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Curettage and electrodessication combined with photodynamic therapy in the treatment of large squamous cell carcinomas in unfit and frail patients

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SUMMARY

A Caucasian female patient in her 90s was referred to the department of plastic and reconstructive surgery for surgical removal of a large invasive squamous cell carcinoma on the anterior chest wall. A skin biopsy prior to the referral indicated that the tumour was moderately differentiated. The patient suffered from severe congestive heart failure with a mechanical valve prosthesis and atrial fibrillation, and was therefore treated with anticoagulants. Hence, a surgical procedure would be hazardous. Therefore, other treatment options were considered. The principal aim was to reduce the amount of tumour tissue to an appropriate size suitable for later excision with primary wound closure. After interdisciplinary discussions, curettage and electrodessication combined with photodynamic therapy was judged the best alternative treatment in this case. At the 1.5 years follow-up after the intervention there was no indication for further surgery. The patient was at that stage content with the treatment and its outcome.

BACKGROUND

Cutaneous squamous cell carcinoma (cSCC) is derived from keratinocytes in the epidermis of the skin, and it is the second most common non-melanoma skin cancer (nMSC) after basal cell carcinoma (BCC). cSCC accounts for approximately 20% of all skin cancers. Depending on the latitude, the incidence of cSCC varies from 5 to 499 per 100 000 individuals.[1] In Sweden, the incidence varies from 74 to 103 per 100 000 individuals (dataset)[2] (online supplemental figure 1). Risk factors for developing cSCC are UV exposure (both natural and artificial), fair skin (Fitzpatrick skin types I–III), old age (average age of onset is in the mid-60s) and immunosuppression. Surgical resection with three-dimensional safety margins is the first line recommended treatment (gold standard) for cSCC and with rare indications for adjuvant chemoradiation based on risk factors.[1]

Curettage and electrodessication (C+E) is a minimally invasive technique used in dermatology to treat superficial basal cell carcinoma (sBCC) and squamous cell carcinoma in situ (cSCCis).[3] The curette is a handheld tool with an open cylinder at the tip, which has at least one sharp edge. After cleansing and application of local anaesthetics to the target area/lesion, the tumour is removed by scraping it down to healthy tissue in the dermis. This curettage is followed by denaturing the tissue with electrodessication.[4] C+E is often repeated up to three times.[3] Between 1965 and 1978, dermatologist Thorsten Bjarke treated 1124 patients with confirmed nMSC on pathology (BCC, cSCC and cSCCis) with C+E and the relapse rates were estimated to be 1.9% for BCC, 2.1% for cSCC and 0 for cSCCis after 5 years of observation.[5] Similar low relapse rates were found in an international review.[4]

Photodynamic therapy (PDT) is a two-step treatment of superficial lesions such as actinic keratosis (AK), sBCC and cSCCis. Curettage of the superficial lesions is followed by application of a drug topically under occlusion, which acts as a photosensitiser, either 5-aminolevulinic acid or methyl aminolevulinate (MAL). Thereafter, the area is illuminated with red light (635 nm) to activate the drug which destroys neoplastic cells through intracellular accumulation of photoactive porphyrins by oxidation.[6]

CASE PRESENTATION

A Caucasian female patient in her 90s was referred to the department of plastic and reconstructive surgery for surgical removal of a large invasive cSCC on the anterior chest wall. A skin biopsy prior to the referral indicated that the tumour was moderately differentiated (figure 1). She was a regular outpatient at the department of dermatology because of her severely sun-damaged skin. Over the years, she had received different types of treatments, both surgical and non-surgical, for her skin dysplasias and non-melanoma skin cancers. Besides her sun-damaged skin, the patient suffered from congestive heart failure with a mechanical valve prosthesis and atrial fibrillation, and was therefore treated with anticoagulants.

Clinical examination revealed an infiltrated tumour area measuring 13×10 cm in the prestsernal skin (figure 2A). There were no clinical suspicions of bone involvement. Ulceration was seen in the centre. Less infiltrated scaly plaques were also found, which is a common sign of cSCCis. Dermatoscopy clues included ulceration, blood spots, polymorphic vessels (dotted, glomerular, linear/hairpin) and white perifollicular circles. These dermatoscopic signs are all indicative of invasive cSCC.[7] No palpable lymph nodes were detected at the neck, supraclavicular, axillar and the inguinal lymph node stations. The tumour was clinically staged to T3N0M0, stage III at the time of this assessment.[8]

Considering the patient's age, comorbidities and anticoagulant therapy, wide excision followed

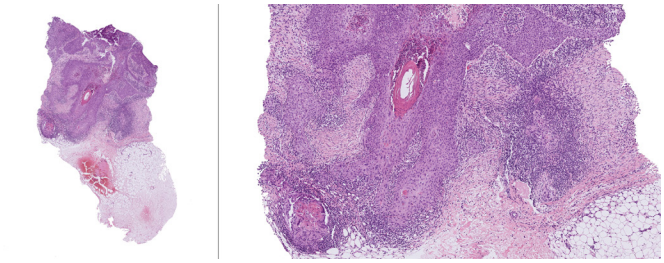

Figure 1 Histopathological images of the 4 mm punch biopsy with overview (left) and detailed view of 8× (right) presenting epidermal, dermal and subcutaneous tissue. The tumour consists of infiltrating sheets of atypical squamous cells with focal keratinisation, moderate pleomorphism and dispersed mitotic figures. In the background, the dermis appears fibrotic and contains foci of foreign body granulomatous reaction around remnants of horn cysts. The tumour infiltrates the subcutaneous tissue focally. The histological picture is consistent with a moderately differentiated squamous cell carcinoma.

by split thickness skin grafting in an outpatient setting under local anaesthesia was deemed to be too unsafe. General anaesthesia was considered as an alternative but would suggest an even higher risk for the patient, taking her comorbidities into account. Radiotherapy (RT) was also ruled out but only for patient-related reasons. Therefore, other treatment options were considered. The principal aim was to reduce the amount of tumour tissue to an appropriate size suitable for later excision with primary wound closure. After interdisciplinary discussions, in which the patient took an interactive part, C+E combined with PDT was considered the best alternative treatment to start with. The medical decision was made with respect to the patient's autonomy.

TREATMENT

After cleansing and injection of anaesthesia (carbocain 10 mg/mL without epinephrine) to the tumour area, the tumour was carefully removed with a curette. Then the wound was denatured with electrodessication (figure 2B). The C+E procedure was repeated two times. There was then a clear and firm sense of healthy dermis at the bottom of the wound. Haemostasis was achieved with the electrodessication. After C+E, the treated area was cleaned for coagulated blood to prepare the area for PDT. The photosensitiser, MAL, was applied to the treated area and occluded with a transparent film to secure penetration of the drug. After 3 hours of occlusion the tumour area was illuminated for 7–8 min with red light to activate the photosensitiser. MAL is the photosensitiser which is routinely used in our unit.

With guidance of our department of coagulation disorders, the patient's ongoing treatment with warfarin was discontinued 4 days before the intervention. Instead, anticoagulation was temporarily achieved by daily injection of low-molecular-weight heparin. One week after intervention, warfarin was reinstituted.

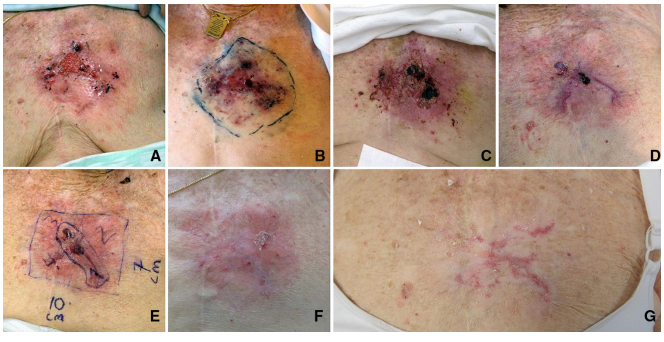

Figure 2 A large invasive squamous cell carcinoma on the anterior chest wall measuring 13×10 cm. Pathology revealed that the squamous cell carcinoma was moderately differentiated. Pictures A–G shows the tumour/treated area before and after treatment. A: before treatment, B: the day of treatment, C: 3 weeks after treatment, D+E: 4 months after treatment, F: 8 months after treatment and G: 1.5 years after treatment.

OUTCOME AND FOLLOW-UP

Three weeks after C+E and PDT, the patient was scheduled to repeat PDT. Clinically, an erythematous ulcer with granulation tissue and a crust was observed. There was an obvious tissue defect in the dermis in the centre of the former tumour but no evident remaining tumour tissue. Consequently, we decided not to repeat PDT. The defect was actually an expected result after deep C+E and PDT (figure 2C).

Four months after deep C+E and PDT, the patient had a follow-up at the department of dermatology. Clinically, a scar with traces of granulation tissue in the centre was observed. No evidence of tumour growth was observed in the treated area (figure 2D). The treated area was divided into four compartments for histopathological mapping prior to possible complementary surgery (figure 2E). Three punch biopsies (4 mm) were taken within compartment 1 and one punch biopsy in each of the other compartments. Histopathological analysis revealed benign tissue with granulation/scar tissue. Surgery was therefore postponed, instead a clinical follow-up was scheduled 4 months later at the department of dermatology.

Eight months after deep C+E and PDT, the patient came to the second follow-up. Clinically, a healed scar with a thin atrophic appearance was observed. No evidence of tumour growth was seen in the treated area (figure 2F). Within the treated area small macular scaly areas and small superficial ulcers were noted. No infiltration was palpated. Clinically, the findings were suggestive of AK and led to suspicion of cSCCis in the superior aspect of the treated area. Surgery was still not indicated at the time of this assessment. An appropriate treatment could have been topical chemotherapy cream such as 5-flourouracil or repeated PDT. The patient's actinic damage had generally progressed at the time of follow-up and clinically many cSCCs and BCCs were observed distant from the treated area. Palpation of lymph nodes at the neck, supraclavicular, axillar and the inguinal lymph node stations was unremarkable. We recommended regular follow-ups for 4 months but agreed on future visits in case of worsening or new lesions.

Approximately 1.5 years after deep C+E and PDT, the patient was referred to our unit due to her various skin lesions. In previously treated area, a depigmented and atrophic scar with telangiectasias was observed. No infiltration was palpated. Xerosis cutis was seen but no hyperkeratosis or ulcers (figure 2G). Palpation of lymph nodes was still unremarkable. The patient's actinic damage had generally further progressed with clinically many cSCCs and BCCs on various locations. We recommended further follow-ups but the patient expressed clearly that she was exhausted by all kinds of treatment. For 15 years she had had frequent hospital visits and treatment sessions and therefore declined further interventions and follow-ups.

DISCUSSION

cSCC is the second most common nMSC, with an average age of onset in the mid-60s. Surgical resection with three-dimensional

safety margins is the first line recommended treatment (gold standard) for invasive cSCC. Primary RT is an effective treatment option and RT can be used in situations where surgery is not applicable or contraindicated.[9] A meta-analysis of 14 observational studies of RT for 1018 primary cSCCs reported a pooled average local recurrence rate of 6.4 %.[10] The recommended radiation dose for cSCC larger than 2 cm according to the European guidelines is 60–66 Gy in fractions of 2 Gy. RT is overall a safe procedure, but it is associated with complications. An acute dermatitis, often erosive, may occur and in the long run depigmentation and telangiectasia may be encountered.[11] RT would require up to 33 sessions in this case which was considered unacceptable by the patient. Therefore, other treatment options came into consideration.

According to previously published data, C+E and PDT achieve favourable results when applied to cSCCis.[4 12] C+E achieves satisfactory results when applied to primary high-differentiated SCCs up to 2 cm in diameter.[4] On the contrary, there is no scientific evidence justifying C+E in the treatment of a low-differentiated cSCC that is larger than 2 cm.[4] Available data for PDT do not currently support its efficacy alone in the treatment of cSCC. A few case series data suggest, however, that PDT may be used as an adjuvant modality in combination with C+E for invasive cSCC.[12] We adopted this strategy in our frail patient with a large tumour where the surgeons judged that surgery would be too invasive. After interdisciplinary team discussions, the principal aim was to reduce the amount of tumour tissue to an appropriate size for later surgery. In theory, this strategy would require three medical consultations only, two for C+E with PDT and one for complementary surgery. Complementary surgery was first postponed and eventually abandoned. The findings at 1.5 years follow-up, with no evident clinical signs of invasive cancer, support this decision.

We staged the patient's tumour using the UICC TNM classification eighth edition and followed the European guidelines.[8] Since there were no suspicion of bone involvement or metastases in our case, we did not proceed with any imaging procedure.

In the daily outpatient setting, anticoagulation therapy is not a major concern in regards to C+E or PDT since dermatologists use these interventions primarily for superficial lesions. However, in this case, we predicted a deeper defect after thorough C+E. Consequently, we adhered to widely accepted routines for handling anticoagulation therapy in connection with surgical procedures.

The patient's follow-up time of 1.5 years is too short to draw any conclusions regarding C+E combined with PDT as a curative treatment for large moderately differentiated cSCC. The ideal follow-up time would be 5 years with regular check-ups every 4–6 months. This was not feasible since the patient declined further follow-ups due to various health and age-related issues.

We propose that C+E combined with PDT can be used as a debulking method prior to surgery for large, moderately differentiated cSCC. We also propose that C+E combined with PDT should be considered a unique treatment option in patients for whom surgery is judged unsuitable due to either patient-related or tumour-related factors, or both. The goal is then to reduce the burden of care and thereby improve quality of life. However, when used in this way, treatment should be followed up clinically at regular intervals for at least 2 years.

Further studies in the field are needed to strengthen the clinical findings in this case report.

Patient's perspective

I am very tired of medical consultations because I have been dealing with frequent hospital visits for the last 15 years. The tumour on my chest started with a small ulcer approximately 1.5 years before and it grew with time and became problematic for me. In the end, it hurt and bled constantly and I got difficulties taking care of it properly. I decided to seek my dermatologist who took a skin biopsy, which confirmed that it was a skin cancer. My dermatologist referred me to the department of plastic and reconstructive surgery where the surgeons told me that surgery would be too extensive. We discussed other treatments including radiation but the one best suited for me became the scraping method combined with light treatment. The suggested treatment is not first line treatment but could potentially make the cancer smaller in size and a complementary surgery would therefore be less complicated. At follow-ups after treatment, the dermatologist found no evidence of cancer in the treated area, which I was happy to hear. The dermatologist suggested further follow-ups but I declined simply because I am tired of medical consultations. In the end, I am happy about the physicians' decision and thankful for how the treatment turned out.

Learning points

- An interdisciplinary team approach is required to achieve appropriate management of invasive cSCC in elderly patients with comorbidities with respect to both patient-related and tumour-related factors.
- For large invasive squamous cell carcinomas, curettage and electrodessication combined with photodynamic therapy is an appropriate debulking method prior to surgery, or even a sufficient treatment in palliative patients, for whom surgery is deemed unsuitable as a first line treatment.
- By this approach, the burden of care may be reduced and quality of life improved for certain fragile patients.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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