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AUTOIMMUNE MECHANISMS OF OVARIAN INFLAMMATION: MORPHOLOGICAL, CLINICAL AND PATHOGENETIC SIGNIFICANCE

Nematova Nargiza Nematilloyevna

Abstract. *Reproductive health in women is directly associated with the functional activity of the ovaries, which play a fundamental role in maintaining hormonal balance, follicular development, ovulation, and preparation of the body for pregnancy. In recent years, evidence has accumulated suggesting that autoimmune mechanisms contribute significantly to the pathogenesis of ovarian inflammatory disorders. These processes disrupt hormonal homeostasis, impair folliculogenesis, and increase the risk of premature ovarian insufficiency and infertility. This paper provides an overview of the pathogenetic mechanisms, morphological characteristics, clinical significance, diagnostic strategies, and potential therapeutic directions in autoimmune ovarian inflammation.*

Keywords: *ovary, autoimmunity, inflammation, infertility, morphology, reproductive health*

Introduction. The ovaries are paired parenchymal organs with dual functions: generative (oogenesis) and endocrine (production of sex steroids). Their activity determines the reproductive capacity of women and influences systemic physiological processes such as bone metabolism, cardiovascular health, and mental well-being. Disorders of ovarian function, particularly when associated with chronic inflammation, represent a serious medical and social problem, contributing to infertility, menstrual irregularities, and early onset of menopausal symptoms.

Traditional gynecological research has emphasized infectious and endocrine causes of ovarian dysfunction. However, emerging data point to autoimmune mechanisms as a critical factor in the pathogenesis of ovarian inflammation. Autoimmune ovarian disorders are characterized by the production of autoantibodies directed against ovarian tissues, infiltration of immune cells into the stroma, and

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progressive destruction of follicles. This perspective introduces new diagnostic and therapeutic challenges that require a multidisciplinary approach involving immunology, endocrinology, and reproductive medicine.

Pathogenetic Mechanisms

Autoimmune ovarian inflammation arises when the immune system loses tolerance to self-antigens and begins attacking ovarian tissue. Several pathogenetic processes are involved:

1. **T-cell mediated cytotoxicity**
   - Activated T-lymphocytes infiltrate ovarian tissue, targeting granulosa cells and oocytes.
   - Cytokines such as interferon-γ and interleukin-17 amplify local inflammation and tissue damage.
2. **Autoantibody production**
   - Autoantibodies may be directed against:
     - Granulosa and theca cells
     - Receptors of FSH and LH
     - Steroidogenic enzymes (aromatase, 17α-hydroxylase)
   - These antibodies disrupt folliculogenesis, impair steroid hormone synthesis, and accelerate follicular atresia.
3. **Molecular mimicry and cross-reactivity**
   - Shared antigens between ovarian tissue and other endocrine glands explain frequent associations with autoimmune thyroiditis, type 1 diabetes, or systemic lupus erythematosus.
4. **Chronic inflammatory microenvironment**
   - Persistent inflammation leads to fibrosis, hyalinization of vessels, and destruction of the cortical layer of the ovary.
   - Eventually, this results in premature ovarian insufficiency (POI).

Morphological and Histological Features

Morphological studies of ovaries affected by autoimmune processes reveal:

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- **Lymphocytic infiltration** of the ovarian stroma, primarily T-helper and cytotoxic T-cells.
- **Destruction of follicles**, particularly primordial and primary follicles.
- **Vascular changes**: hyalinization of arterioles, sclerosis, and reduction in cortical blood supply.
- **Fibrosis** of the ovarian capsule and stroma, impairing follicle development.
- **Follicular atresia** accompanied by reduced cortical thickness.

Histological examination confirms the depletion of the follicular reserve, which clinically correlates with ovarian insufficiency and infertility. These changes highlight the strong association between morphological and functional disturbances in autoimmune ovarian inflammation.

Clinical Significance

Autoimmune ovarian inflammation manifests through a wide range of clinical symptoms:

- **Menstrual irregularities**: oligomenorrhea, secondary amenorrhea, or dysmenorrhea.
- **Infertility**: due to chronic anovulation and destruction of follicles.
- **Signs of hypoestrogenism**: endometrial atrophy, osteoporosis, vasomotor instability, mood disturbances.
- **Hyperandrogenic symptoms**: hirsutism, acne, seborrhea, linked to disrupted steroidogenesis.
- **Systemic associations**: thyroid dysfunction, adrenal insufficiency, type 1 diabetes mellitus, forming part of autoimmune polyglandular syndromes.

These clinical features highlight the dual impact of autoimmune ovarian inflammation: local reproductive dysfunction and systemic endocrine consequences.

Diagnostic Approaches

Diagnosis remains challenging due to the nonspecific nature of clinical symptoms. A comprehensive approach is required:

1. **Laboratory tests**

- Measurement of gonadotropins (FSH, LH), estradiol, and progesterone.
- Detection of ovarian autoantibodies (anti-ovarian, anti-FSH receptor, anti-steroidogenic enzyme antibodies).

2. **Imaging techniques**

- Transvaginal ultrasound to assess ovarian size, volume, and follicular reserve.
- Doppler studies to evaluate vascular changes.

3. **Histological and immunohistochemical studies**

- Confirm lymphocytic infiltration, follicle destruction, and vascular sclerosis.

4. **Exclusion of other causes**

- Differential diagnosis should consider infectious oophoritis, premature menopause of non-autoimmune etiology, and endocrine dysfunction.

Therapeutic and Preventive Strategies

Management of autoimmune ovarian inflammation requires a combination of endocrine support and immunomodulatory therapy.

- **Hormone replacement therapy (HRT):** Used to compensate for hypoestrogenism, preventing osteoporosis and cardiovascular complications.
- **Ovulation induction and assisted reproductive technologies (ART):** For women seeking fertility, IVF with donor oocytes may be considered in advanced cases.
- **Immunotherapy:**
  - Corticosteroids to suppress immune activity.
  - Immunomodulators and targeted biologics (anti-TNF, anti-IL-17, CTLA-4 inhibitors) as potential future therapies.
- **Preventive strategies:** Early identification of high-risk women with autoimmune comorbidities. Regular monitoring of ovarian reserve (AMH, antral follicle count).

Future Directions

Research on autoimmune ovarian inflammation is expanding, with several promising directions:

- **Genetic predisposition**: Polymorphisms in HLA genes and immune-regulating loci increase susceptibility.
- **Biomarker development**: Identification of specific ovarian autoantibodies may improve early diagnosis.
- **Personalized medicine**: Tailoring therapy based on genetic, hormonal, and immunological profiles.
- **Targeted immunotherapy**: Biologic agents modulating specific immune pathways represent a future alternative to nonspecific immunosuppressants.

Conclusion

Autoimmune mechanisms play a crucial pathogenetic and clinical role in ovarian inflammatory processes. They disrupt folliculogenesis, impair steroidogenesis, and predispose to premature ovarian insufficiency and infertility. Morphological findings, including lymphocytic infiltration, fibrosis, and follicular atresia, support the close association between immune-mediated damage and clinical outcomes.

Timely diagnosis using immunological markers, hormonal monitoring, and morphological studies enables early detection and intervention. Advances in immunotherapy and personalized medicine hold promise for improving outcomes and preserving reproductive health in women.

Autoimmune ovarian inflammation thus represents a multidisciplinary challenge, requiring cooperation between gynecologists, endocrinologists, immunologists, and reproductive specialists.

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