectiveness of reproductive rehabilitation; a factor affecting obstetric and perinatal outcomes. The measurement of waist circumference (WC) to determine abdominal (visceral) obesity is also an important study. If the distribution of adipose tissue is male, which is associated with a higher risk of functional carbohydrate disorders and cardiovascular disease formation, patients have a WC greater than 80 cm. Patients with CTPJ are more likely to have abdominal obesity associated with metabolic diseases. The distribution of abdominal adipose tissue is more correlated with IR. Determination of OT in centimeters is an informative and simple anthropometric method that indicates the presence of metabolic dysfunction, as it is directly related to the amount of abdominal adipose tissue.

Obstructive sleep apnea syndrome usually occurs in obese women and is manifested by snoring, daytime sleepiness and increased fatigue. This is the reason for referring a woman for polysomnography to specialized institutions. Cardiovascular disease risk assessment in women with this syndrome is of great importance in evaluating long-term risk factors. Blood pressure is measured during the annual dynamic follow-up of patients; if complaints arise, the therapist or cardiologist determines the frequency of follow-up according to the results of the examination.

The lipid profile is initially assessed by biochemical blood testing; later, when disorders of lipid metabolism are detected by biochemical testing and in combination with an increased risk of cardiovascular disease, the frequency, rate and volume of testing depends on the pathology detected in the woman. The indications for triglyceride studies as part of a set of analyses of lipid profile are the diagnosis of primary and secondary disorders of lipid metabolism, assessment of the risk of atherosclerosis and its complications.

Diagnostic examination is required when there are certain complaints and in cases of anxiety and depressive disorders in patients with CKD due to the increased risk of formation of such changes.

Laboratory tests consist of evaluating hormone levels. In suspected CBC, especially if there are manifestations of hypothyroidism, anovulation, amenorrhea, oligomenorrhea, the level of free testosterone in the blood is first examined and the free androgen index (FAI) is calculated. A significant portion of circulating testosterone is bound to sex hormone binding globulin (hsBG), a smaller portion is bound to albumin, although mostly it is easily released and bioavailable, and only a small portion of testosterone is in free form. If the amount of transport proteins is altered, this ratio may change and therefore, in addition to determining total testosterone, it is appropriate to test this globulin. ISA is an index of the ratio of total testosterone to hsCRP and the following formula is used: ISA = total testosterone (nmol/l) / HGH (nmol/l) · 100. The normal value of ISA in women of reproductive age ranges between 0.8 and 11%. For confirmation of biochemical hyperandrogenemia in patients with suspected CSF, liquid chromatography or gas chromatography with mass spectrometry, as well as radioimmunoassay studies with organic solvent extraction and further chromatography are recommended. Direct methods for the determination of free testosterone are not desirable.

Methods for the determination of free testosterone. Determination of dehydroepiandrosterone sulphate is considered an auxiliary criterion for biochemical hyperandrogenemia. This hormone is usually tested in women in whom total and free testosterone levels are not elevated, although these criteria only provide relevant information for the identification of PCOS. If a woman with PCOS is taking combined oral contraceptives or other hormone-containing medications, evaluation of biochemical hyperandrogenemia may show false results. In such cases, these drugs should be discontinued for 3 months.

Modern hormonal contraception defines a new quality of life for modern women, is prescribed for gynecological diseases and syndromes, allows to maintain reproductive health and in some cases even increases life expectancy. Therefore, the use of modern hormonal contraceptives for therapeutic and preventive purposes in women who do not need contraception is nowadays considered a progressive trend in gynecology and reproductive medicine, and for this purpose women with CKD often take combined oral contraceptives.

To detect carbohydrate disorders, the glycaemic status of patients with CHD is studied and fasting glucose levels, oral glucose tolerance test (GTT) or glycosylated haemoglobin levels are mandatory. A 2-hour oral glucose tolerance test is indicated in the presence of a BMI above 25 kg/m2, hyperglycaemia, impaired carbohydrate tolerance, gestational diabetes in a previous pregnancy and a complicated hereditary history of DM. The most common indication for oral HTT in patients with DM is the prenatal stage. There is an opinion that it is necessary to conduct studies to diagnose disorders of carbohydrate metabolism in the dynamics of 1-3 years. Routine testing of plasma immunoreactive insulin levels in patients with confirmed CHD is also considered unpopular. Meanwhile, indirect assessment of IR is performed by determining the HOMA and Caro index.

Quantitative determination of antimüllerian hormone is not performed unless specifically indicated.

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To confirm ovulatory dysfunction in patients of reproductive age, progesterone is tested on the 6th or 8th day after ovulation [2]. If regular menstrual cycles are present, ovarian function is assessed by echographic examination of the ovaries and other reproductive organs on the 21st-22nd day after the onset of the menstrual cycle. During the menstrual cycle, progesterone secretion begins to increase during the premenstrual period, reaching a peak in the middle of phase II. Its concentration returns to baseline at the end of the cycle and this sharp drop in progesterone concentration causes menstrual bleeding. A progesterone level of less than 3 ng/ml in the middle of the progesterone phase indicates that ovulation did not take place in the cycle. If the progesterone level is less than 10 ng/ml or if the sum of the progesterone levels in 3 consecutive menstrual cycles is less than 30 ng/ml, this indicates phase II failure, that subclinical markers of cardiovascular disease, such as coronary artery calcium, C-reactive protein, carotid endometrial thickness and endothelial dysfunction, are more likely to be elevated in women with CHD. Although the association between CHD and cardiometabolic abnormalities is well documented, it is not clear whether CHD is associated with subclinical and clinical cardiovascular disease independently of these cardiovascular risk factors.

Among the instrumental diagnostic tests for SPCJ, pelvic ultrasound is the main diagnostic test . The following ultrasound criteria of polycystic ovaries are used: using a transvaginal transducer with 8 MHz - presence of more than 20 follicles with a diameter of 2-9 mm in any ovary or an increase in the volume of any ovary above 10 cm3 (absence of luteal body, cysts or dominant follicles), with lower resolution characteristics of the ultrasound device or with the transvaginal transducer - an increase in the volume of any ovary above 10 cm3. If the examination shows evidence of corpus luteum, cysts, dominant follicles, the next ultrasound examination is scheduled after automatic or induced menstruation.

Ultrasonographic evidence of polycystic ovaries is not used as a diagnostic criterion in adolescent girls with suspected CSF within 8 years after menarche, due to the high incidence of polycystic ovarian structure at this age .

The specificity of diagnosing PCOS by ultrasound examination is the use of transvaginal access in sexually active women with an existing menstrual cycle in the follicular phase and, in case of amenorrhea, after menstruation induced by progesterone use (progesterone test) .

Other diagnostic tests include detection of anorexia and identification of diagnostic criteria for irregular menstrual cycles in women of reproductive age: cycle length greater than 35 days or less than 8 menstrual cycles per year in women; cycle length less than 21 days . In adolescents, the following criteria for irregular cycles should be used more than 90 days for each cycle in the first year after menarche; less than 21 days or more than 45 days between 1 and 3 years after menarche; primary amenorrhoea by age 15 years or after 3 years after menarche; less than 21 days or more than 35 days or less than 8 cycles per year between 3 years after menarche.

CONCLUSION

In summary, current diagnostic criteria for CJD are reviewed with emphasis on stratification of subtypes according to metabolic features. Then, depending on the identified subtype, treatment options are reviewed according to the goal of patient management: alleviation of hyperandrogenemia symptoms, regulation of menstrual flow, and restoration of fertility. There are also peculiarities in the diagnosis of PCOS in adolescence. It is believed that the subsequent focus should be on the health consequences of postmenopausal women with PCOS. Most meta-analyses of women of reproductive age show an increased risk independent of obesity. Longitudinal and cross-sectional studies including women with PCOS over 40 years of age are limited in number and design, but many demonstrate that some of these comorbidities persist. All healthcare providers involved in the comprehensive management of women with CKD should be aware of these long-term health risks in order to provide appropriate counseling, testing, and treatment options.

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