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Cytolytic Vaginosis: A Common Yet Under-Diagnosed Entity

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Abstract

Objective: To study the incidence of cytolytic vaginosis among patients undergoing cervico-vaginal cytology for vaginal discharge, pruritis, dyspareunia and other symptoms. Cytololytic vaginosis is also known as lactobacillus overgrowth syndrome or Doderlein's cytolysis. It is characterized by abundant growth of Lactobacilli resulting in lysis of vaginal epithelial cells.

Method: A total of 308 women presented to gynecological OPD. All of the patients were subjected to Pap test with the help of cytobrush. The cervico-vaginal smears were fixed in methanol, stained with papanicolaou stain and studied under microscope independently by two pathologists.

Result: Out of 308 patients, 190 (61.7%) had inflammatory lesion and were negative for intraepithelial malignancy. Out of 190 cases, 31 (16.3%) were diagnosed as cytolytic vaginosis based on clinical and morphological features.

Conclusion: Cytolytic vaginosis is a fairly common entity often misdiagnosed as candidiasis. Morphological features play an important role in identifying cytolytic vaginosis. The results of this study may contribute to reports in the literature indicating the importance of correct diagnosis cytolytic vaginosis leading to appropriate treatment.

Keywords: Cytolytic vaginosis; Candidiasis; Lactobacilli; Bethesda

Introduction

Vaginal discharge is one of the most common complaints encountered among women of reproductive age group. Infection with candida, Trichomonas and cocco-bacilli account for majority of cases with vaginal discharge. Some of the patients presenting with vaginal discharge may be un-responsive to treatment with above mentioned infections. These patients may be suffering from Cytolytic vaginosis. Cytololytic vaginosis (CV) is also known as lactobacillus overgrowth syndrome or Doderlein's cytolysis. It is characterized by abundant growth of *Lactobacilli* resulting in lysis of vaginal epithelial cells; and therefore, called cytolytic vaginosis [1]. The normal vaginal flora was first described by Doderlein as consisting of acid producing gram-positive, immobile, non-spore forming anaerobes, now referred as *lactobacillus* species. Healthy women of reproductive age groups are colonized by *lactobacillus*. It is also suggested that the presence of estrogen and *lactobacillus* are needed to achieve an optimal vaginal pH of 4.0-4.5. Lactobacilli produce lactic acid from glucose, keeping the vagina at an acidic pH. After puberty, glycogen is deposited in the vaginal epithelial cells under the influence of estrogen which is metabolized by vaginal epithelial cells to glucose. *Lactobacillus* converts glucose to lactic acid [2]. They occur in abundance in the late luteal phase and in pregnancy, prefer an acid environment, and are common among women using hormonal preparations (contraceptives and replacements) and in the premenarchal and menopausal age groups [3]. Lactobacillus has a protective role also. Some species of Lactobacillus produce hydrogen peroxide, which is toxic to various micro-organisms. This may prevent overgrowth of organisms such as *E.coli*, *Candida species*, *Gardnerella vaginalis* and *Mobilincus* species. According to several studies, *Lactobacilli* build up a barrier against candidal overgrowth by blocking the adhesion of yeast to vaginal epithelial cells through competition for nutrients [4].

In health, low number of *Lactobacilli* (five bacilli per ten squamous cells) is considered protective against candidiasis by blocking the adhesion of candidal yeast cells to vaginal epithelial cells, through competition for nutrients [5]. Overgrowth of Lactobacilli may occur in individuals of reproductive age group by causing dissolution and damage to vaginal intermediate epithelial cells. It has been observed that in the luteal phase, there is remarkable rise in number of colonizing *Lactobacilli*. It has been claimed that the Lactobacilli are more abundant in women with diabetes mellitus.

The entity is included in current Bethesda system for reporting cervical cytology, as 'unsatisfactory for evaluation'. In these cases, the reason for 'unsatisfactory smears' should be mentioned in the report. Awareness about this entity and its characteristic morphological features is necessary to avoid suffering and unnecessary medication of patients.

Method

A total of 308 cases of cervical smears over a period of one year were received at our clinical laboratory from the gynecology OPD. The cervical smears were prepared using cytobrush. All smears were fixed in methanol, stained with papanicolaou stain and examined independently by two pathologists.

Results

Out 308 cases of cervical smears, 190 were inflammatory (61.7%). Out of inflammatory cases, 31 were of cytolytic vaginosis (16.3%). The most common presenting symptoms in patients with cytolotylic vaginosis were increased vaginal discharge and pruritis vulva. The age groups ranged from 24 years to 61 years with median age being 39 years. The parity of patients ranged from P0+0 to P6+0. Out of 31, 19 (61%) were in luteal phase and this finding corroborates with the literature

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[6]. The colposcopic findings ranged from cervical erosion, vaginitis, vulvitis and discharge as shown in Table 1. The cytological findings were increase in number of *Lactobacilli*, paucity of white blood cells, presence of cytolysis, stripped or naked nuclei and absence of fungus, coccobacilli or *Trichomonas* as shown in Figures 1 and 2. Based on the clinical and cytological features, these cases were diagnosed as cytolytic vaginosis with advice to repeat cervical smears after treatment.

Discussion

Cytolytic vaginalis presents clinically with vaginal discharge, pruritis, dyspareunia and vulval dysuria. Cyclical increase in symptoms is observed in luteal phase. CV is characterized by vaginal pH between 3.5 and 4.5. Microscopically, the papanicolaou stained cervico-vaginal smears show abundant *Lactobacilli*, paucity of pus/polymorphonuclear cells, bare/naked nuclei, cytoplasmic fragments and absence of fungal spores/hyphae, cocco-bacilli or Trichomonas. The microscopic features of CV are based on study conducted by Hu et al. to observe the morphological characteristic of vaginal discharge in patients with CV under the microscope. The clinical features of CV are similar to vulvo-vaginal candidiasis (VVC), thus, it is important to exclude candidiasis by investigations. CV can be distinguished from bacterial vaginosis (BV) by pH measurement and whiffs test. The pH in case of BV is more than 4.5 and Schiff test is also positive. The large number of Lactobacilli covering squamous cells can mimic clue cells seen in BV, however, can be distinguished by careful examination. The key points of differentiation between CV, candidiasis and BV have been tabulated in Table 2.

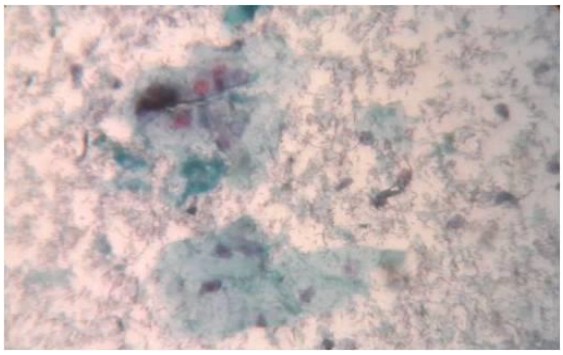

Figure 1: Cervical smear showing cytolysis of squamous cells in background full of *Lactobacilli* (x40, Papanicolaou).

S.No	Age	Chief complaint	Parity	Time of cycle	Per speculum findings
1.	47	Increased vaginal discharge	P3+0	Follicular phase	Cervix and vagina inflamed, small anterior lip polyp
2.	56	Increased vaginal discharge, pruritis vulva	P3+0	Menopausal	Inflamed vagina, discharge
3.	32	Increased vaginal discharge	P2+0	Follicular phase	Inflamed vagina, discharge
4.	38	Increased vaginal discharge	P2+0	Luteal phase	Inflamed vagina, mixed discharge
5.	31	Increased vaginal discharge	P0+A0	Luteal phase	Cervix healthy, mixed discharge
6.	31	Increased vaginal discharge, pruritis vulva	P2+0	Follicular phase	Inflamed vulva, thin discharge
7.	31	Pruritis vulva, increased vaginal discharge	P0+0	Follicular phase	Inflamed vulva and vagina, mixed discharge
8.	24	Increased vaginal discharge, foul smelling	P0+0	Luteal phase	Inflamed vagina, foul discharge
9.	43	Increased vaginal discharge	P2+0	Luteal phase	Inflamed vagina, mixed discharge
10.	26	Increased vaginal discharge	P1+0	Follicular phase	Cervical erosion, mixed discharge
11.	43	Increased vaginal discharge	P2+0	Luteal phase	Cervical erosion, mixed discharge
12.	38	Increased vaginal discharge	P1+0	Luteal phase	Cervical erosion, mixed discharge
13.	32	Increased vaginal discharge	P2+0	Luteal phase	Cervical erosion, mixed discharge
14.	38	Increased vaginal discharge, pruritis vulva	P2+0	Follicular phase	Inflamed vulva and vagina, thick discharge
15.	40	Increased vaginal discharge	P2+0	Follicular phase	Thick discharge
16.	40	Increased vaginal discharge	P2+0	Luteal phase	
17.	61	Pruritis vuvla, urge incontinence	P2+0	Luteal phase	Cervix and vagina normal, discharge
18	30	Increased vaginal discharge	P6+0	Follicular phase	Cervix, vagina normal, mixed discharge
19	37	Increased vaginal discharge		Luteal phase	Cervical erosion, mixed discharge
20	30	Increased vaginal discharge	P2+0	Luteal phase	Cervix and vagina congested, foul smelling discharge
21	40	Increased vaginal discharge	P2+0	Luteal phase	
22	30	Increased vaginal discharge	P1+0	Follicular phase	Circumferential erosion, mixed discharge
23	30	Increased vaginal discharge	P0+0	Follicular phase	Cervix and vagina inflamed, Discharge
24	46	Foul smelling discharge	P2+0	Follicular phase	Inflamed cervix, mixed discharge
25	36	Increased vaginal discharge	P2+0	Luteal phase	Inflamed cervix, vagina congested, mixed discharge
26	21	Increased vaginal discharge	P0+2	Luteal phase	Inflamed cervix and vagina, mixed discharge
27	47	Increased vaginal discharge	P2+0	Luteal phase	Cervix, vagina congested, mixed discharge
28	31	Increased vaginal discharge	P2+0	Luteal phase	Cervical erosion
29	48	Pruritis vulva		Luteal phase	Inflamed cervix and vagina, mixed discharge
30	49	Increased vaginal discharge	P3+0	Luteal phase	Cervix and vagina normal
31	52	Menorrhagia, increased vaginal discharge	P2+0	Luteal phase	Cervix and vagina healthy, mixed discharge

Table 1: Clinical findings in patients of cytolytic vaginosis.

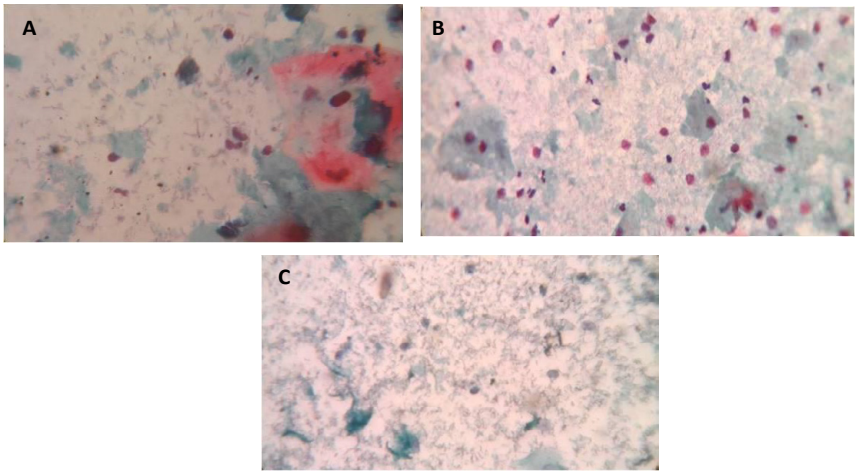

Figure 2: (a-c) Cervical smear showing cytoplasmic debris, bare nuclei and abundant *Lactobacilli* in background (x40, Papanicolaou).

S.no	Parameter	Cytolytic vaginosis	Vulvovaginal candidiasis	Bacterial vaginosis
1.	pH	3.5-4.5	<5	>4.5
2.	Whiff test	Negative	Negative	Positive
3.	Microscopy			
(i)	Lactobacilli	Abundant	Not increased	Few/Absent
(ii)	Pus cells	Few	Abundant	Few
(iii)	Cocco-bacilli	Absent	Absent	Abundant
(iv)	Clue cells	False clue cells	Absent	Present
(v)	Bare / Naked nuclei	Present	Absent / Few	Absent/Few
(vi)	Cytolysis	Present	Absent	Absent
(vii)	Fungal spores / hyphae	Absent	Present	Absent
(viii)	Culture	No growth	Fungal growth of Sabourand dextrose agar	Bacterial growth on aerobic culture medium

Table 2: Comparative investigatory findings in CV, candidiasis and BV.

CV is not an uncommon condition; however, it is often misdiagnosed because it is confused with candidiasis. Many practitioners rely on their clinical judgment alone rather than investigations. Compounding the problem of misdiagnosis is that patients assume that their symptoms are caused by a yeast infection, which results in telephone requests for medication from their physicians instead of an office consultation [7]. Cerikeioglu *et al.* in their study of 210 women with vaginal discharge and other symptom/signs of genital pathology, suggestive of VVC, observed that fifteen patients (7.1%) were diagnosed with CV. All of these cases were in the reproductive age groups of 25-40 years and five were in the luteal phase, with enhanced complaints of discharge and pruritus. In another study conducted by Demirezen S to detect the rate of CV in patients with symptoms resembling that of candidiasis and to distinguish them from candidiasis cases by examining of 2947 papanicolaou stained cervico-vaginal smears. 54 of 2947 patients (1.83%) were diagnosed as having CV based on cytological/ morphological criteria [8].

The treatment of CV is directed towards reducing the number of *Lactobacilli* by elevating vaginal pH. The vaginal pH is elevated by douching with sodium bicarbonate solution or suppository vaginally. Douches are carried out twice weekly for every two weeks. Douching solution is prepared by mixing 1-2 table spoons of baking soda with four cups of warm water. Suppository is prepared by filling gelatin capsules with baking soda. Elevating vaginal pH resolves the symptoms by restoring the normal vaginal environment. If symptoms persist or worsen beyond 2-3 weeks after initiating treatment, re-evaluation is required.

Conclusion

The study emphasizes the need for correct diagnosis of vaginal discharge wherein CV should be considered as possible culprit. It is not as common as candidiasis or bacterial vaginosis; however, it is sometimes confused with the former. A misdiagnosis can lead to patient suffering and unnecessary medication for other cause. Morphological features play an important role in identifying possible cause of vaginal discharge and cervico-vaginal smears should be studied for all patients with vaginal discharge. The results of this study may contribute to reports in the literature indicating the importance of CV which is included in current system for reporting of cervical cytology under 'unsatisfactory for evaluation'. The reason for 'unsatisfactory smears' should be mentioned in report so that these patients can be treated correctly.

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