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Authors

Brewer, Christopher F
Deutsch, Christopher J
Jemec, Barbara

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Is radiation therapy as a primary treatment modality for squamous cell carcinoma of the hand the best choice? Case series and review of the literature

Christopher F Brewer, Christopher J Deutsch, Barbara Jemec

Affiliations: Department of Plastic Surgery, Royal Free Hospital, Hampstead, London, United Kingdom

Corresponding Author: Christopher Felix Brewer, Royal Free Hospital, London, United Kingdom, Tel: 44-7969278019, Email: Christopher.bre@nhs.net

Abstract

Background: Squamous cell carcinoma (SCC) is the most common malignancy of the upper limb and can pose a significant therapeutic challenge. Early treatment needs to be radical whilst maintaining function.

Methods: We describe two cases of upper limb squamous cell carcinoma treated with radiotherapy, review the literature on radiotherapy as a primary treatment modality, and discuss the specific difficulties treating SCC in the hand.

Results: Radiation therapy was inadequate in tumor clearance in both cases, with recurrence both extensive and distal to the initial focus. Moreover, both patients developed progressive functional loss related to pain, swelling, and stiffness.

Conclusion: The evidence basis for radiation therapy as a primary modality is limited, although clearance rates are comparable to surgery. Both radiotherapy and surgery can be utilized to treat SCC. However, we make the case for the hand being especially susceptible to the unwanted side effects of radiotherapy.

Keywords: squamous cell carcinoma, hand, radiotherapy, surgery

Introduction

Squamous cell carcinoma (SCC) is the most common malignancy of the hand, accounting for 58% to 90% of all hand cancers [1, 2]. There is significant heterogeneity amongst clinical presentations, reflecting the varying degree of differentiation, although most cancers arise from areas of already photo-damaged skin [3]. Management of SCC of the

hand is primarily surgical, including Mohs microsurgery, radical excision, and/or amputation [4]. However, radiation therapy has been advocated as a primary treatment modality in cases not amenable to surgery or when surgery is believed to give a less favorable outcome. Radiation therapy may also provide an adjunct to decrease likelihood of recurrence [1, 5].

We report two cases of recurrent SCC on the hands after radiotherapy treatment, which were then managed surgically and review the literature on the use of radiation therapy as a primary treatment modality compared to surgical techniques.

Case Synopsis

Case 1

A 92-year-old man presented with a well differentiated >2.5mm vertical thickness ulcerated SCC on the dorsum of his right middle finger over the middle phalanx without clinical lymphadenopathy. The patient opted primarily for radiotherapy, consisting of 45Gy delivered via a Trubeam system (electron radiotherapy, 9MeV) to the affected area in 10 fractions over two weeks. At 9 months after the initial radiotherapy treatment, he developed new ulceration and inflammation over the same site. This was initially treated as an infection, but biopsy confirmed recurrence of SCC. Following consultation with the plastic surgery team, a decision was made with the patient to amputate the right middle finger. Histology confirmed high risk SCC with close volar excision margins. The tumor had invaded vertically though through the middle phalanx and radially along the volar aspect of the finger, demonstrating

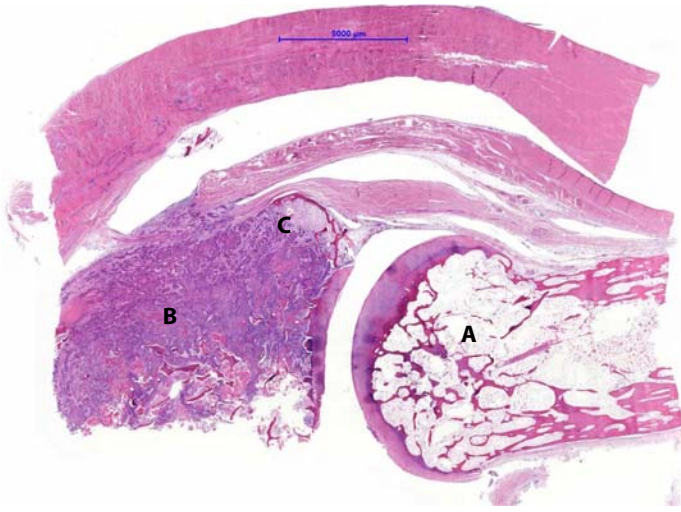


Figure 1. Histological specimen from case one showing primary interphalangeal joint and surrounding soft tissue of amputated right middle finger. H&E, 4.3x. **A**-Intact proximal phalanx, **B**-SCC having invaded vertically through middle phalanx virtually replacing bone, **C**-SCC invading remaining area of middle phalanx.

extensive recurrence beyond initial presentation (**Figure 1**). In the following 5 months the patient developed SCC of the glottis and passed away the following year.

Case 2

A 72-year old woman with a background of photosensitivity (attributed to prior hydroxychlorothiazide treatment for hypertension for greater than 10 years) presented with a biopsy proven recurrent 5x2cm SCC on the 1st dorsal web space of the right hand after previous excision, as well as a smaller primary 3x2cm SCC on the dorsum of her left hand

(**Figure 2**). Pathology showed moderate-poorly differentiated SCC of both specimens. She underwent radiation therapy for both tumors, using the Truebeam system consisting of a total dose of 55Gy delivered in 20 fractions (220kV each, electrons) over four weeks to each hand. Shortly after the treatment, the patient developed moist desquamation and skin soreness, along with significantly impaired functional mobility related to progressive stiffness of her digits.

At 8 months following radiotherapy, she developed new ulceration over the 1st webspace of her right hand (**Figure 3**). Punch biopsy of this lesion revealed high risk SCC and she subsequently underwent excision, which confirmed SCC with a vertical thickness greater than 6mm and extension beyond peripheral margins. Owing to the incomplete margins, along with the non-functioning extensively ulcerated index, thumb, and 1st webspace, with poor function of the index finger, a decision was made to amputate her right thumb and index finger; reconstruction with radial forearm flap was performed.

At 14 months post radiotherapy, the patient presented with poorly healing skin lesions over her left 1st web space and dorsum of left hand (**Figure 3**). Biopsy confirmed well differentiated SCC, which on excision demonstrated a vertical thickness of 8mm and maximum diameter of 82mm again involving peripheral margins. In lieu of the incomplete excision and functional loss, she underwent amputation of

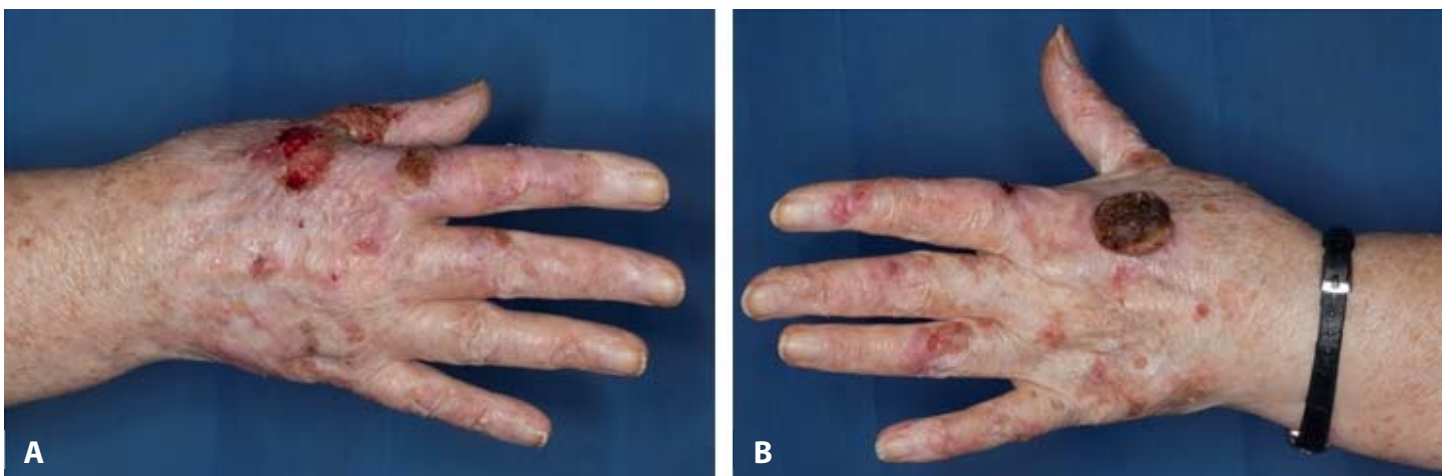


Figure 2. **A)** Right hand, and **B)** left hand at initial presentation to plastic surgery clinic.



Figure 3. A) Right hand 1st web-space 9 months post radiotherapy, B) left hand 14 months post radiotherapy.

her left index finger two months later with reconstruction using a Becker flap (ulnar perforator) and full thickness skin graft. Final histology confirmed full excision in both cases. Nonetheless, 12 months following this surgery she developed another SCC recurrence over the left 1st web space. She has subsequently been started on a course of intravenous cemiplimab, a monoclonal antibody therapy recently licensed for locally advanced cutaneous squamous cell carcinoma.

Case Discussion

A variety of treatment strategies exist for SCC [4]. Judicious selection requires consideration of multiple variables, including size of tumor, location, patient health and comorbidities, and grade and stage of tumor to balance the risk of local damage and loss of function with risk of recurrence.

Surgical excision, whether conventional or as Mohs micrographic surgery are the mainstay of treatment for cutaneous SCC [4]. Using excision margins of 6-10mm for high risk lesions and 4mm for all others, histological tumor clearance is achieved in 95% of cases, equating to a 92% 5-year cure rate [6]. Outcomes for SCC of the upper limb are generally less favorable, with recurrence rates estimated between 2-18% [2,7,8]. Although any surgery on the upper limb can be undertaken utilizing regional anesthesia, of course surgery can lead to significant loss of function in cases of radical excision or amputation.

Radiation therapy as a primary intervention has received less focus, despite obviating the need for surgery and potentially significant tissue loss. For all body sites, radiation therapy has been shown to be marginally inferior compared to surgery for cutaneous SCC [9]. However, there are few reports specific to its application in the upper limb (**Table 1**). Cheo et al. describe a case of SCC involving both palmar and dorsal aspects of the hand successfully treated with electron beam radiotherapy [5]. Somanchi et al. used brachytherapy for 25 patients with SCC of the hand, demonstrating 100% cure at 5 years [10]. Functional outcomes were comparable with the unaffected hand in all cases, with the exception of one patient who underwent subsequent amputation of a digit for radiation induced necrosis. Similar outcomes have also been reported in another case series [11]. Radiation therapy has also been used as a primary intervention in subungual SCC, a rare variant of cutaneous SCC, with cure rates comparable to surgery [12,13].

Complication rates for primary radiation therapy to the hand are difficult to assess owing to the limited case numbers. Larger numbers exist in the treatment of Dupuytren disease, however the radiation doses used are far less than in SCC [14]. A recent systematic review by Kadhum et al. which included 770 Dupuytren hand cases (average total radiation dose 30Gy) recorded acute complications as high as 43% (erythema, skin dryness, and desquamation), with persistent long term issues including skin dryness (5-64%) and atrophy (5-12%), [15].

More recently, immunotherapy has received attention for management of locally advanced or metastatic cutaneous SCC. Phase one and phase two trials using a monoclonal antibody directed against programmed cell death receptor-1 (cemiplimab) have shown response rates of up to 50% and durable disease control in 61–65% of patients [16]. Although not specifically trialed for upper limb SCC, this therapy may become an increasingly favored modality for advanced cases not amenable to radiation therapy or surgery, as was indeed the case for our second patient with frequent recurrence.

The priority for primary treatment of SCC is the clearance of all margins to prevent local and deep recurrence. We present one case of extensive recurrent SCC following radiation therapy, which invaded vertically through bone then radially along the volar surface from a dorsal focus. This may indicate inadequacy of radiotherapy in clearing deeper neoplastic cells, which is especially concerning given the thin skin and limited soft tissue coverage on the dorsum of the hand. The second point to note in this case is that post-radiotherapy ulceration must be suspected to herald recurrence above infection, and biopsy should be mandatory.

Table 1: Studies reporting on radiotherapy as a primary treatment strategy for SCC of the upper limb.

Study, Year	Title	Age (range)	n (patients)	M:F	Site	Radiotherapy	Recurrence	Avg. Follow-up
Cheo et al., 2016 [5]	Long-term remission after low dose radiotherapy in patient with extensive squamous cell carcinoma of the hand: A case report.	69	1	1:0	L hand dorsal + palmar aspects PIPJ LIF, LMF, LRF.	36Gy, 12 F over 2.5 weeks. 6MV photons with 1cm margin.	Nil	22 months
Grootenboers et al., 2007 [15]	Radiotherapy preserves fingers in the management of subungual squamous cell carcinoma, obviating the need for amputation	67 (42-82)	12	9:3	Subungual	49 - 66 Gy, fraction size from 2 to 3.5 Gy, electrons/ orthovolt/ iridium/ cobalt	8%	62 (4-192) months
Hunt et al., 2013 [14]	Multiple-digit periungual Bowen's disease: a novel treatment approach with radiotherapy.	36	1	1:0	Subungual, 8 digits	50 Gy in 15 fractions over 3 weeks, electrons	100%	6 months
Rosen et al., 2010 [13]	Subungual Squamous Cell Carcinoma: Radiation Therapy as an Alternative to Amputation and Review of the Literature	61 (46-83)	3	1:2	Subungual	6 MeV 2.5Gy x 20, Boost 2.5Gy x 5 over 5 weeks	Nil	48 (36-52) months
Yaparalvi et al., 2003 [12]	Radiation therapy for the salvage of unresectable subungual squamous cell carcinoma.	69	1	0:1	Left thumb	External beam	Nil	17 months
Fabrini et al., 2008 [11]	High-dose-rate brachytherapy in a large squamous cell carcinoma of the hand		1		LIF, thenar, palm	192Ir-based brachytherapy, 50 Gy was administered in 10 fractions	Nil	9 months
Somanchi et al., 2008 [10]	Hand Function after High Dose Rate Brachytherapy for Squamous Cell Carcinoma of the Skin of the Hand	74 (53-93)	25	14:11	Fingers (15) dorsum of hand (10)	4000–4500 cGy on the skin surface in eight fractions given on 5 consecutive days.	Nil	5 years

Abbreviations: Gy, Gray; Ir, Iridium; LIF, Left index finger; LMF, left middle finger; LRF, left ring finger; PIPJ, proximal interphalangeal joint; V, volts

Acute inflammation in the hand, especially in the digits are the main cause of adhesions post-surgical repair of tendon lacerations, which of course can produce poor mobility and loss of function. A similar process is induced by radiation therapy and is illustrated by our second case, which resulted not only in extensive recurrence, in a similar vein to the first case presented, but also in stiff, painful, and useless digits. In addition, this case highlights the importance of vigilant follow up.

Conclusion

Several treatment strategies are available for managing cutaneous SCC of the upper limb and careful consideration of patient and disease factors is needed to achieve optimal outcomes. Radiation

therapy has been used in a limited number of studies with good results, although consensus is needed regarding dose and administration technique. However, as a primarily modality in two cases of SCC of the hand, we found radiation therapy to be inadequate for tumor clearance, with recurrence both extensive and distal to the initial focus. Moreover, functionality of the hand was readily impaired by the inflammation caused by radiation therapy in the dosages used to treat SCC. We therefore advise caution when using radiation therapy for SCC of the hand and suggest limiting its use to cases not amenable to primary surgery.

Potential conflicts of interest

The authors declare no conflicts of interests.

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