

CASE REPORT

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Coexistence of Condylomata Acuminata with Warty Squamous Cell Carcinoma and Squamous Cell Carcinoma

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ABSTRACT

Introduction: Condyloma acuminatum has previously been considered to be a benign growth with no malignant potential, but a review of the literature supports the concept that condylomata acuminata may precede or be associated with invasive squamous cell carcinoma (ISCC) or warty squamous cell carcinoma (WSCC). **Case report:** We present a clinical case of a 58-year old woman with large, slow-growing, exophytic tumor of external genitalia shaped like a cauliflower with the propagation to both legs and behind. We performed multiple biopsies to detect potential malignancy but malignancy was not confirmed histologically. The presence of HPV (human papilloma virus) low and high risk was discovered. Inguinal lymph nodes were enlarged both sides, but cytologic examination identified no malignant cells. The patient was initially treated by the loop electro surgical excision procedure (LEEP) and podophilin solution on the rest of the condylomas. Condyloma acuminatum was confirmed histologically. Later, we performed a wide surgical excision of the rest of the condylomas. The new changes on the previously treated region were removed using LEEP. WSCC and ISCC were confirmed histologically so were radical vulvectomy and inguinal lymphadenectomy performed. The patient was advised to remain under close follow-up.

Keywords: condyloma acuminatum, vulvar cancer, HPV.

1. INTRODUCTION

Genital HPV infections are among the most common sexually transmitted diseases (STD). HPV is associated with a spectrum of diseases, ranging from benign vulgar verrucae and condylomata acuminata or genital warts to malignant cancers of the cervix, vulva, anus and penis(1,2). Approximately 50 different types of HPV can infect the anogenital tract. Most genital condylomata are due to infection by HPV-6 or HPV-11. However, invasive squamous cell carcinoma (ISCC) of the vulva is an uncommon disease. Warty squamous cell carcinoma (WSCC) is a rarely described lesion that can often be

confused with other verruciform tumors. This tumor has been associated with a history of vulvar intraepithelial neoplasia, young age, and the presence of HPV deoxyribonucleic acid (DNA) (3). No antiviral treatment exists for HPV to date. The standard treatment options are cryotherapy with liquid nitrogen, trichloroacetic acid, salicylic acid, imiquimod, podophyllotoxin(2). Other modalities in resistant cases include electrotherapy, laser excision and surgical excision (1).

2. CASE REPORT

A 58-year old female was referred for evaluation due to persistent exo-



Figure 1. 58-year old woman with large,slow-growing, exophytic tumor of external genitalia shaped like a cauliflower with propagation to both legs and behind.

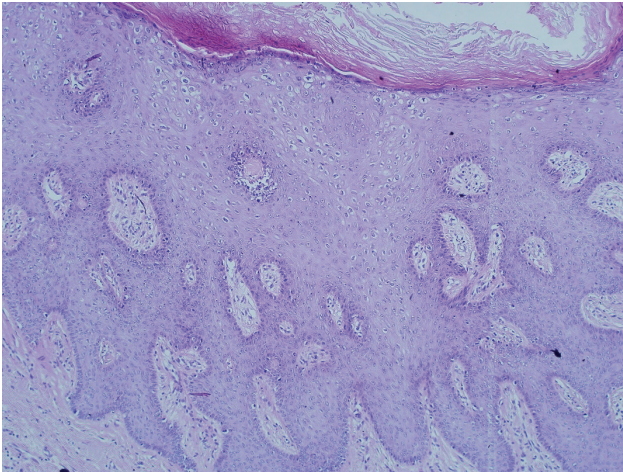


Figure 2. PHD 10814/2010 Condylomata acuminata 100 x JPEG

phytic tumor of external genitalia shaped like cauliflower with propagation to legs and behind persisting for more than 10 years (Fig. 1). Examination of the vulvar skin revealed a 15 x 20 cm fleshy, vascular mass. Vaginal mucosa and cervix appeared normal. PAP smear of cervix and vulva revealed no abnormality. Vulvar smear was screened to detect HPV DNA.

We used *polymerase chain reaction (PCR)*. HPV types of high risk and low risk groups were detected. Colposcopy did not detect any HPV lesion. Proctoscopy was refused. Inguinal lymph nodes were enlarged both sides and fine needle aspiration cytology was done, but cytologic examination identified no malignant cells. Routine laboratory tests, including a complete blood count, blood chemistry, urinalysis, immunological, and serological investigations like The Venereal Disease Research Laboratory (VDRL) and Human Immunodeficiency Virus (HIV), hepatitis A, B and C were negative. Electrophoresis of serum proteins and immunoelectrophoresis revealed no abnormality. Tumor markers were normal. Chest X-ray investigation, electrocardiography, abdominal and pelvic ultrasound and computed tomography (CT), as well as cystoscopy were unremarkable. After we detected a wide base of condylomas predominantly in



Figure 3. The patient was initially treated by the loop electrosurgical excision procedure (LEEP) and podophillin solution on the rest of the condylomas.

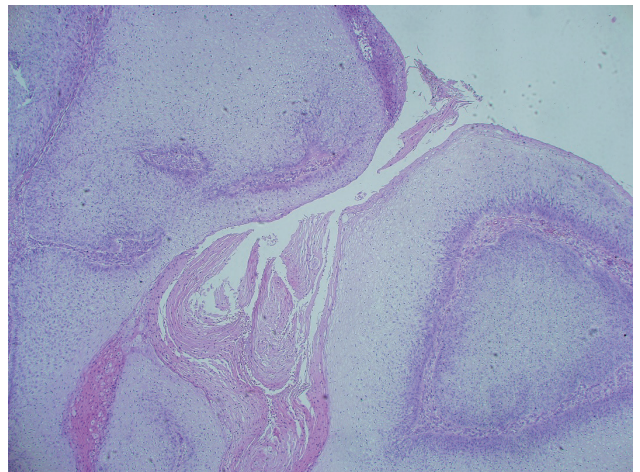


Figure 4. PHD 11405/2010 Ca condylomatousum et condylomata acuminata 50 x JPEG

vulvar region, we performed multiple biopsies to detect potential malignancy.

However, malignancy was not confirmed histologically. The diagnosis of large benign condyloma acuminatum was made (Fig. 2). The patient was initially treated by the loop electrosurgical excision procedure (LEEP) and podophillin solution on the rest of the condyloma (Fig. 3). Condylomata acuminata and plana were confirmed histologically. Later, we performed a wide surgical excision of the rest of the condylomas. Condyloma acuminatum, WSCC and ISCC were confirmed histologically (Fig. 4, 5). Radical vulvectomy and inguinal lymphadenectomy was performed. The patient was advised to remain under close follow-up. Recurrence of condylomas was confirmed several times during follow-up (Fig. 6). All were removed surgically and confirmed pathohistologically.

3. DISCUSSION

Condyloma acuminatum results from infection with the double-stranded DNA virus, HPV, of which over 150 subtypes are now recognized. HPV infection is a sexually transmitted disease (2, 3, 4, 5). Condylomata acuminata



Figure 5. The appearance of vulvar region after the end of therapy.

are associated with HPV types 6, 11, 16, 18, 31, 33 particularly 6 and 11.

The genital warts initially are usually small finely branched structures with a narrow stalk; they may later form large cauliflower masses. Although the vulva and the perianal skin are the sites most frequently involved, lesions may occur within the vagina, cervix or mons pubis in females. Extraanogenital localisation is extremely rare in immuno competent patients (2, 6, 7, 8, 9), and they only rarely turn malignant.

Condylomata plana are subclinical condylomas that are not visible by naked eye. They are associated with HPV 16, 18, 31, 33. Diagnosis of condyloma is generally made on clinical grounds (physical examination and examination in specula). Vulvoscopy and colposcopy are recommended. (4). A biopsy is recommended for women with a history of vulvar dysplasia, postmenopausal women, women who fail medical therapy, in the case of clinical doubt about the diagnosis, and suspicion of malignancy (10, 11, 12, 13).

Biopsy of vulvar skin associated with condyloma shows evidence of complex branching papillary architecture with vascular papillae, hyperkeratosis, acanthosis and parakeratosis. A chronic inflammatory infiltrate is often observed within the dermis. Koilocytosis is commonly observed in the superficial epithelial cells. HPV typisation is recommended.

The standard treatment options are cryotherapy with liquid nitrogen, trichloroacetic acid, salicylic acid, imiquimod, podophyllotoxin including possible options like interferon, isotretinoin or 5-fluorouracil (14, 15, 16, 17). Other modalities in resistant cases include electrotherapy, laser excision and surgical excision (18). Giant condyloma acuminatum, the Buschke-Loewenstein tumor is presented clinically as a malignant formation. It is a large, slow-growing, exophytic, tumor of the external genitalia looking like cauliflower. It is histologically a benign lesion, largely associated with HPV infection, mostly with types 6, 11, 16 and 18.

The main differential diagnosis includes verrucous carcinoma (19, 20, 21, 22). Pathohistological examination shows marked condylomatous epithelial proliferations, hyperkeratosis and parakeratosis. The differentiation

between these two types of tumors is important with respect to treatment and prognosis. Surgery is the only therapy. It is generally observed in male subjects and rarely occurs in women. ISCC of the vulva is an uncommon disease accounting for 3-5% of female genital tract cancers. In recent years, it appears that this incidence has been increasing.

The continued rise in the average age of the female population, causes an increase in the number of women at risk for development of the disease. Vulvar cancer appears most frequently in women between 65 and 75 years old. About 15% of all vulvar cancers occur in women younger than 40 years of age. This cancer is in 40% of cases associated with HPV infection, in 80% with type 16 (3). In typical squamous cell carcinoma (65% of all cancers) HPV infection is rare.

The recommended therapy is radical vulvectomy (21, 22). WSCC is a rarely described variant of invasive squamous cell carcinoma, usually described as a hybrid feature of condyloma and invasive cell carcinoma. It has been described in the vulva, uterine cervix, penis, anus, oral mucosa and urinary bladder. It resembles verrucous carcinoma, being large and exophytic with a papillary appearance, but the surface has a characteristic feathery appearance. It can often be confused with other verruciform tumors, such as condyloma acuminatum and verrucous carcinoma.

This tumor has been associated with a history of vulvar intraepithelial neoplasia, young age, and the presence of HPV DNA type 6, 11, 16, 18, 33 (21). It makes 10% of invasive cancers and has less aggressive behavior. The risk of regional metastases is bigger. It should be differentiated from other verruciform neoplasms based on its histologic findings (3). Although WSCC is histologically similar to typical squamous cell carcinoma, it contains many squamous cells that displayed marked nuclear pleomorphism, enlargement, atypia, and multinucleation in conjunction with cytoplasmic cavitation, resembling koilocytotic atypia in intraepithelial lesions. It has fibrovascular cores within papillary fronds, unlike verrucous carcinoma (22).

Verrucous carcinoma is a rare variant of epidermoid carcinoma, with distinct clinical and pathologic features. The lesion may involve the cervix and vagina as well as the vulva. It presents as a fungating, ulcerated mass with a bulky, elevated appearance reminiscent of benign HPV lesion. It has local invasive growth and is associated with HPV type 6 (21). In the past, this tumor has been reported as giant condyloma acuminatum (of Buschke-Loewenstein), but the implication that this tumor is a type of condyloma is erroneous and confusing and therefore the term is no longer used (22).

It is slow-growing invasive malignant tumor. The epithelium lacks significant cytologic atypia and mitotic activity. The base of the tumor is composed of invasive nests of epithelium with circumscribed pushing margin. Verrucous carcinoma should be distinguished from warty carcinoma and condyloma acuminatum. Distinction from ordinary condylomata is aided by the absence of fibrovascular cores within the proliferating papillary

masses of tumor (22). Identification of this variant is important because the biologic behavior of the disease influences therapy. Warty and verrucous carcinoma have good prognosis.

They recur locally but do not metastasize so surgical excision is the foundation of therapy. Lymphadenectomy is of questionable value except when nodes are obviously involved. Radiotherapy is contraindicated (12, 13, 14, 15). There is delay in diagnosis and treatment of vulvar cancer. Patient has symptoms for 2-16 months before seeking medical help or medical treatment continues for up to 12 months without biopsy for definitive diagnosis. Vulvar cancer is painless, extends slowly and metastasizes fairly late.

In 70 % of cases tumor arises primarily on the labia majora, labia minor, clitoris, perineum. It looks mostly like a small nodule that may ulcerate or form warty or cauliflower like growths. Diagnosis of cancer is made after physical examination, taking PAP smear from the lesion and from the cervix, Collins test and vulvoscopy and colposcopy applying of 3-5 % acetic acid (4). It is of great importance to have examination specula and evaluation of the groin lymph nodes.

Biopsy or excision of the lesion and PHD analysis must be done. HPV typisation is not obligatory, but recommended. Further diagnostic techniques are routine laboratory tests, chest X-ray, pelvic ultrasound examination, abdominal and pelvic CT scan, cystoscopy and proctoscopy. The treatment modalities of carcinoma vulvae are surgery, radiotherapy and chemotherapy (10, 11, 12, 13, 21). The preventive protocol includes: sexual education, responsible sexual behavior, latex condoms and quadrivalent HPV vaccine to HPV types 6, 11, 16, 18. They can lower the risk of getting HPV infection (2, 5) but the complete prevention can not be achieved.

4. CONCLUSION

Vulvar condyloma acuminatum is usually a benign disease, but may grow locally to an excessive extent. The incidence of malignant transformation is rare. ISCC of the vulva is an uncommon disease accounting for 3-5 % of female genital tract cancers. In recent years, it appears that this incidence has been increasing. WSCC is a rarely described variant of invasive squamous cell carcinoma. It can often be confused with other verruciform tumors, such as condyloma acuminatum and verrucous carcinoma.. It should be differentiated from other verruciform neoplasms based on its histologic findings.

There is delay in diagnosis and treatment of vulvar cancer. Patient can experience symptoms for 2-16 months before seeking medical help, or medical treatment continues for up to 12 months without biopsy having performed for definitive diagnosis. The current treatments do not reliably eradicate HPV infections. The result of our surgical treatment of cancer is satisfactory. However, complete clearance of condyloma has not been achieved. The successful therapy of anogenital warts is characterized by their complete clearance, and no recurrence.

• The authors declare no conflict of interest.

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