



Spectrum of Vulvar Lesions in an Obstetrics and Gynecology Outpatient Clinic

Ozhan Ozdemir, Mustafa Erkan Sari, Funda Arpaci Ertugrul, Ertugrul Sen, Bunyamin Ugur Ilgin, Cemal Atalay

Ankara Numune Education and Research Hospital, Department of Obstetrics and Gynecology, Ankara, Turkey

Abstract

Wide range lesions may occur in the vulvar region. The aim of the present study is to have an insight into the diverse morphologic spectrum of vulvar lesions. Total of 263 patients with primary vulvar complaints seen in Ankara Numune Training and Research Hospital Gynecology and Obstetrics Outpatient Clinic were recruited into study. The present retrospective study was carried out by compiling the data from archival records from January 2010 to May 2014. The vulvar biopsies specimens were studied for histomorphological features. The lesions were categorized as non-neoplastic, neoplastic and inconclusive; neoplastic ones were further divided into benign, malignant and premalignant. The age of the women ranged from 11 to 85 years (mean 46.27 ± 14.32) with the maximum number of patients between 41 to 50 years of age. Most common clinical presentation was itching (126 cases; 47.9%). The commonest site of vulvar lesions was labia majora (145 cases, 55.1%). Non neoplastic lesions were more common ($n = 172$; 65.4%) than the neoplastic lesions ($n = 91$; 34.6%). There were 81 (30.8%) benign lesions while 10 cases (3.8%) were malignant or premalignant ones. Amongst the non-neoplastic lesions, the most common histopathologic diagnosis was of lichen sclerosus et atrophicus (46 cases; 17.5%). Early recognition of vulvar lesions and a prompt biopsy diagnosis for all lesions with suspicious changes is of great significance.

Key Words: Vulvar lesion, biopsy, non-neoplastic tissue, neoplastic tissue

(Rec.Date: Jul 10, 2014 Accept Date: Aug 21, 2014)

Corresponding Author: Ozhan Ozdemir, Department of Obstetrics and Gynecology, Ankara Numune Training and Education Hospital, 06010, Ankara, Turkey

E-mail: seyozi@hotmail.com

Introduction

Wide range of benign, premalignant and malignant lesions may occur in the vulvar region. The spectrum of vulvar lesions is large, ranging from dystrophy to a frank carcinoma. Individual variations in care of the genital region, defined by personal and societal “norms” may at times exacerbate vulvar problems. The most common symptom of both benign and malignant vulvar lesions is vulvar itching [1].

Embryologic and immunologic aspects of the vulva contribute to the diagnostic and therapeutic challenges of managing vulvar problems. The vulvovaginal region arises from the close juxtaposition of epithelium derived from all three embryologic layers (endoderm, mesoderm, and ectoderm), a condition found in no other part of the body. Each of the three embryologic derivatives differs in epithelial and glandular structure, hormonal responsiveness, neural distribution, immune response, and relationship to disorders of other body systems [2].

Microscopically, vulva is covered by different types of epithelia, depending on the area of interest, including, from its lateral to medial region, keratinized hair bearing skin, partially keratinized hairless skin, and, mucous membrane of the vestibule. A large number and variety of adnexal structures are associated with vulvar skin in its different sections, such as pilosebaceous units, sebaceous and sweat glands, mucous secretory glands, muscle fibers, and deeper major or minor vestibular glands. Vicinity of underlying vascular structures can also modify vulvar aspects. Therefore, any component of blood and lymphatic vessels can be affected through malformations, tumors, or dystrophic changes [3].

The general approach for evaluation of vulvar lesions includes a pertinent clinical history, physical examination and diagnostic studies. In lesions clinically suspicious for malignancy (asymmetry, border irregularity, color variation, rapid change, bleeding, non-healing) one or more vulvar biopsies are recommended. Biopsy is certainly an important diagnostic step in many circumstances. As biopsy is an invasive procedure, especially on the vulva, special care should be taken. The aim of the present study is to have an insight into the diverse morphologic spectrum of vulvar lesions.

Materials and Methods

This retrospective study includes a single-institution series and compiles the data from archival records from January 2010 to May 2014. The clinical data including the age, patients' complaints, findings on general physical examination and local examination along with the clinical possibilities were noted from the file records. A total of 263 vulvar biopsies reviewed. The lesions were categorized as non-neoplastic, neoplastic and inconclusive; neoplastic ones were further divided into benign, malignant and premalignant.

Results

The age of the women ranged from 11 to 85 years (mean 46.27 ± 14.32) with the maximum number of patients between 41 to 50 years of age. Most common clinical presentation was itching (126 cases; 47.9 %); other presentations white plaque, being swelling, nodularity, ulcer and discharge. The commonest site of vulvar lesions was labia majora (145 cases, 55.13%), followed by labia minora (102 cases, 38.78%). In 16 cases the biopsies were taken from multiple sites including clitoris, fourchette, labia majora and labia minora.

In 263 women who underwent vulvar biopsy, a spectrum of lesions (neoplastic and non-neoplastic) was noted as shown in Table 1. There were 172 (65.4 %) non-neoplastic lesions while 91 cases (34.6%) were neoplastic (benign, premalign or malign) lesions. Amongst the non-neoplastic lesions, the most common histopathologic diagnosis was of lichen sclerosis et atrophicus (LSA) (46 cases; 17.5%). The next in frequency was squamous hyperplasia (35 cases; 13.3%) and Lichen simplex (29 cases; 11.0%). Among the cystic lesions, a diagnosis of Bartholin cyst was rendered in 4 cases (1.5%). Two biopsies had the clinical suspicion of Behcet's disease (leukocytoclastic vasculitis). 15 cases (5.7%) revealed nonspecific inflammation and were diagnosed as non-specific vulvitis.

There were 81 (30.8%) benign lesions while 10 cases (3.8%) were malign or premalign ones. Among the neoplastic benign lesions, the most common tumor was condyloma acuminatum in 31 cases (11.8%) followed by 19 cases (7.2%) fibroepithelial polyp and 18 cases (6.8%) squamous papilloma. One case each of angiomyolipoma, leiomyoma, hemangioma, lymphangioma and lipoma was reported. Among the neoplastic malign or premalign lesions, the most common tumor was vulvar intraepithelial neoplasm (VIN) in 5 cases (1.9%) followed by 4 cases (1.5%) squamous cell carcinoma (SCC) and 1 cases (0.4%) verrucous carcinoma.

Table 1. Histopathological diagnosis in vulvar lesions.

Non Neoplastic (n=172; 65,4%)		Neoplastic (n=91; 34.6%)			
		Benign (n=81; 30,8%)		Malign & Premalign (n=10; 3,8%)	
LSA	46 (17,5%)	Condyloma acuminatum	31 (11,8%)	VIN	5 (1,9)
Squamous hyperplasia	35 (13,3%)	Fibroepithelial polyp	19 (7,2%)	SCC	4 (1,5)
Lichen simplex	29 (11,0%)	Squamous papilloma	18 (6,8%)	Verrucous carcinoma	1 (0,4)
Dermatitis	21 (7,9%)	Hidradenoma	5 (1,9%)		
Non-specific vulvitis	15 (5,7%)	Mesenchymal neoplasm	2 (0,8%)		
Seborrheic keratoses	8 (3,0%)	Angiomyolipoma	1 (0,4%)		
Mollosom contagiosum	7 (2,7%)	Leiomyoma	1 (0,4%)		
Bartholin's cyst,	4 (1,5%)	Hemangioma	1 (0,4%)		
Lentigo	3 (1,1%)	Syringoma	1 (0,4%)		
Leukocytoclastic vasculitis	2 (0,8%)	Lymphangioma	1 (0,4%)		
Vitiligo	1 (0,4%)	Lipoma	1 (0,4%)		
Psoriasis	1 (0,4%)				

LSA: Lichen sclerosus et atrophicus

VIN: Vulvar Intraepithelial Neoplasia

SCC: Squamous cell carcinoma

Discussion

The incidence of vulvar skin disorders is not known. A community-based survey has estimated that 20% of women have vulvar symptoms lasting more than 3 months during their lifetime [4]. Patients with vulvar disorders are well managed by a multidisciplinary approach with the expertise of both gynecologist and dermatologist. Most of the authors have emphasized the role of vulvar skin biopsy with subsequent histological analysis by a dermatopathologist in diagnosing vulvar diseases [1].

Classification of the Internal Society for the Study of Vulvar Diseases (ISSVD) appears credible as it is periodically revisited and as it is the result of consensus between gynecologists, dermatologists, and pathologists. At the present time, 2006 ISSVD Classification is still relevant (Table 2) [5]. But, as this classification is of minor help for diagnosis, ISSVD formulated in 2011 a complementary classification as an approach to clinical diagnosis [6].

Non-specific symptoms such as pruritus, pain and changes in skin color and texture are the common presenting symptoms in vulvar skin disorders. Possible causes include vulvar dermatoses, infection, contact dermatitis, hormone deficiency and systematic skin disorders. Self-medication or previous inadequate or inappropriate treatments may contribute to symptoms.

Table 2. 2006 World Congress ISSVD classification of vulvar dermatoses

Pathologic Subset	Clinical Correlation
Spongiotic pattern	Atopic dermatitis Allergic contact dermatitis Irritant contact dermatitis
Acanthotic pattern	Psoriasis Lichen simplex chronicus - Primary (idiopathic) - Secondary
Lichenoid pattern	Lichen sclerosus Lichen planus
Dermal homogenization/sclerosis pattern	Lichen sclerosus
Vesiculobullous pattern	Pemphigoid, cicatricial type Linear IgA disease
Acantholytic pattern	Hailey-Hailey disease Darier disease Papular genitocrural acantholysis
Granulomatous pattern	Crohn's disease Melkersson-Rosenthal syndrome
Vasculopathic pattern	Aphthous ulcers Behçet disease Plasma cell vulvitis

It is essential to explore a wide relevant history to elucidate possible causal or contributing factors. Pruritus is the most common symptom of vulvar disorders and optimal management should be to search for the underlying cause of the problem so that appropriate treatment can be given. In particular, it is important to differentiate between benign, premalignant, and malignant conditions [7].

Biopsy is the primary diagnostic tool for vulvar lesions. Skin biopsy is not necessary when a diagnosis can be made on clinical examination. Biopsy is required if the woman fails to respond to treatment or there is clinical suspicion of VIN or cancer. The important question here is to accurately determine the site of the biopsy. For an accurate diagnosis, judicious

selection of biopsy sample locations is important. For palpable tumors, biopsy should contain the tumor mass with surrounding normal skin to comment on the extent of invasion. In patients with indistinct tumor boundaries, topical agents like diluted acetic acid may be used for identification of acetowhite/suspicious areas. To increase the sensitivity and specificity of vulvar biopsy, Collins toluidine blue test can be used to define more accurately the areas of vulvar abnormalities [8].

The most common dermatologic conditions encountered in our study were lichen sclerosus as reported in other studies [9,10]. Lichen sclerosus is a chronic inflammatory skin disorder that affects approximately 1 in 70 women, usually presenting in premenarchal girls and menopausal women. There is a 5% associated risk of vulvar squamous cell carcinoma, and it is unclear if treatment decreases this risk. Physical examination reveals ivory white atrophic plaques with a “cigarette paper” appearance. Although vulvar lichen sclerosis can be a clinical diagnosis, skin changes may be difficult to differentiate from vulvar intraepithelial neoplasia, and a biopsy should be performed before treatment with topical steroids is initiated. Biopsies in cases of lichen sclerosis are useful for confirmation of clinical diagnosis and to exclude early invasive malignancy [11]. Lichen simplex chronicus of the vulva is a chronic eczematous condition characterized by intense and unrelenting pruritus, leading to scratching and lichenification. A biopsy is often necessary to exclude lichen sclerosus, lichen planus, or vulvar intraepithelial neoplasia [12]. Lichen planus, an autoimmune inflammatory mucocutaneous disorder, affects approximately 1% of women [13].

Contact dermatitis is one of the most common and often avoidable problems. Exogenous agents cause inflammation of the skin. Clinical examination may reveal a range of findings from mild erythema and swelling to severe erythema, fissures, skin thickening, erosion and ulceration [14]. A detailed history and physical examination are keys to diagnosis; however, physicians should have a low threshold for biopsy to rule out coexisting conditions. Patients who do not respond to treatment will need reevaluation and a biopsy to exclude other conditions. In our study dermatitis was seen in 21 cases.

Seborrheic keratosis involves hair-bearing squamous epithelium of the vulva. The lesion is characterized by symmetric squamous acanthosis, papillomatosis, and hyperkeratosis with keratin horn cysts. Cytologic atypia and HPV-related koilocytosis are absent [15]. Common non neoplastic tumor-like conditions include epidermal inclusion cyst, Bartholin cyst, mucinous cyst and ciliated cyst.

Among the neoplastic benign lesions, the most common tumor was condyloma acuminatum, followed by fibroepithelial polyp and squamous papilloma in our study. Condyloma acuminatum is a common, sexually transmitted, papillomatous squamous proliferation related to HVP 6 and 11, and is not considered progressive toward invasive cancer. Its appearance is clinically distinct with a verrucous growth and is frequently multifocal, and even confluent, involving large areas. Histologically, the lesion consists of papillomatous squamous proliferation with fibrous stroma. Marked acanthosis, parakeratosis, and hyperkeratosis are common. Distinguishing from a squamous papilloma requires the presence of koilocytes, and when in doubt, the presence of Ki-67 positive nuclei in the upper half of the epithelium favors a diagnosis of condyloma [16].

Fibroepithelial stromal polyps are a type of mesenchymal lesion that typically occur in women of reproductive age. The margins of these polyps merge with normal tissue and their vascular supply is usually thick-walled with a central core. Malignancy must be excluded in every diagnosis of fibroepithelial stromal polyp [17]. Squamous papilloma of the vulva may be multiple and consists of simple papillary proliferation of squamous epithelium without complex branching. The absence of definite HPV koilocytosis distinguishes it from a condyloma [18].

Hidradenoma is the most common vulvar benign glandular tumor. It is usually asymptomatic and small (less than 1 cm), frequently involving the labia majora. Majority of cases of hidradenoma papilliferum are nodular and composed of compact glandular or tubular epithelial growth with papillary formations [19]. Leiomyoma in the vulvar region are rarely seen in daily practice, but important in the diagnosis of vulvar masses. The main problem is the differentiation of benign and malignant lesion [20].

The Vulvar Intraepithelial Neoplasia (VIN) is divided into 3 grades depending on the extent of thickness of epithelium involved in neoplastic process. Extension of the neoplastic cells into the stroma is invasive vulvar cancer. The lesions clinically present as erythematous patches, or verruciform or even pigmented plaques. They may be multiple and involve large areas including the perineum. The distinction between VIN lesions and early invasive SCC can only be done on histopathologic examination, hence necessitating a biopsy of all suspicious vulvar lesions [21]. In our study VIN was seen in five cases.

Squamous cell carcinoma comprises about 90% of all vulvar cancers, the others being melanoma, Paget's disease, Bartholin's gland tumor, adenocarcinoma and basal cell carcinoma. Verrucous carcinoma is seen in <1% cases [22]. In our study vulvar squamous cell carcinoma was seen in 4 cases while verrucous carcinoma was reported in a single case.

Conclusion

Wide range lesions may occur in the vulvar region. The task of making a distinction between normal variants, benign entities and potentially serious vulvar pathology is challenging. Early recognition of vulvar lesions and a prompt biopsy diagnosis for all lesions with suspicious changes is of great significance. We believe it is essential to make more detailed epidemiologic studies about vulvar diseases.

References

1. Mohan H, Kundu R, Arora K, Punia RS, Huria A. Spectrum of vulvar lesions: a clinicopathologic study of 170 cases. *Int J Reprod Contracept Obstet Gynecol.* 2014; 3(1):175-80.
2. Foster DC. Vulvar disease. *Obstet Gynecol.* 2002;100(1):145-63.
3. Doyen J, Demoulin S, Delbecque K, Goffin F, Kridelka F, Delvenne P. Vulvar skin disorders throughout lifetime: about some representative dermatoses. *Biomed Res Int.* 2014;2014:595286.
4. Eva LJ. Screening and follow up of vulvar skin disorders. *Best Pract Res Clin Obstet Gynaecol.* 2012;26(2):175-88.
5. Lynch PJ, Moyal-Barracco M, Bogliatto F, Micheletti L, Scurry J. 2006 ISSVD classification of vulvar dermatoses: pathologic subsets and their clinical correlates. *J Reprod Med.* 2007;52(1):3-9.
6. Lynch PJ, Moyal-Barracco M, Scurry J, Stockdale C.J Low. 2011 ISSVD Terminology and classification of vulvar dermatological disorders: an approach to clinical diagnosis. *Genit Tract Dis.* 2012;16(4):339-44.
7. Bohl TG. Overview of vulvar pruritus through the life cycle. *Clin Obstet Gynecol* 2005;48(4):786–807
8. Fatoohi BY. Collins test in patients with vulvar pruritus. *Int J Gynaecol Obstet.* 2009;104(1):76.
9. O'Keefe RJ, Scurry JP, Dennerstein G, Sfameni S, Brenan J. Audit of 114 non-neoplastic vulvar biopsies. *Br J Obstet Gynecol* 1995;102(10):780-6.
10. Bowen AR, Vester A, Marsden L, Florell SR, Sharp H, Summers P. The role of vulvar skin biopsy in the evaluation of chronic vulvar pain. *Am J Obstet Gynecol* 2008;199(5):467.

11. Murphy R. Lichen sclerosis. *Dermatol Clin*. 2010;28(4):707-15.
12. Burrows LJ, Shaw HA, Goldstein AT. The vulvar dermatoses. *J Sex Med*. 2008;5(2):276-83.
13. Goldstein AT, Creasey A, Pfau R, Phillips D, Burrows LJ. A double-blind, randomized controlled trial of clobetasol versus pimecrolimus in patients with vulvar lichen sclerosis. *J Am Acad Dermatol*. 2011;4(6):e99-104.
14. Bhate K, Landeck L, Gonzalez E, Neumann K, Schalock P. Genital contact dermatitis: a retrospective analysis. *Dermatitis*. 2010;21(6):317-20.
15. Grazzini M, Gori A, Rossari S, Lotti T, Scarfi F, Massi D, de Giorgi V. Seborrheic keratosis of the vulva clinically mimicking a genital wart: a case study. *Int J Dermatol*. 2013;52(9):1156-7.
16. Léonard B, Kridelka F, Delbecq K, Goffin F, Demoulin S, Doyen J, Delvenne P. A clinical and pathological overview of vulvar condyloma acuminatum, intraepithelial neoplasia, and squamous cell carcinoma. *Biomed Res Int*. 2014;2014:480573.
17. Madueke-Laveaux O S, Gogoi R, Stoner G. Giant fibroepithelial stromal polyp of the vulva: largest case reported. *Annals of surgical innovation and research* 2013;7(1):8.
18. Mehta V, Durga L, Balachandran C, Rao L. Verrucous growth on the vulva. *Indian J Sex Transm Dis*. 2009;30(2):125-26
19. Duhan N, Kalra R, Singh S, Rajotia N. Hidradenoma papilliferum of the vulva: case report and review of literature. *Arch Gynecol Obstet*. 2011;284(4):1015-7.
20. Ozdemir O, Sari ME, Yakut K, Erkilinc G, Unal DT, Atalay C. Leiomyoma in the vulva of a postmenapousal woman: Case report. *Turkiye Klinikleri J Gynecol Obst*. 2014;24(1):67-70.
21. Del Pino M, Rodriguez-Carunchio L, Ordi J. Pathways of vulvar intraepithelial neoplasia and squamous cell carcinoma. *Histopathology* 2013;62(1):161-75.
22. Robinson Z, Edey K, Murdoch J. Invasive vulvar cancer. *Obstet Gynaecol Reprod Med*. 2011;21(5):129-36.