Reminder of important clinical lesson

Multifocal intraepithelial neoplasia and the psychological consequence of vulvectomy

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Correspondence to Dr Shahid Hussain Shah, shahidshah@doctors.net.uk**Summary**

A 41-year-old female with significant psychiatric history presented with persistent vulvar lesions that were refractory to common clinic and home based wart therapies. Vulvoscopy directed biopsies confirmed invasive vulvar squamous cell carcinoma and further investigation revealed cervical and anal intraepithelial neoplasia in a patient who remained HIV negative with no other cause of immunosuppression detected other than smoking. Vulvectomy following cancer diagnosis led to a relapse of her psychiatric illness and excessive alcohol intake. Her psychiatric illness in turn affected her further management and follow-up. This case highlights the need for the case based, medical, surgical, psychological and social considerations when managing persistent anogenital warts and anogenital neoplasia as well as the psychological impact of vulvectomy.

BACKGROUND

Our case illustrates the need for medical, surgical, psychological and social considerations when managing persistent anogenital warts and anogenital neoplasia. The case not only highlights the common medical interventions used and the importance of investigating persistent lesions but also illustrates the profound psychological effects of disfiguring genital surgery in a patient with a known significant psychiatric history and risk factors with the impact that this can have socially and on ongoing medical care. Finally, the case reminds the reader how multifocal intraepithelial neoplasia can occur in HIV negative and otherwise immunocompetent patients and the importance of continued follow-up for recurrent disease.

CASE PRESENTATION

A 41-year-old woman presented with a 7-year history of persistent and recurrent vulvar warts refractory to multiple treatment regimes from several hospitals including topical podophyllotoxin, cryotherapy and imiquimod. She had a history of menorrhagia, a right ectopic pregnancy that led to laparotomy and salpingectomy. She later had left tubal ligation after giving birth to four children and subsequently a tubo-ovarian abscess which needed laparoscopic drainage. Her youngest child on presentation was 16 years of age. She gave a history of an abnormal cervical smear (borderline nuclear abnormality) 6 months earlier and a family history that included her mother being diagnosed with cervical carcinoma at the age of 25 requiring a hysterectomy. Her psychiatric history included an attempted overdose and a long history of depression and panic attacks. Her medication on presentation included citalopram and temazepam. She smoked 5–10 cigarettes per day but had previously smoked more and had been smoking since the age of 12. She was drinking 3 to 4 units of alcohol every other day.

INVESTIGATIONS

On presentation, she informed us that she had discontinued her most recently prescribed wart treatment, imiquimod, due to a burning sensation that she could not tolerate. Examination revealed anogenital warts with plaque-like lesions and increased pigmentation extending from the labia minora to the perianal area. Due to the atypical and suspicious features on examination, vulvoscopy directed biopsies were undertaken, the results of which revealed a moderately differentiated invasive squamous cell carcinoma with a background of vulvar intraepithelial neoplasia III (VIN III) (figures 1 and 2). Two weeks after her initial presentation she was informed of her diagnosis of vulvar carcinoma and referred to a tertiary centre for further management. Other baseline investigations including a HIV test were negative, with no identifiable immunocompromisation.

She was reviewed at a joint gynaecology oncology clinic which confirmed the entire lower half of the vulva having warty lesions involving the labia minora and majora extending down to the anal verge. Colposcopy revealed a low-grade cervical abnormality which was biopsied. The management plan was to investigate for possible spread of the carcinoma, to undertake proctoscopy and to prepare for radical excision of the vulvar lesion.

TREATMENT

The report of the cervical biopsy taken at colposcopy revealed cervical intraepithelial neoplasia II (CIN II) and large loop excision of the transformation zone (LLETZ) procedure was carried out. High-resolution anoscopy was performed which revealed an acetowhite abnormality within the transformation zone in the anal canal. An excision biopsy of this lesion confirmed anal intraepithelial neoplasia II (AIN II). Therefore at this stage, our patient had been diagnosed with vulvar carcinoma, VIN III, CIN II

Figure 1 Warty pigmented and de-pigmented lesions at fourchette, representing vulvar intraepithelial neoplasia (VIN3).

Figure 2 High power view of mid-zone of the vulva showing an area of microinvasive carcinoma.

and AIN II. Our patient then underwent vulvectomy and bilateral node excision at the tertiary centre.

OUTCOME AND FOLLOW-UP

This patient was not followed up at our hospital until 4 months after her vulvectomy. We repeated her high-resolution anoscopy examination which confirmed complete removal of the AIN II lesion at excision biopsy with no new anal disease. It was also noted at this visit that the patient had been drinking alcohol excessively with objective and subjective evidence of self neglect and a reported increase

in panic attacks. She was referred to our on site psychologist who reviewed the patient 6 days later. Her psychiatric history was as previously described. It was also revealed that she had just separated from an 18-year relationship with her partner, had a background of domestic abuse and violence and had a brother who had committed suicide. Her mother had left when she was 11 years old and she was left to take care of her six siblings. Her only coping mechanism in the past was to turn to drinking alcohol to block out thoughts of her life. She described how being diagnosed with cancer and particularly after vulvectomy

her mood had further worsened and she had relapsed to drinking alcohol excessively again as she slipped further into depression. Despite counselling, she refused further psychiatric input. It was clear, however, that the diagnosis of cancer compounded by vulvectomy and the way she now felt and perceived herself physically had had a serious psychological effect on somebody with a known significant psychiatric history.

A repeat cervical smear was normal, however, repeat vulvoscopy and biopsy revealed VIN III in the periclitral area which was reviewed by a dermatologist and the patient was commenced on topical imiquimod. Several months later at a joint vulval clinic it was found that she had responded well to imiquimod and had no evidence of AIN. She was then lost to follow-up. She attended 3 years later, in June 2010 at our hospital. Repeat high-resolution anoscopy and vulvoscopy with biopsy revealed 'new' AIN II and VIN III disease. She was given the option of laser ablation or surgical excision of her VIN III and AIN II disease. She opted for laser therapy, stating she 'didn't want to be cut up anymore' which was completed 2 months later and 6 months later, respectively. She has remained HIV negative throughout this presentation.

DISCUSSION

Anogenital warts are described as the most prevalent viral sexually transmitted infection (STD) in the UK¹ and the most common STD seen in genitourinary clinics.² It is recognised that central to the development of anogenital warts is the human papillomavirus (HPV) of which there are many types. The low-risk types such as genotypes 6 and 11 are found in >90% of anogenital warts, however, patients with visible warts may also be infected with oncogenic HPV such as types 16 and 18 that may cause intraepithelial neoplasia, and lead to anogenital cancer.³ Anogenital warts in themselves can have both physical and psychological effects and it is recognised that for some patients the psychological impact of warts is worse than the disease itself.⁴ There are a number of home-based and clinic-based treatments available for anogenital warts. Our patient had tried many of these interventions with little effect over several years. It was due to the persistence and morphology of the 'warts' that biopsies were taken on presentation, that revealed invasive vulvar carcinoma and we feel that this case therefore illustrates the importance of biopsy in such persistent or treatment-resistant cases.

Vulvar cancer is reported to represent 3–5% of all gynaecological malignancies with squamous cell carcinoma, as identified in our patient, accounting for 85–90% of vulvar cancers.⁵ HPV is detected in up to 60% of cases of vulvar warts, VIN and invasive vulvar cancer and HPV infection is believed to play an early role in the process of vulvar carcinogenesis.⁶ This is important as our patient was found to have intraepithelial neoplasia at multiple sites (cervical, anal and vulvar) all of which are believed to be associated with HPV. Interestingly, our patient was not immunocompromised. Intraepithelial neoplasia and particularly AIN are commonly described in association with immunosuppression and in patients who are HIV positive. In women with high grade CIN, the presence of HIV increases the likelihood of development of AIN.⁶ This case illustrates that although it is important to test for HIV in patients found to

have high grade intraepithelial neoplasia at multiple sites, it must not be assumed that such patients have HIV or are immunosuppressed. Once our patient had been diagnosed with vulvar carcinoma, we decided to carry out colposcopy and anoscopy. On the question of whether all women with genital intraepithelial neoplasia should undergo anoscopy, one author recommends that in HIV seronegative women the clinician should use their judgement with the knowledge that HPV disease may be multifocal and that women who are found to have a high grade cervical, vulvar or vaginal intraepithelial neoplasia may be at risk of anal disease.⁷ Our case clearly supports this recommendation.

Stanley Way introduced radical vulvectomy with bilateral lymphadenectomy in the early 1950s as the standard management for vulvar cancers, which confers a 5-year survival of 70% in non-metastatic malignancy.⁵ It is, however, recognised that although surgical procedures are highly effective at excising the carcinoma, the adverse effects are many and include physical deformity, which may cause cosmetic disfigurement and compromise quality of life in women. Laser ablative treatment is a recognised intervention for vulvar intraepithelial neoplasia that despite being potentially associated with increased risk of recurrence preserves sexual function and physical appearance with less adverse effects.⁸ It is no surprise that our patient had opted for laser as opposed to surgical therapy on re-presentation with high grade AIN and VIN. Understandably, the diagnosis of cancer triggers changes in the way that people view themselves and their life. The surgical treatment of gynaecologic cancers has the added stressor of disfiguring surgery and irreversible physical damage and so it has been described that managing psychosocial issues may be a promising focus of intervention in sexual rehabilitation.⁹ Our patient already had a background of psychiatric illness and many risk factors for depression as well as a background of excessive alcohol intake. In such a patient, unsurprisingly, the added stressors of persistent warts, a diagnosis of cancer, and the psychosocial effects of disfiguring surgery and frequent hospital attendances triggered a relapse of her psychiatric illness and significantly affected her life, ongoing follow-up and medical care. Our case illustrates the importance of considering the psychological effects of gynaecological surgery and perhaps the need for adequate psychiatric input from the point of diagnosis in a patient with a significant psychiatric history. Our patient was lost to follow-up for 3 years and re-presented with multifocal high grade intraepithelial neoplasia, a situation that may have been better managed had her psychological status been better monitored and supported from the outset. Our patient has not felt able to have an intimate relationship with somebody since the diagnosis of cancer and the interventions that followed. She has informed us that she felt she would have continued in a spiral of alcohol fuelled depression had it not been for the birth of her granddaughter that helped to put her life into perspective. Unfortunately, research on the psychological aspects of vulvectomy is lacking and the psychological, social and sexual adaptation of women following mutilating surgery of the external genitalia is reportedly one of the least studied areas of oncologic psychology despite it being recognised that young women even develop suicidal inclinations after vulvectomy.¹⁰

Learning points

- It is important to consider biopsy in long-standing or treatment-resistant cases of anogenital warts to investigate potential malignancy
- HIV negative patients can have multifocal intraepithelial neoplasia although immunosuppression is an important risk factor that should be investigated
- High-resolution anoscopy should be considered in all patients with high grade genital intraepithelial neoplasia
- Vulvectomy can be associated with significant psychosocial adverse effects, and hence patients, particularly those with a significant past psychiatric history, should be adequately supported from a psychiatric perspective through diagnosis, care and follow-up for recurrence.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **McClean H**, Shann S. A cross-sectional survey of treatment choices for anogenital warts. *Int J STD AIDS* 2005;**16**:212–16.
2. **Carey FM**, Quah SP, Dinsmore W, *et al*. Patient assessment of anogenital warts and the success of treatment with home applied therapy. *Int J STD AIDS* 2004;**15**:316–18.
3. **von Krogh G**, Lacey CJ, Gross G, *et al*. European guideline for the management of anogenital warts. *Int J STD AIDS* 2001;**12**:40–7.
4. **Maw R**. National guideline for the management of anogenital warts. *Sexually Transmitted Infections*. 1999; **75**: S71–5.
5. **Sznurkowski JJ**, Emerich J. Characteristic features of recurrences of squamous cell carcinoma of the vulva. *Ginekol Pol* 2010;**81**:12–19.
6. **Zbar AP**, Fenger C, Efron J, *et al*. The pathology and molecular biology of anal intraepithelial neoplasia: comparisons with cervical and vulvar intraepithelial carcinoma. *Int J Colorectal Dis* 2002;**17**:203–15.
7. **Eckert L**. Screening for anal dysplasia in women with cervical, vaginal, or vulvar dysplasia: yes, no, maybe? *Obstet Gynecol* 2010;**116**:566–7.
8. **von Gruenigen VE**, Gibbons HE, Gibbins K, *et al*. Surgical treatments for vulvar and vaginal dysplasia: a randomized controlled trial. *Obstet Gynecol* 2007;**109**:942–7.
9. **Willibrord C**, Schultz W, Harry B, *et al*. Psychosexual functioning after the treatment of cancer of the vulva. *Cancer*. 1990;**66**:402–7.
10. **Swartz S**, Williams D. Psychologic aspects of gynecologic surgery. *CME Journal of Gynecologic Oncology* 2002;**7**:268–79.

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