Study on autoimmune antibody of infertile women based on ultrasound images

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Abstract. Objective: to study the clinical value of reproductive immune autoantibody based on ultrasound image in the diagnosis of infertility. Methods: Eighty infertile women who were admitted to our hospital from June 2019 to May 2020 were included in the study. ELISA was used to detect the serum reproductive immunity antibodies of the patients, including anti-sperm antibody (AsAb), anti-endometrial antibody (EMAb), anti-ovarian antibody (AOAb) and anti-cardiolipin antibody (ACA). Results: the results of reproductive immune antibody test indexes of female infertility patients with different types were compared, and the difference was statistically significant (p < o. 05). conclusion: the detection of reproductive immune autoantibody in clinic can be used for the diagnosis of female infertility, and has important clinical value.

Keywords: Ultrasound images; Infertility; Autoimmune antibody

1. Introduction

Infertility has become a common clinical problem at this stage, and the probability of infertility for couples of childbearing age is as high as 10% – 15% [1]. Clinical studies have found that female factors, male factors and both factors may lead to infertility [2]. There are many causes for female infertility, and the effect of immune factors has attracted increasing clinical attention. For this part of unexplained infertility, it is currently tended to think that its pathogenesis is related to immunity [3].

The common mechanisms of inducing factors leading to immune infertility are as follows: On one hand, precipitating factors such as infection and trauma destroy the isolation state of reproductive tract autoantigen from the immune system, causing the overflow of super physiological amount of autoantigen; Second, the resulting inflammatory reaction causes a large number of immunocompetent cells, such as T lymphocytes and mononuclear macrophages, to infiltrate into the tissues of the reproductive system so that they can fully contact with their own antigens to stimulate autoimmune reactions. There are four antibodies in infertility patients: antisperm antibody (ASAb), anti-endometrial antibody (EMAb), anti-ovarian antibody (AOAb) and anticardiolipin antibody (ACA). The main disease of infertility is due to the abnormalities of these antibodies [4 - 5]. In this paper, based on ultrasound images from the serum reproductive immune antibody detection, through the detection and analysis of 80 patients in our hospital, and obtained the relevant clinical value, which is now reported as follows.

2. Research progress on the production of reproductive immune antibodies and the mechanism of infertility

2.1 Normal reproductive process

Mature sperm enter the female reproductive tract through sexual intercourse, and under the action of degradation enzymes in the female reproductive tract, the desensitizing factors on the surface of the acrosome are degraded to enable the sperm to be capacitated. The obtained sperm run to the ampulla of fallopian tube and meet with egg, and the sperm contacts with cumulus cells to produce acrosome reaction; acrosome enzyme releases and dissociates follicle cells of radioactive crown to decompose zona pellucida, so that the sperm and egg can directly contact to complete fertilization process and form fertilized egg. The fertilized eggs move from the fallopian tube to the

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uterine cavity in the process of continuous cell division, and gradually embed into the endometrium to develop into a normal fetus [6].

2.2 Anti-endometrial antibody

Anti-endometrial antibody is an autoantibody that targets endometrium and causes a series of immunopathological reactions. It has been reported [7] that 37%-50% of patients with infertility, abortion and endometriosis have positive EmAb. The incidence of eab among women after induced abortion is as high as 24%-6 1%. E mAb binds to endometrial target antigen and injures the endometrium through two main self-injury mechanisms: activation of the complement system produces cytotoxic injury, which chemotaxis and activates T lymphocytes and mononuclear macrophages, causing lymphoid and mononuclear cell infiltration in the endometrium and antibody-mediated cytotoxic injury.

EmAb often coexists with endometriosis and is a signature antibody against endometriosis. It has been reported in the literature that the detection rate of EmAb in patients with endometriosis is as high as 70% - 80% [8]. Therefore, determination of EmAb contributes to the diagnosis of endometriosis, observation of curative effect, and improvement of treatment effect for infertility patients caused by this factor. For secondary infertility, positive EmAb indicates that immune infertility is one of its infertility mechanisms, and whether to adopt immunosuppressive therapy is still an uncertain problem. For primary infertility, eab can be used as an indicator for immunosuppressive therapy and an indicator for efficacy observation.

2.3 Antisperm antibody

Antisperm antibodies may be present in both men and women. In semen, there are a variety of antigens that can be absorbed by the cervical epithelium in the female genital tract and produce an immune response that produces antisperm antibodies locally in the woman's blood and genital tract. This antibody can affect the movement of sperm, leading to infertility. Normally, men do not produce their own antisperm antibodies. However, antisperm antibody can be produced under the action of certain precipitating factors, most commonly reproductive tract infection or damage of reproductive tract mucosa. In this condition, sperm serves as an antigen to stimulate T cell immunity of the body, thereby inducing the production of antisperm antibody. If the male seminal plasma in the immune material lack, causes the spouse to have the allergic reaction to the seminal plasma, may also produce the antisperm antibody; At the same time, because the endometrium after artificial abortion is damaged, before it is not repaired, sperm may enter the body through the damaged part and cause AsAb in the body. Multiple artificial abortions aggravate local infection and injury of reproductive tract. The strengthening of immune response causes AsAb in the body to rise step by step, aggravating infertility.

According to available data [9 - 10], the positive rates of AsAb in serum and cervical mucus in the abortion secondary infertility group were as high as 35.56% and 47.78%, significantly higher than 21.82% and 39.09% of the primary infertility group, and 5.00% and 6.25% of the normal control group (P < 0.01). With the increase of induced abortion times, the positive rate of AsAb in serum and cervical mucus of infertility group after induced abortion increased significantly.

2.4 Anticardiolipin antibody

Anticardiolipin antibodies are a group of antibodies that can react with a variety of antigens containing phospholipid structures. They can prevent the production of prostaglandins in the body, increase the ratio of thrombus to prostaglandins, and cause spasm and ischemia of the whole body and placenta.

The mechanism of anticardiolipin antibody induced infertility mainly has four aspects:

(1) Interference with normal fertilization process. It can change the function of sperm mainly by combining with phospholipid component on the surface of sperm.

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(2) Destroy the implantation of fertilized eggs or cause the dysplasia of fertilized eggs that implant. It is mainly caused by immune inflammation in endometrium [11].

(3) Interfering with the embryo implantation and early post-implantation development. Cell damage occurs primarily through binding to cardiolipin on the surface of the trophoblasts.

(4) Cardiac phospholipids that act on vascular endothelial cells and platelet membrane damage the vascular endothelium, resulting in increased systemic small vessel tension and microthrombosis, and finally adverse pregnancy outcome [12].

More and more attention has been paid to the relationship between ACA immune dysfunction and spontaneous abortion. Studies have shown that immune dysfunction and abnormal autoimmune response are the important basis of pathological changes in spontaneous abortion, while ACA is the result of excessive antibody immune recognition and immune response imbalance, as well as the manifestation of abnormal autoimmune response [13].

In the patients with spontaneous abortion and positive serum ACA-IgG type, about 70% of the untreated pregnant women may suffer from spontaneous abortion and intrauterine fetal death. In particular, IgM type ACA can be used as a forward-looking indicator of spontaneous abortion or fetal death. Therefore, ACA is considered to be a relatively sensitive indicator for predicting whether high-risk women have abortions. Studies have shown that the positive rate of ACA and other antibodies in serum of patients with spontaneous abortion is significantly higher than that in the normal control group, with significant differences [14].

2.5 Anti-ovarian antibody

The ovary contains many tissue components such as oocytes, zona pellucida, and granulosa cells in different stages of development, each of which may lead to the generation of AoAb due to the abnormal expression of its antigen. The overflow of ovarian antigen caused by ovarian damage, infection, inflammation, and other reasons induces the generation of AoAb in individuals with certain immune dysfunction. AoAb further aggravates ovarian damage and leads to the dysfunction of uterus and placenta, causing infertility and abortion.

AOAb is an autoantibody whose target antigen is located in ovarian granulosa cells, oocytes, corpus luteum cells and interstitial cells. The activity of AOAb in unexplained infertility women is significantly higher than that with a clear cause. The higher serum AOAb levels in women undergoing multiple embryo transfer (IVF-ET) treatment cycles may be related to the increased AOAb synthesis promoted by follicle puncture. A large amount of ovarian antigen is released in the case of infection and trauma, which can stimulate the local reaction of the body to produce antigen and antibody, leading to the production of AOAb. Studies have shown that the anti-fertility effect of AoAb results in more infertility than abortion [15]. Recent studies have shown [16] that AoAb can be detected in the blood of most patients with polycystic ovary syndrome. At the same time, it is considered that immune response causes inflammation of ovary, and inflammation causes abnormal cytokine production, which eventually leads to obvious biochemical changes of polycystic ovary syndrome and leads to infertility. This new theory needs further study [17].

3. Materials and methods

3.1 General information

A total of 80 cases of female infertility patients were selected from June 2019 to May 2020 in our hospital. Their age ranged from 26 to 35 years old, with an average of (28.56 ± 2.31) years old. The duration of infertility was 3 - 9 years, with an average of (4.35 ± 1.65) years; There were 20 cases of primary infertility, 15 cases of recurrent abortion, and 35 cases of secondary abortion. Exclusion criteria: (1) females not in childbearing age; (2) Patients with severe diseases of other systems; (3) patients who failed to fully cooperate with the experiment.

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3.2 Method

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After 2mL venous blood was collected and allowed to stand, serum was separated and stored at 4 C. Detection should be completed within 3 d. Enzyme-linked immunosorbent assay (ELISA) was selected to test AsAb, EMAb, AO Ab and ACA. When taking out the refrigerated specimen for testing, the serum should be thawed, and then tested when it is balanced to room temperature, so as to avoid the temperature factor affecting the test results of patients. Testing operations should be performed using instruments and reagents correctly and in strict accordance with the instructions.

3.3 Detection Indicator

Six reproductive immune indexes in serum were detected, which were anti-ovarian antibody, anti-cardiolipin antibody, anti-endometrial antibody, anti-sperm antibody, anti-chorionic gonadotropin antibody, and anti- β 2 glycoprotein antibody. According to the positive rate of reproductive immune antibody detection and comparison.

3.4 Statistical analysis

SPSS19. 0 statistical software was used to analyze the data. χ^2 test was used for counting data and T test was used for measuring data. The confidence interval was 95%, and the difference was statistically significant with P < 0.05.

4. Result

4.1 Detection results of serum reproductive immune antibodies in 80 patients

After serum reproductive immune antibodies were detected in 80 patients selected from our hospital, 55 patients were positive, and the antibody positive rate was 68.75% (Table 1).

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Test item	Number of positive cases	Proportion(%)		
AsAb	20	25.00		
AOAb	15	18.75		
EMAb	9	11.25		
ACA	11	13.75		

Table 1. Detection results of serum reproductive immune antibodies in 80 patients

4.2 Detection results of serum reproductive immune antibodies in 80 patients at different ages

According to the different age distribution of patients, the detection results of serum reproductive immune antibodies of patients are classified and analyzed as follows (Table 2).

Table 2. Detection results of serum reproductive immune antibodies in 80 patients at different

ages						
Age bracket	AsAb(+)	EMAb(+)	AOAb(+)	ACA(+)		
22-30	8	4	3	6		
30-38	14	7	9	10		

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5. Discussion

According to clinical statistics, the incidence of infertility and spontaneous abortion is increasing gradually, and there are many reasons leading to infertility, including endocrine, infectious and hereditary, etc. In addition to the above factors, immune dysfunction is considered to be an important cause of diseases, and it is also a research hot spot at present. Clinical research shows that the related factors affecting female infertility are extremely complex, which can be divided into genetic defects, anatomical abnormalities, endocrine disorders, systemic diseases, environmental factors and lifestyle. The treatment of female infertility requires correct analysis of the causes and symptomatic treatment, otherwise it is difficult to achieve good results.

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There are immunosuppressive substances in seminal plasma, so women will not have anti-sperm immune response under normal circumstances when they encounter sperm antigen of their spouse. Immunosuppressive substances are highly effective. When they adhere to sperm surface, they will cause sperm antigenic determinants to change or be obscured, which will not only cause female immunocompetent cells not to recognize sperm antigens effectively, but also affect their reaction ability. In our hospital, 70 female patients with infertility were selected as research objects, including primary infertility patients, recurrent abortion patients and secondary abortion patients. From the detection results of immune antibodies in female patients, the positive rate of AsAb in patients with primary infertility is the highest, and the reason of infertility is mainly affected by AsAb; Among patients with recurrent abortion, ACAb has the highest positive rate, followed by EmAb and AhAb.

Clinical observation showed that AsAb positive patients had a history of abnormal bleeding of reproductive organs during sexual intercourse, or complicated with inflammation of reproductive system such as endometrium and fallopian tube. There are more positive cases of serum reproductive immune antibody in older female patients, accounting for 37% of the total antibody positive cases, while the number of positive cases in younger female patients is far less than the former, accounting for only 15%. To sum up, the detection of serum reproductive immune antibodies can clearly distinguish the impact of each antibody on patients, and then identify the causes of illness, which has guiding significance for clinical treatment.

EMAb can combine with the antigen in endometrium, produce antigen-antibody reaction, activate complement system, impair the function of endometrial gland, lead to insufficient glycogen secretion of nutritious embryo, interfere and hinder the implantation of fertilized egg and the development of embryo sac, and lead to infertility [18]. Endometrial damage mainly causes hyposecretion of endometrial glands, which is not conducive to blastocyst implantation I Endometrial inflammatory environment causes embryonic development disorders, and is prone to abortion. After the EmAb is induced by endometriosis, the normal endometrium is damaged through EmAb-mediated immune damage, which has become one of the mechanisms of infertility caused by endometriosis. ACAb reduces the synthetic release of prostacyclin by acting on membrane phospholipids of placental vascular endothelial cells. AOAb and infertility. For elderly pregnant women, the aging of ovarian function is the main cause of infertility. Due to ovarian damage, infection or inflammation, corresponding anti-ovarian antibodies will be produced to inhibit the normal secretion of ovaries. The infertility is finally caused by the lack of hormones during pregnancy. ACAb can cause infertility or abortion by interfering with the normal operation of coagulation in the body and inducing microthrombosis at the mother-fetal interface and affecting the normal supply of blood night to the placenta and decidua.

ACAb can directly interact with membrane phospholipids of placental vascular endothelial cells to reduce the synthesis and release of prostacyclin; At the same time, the antibody can inhibit the release of fibrinogen solvent activator and thrombomodulin to inhibit anticoagulant protein I and antithrombin III, affect the activation of protein C system, and reduce the ability of protein S and protein C to inactivate factor V. High k β 2 causes blood coagulation dysfunction, which is easy to lead to the formation of thrombosis, and is related to abortion and stopped development of embryos. At the same time, it also leads to the increased incidence of infertility. The antibody can cause abortion of placental obstruction by cause myometrial cysts, can also cause placental angiitis to cause that for fetus to die due to insufficient oxygen supply, and can also cause the fetus to die due to insufficient blood supply through placental vasoconstriction; and the antibody is easy to cause repeated abortion of pregnant women during pregnancy and is easy to cause the fetus to die in uterus.

6. conclusion

The results of this study show that autoimmune antibody is the main cause of infertility, which is closely related to the occurrence of infertility. Detection of autoimmune antibodies based on ultrasound images can provide scientific basis for diagnosis of infertility.

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