CASE REPORT
DERMATOLOGY

Diseases & Research

‘Warts and All’ - Consider Even Definitive Salvage Radiotherapy for Recalcitrant Adult Viral Warts

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Abstract: Recalcitrant adult viral warts can cause significant functional and cosmetic impacts. A 60-year-old adult male with a five-year history of recurrent, recalcitrant, and progressive warts of both hands had failed prior treatments with laser, cryotherapy, and topical therapies. Salvage radiotherapy (RT) was considered. RT volumes were administered to gross disease only with the margin to field edge dependent on modality. Using superficial radiotherapy (SXRT) with beam quality of half value layer of 1.9 millimeters aluminium equivalent, an area on the dorsum of the non-dominant (left) hand measuring 4 × 3 centimetres (cm) received 19.8 Gray (Gy) to skin surface in 11 daily fractions of 1.8 Gy. When little reaction was noted, the fraction size was increased to 3 Gy, delivering another nine fractions to 27 Gy, giving a total dose of 46.8 Gy. Wart lysis, erythema, and desquamation healed over four weeks, this complete response (CR) continuing at more than two years. We then considered SXRT dose of 50 Gy in 20 fractions over four weeks to be the correct SXRT dose. A further 39 areas were treated with SXRT over a year with continuing CR, continuing for at least a year following the last area treated. A larger area of 11 × 4 cm on the dorsum of his dominant right hand received 60 Gy in 24 fractions using Volumetric Arc Therapy (VMAT) had CR also continuing at two years post treatment. Radiotherapy to a high dose may be considered for salvage of recalcitrant adult viral warts. More research is needed.

Keywords: Viral warts; Benign; Radiotherapy; Case study; Australia; Adult.

Introduction

A wart is a raised, benign growth on the skin caused by the human papillomavirus (HPV). Infection in the basal layer of keratinocytes is followed by clonal proliferation, resulting in a visible lesion, weeks or even months after infection[1,2]. Infection is common in children. Children’s warts are usually relatively short-lived, with two-thirds clearing after two years. Adult warts can persist from five to ten years, but may persist longer[1]. Salicylic acid is the primary treatment for warts, with other treatments including cryotherapy, vitamin A, bleomycin, 5-fluorouracil, and laser[2,3]. Cutaneous warts caused by HPV are usually benign, so treatment is only necessary if the warts cause discomfort, such as by limiting mobility or causing cosmetic bother[3].

Skin is one of the most sensitive tissues to ionising radiation[4]. Hence, radiotherapy (RT) is often used as a treatment for skin malignancies, most commonly keratinocytic cancers. Clinically, RT provides the potential for treatment without major surgical procedures, while providing comparable cure rates, tissue conservation, and potentially better cosmetic and functional outcomes[5]. RT has also been proved to be effective in treating benign conditions[4]. Over 100 different benign conditions have been successfully treated using RT, ranging from hyperproliferative, to inflammatory to other functional diseases[6].

Though benign, pathogenesis of warts shares some similarities with the development of keratinocytic cancers[7]. Could RT be used in recalcitrant cases? A literature search showed that there had been some response to radiotherapy in previous studies for this condition[8]. Other benign conditions treated with RT usually require lower doses, decreasing the associated risks[9]. Additionally, advances in radiotherapy such as volumetric modulated arc therapy (VMAT) further reduce any risks. VMAT delivers highly conformal dose distributions to the affected site, reducing unnecessary irradiation compared to traditional conformal radiation therapy (CRT), thereby reducing risks of side effects to surrounding healthy tissue[10]. The main risk of benign treatment is radiation induced malignancy (RIM), hence the “warts” of RT. However, this risk is rare and decreases with the patient's age at radiation exposure. Patients over 60 treated with RT to the skin have a one in 1000 risk of RIM every ten years. The usual RIM after skin RT is a basal cell carcinoma (BCC) which is treated on its merits[11].

We present a case involving recurrent recalcitrant adult viral warts on the dorsum of both hands that progressed despite treatments including laser, cryotherapy, and topical agents over the

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course of five years. Definitive salvage RT including VMAT continues to be effective at least 12 months following cessation of RT.

Case Presentation

A 60-year-old adult male presented with a five year history of recurrent, recalcitrant, and progressive adult viral warts of both hands. The patient's disease had a negative impact on his function, cosmesis and self-esteem. He described that his family was embarrassed of his warts and that he would take the time to wrap up his hands to conceal them. The patient also described a fear of transmitting HPV to his loved ones. Horizontal transmission of untreated HPV has been largely discussed in various studies[12], validating our patient's concern.

The dorsum of the right hand, his dominant hand, was the most bothersome. He had had previous therapies of laser, cryotherapy and topical therapies over five years but these had failed. The most successful had been laser with a forty percent reduction, but the disease was once again progressing. Past medical history included medicated ischemic heart disease, type 2 diabetes, and hypertension. He had not had a virological test for HPV nor had he suffered from symptoms of human immunodeficiency virus (HIV) nor had he been tested for this. He has six adult children and seven grandchildren. Due to his progressive disease, the parents of his grandchildren would not let the grandchildren play with their grandfather for fear of contracting the virus. This was the major reason why he sought treatment.

On examination, there were many areas of warts on both hands mainly on the dorsum. They were not tender but the mass effect did impact some function. He could not fully flex his hands to make tight fists, worse on the right where he had more bulky disease. In particular, there was a 3 by 3.5 centimetre (cm) mass of warts on the dorsum of the left hand. There was also a 11 by 4 cm area on the dorsum of the right hand that stretched from the ulnar to the radial side of the hand at the metacarpal-first phalangeal junctions, See Fig. 1.

The rationale, process, and side effects of RT were explained to the patient. He consented to treatment and to having his de-identified data used for teaching, research, and publication. To make sure that the radiotherapy was safe, well tolerated, and efficacious, the smaller area of confluent disease on the dorsum of the left hand was treated first.

The radiotherapy details for this patient were as follows. An area on the dorsum of the non-dominant (left) hand was identified, measuring 4 × 3 cm in size. Initially, 11 daily fractions of 1.8 Gray (Gy), a subtotal of 19.8 Gy, was delivered to the surface using a WOMED T-105 (Wolf-Medizintechnik GmbH St. Gangloff, Germany) superficial machine (SXRT) with a source surface distance (SSD) of 30 cm. The SXRT used a filter 3 with equivalent half value layer of 1.9 millimeters aluminium. When little reaction was noted, the fraction size was increased to 3 Gy, delivering another nine fractions for a subtotal of 27 G. A total dose of 46.8 Gy was delivered to the left hand. He had the expected wart lysis, erythema, and desquamation within the treatment field. Side effects peaked at the end of treatment. With appropriate nursing care, the left hand healed over a period of four weeks, resulting in a complete response (CR) from the warts and re-epithelialization of the normal skin over the treated area. This response continues at more than two years. We then regarded the SXRT dose of 50 Gy in 20 fractions over four weeks to be the correct dose.

To document the effect of the radiotherapy, biopsies were done prior to treatment, see Fig. 2 and again one month after RT, see Fig. 3.

Following treatment on his left hand, the patient requested further treatment. Once again, he consented to treatment, this time to the right hand. Because of the curvature and size covering a total area of 11 × 4 cm of the affected area on the right hand, it was decided to use VMAT. The gross tumour volume (GTV) comprised the palpable warts seen on direct vision and on the planning CT scan. There was an expansion to the planning target volume (PTV) of two millimetres. 50 Gy in 20 fractions was prescribed. After four weeks, little reaction was noted. An extra 10 Gy was given to a total dose of 60 Gy in 24 fractions with adequate reaction. This healed in four weeks, resulting in complete destruction of the warts and recovery of the infield and surrounding normal tissue. Due to excellent VMAT dosimetry, there was no spillage of dose onto the palmar surface, so the patient was able to use his dominant hand as usual during the treatment. See Fig. 4. for the RT planning details.

The patient requested further treatment to eradicate all signs of viral warts on the palmar and dorsal surfaces of both hands. He was treated to a total of 41 superficial areas using the same dose. The usual SXRT applicator was two centimetres in diameter. He was treated to a maximum of six areas in any one treatment course. Only one hand at a time was treated so that there would

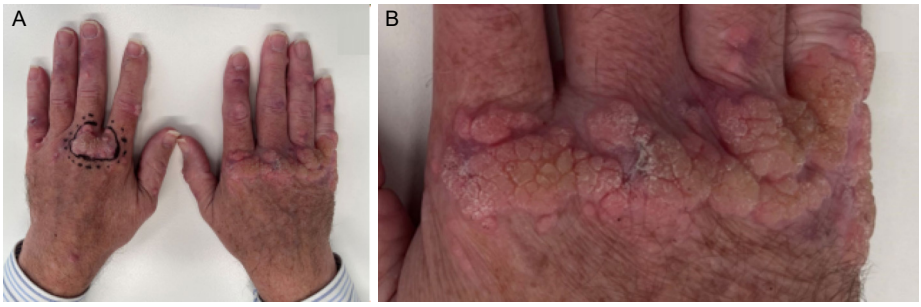

Fig. 1. Patient's hands presented prior to RT treatment.
A. Hands at presentation showing an area 3 × 3.5 cm on the left hand marked up for SXRT.
B. Hands at presentation - close up of an area on the dorsum of the right hand that stretches from the ulnar to the radial side of the hand at the metacarpal - first phalangeal junctions.

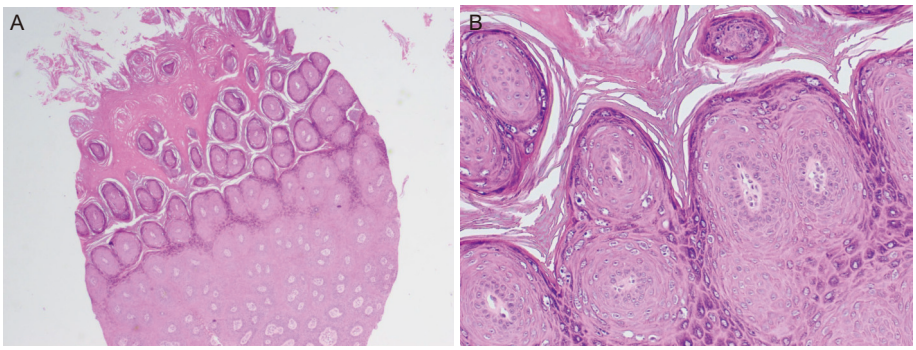

Fig. 2. Haematoxylin and eosin stained sections prior to radiotherapy show verruca vulgaris with papillomatosis, hypergranulosis, hyperkeratosis and koilocytes.
A. Low power stained sections prior to radiotherapy.
B. High power stained sections prior to radiotherapy.

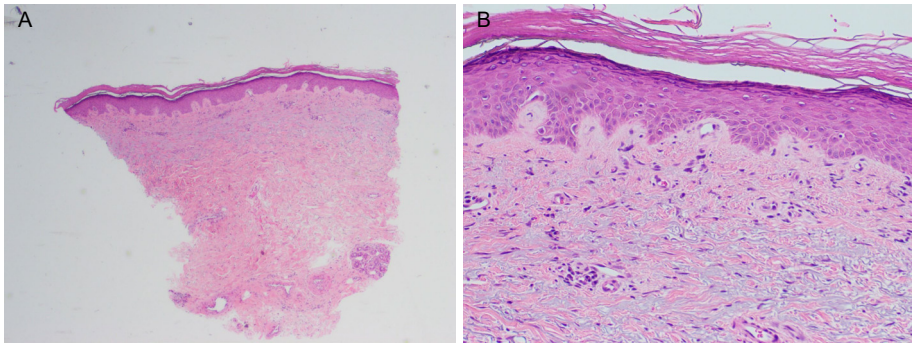

Fig. 3. Haematoxylin and eosin stained sections post-RT demonstrate skin with no residual viable verruca vulgaris. There is fibrosis within the dermis and reactive fibroblasts secondary to radiotherapy effect.
A. Low power stained sections after radiotherapy.
B. High power stained sections after radiotherapy.

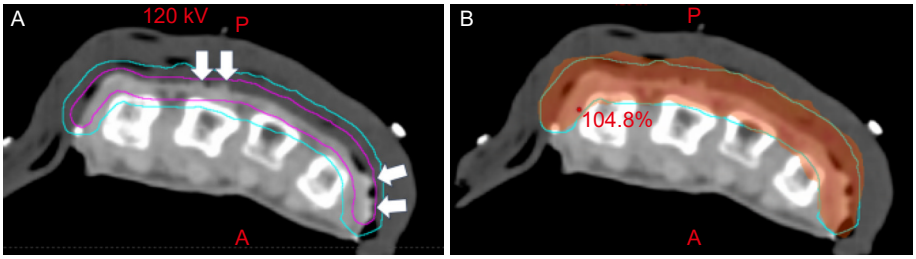

Fig. 4. Volumetric modulated arc therapy (VMAT) radiotherapy planning details.
A. The VMAT contouring on the axial cuts of the planning CT scan. The pink volume is the clinical target volume (CTV) which encompasses the thickened epithelium and the peaks of the warts. The blue volume is the planning target volume (PTV) to ensure that each day the total CTV is covered. The white arrows show the peaks of the viral warts on the CT.
B. The VMAT dosimetry at the therapeutic dose hugs the blue planning target volume with no spillage onto the palmar surface. There were no side effects on the palm, ensuring he was able to use his dominant hand as usual during the treatment.

be no side effects on the other hand, enabling him to continue work throughout his treatment. Fig. 5 shows a typical markup for treatment to six areas on one hand.

Sequential RT lasted 13 months and comprised nine separate courses. He was reviewed one year after his last treatment, two years after his VMAT treatment. All the treated areas remain in CR. There are still some small areas of untreated disease, however, he has achieved his goal of being able to once again have physical contact with his grandchildren and is not interested in having more treatment at this stage to these remaining areas. See Fig. 6.

Discussion

This case study documents a 60-year-old male patient treated with salvage RT following a five year history of recalcitrant viral warts on both hands that had no durable response to typical treatments. The patient demonstrated a CR two years post-VMAT and at least one year following the last SXRT course. The administration of SXRT, and later on VMAT, resulted in the eradication of all targeted lesions and there were no reported side effects in healthy tissue at last follow-up, a year after the last RT treatment. This response indicates RT's potential as a possible salvage treat-

Fig. 5. A typical markup for SXRT treatment to six areas on one hand.

Fig. 6. Shows dorsum of hands 18 months post the first treatment. No signs of in-field recurrence were detected.

ment for recalcitrant adult viral warts. As RT was the only treatment that has led to a definitive solution in this patient, why should RT not be considered earlier in the patient journey?

The role of RT has expanded beyond its traditional use of treating cancers as a treatment for benign diseases[4]. This is due to advancements in RT technology such as VMAT in the treatment of various benign diseases and a reduction in the risks of RIM with better dosimetry, thereby sparing surrounding normal tissues from any unwanted RT. Benign conditions require less radiation (3-50 Gy) than malignant disease (>50 Gy)[13]. Radiotherapy has been used in the treatment of certain benign conditions, particularly inflammatory and proliferative conditions[4]. Currently, there is regular low dose RT used for the treatment of heterotopic ossification[8], keloids[14], pterygium, Dupuytren's contracture, and osteo-arthritis[7,15]. RT also carries other benefits such as being an option for patients who are not good surgical candidates or when surgery could be detrimental to cosmesis or function[4]. SXRT and VMAT were used as these were the only modalities available in the department. Other modalities such as brachytherapy and electrons are other common motilities that may be used[16,17].

Clinicians weigh the risks of RT against the option of leaving the condition untreated, taking into account the fact that benign conditions such as HPV are not life-threatening, but still pose a significant impact on a patient's quality of life (QoL). In this case of recalcitrant viral warts, RT treatment led to a substantial improvement in our patient's QoL. Previously attempted treatments such as laser removal and cryotherapy were unsuccessful and resulted in considerable pain and financial cost. In contrast, RT resulted in eradication of the warts within treated regions while offering a better and more durable QoL post treatment. The patient only reported mild soreness after RT which was much more tolerable than the discomfort caused by other treatments, and these acute symptoms quickly resolved with appropriate care.

Conclusion

This case demonstrates that radiotherapy provides a viable salvage treatment of recurrent recalcitrant adult viral warts. Following at least one year after treatment, there have been no signs of recurrence. Radiotherapy provided excellent quality of life benefits for our patient by eradicating the patient's functional and cosmetic bother and eliminating their concerns of viral transmission. Treatment was conducted with minimal discomfort, especially when compared to traditional treatment methods. This research may be of benefit to patients suffering with recalcitrant adult viral warts. However, further research is necessary to assess the effectiveness of radiotherapy on warts in general populations.

Abbreviations

BCC, basal cell carcinoma; cm, centimetre; CR, complete response; CRT, conformal radiation therapy; CT, computed tomography; CTV, clinical target volume; GTV, gross tumour volume; Gy, Gray; HIV, human immunodeficiency virus; HPV, human papillomavirus; PTV, planning target volume; QoL, quality of life; RIM, radiation induced malignancy; RT, radiotherapy; SSD, source surface distance; SXRT, superficial radiotherapy; VMAT, Volumetric Arc Therapy.

Ethical approval and consent to participate

Written consent by the patient was obtained to use de-identified data including photos for publication.

Conflicts of interest

All authors declared that there are no conflicts of interest.

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Authors' contributions

JT and VS retrieved data and wrote the manuscript. AC and GBF

were all intimately involved in the care of the patient during treatment and writing of the manuscript. ALC prepared and reported on the histopathology.

Consent for publication

The patient consented to treatment and to having his de-identified data used for teaching, research, and publication.

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