Review Article

Genitourinary Syndrome of Menopause (GSM): Pap test and Gram findings

Abstract:

The loss of ovarian function, prematurely or due to menopause, causes a decrease of the vaginal epithelium trophy. However, with the end of the menstrual cycle and the consequent hypoestrogenism, the epithelial thickness also decreases, with only the parabasal and basal layers remaining with low glycogen reserves. A thinner epithelial thickness associated with a pH greater than 4.5 and a microbiota without protective bacteria (*Lactobacillus* sp) can lead to an inflammatory condition not necessarily related to the action of a pathogen but mainly the atrophy itself. Atrophic vaginitis is often confused with genitourinary syndrome of menopause (GUSM). Laboratory findings do not necessarily coincide with symptoms but could help in diagnosing. Examinations such as bacterioscopy of vaginal smear (Gram) and cytology (Pap test or cytology in liquid medium) have findings that may suggest a picture of intense hypoestrogenism. However, the clinical-laboratory correlation is essential.

Key-words: Genitourinary Syndrome of Menopause, Vaginitis, Papanicolaou Test, Cytology

Introduction

The loss of ovarian function, prematurely or due to menopause, causes a decrease of the vaginal epithelium trophy. Sometimes the women refer to localized symptoms leading to discomfort and influencing sexual activity. (1).

In 2014 the International Society for the Study of Women's Sexual Health and the North American Menopause Society introduced genitourinary syndrome of menopause (GSM) as changes associated with lack of estrogen. Sometimes the term GSM is confounding with atrophic vaginitis, but this is only a possible finding in the syndrome, besides urinary and sexual complaints (2-). However, it is essential to understand that the laboratory finding of atrophy with inflammatory infiltrate does not always correspond to complaints and clinical findings. (3)

Pathophysiology

The vaginal epithelium originated from the urogenital sinus and the Müllerian duct, is a non-keratinized stratified epithelium that modifies its thickness according to the estrogen stimulus. There are the following layers in the entire thickness of the epithelium: basal, parabasal, intermediate, and superficial. Depending on the menstrual cycle phase and, therefore, on the estrogenic and progestin influence, there is a greater glycogen accumulation in the epithelium's intermediate layer (post-ovulatory phase). The glycogen is

metabolized to produce lactic acid and maintain physiological pH in the vagina (<4.5). (4, 5)

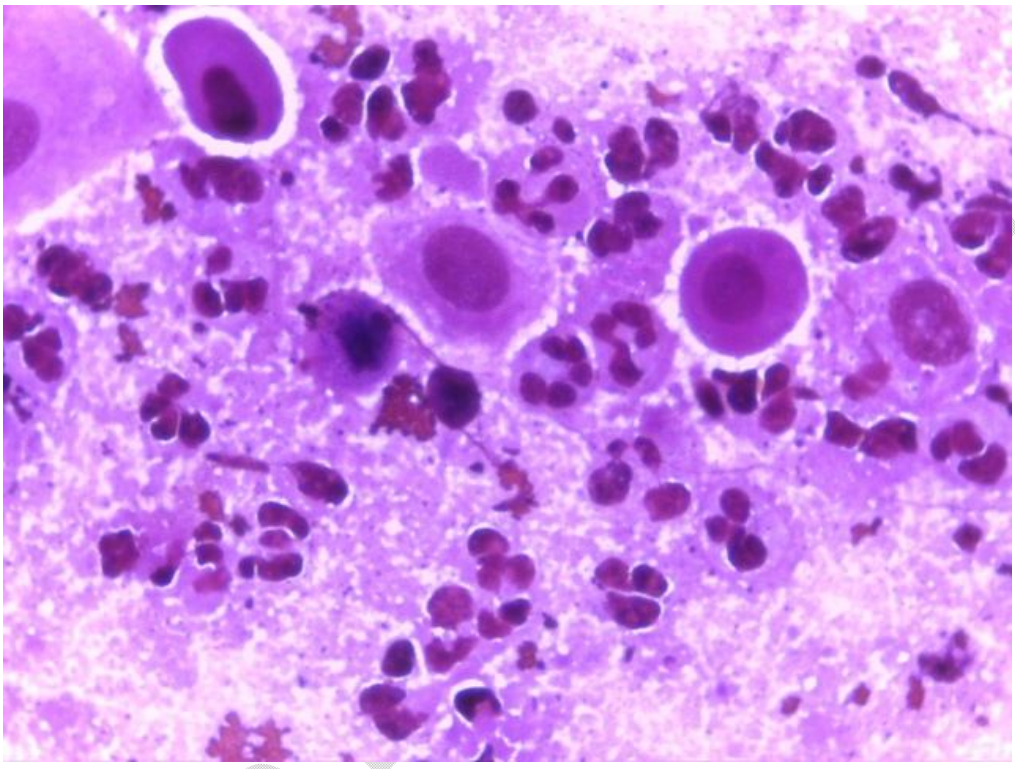
In women who have a menstrual cycle, the highest level of epithelial thickness occurs in the periovulatory period, when there is also a higher estrogen level. However, with the end of the menstrual cycle and the consequent hypoestrogenism, the epithelial thickness also decreases, with only the parabasal and basal layers remaining with low glycogen reserves. A thinner epithelial thickness associated with a pH greater than 4.5 and a microbiota without protective bacteria (*Lactobacillus* sp) can lead to an inflammatory condition not necessarily related to the action of a pathogen but mainly the atrophy itself. (6)

Laboratory exams

Some tests can be used to help diagnose the atrophyc vaginitis.

Gram: in cases of women with hypoestrogenism (atrophy) the microbiota study in a Gram-stained smear identifies a microbiota of sparse Gram-positive cocci, sometimes Gram-negative, amid rounded cells (parabasal). This finding differs from oestrogenized women with a well-developed microbiota, with a predominance of gram-positive medical bacilli (*Lactobacillus* sp). However, atrophy with inflammation or atrophic vaginitis is characterized by infiltrating inflammatory cells, predominantly polymorphonuclear leukocytes, in addition to the criteria defined above. (7).

Figure 1. The aspect of cytological atrophy in vaginal smear (Gram 1000x). We can observe the parabasal cells (rounded), numerous leukocytes and scarce cocaceous microbiota.

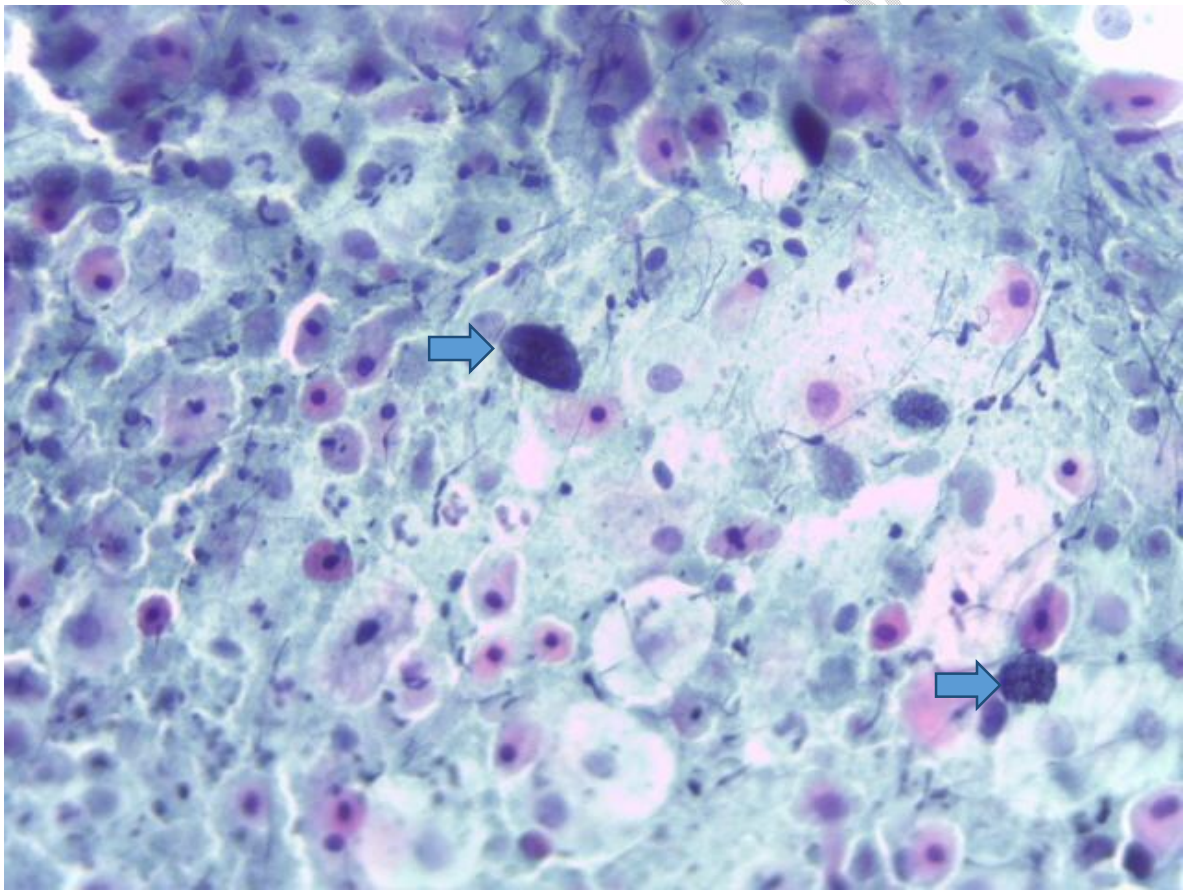


Pap test: the Pap smear is a widely used method in secondary prevention of cervical cancer, but it can observe other findings that help diagnose different diseases. But, for a long time, the Pap smear was also used to assess hormonal status. Analyzing the cell types of vaginal smears, it was possible to suggest the action or not of estrogen and progesterone.

Today, cytology reports follow the Bethesda system, which classified atrophy as "non-neoplastic findings" in its latest version. (8)

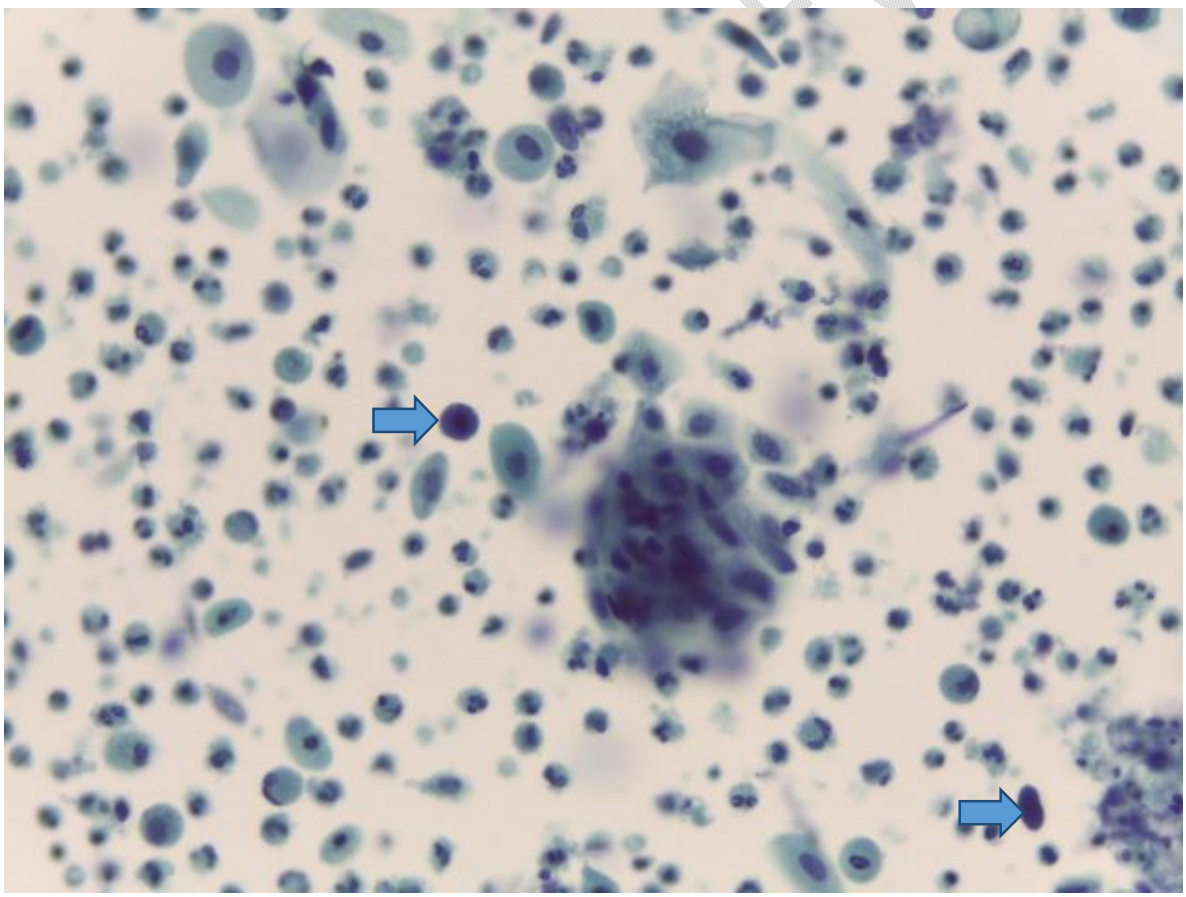
Criteria for diagnosing atrophy and atrophic vaginitis are monolayer sheets of round cells with the high nucleo-cytoplasmic rate (parabasal cells), as well dispersed and isolated cells. Sometimes only nuclei are observed without cytoplasm (autolysis). When abundant inflammatory cells and rounded blue bodies ("blue blobs") are present, we think about extreme atrophy or atrophic vaginitis. (9, 10).

Figure 2. Findings of atrophy with inflammation in conventional cytology (Pap 400x). We can see parabasal cells, inflammatory infiltrate, scarce microbiota, filaments, and blue blobs (arrow)



Liquid-based cytology: the liquid-based cytology, which uses the same polychromatic stain, has slightly different findings. The smear background is clean, parabasal cells are better observed, and autolysis is absent. However, the inflammatory infiltrates and "blue blobs" indicate, as in the conventional cytology (Pap test), atrophic vaginitis (10).

Figure 3. Atrophy with inflammation in liquid-based cytology (Surepath 400x). We can observe isolated and grouped well-preserved parabasal cells, inflammatory infiltrate, sparse microbiota and blue blobs.



Crothers et al. (11) studied conventional cytology and two methods most used in liquid cytology (Thinprep and Surepath). The authors concluded that in Thinprep, cases

were often considered unsatisfactory. Even Surepath having fewer unsatisfactory cases was more discordant in diagnosing atrophy with inflammation than the conventional smear.

Conclusion:

GSM is a syndrome that can have in the morphological laboratory exam, Gram and cytology, a tool to aid diagnosis. However, the finding of a picture suggestive of atrophy with inflammation does not necessarily indicate the need for treatment. The clinical-laboratory correlation is vital for a correct diagnosis and adequate management.

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