CASE REPORT

Vulvar cancer in young woman—case report

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Abstract

Vulvar cancer is rare with incidence of 45,240 new cases globally which account for 4% of all genitourinary tract neoplasma. It is considered a postmenopausal disease, however incidence age has decreased over the years because of high prevalence of persistent high-risk human papillomavirus (hrHPV) infection. Vulvar cancer diagnosis in young women is challenging. Prompt and adequate diagnosis, and treatment can ensure the life quality. A 23 years old patient was admitted to Department of Operative Gynecology for treating malignant vulvar neoplasma. She was reffered to our clinic for electrocauterization after being diagnosed of condylomata acuminata. Physical examination revealed vulva atrophy with smooth discolored skin patches on both sides. A 2 cm exophytic lesion was noted ~10 mm from clitoris on right labia majora. Multifocal biopsy was performed for suspect finding which proved invasive vulvar squamous keratinizing cancer. Positron emission tomography-computed tomography (PET/CT) scan showed individual lymph nodes on right inguinofemoral region which were moderately metabolically active. Wide excision of cancer was performed with unilateral inguinofemoral lymphadenectomy. Macroscopic evaluation of entire specimen depicted 2.4 × 2.2 × 0.5 cm HPV associated invasive vulvar squamous keratinizing cancer, vulvar high grade squamous intraepithelial lesion (vHSIL) or usual type vulvar intraepithelial neoplasia (uVIN3) and lichen sclerosus. Healthcare professionals in primary care centers should be adequately trained, aware of and familiar with vulvar malignancies in younger women despite their rarity. Early diagnosis can improve outcomes in vulvar cancer via reducing morbidity and mortality. The individualized surgical treatment is the preferred strategy for patients at present.

Keywords

Vulvar cancer; HPV infection; Young women; Lichen sclerosus

1. Introduction

Vulvar cancer is rare with global incidence of 45,240 new cases which account for 4% of all genitourinary tract neoplasma [1]. It is considered a postmenopausal women disease, however evidence shows incidence age being decreased over the years because of high prevalence of persistent high-risk human papillomavirus (hrHPV) infection [2]. There are two forms of vulvar squamous cell cancer having different pathogenetic mechanisms. The first form is associated with hrHPV infection and generally seen in younger women of 35–65 years’ age. The second form is linked with chronic vulvar inflammatory epithelial condition, particularly the lichen sclerosus (LS), and normally seen among women in their 70 s [3]. Both forms are preceded by vulvar squamous intraepithelial lesions (vSIL), however HPV associated type is termed as high-grade SIL of vulva (vHSIL), formerly known as “vulvar intraepithelial neoplasia usual type” (uVIN), while that with dermatoses is termed as differentiated vulvar intraepithelial neoplasia (dVIN) [4]. Vulvar cancer appears as palpable lump with symptoms of pruritis, irritation, pain, bleeding, vaginal discharge and dryness or dysuria [5]. The common sites are labia majora and clitoris. Vulvar cancer can spread locally, hematogenously, in inguinal and femoral lymph nodes, and the pelvic and paraaortic lymph nodes. Vulvar cancer diagnosis in young women is challenging. Early diagnosis and suitable treatment can ensure the life quality.

2. Case report

A 23 years old patient was admitted to Department of Operative Gynecology for treating malignant vulvar neoplasma. She had periodic episodes of mild pruritis of vulva for the last couple of years. She noticed a small lesion one year ago and thus went to the gynaecological department in Primary Health Care Centre. The lesion was conservatively treated with imiquimod topical cream but without improvement. She was diagnosed with condyloma acuminata at another primary gynaecological facility and reffered to our clinic for electrocauterization. Her history revealed that she was an active smoker for the past eight
years smoking 20 cigarettes a day. She had more than five sexual partners and the first sexual intercourse was at 14 years’ age. She was not vaccinated for HPV. Pap test was negative for intraepithelial lesion or malignancy (NILM), while HPV test was positive for hrHPV type 16. Physical examination depicted vulva atrophy with smooth discolored skin patches on both sides. A 2 cm exophytic lesion was noted ~10 mm from clitoris on right labia majora. The urethra or vagina had no involvement. Colposcopic findings of vagina and cervix were normal. Multifocal biopsy was performed due to suspect finding. Biopsy depicted invasive vulvar squamous keratinizing cancer and HPV associated high grade vSIL (uVIN3) with p16 positive in immunohistochemical analysis and wild type p53 gene. Pelvis magnetic resonance imaging (MRI) (Fig. 1) pointed out suspicious inguinofermal lymph nodes on both sides but predominantly on the right. PET/CT scan was then conducted.

**FIGURE 1.** Pelvis MRI showing suspicious inguinofermal lymph nodes on both sides but predominantly on the right.

PET/CT scan (Fig. 2) showed metabolically active focus in right labia majora region corresponding to primary tumor deposit. There were individual lymph nodes on right inguinofermal region which were moderately metabolically active, while they were smaller without metabolic activity on the left side.

Wide excision of cancer was conducted with inguinofermal lymphadenectomy (Fig. 3). Macroscopic evaluation of entire specimen exhibited 2.4 × 2.2 × 0.5 cm HPV associated invasive vulvar squamous keratinizing cancer, vHSIL (uVIN3) and lichen sclerosus (Fig. 4). Margins were tumor-free with proximal margin 0.7 cm near clitoris and lateral margin 1.2 cm from well-defined lesion. The greatest invasion depth was 2.5 mm. Inguinofermal lymphadenectomy histological report depicted 10 lymph nodes with lymphadenitis chronica reactiva. Lymphovascular or perineural space involvement was not seen. According to the latest staging of the International Federation of Gynecology and Obstetrics (FIGO)

**FIGURE 2.** PET/CT scan with metabolically active focus in right labia majora region, and moderate metabolically active lymph nodes on right inguinofermal region.

**FIGURE 3.** Marked planning for wide excision.

**FIGURE 4.** Histomicrographs. (a) Invasive squamous vulvar carcinoma-biopsy, HE×50. (b) Invasive squamous vulvar carcinoma-resection specimen, HE×100. (c) Invasive squamous vulvar carcinoma-resection specimen, 50×HE. (d) Invasive squamous vulvar carcinoma-resection specimen, 50×HE.
it was stage Ib [6]. Postoperative course was uneventful. As per the decision of oncology committee, there was no need of adjuvant therapy based on histopathological findings. The ultrapotent local corticosteroid therapy (betamethasone dipropionate ointment 0.05%) was prescribed to the patient because of lichen sclerosus. According to the protocols, the patient had gynecological examination every three to four months for the next two years and after that less often, however lifelong follow-up was recommended.

3. Discussion

Evidence shows that there has been striking increase worldwide in the incidence of vSIL and vulvar cancer, among young women. High-risk HPV infection has role in vulvar HSIL development (86.7% cases) and “predilection” for women in 30 s and 40 s, however it is rare in women under 30 years’ age [7]. The risk factors for vHSIL are linked to HPV-related lesions: multiple partners, early sexual activity, oral contraceptive usage, smoking and immunodeficiency conditions [8]. Our patient history indicates risky sexual behavior and active smoking for almost a decade which are the known risk factors of HPV infection. She had a cervical HPV16 infection, and large cohort study concluded increased vHSIL risk in those women (hazard ratio (HR) = 2.6; 95% confidence interval, 1.2–5.5) compared to HPV negative [9]. Malignant transformation of vHSIL in young women is 5.7%, and that the depressed immunity is a predisposing factor [10]. Most VIN exhibiting women have localized pruritis or lesions that can be confused with condylomas, which also occurred in our case. Vulvar cancer was initially misdiagnosed because of her age and inexperienced gynaecologist. Vulvar cancer diagnosis is not difficult in postmenopausal women with known subjective symptoms, prior diagnosis of high risk HPV types, autoimmune or chronic vulvar disease and visible raised, warty or flat lesions of vulva. It is a challenge to diagnose young women with rare chronic disease in early 20 s. Lichen sclerosus is a chronic inflammatory condition with unknown but probably autoimmune etiology [11]. The true LS prevalence is unknown as it remains underrecognized and undertreated. A study showed 1.7% LS prevalence diagnosed in women with mean age of 52.6 years by the private gynecological practice, where one third was asymptomatic [12]. An inexperienced gynecologist can overlook the reality that an immunologically affected person may develop a disease in whom the molecular milieu has changed and it is not the characteristic of subjects’ age [13]. In our case, it is probable that pathogenetic mechanism that led to invasive cancer in our very young patient is an unrecognized and untreated vHSIL lesion in the chronic inflammatory disease setting, such as lichen sclerosus. Lichen sclerosus has a non-negligible risk (4–6.7%) of vulvar squamous cell cancer, and treatment with ultrapotent topical corticosteroids is thus needed [14, 15].

Efforts have been made in the last twenty years, particularly in younger women, to individualize the patients’ treatment with less radical procedures because of severe post-surgical complications and psychosexual disorders caused by highly deforming operations. In early-stage vulvar cancer patients, the gold standard treatment is surgery (radical wide excision of tumor with adequate margins) and inguinofemoral lymphadenectomy, or a sentinel node procedure in appropriate patients [16]. Ipsilateral inguinofemoral lymphadenectomy should be performed immediately in patients with unifocal lateral lesions of less than 4 cm, if enlarged lymph nodes are diagnosed preoperatively [16]. According to the current guideline of European Society of Gynecologic Oncology (ESGO), a surgical excision margin of at least 1 cm is recommended, while a narrower margin is acceptable when tumor lies close to midline structures (clitoris, urethra, anus) and preserving their function is desirable [17]. Patients with associated VIN or lichen sclerosus have higher local recurrence risk and require careful and lifelong follow-up [10, 18].

4. Conclusions

Healthcare professionals in primary care centers should be sufficiently trained, aware of and familiar with vulvar malignancies in younger women despite their rarity. It is imperative to diagnose the patients at early stage and refer to tertiary center for multi-dimensional treatments by gynecologists, oncologists and pathologists. Early diagnosis can improve outcomes in vulvar cancer via reducing the morbidity and mortality. The individualized surgical treatment is the best strategy for patients at present.

ABBREVIATIONS

HPV, human papillomavirus; hrHPV, high risk human papillomavirus; LS, lichen sclerosus; vSIL, vulvar squamous intraepithelial lesions; vHSIL, vulvar high grade squamous intraepithelial lesions; uVIN, usual type vulvar intraepithelial neoplasia; dVIN, differentiated vulvar intraepithelial neoplasia; PET-CT, positron emission tomography-computed tomography; NILM, negative for intraepithelial lesion or malignancy; MRI, magnetic resonance imaging; FIGO, The International Federation of Gynecology and Obstetrics; ESGO, The European Society of Gynecologic Oncology.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

MP—designed the research study and revised the draft. MS—oversaw medical photography. MP—performed pathological analysis. LJMS—advised on manuscript development. BB and AK—wrote the manuscript. BB—was responsible for submitting manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The patient gave informed consent prior to her inclusion in case report. The case report was exempted from requiring ethics
approval for being a review of clinical practice outcome. This was approved by The Ethics Review Committee of Clinic for gynecology and obstetrics in Novi Sad 00-6/342.

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CONFLICT OF INTEREST
The authors declare no conflict of interest.

REFERENCES