Vulvar pruritus

Differential diagnostic in medical practice

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Vulvar pruritus, defined as itching of the external female genitalia, is a common symptom in females of all ages (1) and may occur in the presence of dermatological disease or with very few skin findings. The list over the next pages is not exhaustive but attempts to cover the vulvar lesions that occur with a greater likelihood in the practitioner's office.

Pathophysiologically, the nerves responsible for pruritus have been identified as unmyelinated C-fibers and histamine is defined as the main peripheral mediator of pruritus. Histamine-induced itch has been shown to activate central motor areas which are linked to the act of scratching, thereby supposing the observed itch-scratch-itch behavior.
Table 1 and *2* give a summary of these pathologies.

Acute vulvar pruritus

Acute vulvar pruritus is often of infectious nature (2), however, allergic and irritant contact dermatitis playing an important role. Identification of these causes may lead to a prompt resolution of pruritus with directed therapies.

Fungal infection
Yeast organisms, especially *Candida albicans*, are normally present in most vaginas, but in small numbers. A yeast infection, then, is not merely the presence of yeast, but the concentration of them in such large numbers as to cause the typical symptoms of itching, burning and typical cottage-cheese appearing discharge. Likewise, to cure yeast infections means that the concentration of yeast has been restored to normal and symptoms have resolved. The diagnosis is often made by history alone, and enhanced by the classical appearance of vaginal discharge. It can be confirmed by microscopic visualization of clusters of thread-like, branching Candida organisms when the discharge is mixed with KOH. Cultures for bacteria and fungi are necessary to precisely identify Candida, bacterial vaginosis, or trichomonas (3).

Viral infection
Viral infection such as Herpes simplex, Poxvirus or Human papillomavirus (HPV) can also lead to vulvar pruritus although it is not the main symptom.
A tingling or itching sensation precedes the development of painful blisters on both sides of the vulva in *acute herpes infection*. The blisters then break and form shallow ulcers that crust over and when the crusts fall off, the underlying skin looks normal. The process takes 7–10 days.
During the ulcerative stage, the pain may be so intense as to require narcotic analgesia. Urinating during this time can be extremely painful due to the hot, salty urine coming in contact with the open sores on the vulva. The diagnosis is made by the typical appearance and confirmed with a herpes immunofluorescence, antigen detection by ELISA, PCR or culture. Recurrences are common. Treatment guidelines have recently been published (4).
Most commonly found on the labia minora, forchette, perineum, and perianal areas, exophytic wart is one manifestation of «*low oncogenic risk*» *HPV infection*. Their classic appearance is helpful for the diagnosis, however, biopsy should be performed to «rule out» Vulvar intraepithelial neoplasia (VIN) or squamous carcinoma in circumstances of rapid growth, increased pigmentation, coexisting ulceration or fixation to underlying connective tissue (5). Misdiagnoses with condyloma latum (secondary syphilis) as a genital wart or overdiagnoses «micropapillomatosis» of the vestibule as evidence of HPV infection are not uncommun.
Virus of the poxvirus family causes small, benign skin tumors to grow on the vulva known as *Molluscum contagiosum*, which are usually symptomless but may sometimes be itching. Confirmatory diagnosis and treatment follow excisional biopsy or dermal curettage.

Allergic and contact dermatitis
A number of topical agents may cause *allergic contact dermatitis* also called eczema, in the genital area. This often presents as an acute eczematous dermatitis with bright red erythema, weeping and significant pruritus.
Two major types of eczema, exogenous and endogenous, occur (6):
Exogenous eczema can be either «irritant» or «allergic». Eczematous lesions are symmetric and found on areas of the vulva that may contact environmental irritants or antigens.
Any chronic pruritic dermatosis of the vulva can lead to scratching and chronic rubbing which eventually leads to the changes of the skin known as *lichen simplex chronicus*. Patch testing is of limited value given the nearly unlimited number of potential irritants and allergens. However, in one study, 49% of women with chronic vulvar dermatoses were patch test positive for a relevant allergen (7). Any topical agents (lanolin in creams and ointments) as well as rubber accelerators associated with condom or diaphragm use, propylene glycol (present in KY Jelly) fragrances in feminine hygiene prepara-

Vulvar pruritus

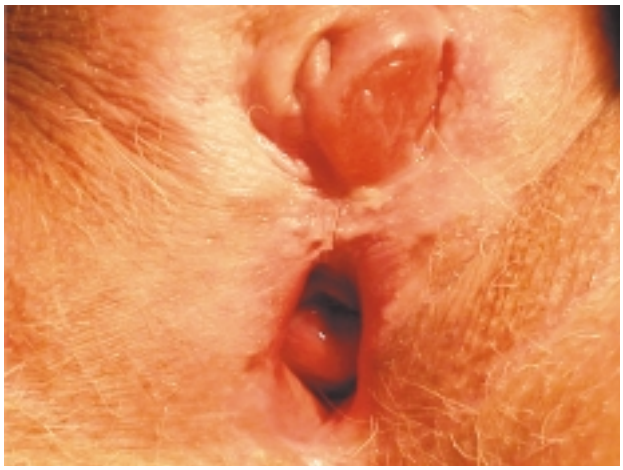

Figure 1: Squamous cell carcinoma coexisting with lichen sclerosus

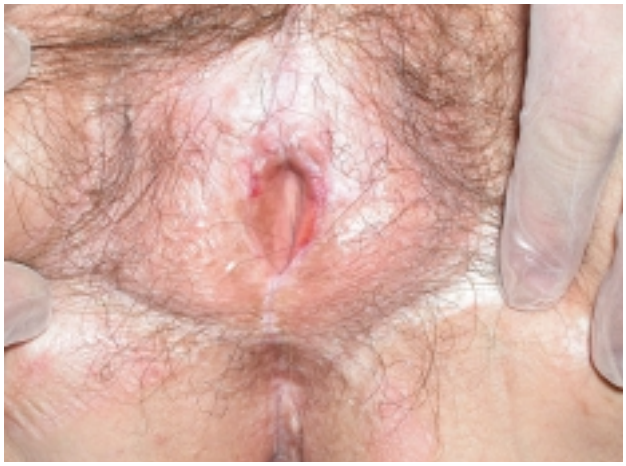

Figure 2: Lichen sclerosus

tions are common causes of exogenous eczema (7).

A large number of women behaviour such as perceiving themselves unclean, and initiating a vigorous or irritating cleansing routine may exacerbate irritant *contact dermatitis*. Feminine hygiene products, fragrances, spray deodorants, and douches have many irritating ingredients, such as alcohol, propylene glycol, or an acidic pH.

Endogenous eczema, also known as atopic dermatitis, may affect multiple sites including the vulva, and may coexist with asthma or allergic rhinitis. Vulval eczema commonly presents with pruritus usually exacerbating during sexual intercourse or menstruation, leading to embarrassment and interference with normal life. This pathology is actually a chronic cause of vulvar pruritus, nevertheless the onset can be perceived as acute by both the patient and physician.

Chronic vulvar pruritus

Chronic vulvar pruritus often has a long history with gradual onset, and may include a large variety of disorders like primary inflammatory disorder, papulosquamous disorders as well as malignancies, mechanical or psychogenic causes.

Malignancies

Malignancies of the vulvar area are often slow growing and can cause low-grade pruritus. VIN, also previously referred to as *Bowen's disease or squamous cell carcinoma in situ,* as well as extramammary Paget's disease may mimic dermatitis with erythematous plaques and variable scale.

There are in fact two distinct types of VIN, one associated and the other not associated with HPV infection. The HPV-associated type of VIN or undifferentiated VIN occurs predominantly in younger patients, tends to be a multicentric and multifocal disease and is of the undifferentiated Bowenoid or basaloid histological type, while the non-HPV associated or differentiated VIN form generally found in older women, is commonly unifocal, unicentric and usually of the differentiated type (8, 9, 10). The potential for progression of undifferentiated VIN 3 to an invasive carcinoma has generally been thought to be low and usually estimated to be no more than 3–4% (11). However according to recent studies, the risk of invasion is not consistently low and it is possible that it has been seriously underestimated in the past, particularly in elderly women in whom progression to an invasive lesion can occur in at least 20% of VIN 3 cases (12, 13) (*figure 1*).

Differentiated VIN is commonly associated with lichen sclerosus and has a very strong association with invasive squamous cell carcinoma in VIN 3 cases (10). Any apparent dermatosis not responding to therapy may warrant a biopsy.

The histogenesis and pathogenesis of *Paget's disease* of the vulva remain unclear, though it is recognized as an intraepithelial adenocarcinoma. About 5% of women with vulvar Paget's disease have regional or distant malignant disease such as cervical adenocarcinoma, transitional cell carcinoma of the urinary tract or breast carcinoma (14).

Occasional cases of vulvar Paget's disease have also been associated with vulvar squamous intraepithelial neoplasia (VIN) 3 or invasive carcinoma (8).

The prognosis, in terms of survival, for patients with vulvar Paget's disease without associated malignant neoplasm is generally very good. However, in a proportion of cases, ranging from 12% to 47%, the intraepithelial lesion gives rise to an adenocarcinoma sometimes leading to death (15, 16). Patients with Paget's disease associated with a regional malignant neoplasm tend to have a poor prognosis (17). Treatment of intraepithelial vulvar Paget's disease is by surgical excision, but recurrence occurs in nearly 40–50% of cases (18).

Dermatoses

Lichen sclerosus is a common cause of whitish lesions of the vulva. The cause of this disorder is unknown, and it can occur at any age, although it is most common in the postmenopausal years. At menarche, symptoms and signs can im-

Vulvar pruritus

Table 1: Causes of acute vulvar pruritis

A Infectious causes

Bacterial:

Staphylococcus aureus, group A Streptococcus, Mycoplasma homini, Haemophilus influenzae, Streptococcus pneumoniae; Neisseria meningitidis, Shigella, Yersinia, Gardnerella vaginalis, Mobiluncus, Bacteroides Trichomonas vaginalis, Neisseria gonorrheae, Chlamydia trachomatis

Fungal:

Candidiasis, Tinea cruris

Infestation:

Scabies, Pediculosis pubis, Pinworms

Viral:

Herpes simplex virus, Herpes zoster, Human papillomavirus, Molluscum contagiosum

B Non-infectious causes

Contact dermatitis

Irritant, allergic

Table 2: Causes of chronic vulvar pruritis

A Malignancies

Extramammary Paget's disease, Vulvar intraepithelial neoplasia

B Dermatoses

Seborrheic dermatitis, Psoriasis, Atopic dermatitis, Lichen sclerosus, Lichen planus

C Atrophic vulvovaginitis

Diabetic patient, obese patient, inadequate hygiene, psychogenic: Depression, Idiopathic pruritus (lichen simplex chronicus)

prove spontaneously, but it is not known whether there is long-term risk of recurrence.

Pruritus is quite characteristic of lichen sclerosous although it can be asymptomatic in its early stages (*figure 2*). There may be loss of the normal architecture with atrophy of the labia minora, constriction of the vaginal orifice (craurosis), synechiae development, ecchymoses, fissures, and telangiectases (19). A clear risk of association with vulvar puritus is well documented (12, 13).

Two types of *Lichen planus* are known:

1. the «classic» type consisting of sharply demarcated, flat-topped plaques on oral and genital membranes and,
2. The «erosive» type consisting of an erosive, erythematous lesion originating in the vestibule and variably extending up the vaginal canal.

Similar to lichen sclerosus, lichen planus may be associated with an increased risk of malignancy (20).

Any times, no etiology is identified and examination reveals either normal skin, or lichenification, lichen simplex chronicus or idiopathic/essential pruritus can be suspected. Lichenified skin is mildly scaly, rather leathery and has increased skin markings. At times, the skin may, in fact, appear completely normal. Symptoms of itching and burning predominate. A number of acute disorders may evolve into lichen simplex chronicus including recurrent vaginal infections and long-standing eczema. Nighttimes itch is a common feature and patients maybe unaware of this behaviour (21). Lichen simplex chronicus may coexist with chronic dermatoses such as lichen sclerosus or lichen planus. Essentially, it is an end-stage disorder that originates from a wide number of irritative or infectious factors.

Papulosquamous disorders or dermatoses such as seborrheic dermatitis, psoriasis and atopic dermatitis rarely present with genital features alone. A history and a full skin exam should reveal some other signs of these conditions.

Finally, an increased tendency for depressive and obsessive-compulsive traits has been identified in patients with chronic pruritic conditions (22, 23). Whether this represents a cause or effect is unclear. It has been shown that depression correlates with the degree of symptomatic pruritus in patients with chronic pruritic dermatological disease.

Conclusion

In conclusion, management of vulvar pruritus is difficult. A detailed history is important, thorough examination and biopsies of the vulva are essential to reach a diagnosis. Better knowledge of these diseases can be achieved by referring the patients to second opinion. ◗

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References:

1. Bornstein, J., Pascal, B., Abramovici, H.: The common problem of vulvar pruritus. Obstetrical & Gynecological Survey 1993; 48 (2): 111–118.
2. Hatch, K.D.: Vulvar and vaginal disorders. Current Opinion in Obstetrics & Gynecology 1992; 4(6): 904-906.
3. Edwards, L.: The diagnosis and treatment of infectious vaginitis. Dermatologic Therapy 2004; 17 (1): 102–110.
4. Buchner, S., et al.: Swiss recommendations for the management of genital herpes and herpes simplex virus infection in the neonate. Swiss Med WKL. 2004; 134: 205–214.

Vulvar pruritus

5. Moscicki, A.B., et al.: Risks for incident human papillomavirus infection and low-grade squamous intraepithelial lesion development in young females. JAMA 2001; 285 (23): 2995–3002.
6. Salim, A., Wojnarowska, F.: Skin diseases affecting the vulva. Current Obstetrics & Gynecology 2002; 12: 81–89.
7. Lewis, F.M., Shah, M., Gawkrodger, D.J.: Contact sensitivity in pruritus vulvae: patch test results and clinical outcome. American Journal of Contact Dermatitis 1997; 8(3): 137–140.
8. Hart, W.R.: Vulvar intraepithelial neoplasia: historical aspects and current status. International Journal of Gynecological Pathology 2001; 20(1): 16–30.
9. Haefner, H.K., et al.: Vulvar intraepithelial neoplasia: age, morphological phenotype, papillomavirus DNA, and coexisting invasive carcinoma. Human Pathology 1995; 26(2): 147–154.
10. Yang, B., Hart, W.R.: Vulvar intraepithelial neoplasia of the simplex (differentiated) type: a clinicopathologic study including analysis of HPV and p53 expression. American Journal of Surgical Pathology 2000; 24 (3): 429–41.
11. Fiorica, J.V., et al.: Carcinoma in situ of the vulva: 24 years' experience in southwest Florida. Southern Medical Journal 1988; 81 (5): 589–593.
12. Crum, C.P.: Carcinoma of the vulva: epidemiology and pathogenesis. International Journal of Radiation Oncology, Biology, Physics 1992; 22 (3): 525-527.
13. Thuis, Y.N., et al.: Contemporary experience of the management of vulvar intraepithelial neoplasia. Int J Gynecol Cancer 2000; 10: 223–227.
14. Fishman, D.A.: Extramammary Paget's disease of the vulva. Gynecologic Oncology 1995; 56 (2): 266–270.
15. Fanning, J., et al.: Paget's disease of the vulva: prevalence of associated vulvar adenocarcinoma, invasive Paget's disease, and recurrence after surgical excision. American Journal of Obstetrics & Gynecology 1999; 180: 24–27.
16. Crawford, D., et al.: Prognostic factors in Paget's disease of the vulva: a study of 21 cases. International Journal of Gynecological Pathology 1999; 18 (4): 351–359.
17. Parker, L.P.: Paget's disease of the vulva: pathology, pattern of involvement, and prognosis. Gynecologic Oncology 2000; 77 (1): 183–89.
18. Zollo, J.D., Zeitouni N.C., The Roswell Park Cancer Institute experience with extramammary Paget's disease. British Journal of Dermatology 2000; 142 (1): 59–65.
19. Carlson, J.A., et al.: Vulvar lichen sclerosus and squamous cell carcinoma: a cohort, case control, and investigational study with historical perspective; implications for chronic inflammation and sclerosis in the development of neoplasia. Human Pathology 1998; 29 (9): 932–48.
20. Jones, R.W., et al.: Vulvar lichen planus: progression of pseudoepitheliomatous hyperplasia to invasive vulvar carcinomas. BJOG: an International Journal of Obstetrics & Gynaecology 2001; 108 (6): 665–666.
21. Virgili, A., Bacilieri, S., Corazza, M.: Managing vulvar lichen simplex chronicus. Journal of Reproductive Medicine 2001; 46 (4): 343–46.
22. Sheenhan-Dare, R.A., et al.: Anxiety and depression in patients with chronic urticaria and generalized pruritus. Br J Dermatol 1990 (123): 769–774.
23. Hatch, M.L., Paradis C., and Friedman S.: Obsessive-compulsive disorder in patients with chronic pruritic conditions. Case studies and discussion. J Am Acad Dermatol 1992; 26: 549–551.

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Solidarität gegen Brustkrebs

Die Diagnose Brustkrebs ist ein Schock für jährlich etwa 4500 betroffene Frauen in der Schweiz. Die Angst vor dem Verlust der Brust, vor Haarausfall und weiteren Nebenwirkungen der Chemotherapie wird ständiger Begleiter. Dabei fürchten die Frauen um die Beziehung, die Familie, ihr Überleben und fühlen sich mit ihren Ängsten meist alleingelassen. Der Arzt kann psychologisch oft zu wenig helfen, die Familie, die Freunde und der Partner sind überfordert. Hier setzt der neue psycho-onkologische Dienst der Krebsliga Zentralschweiz an: Ab Januar 2005 wird die Psycho-Onkologin Carmen Schürer betroffenen Frauen mit Rat und Tat zu Seite stehen.

Um dem neuen Projekt eine kleine Starthilfe zu geben, organisierte die «Luzerner Solidaritätswanderung» einen geselligen Abend mit Schifffahrt auf dem Vierwaldstättersee, Kurzspielfilm und Benefizkonzert. Der Reinerlös wird dem psycho-onkologischen Dienst der Krebsliga Zentralschweiz zugute kommen. Fast 170 Personen nahmen teil und unterstützen den guten Zweck. Nicht zuletzt dank des Hauptsponsors Essex Chemie können der Krebsliga Zentralschweiz 12 000 Franken zur Verfügung gestellt werden.

Wie gross die psychische Belastung von Brustkrebspatientinnen ist, zeigt der Kurzspielfilm «Busenfreundinnen» von Gabriele Schärer. Einfühlsam und eindringlich thematisiert der Film die Sprachlosigkeit und Ängste von Brustkrebspatientinnen und mündet in betroffenem Schweigen. Dabei gibt es, wie Professor Dr. Rudolf A. Joss, Chefarzt Onkologie am Kantonsspital Luzern, betont, medizinische Entwicklungen, die nicht nur die Heilungschancen erhöhen, sondern auch weniger belastend als ältere Methoden sind. Dazu gehören brusterhaltende Tumoroperationen und nebenwirkungsärmere Chemotherapien.

Chemotherapien mit modernsten Brustkrebsmedikamenten, etwa dem eingekapselten Doxorubicin Caelyx, verursachen heute bei maximaler Wirksamkeit deutlich weniger Nebenwirkungen als herkömmliche Behandlungen. Studien belegen, dass Haarausfall, Übelkeit und Erbrechen wesentlich seltener auftreten. Dennoch brauchen Brustkrebspatientinnen dringend die Hilfe, die ihnen der neue psycho-onkologische Dienst in Luzern geben kann. ◗

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