

External beam radiotherapy for large genital warts: Does it work?

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Summary

Introduction: The management of very large vulval condyloma acuminata is challenging since surgery is associated with significant morbidity. **Materials and Methods:** Fifty-four patients with very large biopsy-proven vulval warts received external beam radiotherapy. Objective tumour response for target lesions was assessed using the Response Evaluation Criteria in Solid Tumours (RECIST) criteria definitions. The retrospective data were analysed by a professional statistician. The data was regarded as purely descriptive. **Results:** There were 40 patients in whom the size of the genital wart ranged from 10-20 cm. Five patients had warts larger than 20 cm. Fifty-two patients were HIV infected, of which 42 patients had CD4 counts greater than 200 cells/ml and 40 patients were receiving antiretroviral therapy. The majority of patients (n=33) demonstrated a partial response to radiotherapy. There were no patients in whom progressive disease was noted. Both HIV non-infected patients had a complete response to treatment, while 14 of the 52 HIV-infected patients had a complete response to radiotherapy. Thirty-two patients received additional laser or electrocautery for residual lesions. **Conclusions:** Radiotherapy represents a novel approach for the management of very large vulval warts not amenable to surgical therapy, and has an acceptable side effect profile.

Key words: Vulval condyloma acuminata; HIV; Genital warts; External beam radiotherapy.

Introduction

HPVs types 6 and 11 are responsible for condyloma acuminata (genital warts), which affect about 5% of the population. These are benign epithelial proliferations which affect the external genitalia and have also been reported to occur in the bladder mucosa [1]. The size of vulval condylomas can vary from small to massive lesions rendering surgical excision hazardous due to haemorrhagic complications. The large Buschke-Lowenstein tumour or giant condyloma acuminata is an uncommon lesion affecting the anogenital region and, although it is histologically benign, it can infiltrate surrounding tissues with considerable morbidity and mortality[2]. The greater frequency of these lesions in immunocompromised patients has been described [3].

Materials and Methods

A retrospective chart review was conducted of 54 women with very large genital warts seen at the combined gynaecology-oncology clinic at Inkosi Albert Luthuli Central Hospital, Durban, South Africa from 2009 to 2011. In all patients, the size, site and number of lesions were determined. Biopsies were taken to exclude pre-invasive or malignant disease of the vulva. All patients also had blood tests for blood count, renal function and human immunodeficiency virus (HIV)-antibodies. If the HIV test was positive, CD4 counts were measured. Clinical assessment in all

patients with measurable disease was performed routinely using a ruler to estimate the size of the lesion and colour photography. An analysis was performed in all patients in relation to the clinical extent of the lesions on presentation, HIV status, CD4 count levels, and treatment response with external beam radiotherapy (EBRT).

All patients with biopsy-proven condylomata acuminata, received primary EBRT. Radiotherapy was administered with conventional fluoroscopy-guided treatment simulation and two-dimensional (2D) dose planning with photons or a clinical mark-up with electrons, based on the extent of disease, to a planned dose of 30 Gy in 3 Gy fractions. Patients were then re-assessed three months post-treatment, and if significant residual lesions were found, these lesions were then treated with either carbon dioxide (CO₂) laser and/or electro-cautery.

Objective tumour response for target lesions was assessed using the Response Evaluation Criteria in Solid Tumours (RECIST) criteria definitions as a guide: complete response (CR): disappearance of all target lesions, partial response (PR): at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters, progressive disease (PD): at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study, and stable disease (SD): neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study [1]. The retrospective data were analysed by a professional statistician. The data was regarded as purely descriptive.

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Table 1. — Patient, disease, and treatment factors.

Descriptive frequency variables	n	%
Age (years)		
1-5	5	9.3
6-10	1	1.9
11-20	11	20.4
≥ 21	37	68.5
Size of vulval warts pre-treatment (cm)		
< 10	9	16.7
10-20	40	74.1
≥ 20	5	9.3
Histological confirmation		
Yes	54	100.0
Urinary/bowel symptoms		
Yes	1	1.9
No	53	98.1
Type of EBRT given		
Electrons	39	72.2
Photons	15	27.8
Dose of EBRT given		
< 30 Gy	1	1.9
30 Gy	53	98.1
> 30 Gy	0	0.0
Response to RT		
Complete response	16	29.6
Partial response	33	61.1
Stable disease	5	9.3
HIV status		
Positive	52	96.3
Negative	2	3.7
CD4 count (cells/ml)		
< 200	12	22.2
200-400	34	63.0
400-600	8	14.8
HAART use		
Yes	40	74.1
No	14	25.9
Side effects from EBRT		
Yes	16	29.6
No	38	70.4
Additional treatment post RT		
Laser	6	11.1
Cautery	26	48.1
Nil additional	5	31.5
Repeat dose RT	17	9.3

EBRT= external beam radiotherapy.

Results

A total of 54 patients were enrolled for the study. Majority of patients (n=37) were older than 21 years of age. There were 40 patients in whom the size of the genital wart ranged from 10 to 20 cm. Five patients had warts larger than 20 cm (Table 1). Histological confirmation of a wart was made in all patients. Fifty-two patients were HIV infected, of which 42 patients had CD4 counts of greater than 200 cell/ml and 40 patients were receiving antiretroviral treatment. Fifty-three patients received a total of 30 Gy dose of



Figure 1. — Pre-radiotherapy.

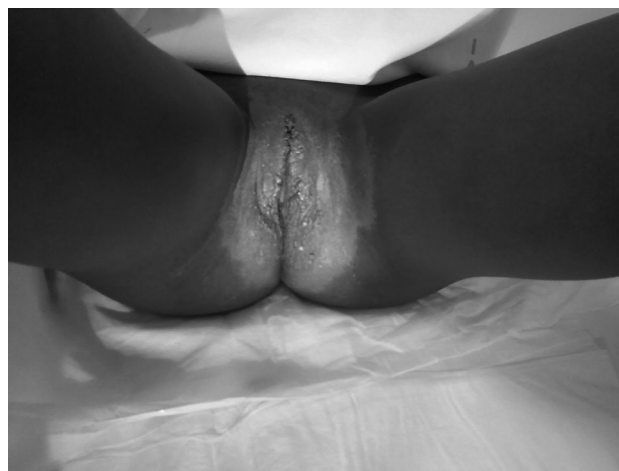


Figure 2. — Post-radiotherapy.

EBRT. The majority of patients (n=33) demonstrated a partial response to radiotherapy (Figures 1 and 2). There were no patients in whom PD was noted. Both HIV non-infected patients had a CR to treatment, while 14 of the 52 HIV-infected patients had CR to radiotherapy. A total of 32 patients (partial responders) received additional laser or electrocautery for minimal residual lesions.

Discussion

Large or extensive genital warts with HIV infection are now a common occurrence in South Africa. These lesions are cosmetically disfiguring, causes morbidity with regards to ambulation, bladder and bowel function, and are not amenable to surgical resection due to haemorrhagic complications. Besides, any attempt to surgically excise these

large/extensive lesions will result in considerable tissue-loss and leave a large crater with potential for infectious sequelae. Surgical resection of large genital warts followed by musculo-cutaneous flaps and faecal stomas have been described [4, 5].

While topical agents, such as podophylin, may be useful for small- to medium-sized genital warts, large or massive genital warts do not respond to such conservative therapies. Sobrado *et al.* described the use of radiotherapy for a giant condyloma acuminata lesion of the vulva with successful results [6]. The risk of malignant transformation of a condylomatous warty lesion is reported to be about 30% and is thought to be more common with the co-existence of carcinogens such as immunosuppressive factors, HIV infection, and poor nutrition [7]. Radiotherapy is generally avoided for benign gynaecological conditions to avoid the risk of secondary radiotherapy-related cancers. The first reported use of radiotherapy was that of a patient with urethral warts resistant to other forms of treatment [8]. A total of 25 Gy EBRT, using 2.5 Gy fractions was used over a period of two and half weeks. The second report described the use of radiotherapy in patients resistant to conservative and surgical therapies for the treatment of giant peri-anal condylomas [6]. A total of 45 Gy using 1.8 Gy fractions was used and a complete response was achieved

The majority of patients in the present study demonstrated a treatment response, with 29.6% of patients showing a CR, and 61.1% having a PR to radiotherapy. A total of 32 patients (59.2%) required additional treatment in the form of laser or cautery for residual disease. Over a five-year follow-up period, only two patients developed recurrent warty lesions. There were no patients in this series who developed secondary malignancies during the five-years follow-up.

The two HIV non-infected patients had a CR to radiotherapy. The five patients who failed to demonstrate a treatment response to EBRT (stable disease), were treated with cautery and laser, but were again poor-responders. The commonest side-effects of radiotherapy were skin-related. Only one of the 54 patients failed to complete the planned 30 Gy of radiotherapy due to skin related toxicity. There was no significant radiotherapy-related bladder or bowel

toxicity warranting treatment interruption or discontinuation.

Conclusions

The authors conclude that radiotherapy using electrons or photons are a useful method of treating very large genital warts that are not suitable for conservative or local therapies and appears to have good overall results with acceptable side-effects.

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