Patologija vulve/izabrane teme

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Apstrakt

Koža vulve se razlikuje od koze drugih regija po različitoj bakterijskoj flori I uslovima trenja. Dermatološke bolesti vulvarne kože i mukoze se dele u dve grupe. Prvu grupu čine dermatoze slične ekstravulvarnim dermatozama, a drugu čine dermatoze koje zahvataju predominantno vulvarnu regiju. Spečificne dermatoze vulve su kontaktni dermatitis, lichen planus, lichen sclerosus. Infektivne bolesti vulve se mogu preneti direktnim kontaktom. Prepoznavanje tipičnih mikroskopskih karakteristika pomaze u dijagnostici scabiesa, herpes virusne infekcije i molluscum contagiosuma. Humani papilloma virusi (HPV) su epiteliotropni virusi i mogu uzrokovati premalgnu i malignu transformatciju epitelnih ćelija. Sledeći kriterijumi kao što su virusne promene, klinički parametri i mikroskopski nalaz upućuju na postojanje dva puta u karcinogenezi skvamoznog karcinoma vulve i to HPV-zavisni put udružen sa Vulvarnom intraepitelialnom neoplazijom/VIN/ klasičnog tipa i ne -HPV sa VIN diferentovanog (simlex) tipa često udruženim sa lichen sclerosusom i/ili vulvarnom hiperplazijom.Invazivni planocelularni karcinom je najčešći karcinom vulve. Procena prognostičkih faktora je neophodna komponenta patohistoloskog izveštaja. Visoki gradus tumora, vaskularna invazija, veće dimenzije tumora i dubina invazije zaslužuju imunohistohemijsku analizu limfnih čvorova radi nalazenja metastaskih ćelija karcinoma. Extramamarna Pagetova bolest je retka. Može biti primarnog kožnog porekla ili udružena sa nekožnim tumorima gastrointestinalnog ili porekla mokraćne bešike. Imunohistohemijskla analiza je važna za odredjivanje primarnog porekla tumora.

Ključne reči: vulve, dermatoza, herpers virus, šuga, Molluscum contagiosum, humanim papiloma virusima (HPV), Vulvar intraepitelna neoplazija / VIN, planocelularni karcinom, ektramamarna Pagets bolesti

Vulvar Pathology - Selected Topisc

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Abstract

Skin of the vulva differs from the other sites from the different bacterial and friction features. Dermatologic diseases of vulvar skin and mucosa can be divided in two groups. The first includes dermatoses similar extravulvar sites,and second includes dermatoses affected predominantly vulvar region.Specific dermatoses of vulva are contact dermatitis, seborrhoic dermatitis, lichen planus, lichen sclerosus. Infectios deseases of vulva can be transmited by direct contact. Recognition of typical microscopic findings can helped for dignosis of scabies,herpes virus,molluscum contagiosum diseases of vulva. Human papilloma viruses (HPV) are epithelitrophic viruses and cause premalgnant and malignant transformation of epithelial cells.According criteria like viral associated changes,clinical paramethars, microscopic features there are two pathways in carcinogenesissquamous cell carcinoma HPV-related pathway associated with Vulvar intraepithelial neoplasia/VIN of the classic type, and the non-HPV related with VIN of the differentiated (simlex) type frequently associated with lichen sclerosus and/or vulvar hyperplasia. Invasive squamous carcinoma is the most common carcinoma of vulva. Prognostic factors like stage, extracapsular nodal spread,infiltrative margins, vascular invasion, degree of differentiation, status of adjacent skin, stromal response, p53 overexpression are necessary for report. High tumor grade, capillary lymphatics invasion, biger tumor size and depth invasion deserve imunohistochemical analysis lymph nodes for metastatic cells of carcinoma. Extramammary Pagets desease is rare neoplasm. Paget desease can be primary cutaneus vulvar disease,or associated with noncutaneous carcinoma gastrointenstinal origin or bladder carcinoma. Immunohistochemical analysis is very helpful to determine primary origin.

Key words: vulva, dermatoses, herpers virus, scabies, molluscum contagiosum, Human papilloma viruses (HPV), Vulvar intraepithelial neoplasia/VIN, squamous carcinoma, extramammary Pagets desease

Introduction

Skin of the vulva differs from the other sites from the different bacterial and friction features. Dermatologic diseases of vulvar skin and mucosa can be divided in two groups. The first includes dermatoses similar extravulvar sites,and second includes dermatoses affected predominantly vulvar region[1].

Specific dermatoses of vulva

Contact dermatitis

Agents like hygienic, synthetic materials may cause inflammatory response of the squamous epithelium. Histologic features are not specific and include intracellular and intercellular edema of squamous epithelim, with edema of dermis and dillatation of blood vessels. Inflammatory infiltrtation consist lymphocytes and histiocytes, and eosinophiles may be or not prominent.

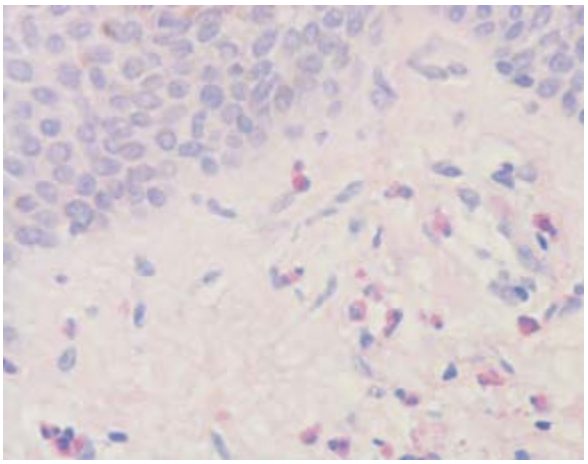

Figure 1. Dermal inflammatory infiltration (HEx40)

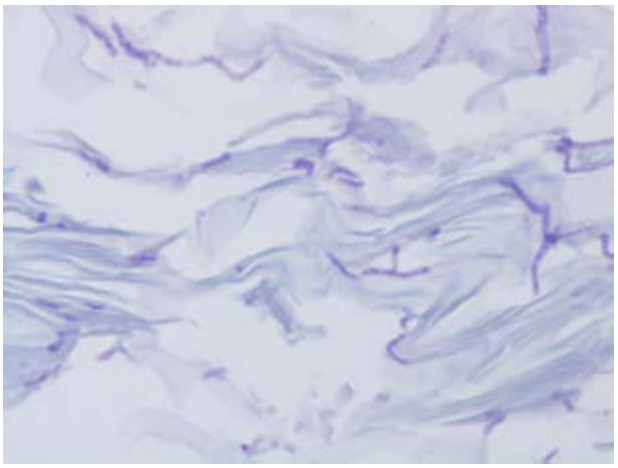

Figure 2. Fungal organisms on surface vulvar skin (PASx40)

Seborrhoic dermatitis

Vulvar erruptions of in obese woman with, frictin cause, exematous apperance can have nonspecific histologic changes. Microscopic features may be akantosis, spongiosis and parakeratosis, with elongation of rete pegs of epidermis.Mild chronic dermal inflammation persist, and finding fungal and other infectious agents are according for the diagnosis sebborhoic dermatitis[2].

Psoriasis

Vulvar psoriasis may be part of generalize disease or affect vulvar region.Erruptions have sharp dermacated areas with red surface covered with white plaques. The clinical course can be persistent with progress in chronic and generalized disease, or have remission. Histologic findings are hypekeratosis, parakeratosis,uniform elongation of rete pegs, lack of granular layer, thinning of stratum malpighii. Munro microabscesses are accumulation neutrofils in the epidermis.Dermal capillares are dilated, and dermis is with edema,with minimal inflammatory cells[1].

Lichen planus

Lichen planus may present like vulvar white plaques or lines with pruritus in the womans after 30 years . It can be localized or generalized and can spontanous regress with exacerbations. Histologic features this interface dermatitis are akantosis, parakeratosis, hypekeratosis and hypergranulosis with elongation of rete pegs. Band-like lymphocytic infiltration next the epidermis is typically present and infiltrate extend in epidermis bassal cells.. Liquefaction degeneration of basal epithelial cells is present. Cytoid bodies present degenerated keratinocytes and dysceratotic cells, and they are localized in the epidermis or superficial dermis.

Lichen sclerosus (et atrophicus)

Lichen sclerosus affected predominantly postmenopausal women, but and young womens may be affected.Desease can affect any or all areas of vulva, and may extend perianal skin, or extragenital sites (neck, extremimites). Microscopic features can vary related to stage of desease. In the advanced the epithelium is atrophic, hyperkeratotic in some cases, with flattened rete pegs.In basal layers of epidermis are present edema and hydropic degeneration what sometimes separate basal cells from the basment membrane in some cases. Infiltration of lymphocytes in the basal and parabasal layers are visibly. Homogenisation, edema, collagenisation of the dermis are in association with mild chronic inflammation[3,4].

Infectious disease of vulva- selected topics

Scabies

Infestation of scabies is related with sexual contact.Pruritic disease cause excoriation, secondary infection. Microscopic features are epidermal irregular acantosis, focal spongiosis, psoriasiform epidermal hyperplasia with exoskeleton on the lower stratum corneum, dermal inflammation with perivascular infiltrate of lymphocites and variable numbers of eosinophils[5].

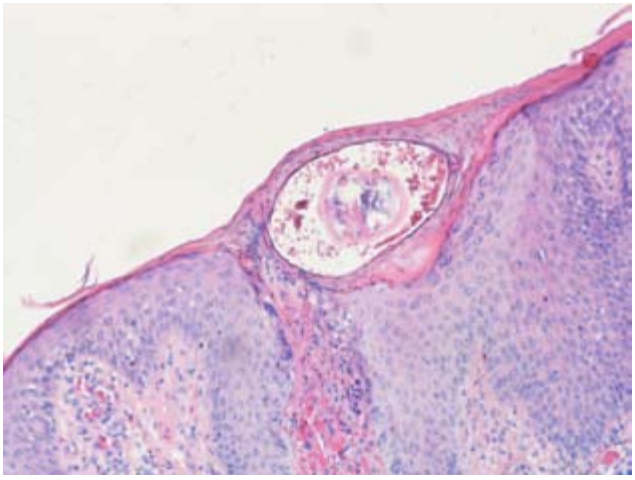

Figure 3. Exosceleton of scabies on the surfaceof vulvar skin(HEx10)

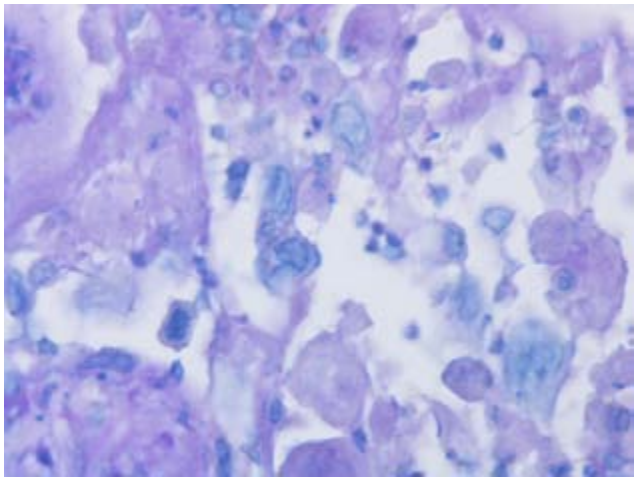

Figure 4. Vulvar herpes simplex (PASx40)

Herpesvirus infection

Herpes simplex virus hominis type 2 can be transmited by direct contact.Fever, inguinal lymphadenopathy, dysuria, urinary retention and vesicles, pustules and painful ulcers are typical clinical findings. Microscopic

features of herpes simpex virus infected epithelial cell is nuclear „ground glass“ appearence and typical eosinophilic intranuclear inclusion body predominantly in the margins of lesion, and finally lysis of cells. Imunohistohemistry for HSV is helpful for diagnosis of viral presence[6].

Molluscum contagiosum

Poxyviral disease transmited with direct contact.Vulvar an perianal pruritic papules with central umbilication or punctum are present, and can be single or multiple. Microscopic findings are acantosis, spongiosis, ballonooning degeneration of epithelial cells which contain intracytoplasmatic eosinophilic inclusion bodies (Henderson-Paterson) which push the nucleus on the periphery of cells.Edema and perivascular inflammation with endothelial vascular proliferation are present in the derm. Recognition of typical microscopic findings can be helped with electron mycroscopy of the virus, but wery rare analisis[7].

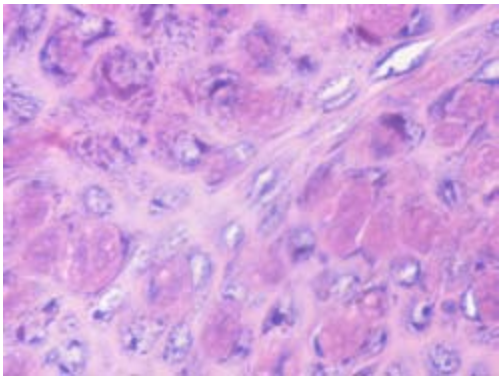

Figure 5. Molluscum contagiosum of vulvar skin (HEx40)

Human papilloma viruses HPV

Human papilloma viruses (HPV) are epithelitrophic viruses and cause premalgnant and malignant transformation of epithelial cells[8]. One-half of womens have other deaseases of genital tract cause HPV. Like other sexually trasmited deseases, direct contact is way for infection.

Low-Risk HPV types for genital premalignant and malignant deseases are 6, 11, 42, 43, 44, Intermediate-Risk HPV types are 33, 35, 39, 51, 52 and High-Risk HPV are types 16, 18, 31, 45, 56. HPV type 6,11,16,18,33 are most commonly in vulva[8,9].

In the geometric style HPV started with disorders in the lowest third of epithelium where HPV include in cell nuclei, and transform and deregulate cell cycle and inhibition of apopthosis.

Condyloma are verrucous, papilary lesions of skin or mucous membrane.This benign neoplasms may be solitary, but may involve cervix, vagina, urethra, peranal skin and anal canal, predominantly in immunosuppresed patients.Central fibrovascular cores covered with squamous epithelium with acantosis, hyperkeratosis, parakeratosis with or without koilocytic atypia in epithelium are microscopic features . Hyperplasia an enlarging of the parabasal cells,with accentation of itracellular bridges and granular layer may be also present. Perinucler „halos“, with picnotic or enlarged nuclei are present in the superfitial cells, and multinucleated cells too, but they may be focal or absent.Abnormal mitosis are absent. Viral cytopathic changes are associated with HPV 6 and 11, but lack of koilocytic atypia does not exclude diagnosis of condyloma,an HPV infection[8].

Vulvar intraepithelial neoplasia (VIN) are precancerous changes of the squamous type. International Society for Study of Vulvovaginal Disease and the International Society of Gineclogical Pathologist recommanded the use of term VIN.

According criteria like viral associated changes,clinical paramethars, microscopic features there are two pathways in carcinogenesis sqimous cell carcinoma HPV-related pathway associated with VIN of the classic type, and the non-HPV related with VIN of the differentiated (simlex) type frequently associated with lichen sclerosus and/or vulvar hyperplasia[9,10].

Vulvar intaepithelial neoplasia, classic type are present like focal or multifocal lesions in womens with HPV infection,and they have concomitant cervical lesion in 50%(). Risk factors are cigarete smokong, immunodeficiency. Microscoping features of VIN are high nucleo-cytoplasmatic ratio, lack of cytoplasmatic maturation of basal and parabasal layers with crowding and cellular disarray,hyperchromasia and nuclear pleomorphism, mitotic figures, parakeratosis, hyperkeratosis,individual-cell keratinisation. Koilocytosis and binucleated and multinucleated cells are present too.Skin appendages are involved often. Imunohistohemichal analisis p16, p63, survivin are very helpful for diagnostic HPV infection in VIN[11,12].

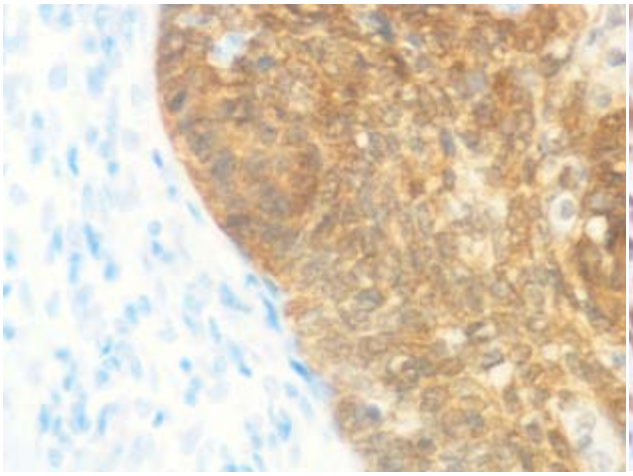

Figure 6. p16 immunoreactivity in cells of VIN (x40)

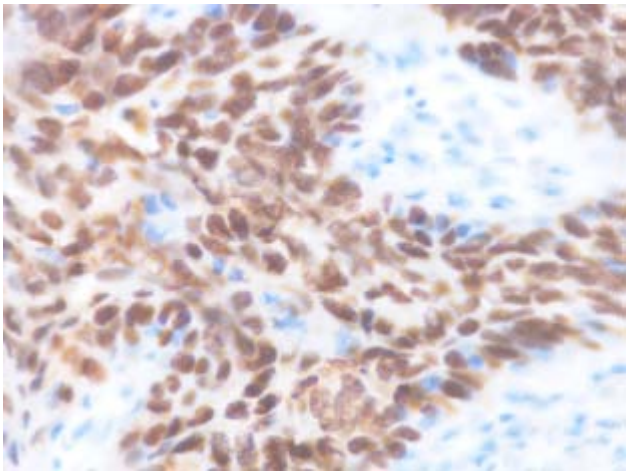

Figure 7. p63 immunoreactivity in cells of VIN (x40)

VIN differentiated (simplex) type affected predominantly older patients, andoften associated with vulvar inflammatory desease or lichen sclerosus. Lesion is predimninatly solitary without assotiation with cervical desease, and HPV infection.The keratinocytes of differetiated VIN are large and pleomorphic, with eosinophilic cytoplasm in the basal and parabasal keratinocytes in the base of rete ridges.Prominent nucleoli in the enlarged nuclei are present predominantly in basal and parabasal keratinocytes.Elongation and anastomosis of rete pegs, and keratin pearl within rete may be present. Parakeratosis is often present[10].

Some patients have “mixed” VIN lesion, and the report of microscoping findings must have predominant type of VIN.

Vulvar malignant epithelial tumors - selected topics

Vulvar squamous cell carcinoma

Invasive squamous carcinoma is the most common carcinoma of vulva. Carcinomas associated with HPV infection affected younger patients in risk groups of smokers, immunosupresion[9,13].

Morphologic subtypes of invasive squamous cell carcinoma include keratinizing, nonkeratinizing, basaloid, warty, spindled, verrucous.Prognostic factors like stage, extracapsular nodal spread,infiltrative margins, vascular invasion, degree of differentiation, status of adjacent skin, stromal response, p53 overexpression are necessary for report[14,15,16].

Some authors sugest to detect dendritic cells by the Cd1a immunohistochemical analysis liike prognostic factor[17].

Figure 8. Immunoreactivity CD1a in squamous cell carcinoma of vulva (x5)

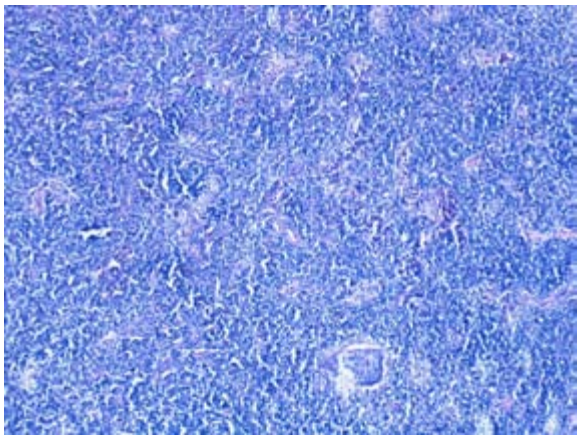

Figure 9. Metastatic cells of squamous cell carcinoma in lymph node(HEx10)

High tumor grade, capillary lymphatics invasion, biger tumor size and depth invasion deserve imunohistochemical analysis lymph nodes for metastatic cells of carcinoma.

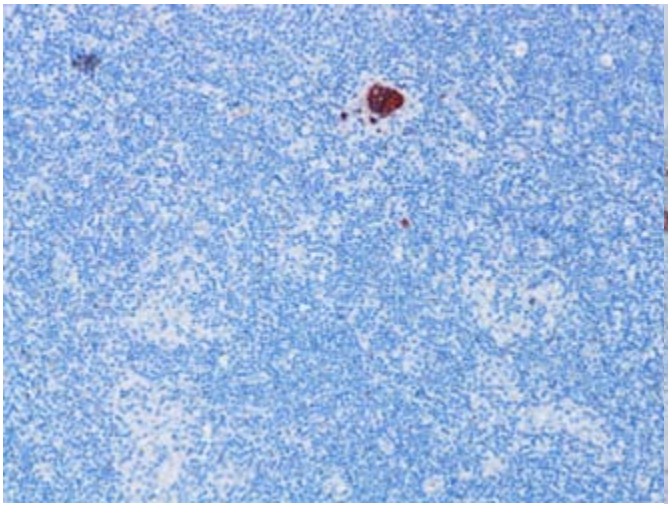

Figure 10. Pancitokeratin immunoreaktivity of metastatic cells of carcinoma in lymph node (x10)

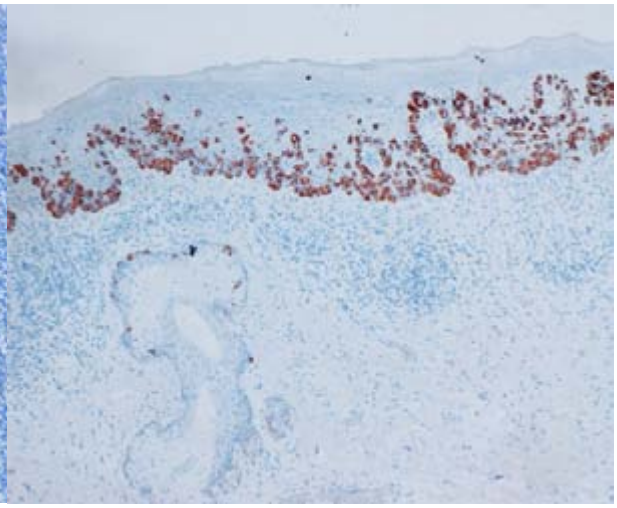

Figure 10. CK7 immunoreactivity in cells ov vulvar Paget desease (x5)

MALIGNANT GLANDULAR TUMOR OF VULVA- selected topic

Vulvar Pagets disease

Extramammary Pagets desease is rare neoplasm, predominantly in the seventh decade. Desease can be focal or extensive. Microscopic features are typical with intraepidermal proliferation of large, atypical gladular-type cells, with granular or vacuolated cytoplasm and round nuclei with prominent nucleoli. Localisation of this cells is predominantly in the parabasal area, singly or in clusters, but may be in diferent layers of epithelium with “Pagetoid spread”. Mitotic figures are present, but not very frequent.

Paget desease can be primary cutaneus vulvar disease,or associated with noncutaneous carcinoma gastrointenstinal origin or bladder carcinoma. Immunohistochemical analysis is very helpful to determine primary origin.

Immunohistochemical finding in primary vulvar cutaneus Paget desease are CK7+, EMA+, CEA+, S100, MelanA-, HMB45-. Immunohistochemical finding in pagetoid rectal adenocarcinoma are CK7-, CK20+, CEA+. Immunohistochemical finding in pagetoid transitional cell carcinoma are CK7+/-,CK20+/-, CEA+, Uroplakin+.[18]

Some author suggest that survivin is useful prognostic marker for vulvar Paget desease[19].

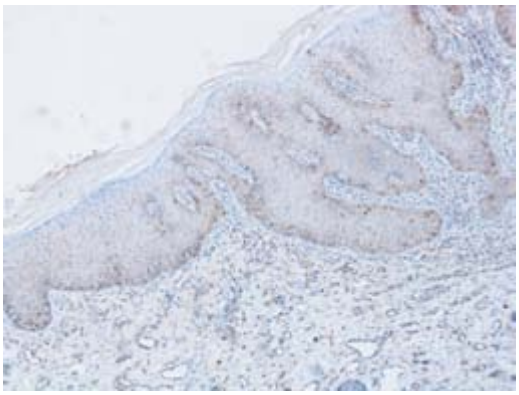

Figure 11. Survivin immunoreactivity in cells of vulvar Paget desease (x5)

Literature

1. Barchino-Ortiz L, Suárez-Fernández R, Lázaro-Ochaita P.Vulvar Inflammatory Dermatoses.
2. Actas Dermosifiliogr. 2012;103(4):260-275.
3. Schwartz JL, Clinton TS. Darier's disease misdiagnosed as severe seborrheic dermatitis.Mil Med 2011;176(12):1457-9.
4. Yasar S, Mumcuoglu CT, Serdar ZA, Gunes P. A case of lichen sclerosus et atrophicus accompanying bullous morphea. Ann Dermatol. 2011;23(Suppl 3):S354-9.
5. Sander BB, Damsgaard K. Lichen sclerosus--a neglected disease.Ugeskr Laeger. 2005;173(46):2951-4.
6. Gaspard L, Laffitte E, Michaud M, Eicher N, Lacour O, Toutous-Trellu L. Scabies.Rev Med Suisse.2006;8(335):718-22,
7. Amaral RL, Giraldo PC, Cursino K, Gonçalves AK, Eleutério J Jr, Giraldo H. Nodular vulvar herpes in an HIV-positive woman.Int J Gynaecol Obstet. 2009;107(3):255.
8. Lin HY, Linn G, Liu CB, Chen CJ, Yu KJ. 4. An immunocompromised woman with severe molluscum contagiosum that responded well to topical imiquimod: a case report and literature review.J Low Genit Tract Dis. 2010;14(2):134-5.
9. Horn LC, Klostermann K, Hautmann S, Höhn AK, Beckmann MW, Mehlhorn G. HPV-associated alterations of the vulva and vagina. Morphology and molecular pathology.Pathologe. 201 ;32(6):467-75.
10. Alonso I, Fusté V, del Pino M, Castillo P, Torné A, Fusté Pet al. Does human papillomavirus infection imply a different prognosis in vulvar squamous cell carcinoma?Gynecol Oncol. 2011;122(3):509-14.
11. Ordi J, Alejo M, Fusté V, Lloveras B, Del Pino M, Alonso I et al. HPV-negative vulvar intraepithelial neoplasia (VIN) with basaloid histologic pattern: an unrecognized variant of simplex (differentiated) VIN.Am J Surg Pathol. 2009;33(11):1659-65.
12. Immunohistochemical staining for p16 and p53 in premalignant and malignant epithelial lesions of the vulva.Santos M, Montagut C, Mellado B, García A, Ramón y Cajal S, et al. Immunohistochemical staining for p16 and p53 in premalignant and malignant epithelial lesions of the vulva.Int J Gynecol Pathol. 2004;23(3):206-14.
13. Brustmann H, Hinterholzer S, Brunner A.Iimmunohistochemical expression of survivin and γ-H2AX in vulvar intraepithelial neoplasia and low-stage squamous cell carcinoma.Int J Gynecol Pathol. 2011;30(6):583-90.

14. Petignat P, Achtari C. Gynecology.Rev Med Suisse. 2010;6(232):105-8.

15. Woelber L, Choschzick M, Eulenburg C, Hager M, Jaenicke F, Gieseking F et al. Prognostic value of pathological resection margin distance in squamous cell cancer of the vulva.Ann Surg Oncol. 2011;18(13):3811-8.

16. Konidaris S, Bakas P, Gregoriou O, Kalampokas T, Kondi-Pafiti A. Surgical management of invasive carcinoma of the vulva. A retrospective analysis and review.Eur J Gynaecol Oncol. 2011;32(5):505-8.

17. Balega J, Butler J, Jeyarajah A, Oram D, Shepherd J, Faruqi A et al. Vulval cancer: what is an adequate surgical margin? Eur J Gynaecol Oncol. 2008;29(5):455-8.

18. Brustmann H. Galectin-3 and CD1a-positive dendritic cells are involved in the development of an invasive phenotype in vulvar squamous lesions.Int J Gynecol Pathol. 2006;25(1):30-7.

19. Shiomi T, Yoshida Y, Shomori K, Yamamoto O, Ito H. Extramammary Paget's disease: evaluation of the histopathological patterns of Paget cell proliferation in the epidermis.J Dermatol. 2011;38(11):1054-7.

20. Shan SJ, Zhang N, Geng SL, Zhou Z, Chen X, Nie T, Guo Zet al Expression of survivin and human telomerase reverse transcriptase in extramammary Paget's disease..J Cutan Pathol. 2010;37(6):635-40..