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CASE REPORT

Surgical Excision Combined with Photodynamic Therapy for Squamous Cell Carcinoma Arising in Lupus Vulgaris

Li Lin[1,*], Zeyu Huang[2,*], Bangsheng Xi[3,*], Xiaoming Qin[1], Kongchao Yang[1], Ruzhi Zhang[1]

[1]Department of Dermatology, The Second Affiliated Hospital of Wannan Medical College, Wuhu, People's Republic of China; [2]Department of Dermatology, The Third Affiliated Hospital of Soochow University, Changzhou, People's Republic of China; [3]Department of Clinical Laboratory, The First Affiliated Hospital of Wannan Medical college, Wuhu, People's Republic of China

*These authors contributed equally to this work

Correspondence: Ruzhi Zhang, Email zhangruzhi628@163.com

Abstract: Cutaneous squamous cell carcinoma (SCC) is a common non-melanoma skin cancer (NMSC). Although most cutaneous SCC in people with lighter skin pigmentation as a result of sun damage, patients with underlying conditions such as skin ulcers and chronic inflammation-including conditions such as lupus vulgaris (LV) and chronic discoid lupus erythematosus—are also predisposed to developing SCC. Here we report a case of secondary SCC diagnosed in a 54-year-old patient with 20 years of lupus vulgaris without prior formal systemic treatment, a rarity in clinical practice. Two months ago, the patient developed papules on the right cheek that ulcerated and discharged purulent fluid. Laboratory tests revealed a positive TSPOT result and histopathological examination confirmed granulomatous lesions, supporting the diagnosis of SLE. However, a tissue biopsy unexpectedly revealed a moderately differentiated SCC of the keratinizing type. In this case, we performed surgical excision of the lesion followed by cosmetic closure and adjuvant photodynamic therapy (PDT). Concurrently, the patient underwent systemic anti-tuberculosis treatment. At 6 months post-treatment, no tumour recurrence was observed and the rash associated with lupus erythematosus had also resolved. The patient was satisfied with the treatment outcome.

Keywords: lupus vulgaris, squamous cell carcinoma, surgical excision, photodynamic therapy

Introduction

Cutaneous squamous cell carcinoma (SCC) is the second most common non-melanoma skin tumour worldwide after basal cell carcinoma (BCC), accounting for 20% of all skin cancers.[1] Currently, surgical resection with three-dimensional safety margins remains the frontline recommended treatment for SCC.[2,3] However, for SCC secondary to primary lupus vulgaris (LV), there are no specific guidelines recommending follow-up treatment after extensive resection.

Recent years have seen the rapid development of many non-surgical therapies. Five-aminolevulinic acid photodynamic therapy (ALA-PDT) has surpassed guideline indications and emerged as a minimally invasive treatment for superficial SCC in situ, effectively improving cosmetic outcomes and patient satisfaction.[4] Existing prospective studies have confirmed the efficacy and safety of PDT for low-risk SCC.[5] However, the efficacy of monotherapy can vary depending on factors such as tumour infiltration depth, size and photosensitiser penetration.[6] Therefore, PDT remains a valuable adjunctive therapy, particularly when combined with surgical excision, which is recognized as a more effective treatment strategy for SCC. This combined approach removes potential lesions postoperatively, thereby reducing the risk of recurrence.[6–8] In addition, some researchers suggest that PDT may have a beneficial effect on Mycobacterium tuberculosis infection, with enhanced therapeutic effects when combined with LV medication.[9] This case report highlights the achievement of satisfactory treatment outcomes through the combination of surgery and PDT.

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Clinical Data

A 54-year-old woman presented with plaques and nodules on the right side of the face for 20 years and a tumour in the right zygomatic region for 2 months. Twenty years ago, a papule measuring approximately 4 mm appeared on the right side of the face without pain or pruritus and without apparent cause. The patient had previously been treated in a clinic but had not receive a definitive diagnosis. Due to the poor outcome, the patient did not seek further treatment. Subsequently, the eruptions gradually increased in number and area, involving the right ear and nasal root. Two months ago, a papule measuring approximately 6 mm appeared on the right cheekbone without any apparent cause and rapidly developed into a plaque with ulceration and weeping. History of hepatitis and tuberculosis, trauma, surgery and blood transfusion was denied. The patient's BMI was 27.69 kg/m². Instrumental examinations including chest radiography, echocardiography and abdominal ultrasound showed no abnormal lymph node enlargement or mass proliferation, suggesting no evidence of SCC metastasis at present.

Dermatological Examination

Dermatological examination revealed infiltrative reddish-brown plaques and nodules on the root of the nose, nose, right side of the face and ears, with an apple-jam-like slide on pressure. The surface of the lesion area was uneven and atrophic scarring was seen. The lesions had clear but irregular borders with some scaling. The right external ear was deformed. Most prominent was an elevated mass on the right zygomatic region, approximately 2.5 cm x 2.5 cm in diameter and approximately 1.5 cm above the skin surface, covered with black crusts. It was firm to the touch, adherent to the surrounding tissues and poorly mobile (Figure 1a and b).

Figure 1 Skin lesions of the patient before and after treatment. A well-defined reddish-brown patch mixed with papules and plaques at the base of the nose, dorsum of the nose and right side of the face and right side (**a**). There was a mass on the right cheekbone covered by a black crust (**b**). Local PDT was administered on postoperative days 5 (**c**), 12 (**d**) and 19 (**e**). Six months after treatment, there was no recurrence of the tumour and the lupus vulgaris lesions had largely disappeared (**f**).

Laboratory Tests

Routine blood count, routine urinalysis, liver and kidney function, tumour-related antibodies, antinuclear antibodies and secretory bacterial culture showed no obvious abnormalities. Blood sedimentation rate is 39 mm/h (normal range: <20 mm/h), fasting blood glucose is 8.86 mmol/L (normal range: 4.4–6.1 mmol/L); triglyceride is 10.37 mmol/L (normal range: <1.70 mmol/L); serum potassium is 3.01 mmol/L (normal range: 3.5–4.5 mmol/L); HBsAg (+), HbeAb (+), HbcAb (+), TB (+), TSPOT (+), PPD (+++), the chest CT shows mild chronic inflammation and fibrocalcified foci in the left upper lung.

Pathological Examination

Pathological biopsy of the right zygomatic mass showed irregular hyperplasia of the epidermis with disorganised arrangement of the entire layer. The dermis showed clumps of squamous epithelial cells with abundant cytoplasm, some of which was vacuolated, and nuclei of variable size, as well as keratinocytes and dyskeratotic cells. A predominantly inflammatory infiltrate of lymphocytes and neutrophils was seen around the tumour masses in the dermis. Postoperative pathological examination of the completely excised mass and surrounding tissues revealed a pathological diagnosis of SCC (keratinised echinoderm type, moderately differentiated), with no cancerous residue seen at the lateral and basal margins of the specimen. Immunohistochemistry showed Ck5/6 (+), Ki-67 (30%+), P63 (+). Meanwhile, a biopsy of the lesion in the mandibular region showed hyperkeratosis and mild epidermal thickening. The dermis was infiltrated by large numbers of histiocytes, lymphocytes and multinucleated giant cells, the infiltrating foci were avascular and there was degeneration of collagen fibres, consistent with a granulomatous lesion. (Figure 2)

Clinical Diagnosis

According to the results of the examination, the diagnosis was lupus vulgaris, squamous cell carcinoma, hepatitis B.

Treatment

Prior to surgery, the patient was treated with potassium supplementation and glycaemic and lipid control. Under general anaesthesia, an extended resection of SCC + kite flap plasty was performed, and the patient's zygomatic mass and surrounding 0.5 cm of tissue were completely removed. The first PDT was administered on postoperative day 5 and then at 1-week intervals for a total of 3 sessions. An Omnilux red light therapy device was used with treatment parameters of wavelength (633 ± 5) nm, light density 60 mW/cm2, a total dose of 60 J/cm2, a distance 20 cm, and vertical irradiation for 20 minutes. The patient was treated with oral anti-tuberculosis therapy with isoflupine and ethambutol hydrochloride tablets, and her liver and kidney functions were monitored regularly. After 6 months, the patient's surgically resected area had almost returned to normal, with no recurrence of the tumour, and the lupus vulgaris rash had resolved (Figure 1).

Discussion

Cutaneous SCC is a heterogeneous group of cutaneous malignancies arising from epidermal keratinocytes. Clinically, cutaneous SCC often presents with irregular raised borders, a tendency to bleed, rapid ulceration and sometimes a foul odour due to infection. Lupus vulgaris (LV), caused by Mycobacterium tuberculosis, is the most common form of cutaneous tuberculosis in adults and typically presents as dark red erythema and irregular plaques, mainly on the face. It is similar to discoid lupus erythematosus (DLE) and verrucous cutaneous tuberculosis (VCTB), but can be distinguished pathologically by characteristic "lupus nodules" and "tuberculous infiltration". The course of the disease, which often lasts years to decades, is often overlooked due to its asymptomatic nature. Malignant tumours have been documented in patients with lupus vulgaris, with an incidence ranging from 0.5% to 10.5%.[10] While SCC stands out as the most common form of secondary malignancy. Our review reveals limited reports of SCC attributed to lupus vulgaris over the past two decades.[8] The exact mechanism linking these two diseases remains elusive, but Kensler et al suggest that free radicals generated by chronic inflammation are involved in tumour development.[11] In addition, the induction of malignant tumours has been linked to DNA damage, p53 gene mutations, and immunosuppression induced by exposure to ultraviolet light.[12] This article documents a patient with lupus vulgaris who has remained untreated for 20 years, an extremely rare occurrence in clinical practice. Based on the patient's history, characteristic pathological features and positive results of relevant laboratory tests, the definitive diagnosis was SCC secondary to lupus vulgaris. Traditionally,

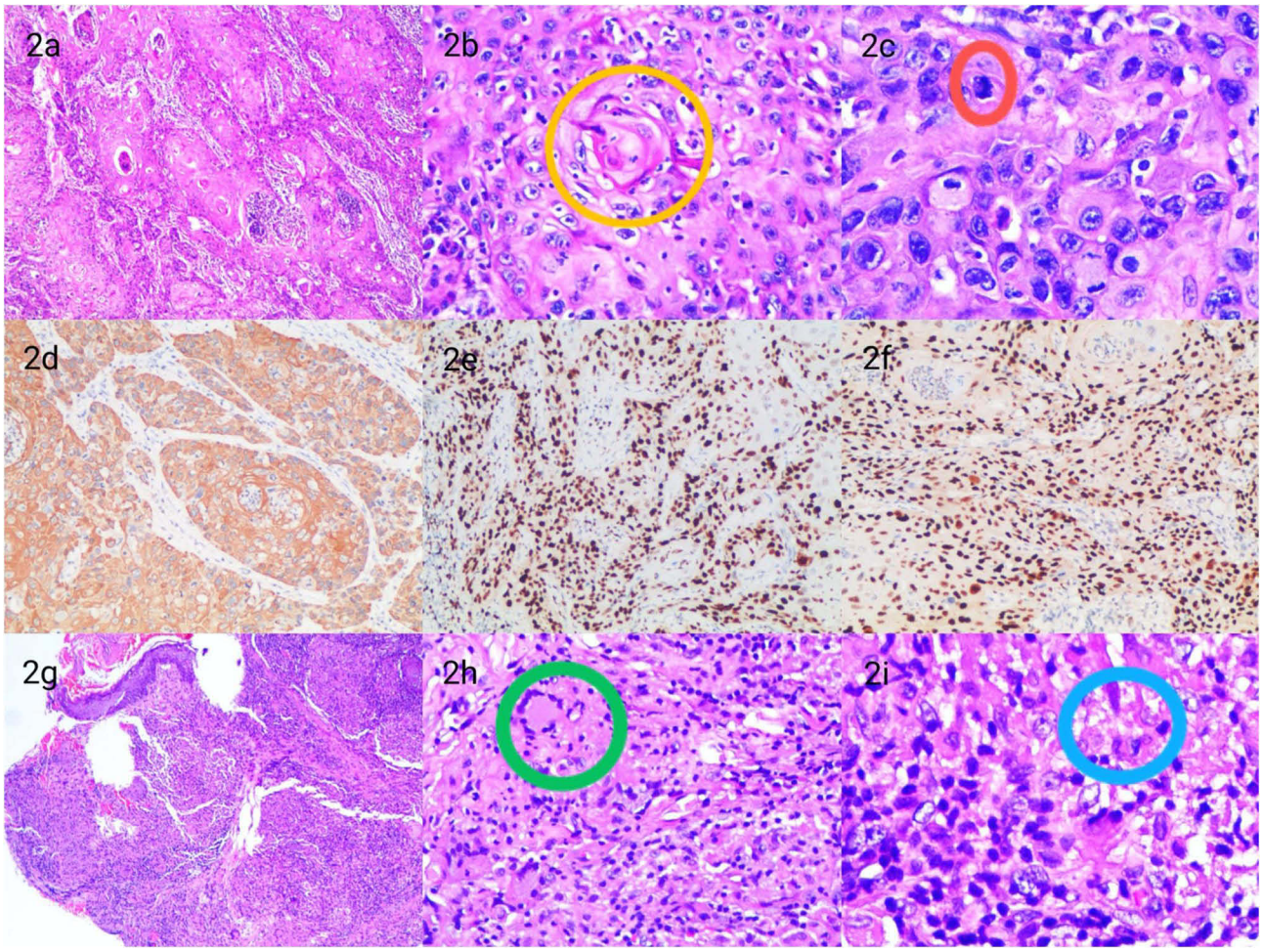

Figure 2 Histopathological and immunohistochemical findings of the skin lesions. The pathology of the zygomatic nodule showed irregular epidermal hyperplasia with disturbed arrangement of the entire layer. The dermis showed clumps of squamous cells surrounded by an inflammatory infiltrate dominated by lymphocytes and neutrophils. Tumour cells had abundant cytoplasm and nuclei of variable size. Keratinocytes and dyskeratotic cells were seen (**a–c**). Immunohistochemistry was positive for Ck5/6 (**d**), Ki-67 (30%) (**e**) and P63 (**f**). Biopsy of the mandibular lesion showed hyperkeratosis and mild thickening of the epidermis. The dermis was heavily infiltrated with histiocytes, lymphocytes and multinucleated giant cells with degeneration of collagen fibres (**g, h** and **i**). Keratin pearls are highlighted within the yellow circle (**b**). Mitotic figures are marked by the red circle (**c**). Multinucleated giant cells are indicated by the green circle (**h**), and necrotic cells are identified within the blue circle (**i**). (**a, d, e, f** and **g**, ×40; **b** and **h** ×100; **c** and **i** ×200).

the treatment of SCC involves extensive excision of lesions followed by skin grafting. However, given the widespread distribution of facial lesions in patients with lupus vulgaris, traditional treatment can significantly affect the patient's appearance. In addition, pre-existing lupus vulgaris may affect skin graft survival of and post-operative recovery.

Several interventional studies and case reports have found PDT to be effective in reducing field carcinogenesis and treating patients with superficial or nodular BCC and cutaneous SCC.[4,5,8,13,14] PDT involves the application of a topical photosensitizer which, when activated by visible light, catalyses the formation of reactive oxygen species (ROS) and induces apoptosis and necrosis of atypical keratinocytes. This method significantly improves post-operative skin healing, shortens the anti-tuberculosis treatment cycle[9] and minimizes scarring without compromising aesthetics. Mohs micro-surgery is also a popular treatment for facial non-melanoma skin cancer, which can maximize facial function and cosmetic effect, but 6% of SCC cases have positive cutting edge and require re-resection.[7] In addition, flap reconstruction is not recommended until tumour clearance is confirmed by pathology, which also affects the patient's postoperative recovery. The patient could not accept the risk of Mohs microsurgery, so we ended up with extended resection + kite flap angioplasty to improve circulation, combined with PDT and anti-tuberculosis therapy to avoid potential risks. Ultimately, the patient was successfully cured and no new skin lesions or lymphadenopathy were observed at six months follow-up.

Of course, further investigation and use of PDT is warranted.[15] Surgical resection remains the cornerstone treatment for high-risk cutaneous SCC. Future treatment paradigms may include the integration of multiple modalities, potentially improving patient prognosis.

Conclusion

The case highlights the effectiveness of a combined treatment approach, including surgical resection, PDT, and anti-tuberculosis treatment, for secondary SCC arising from lupus vulgaris. This comprehensive strategy offers a viable alternative for the management of complex cases. In addition, exploring the synergy of multiple treatments is promising and warrants further research efforts in in this area.

Institutional Approval

The Ethics Committee of the Second Affiliated Hospital of Wannan Medical College granted permission to report this case.

Consent to Participate

Written consent was obtained from the patient for publication of case details along with imaging or videos.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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