

Simple shaving combined with photodynamic therapy for refractory bowen disease

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ARTICLE INFO

Keywords:

Simple shaving
Photodynamic therapy (PDT)
Bowen disease (BD), 5-ALA

ABSTRACT

Bowen Disease (BD), also known as squamous cell carcinoma *in situ*, requires treatment to prevent progression to invasive cancer. Photodynamic therapy (PDT) has been widely employed to treat BD. However, there are BD patients who undergo PDT but experience poor efficacy and recurrence. We have considered that for some, the reason is the depth of PDT penetrating tissue to be limited. Therefore, we combined simple shaving with PDT to treat 10 patients with a total of 44 advanced BD lesions. After local injection of anesthesia, the lesions were shaved once *in situ*, then a total of three PDT sessions were applied for each patient. At 12 weeks, all of BD lesions (100%) have shown complete clinical response. After more than 12 months follow-up, the RR was 0, and all lesions showed a good or excellent cosmetic outcome. The patient's symptoms were alleviated with improvement in the quality of life. For those with advanced BD, which are more than 3 cm in diameter, with unclear borders, ulcers, multiple occurrences and those that appear on the face and neck that are not suitable for extended resection by routine surgery, combined simple shaving with PDT is recommended.

1. Background

Bowen disease is also known as squamous cell carcinoma (SCC) *in situ*, which may further develop into invasive SCC in 3%–5% cases [1]. Therefore, Bowen disease should be treated actively. The latest guidelines [1] indicate that PDT is an effective measure to treat for BD. However, the clinical response rate (CRR) following PDT therapy was 52–100% [2]. We have considered that one reason for poor outcomes may be that the depth of PDT penetrating tissue to be limited. PDT combination therapies for BD, generally appear to have better curative effect than PDT alone [3–6]. We looked at combining the simple shaving technique with PDT in advanced cases of BD.

2. Aims

To increase the penetration depth of photosensitizer in our present study, simple shaving combined with PDT was used to treat 10 refractory BD patients who were not suitable for surgery due to special reasons, such as large lesions, multiple or special anatomical sites and

so on. The efficacy of combination treatment was observed.

3. Methods

3.1. General information

We have recorded 10 patients' age, size, number, location, healing time, recurrence rate, pain during treatment, satisfaction with treatment score (after 12 months treatment) and dermatological quality of life index (DLQI) (Table 1).

3.2. Simple shaving with photodynamic therapy

Simple shaving (Fig. 1b–c) was only performed once before the first PDT. Razor blade (brand: Gillette, very cheap, and can be used after strict disinfection) with routine sterilization were used to cut the lesions *in situ*. The epidermis and tumors were removed routinely, and the shaving depth was as deep as the superficial dermal layer. It only takes about 10 min for each lesion and simple operation. PDT (Fig. 1d–e) was

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<https://doi.org/10.1016/j.pdpdt.2019.04.001>

Received 26 January 2019; Received in revised form 31 March 2019; Accepted 1 April 2019

Available online 02 April 2019

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Table 1
Clinical datum and follow-up information.

Patient Number	Gender	Age (year)	Location	Size (cm ²)	Number	Healing Time (days)	Recumance (More than 12 months)	Satisfaction with treatment (score)	Pain	DLQI P		
										before the treatment	after the treatment	0.000
1	Female	46	Tempus	1*1	1	8	No	9	2	16	2	
2	Female	59	Trunk	5*4	32	9	No	8	6	20	6	
3	Male	68	Tempus	2.5*2.5	1	7	No	9	2	22	2	
4	Male	71	Face	1.5*1.5	4	9	No	8	2	22	7	
5	Male	81	Tempus	3*4	1	8	No	8	3	20	5	
6	Male	46	Face	1.5*1	1	6	No	8	2	20	2	
7	Male	61	Tempus	3*3.5	1	22	No	9	3	22	6	
8	Male	54	Waist	5*6	1	18	No	9	4	22	4	
9	Female	66	Face	1*1	1	7	No	9	2	24	6	
10	Male	68	Abdomen	9*8	1	10	No	9	5	24	7	

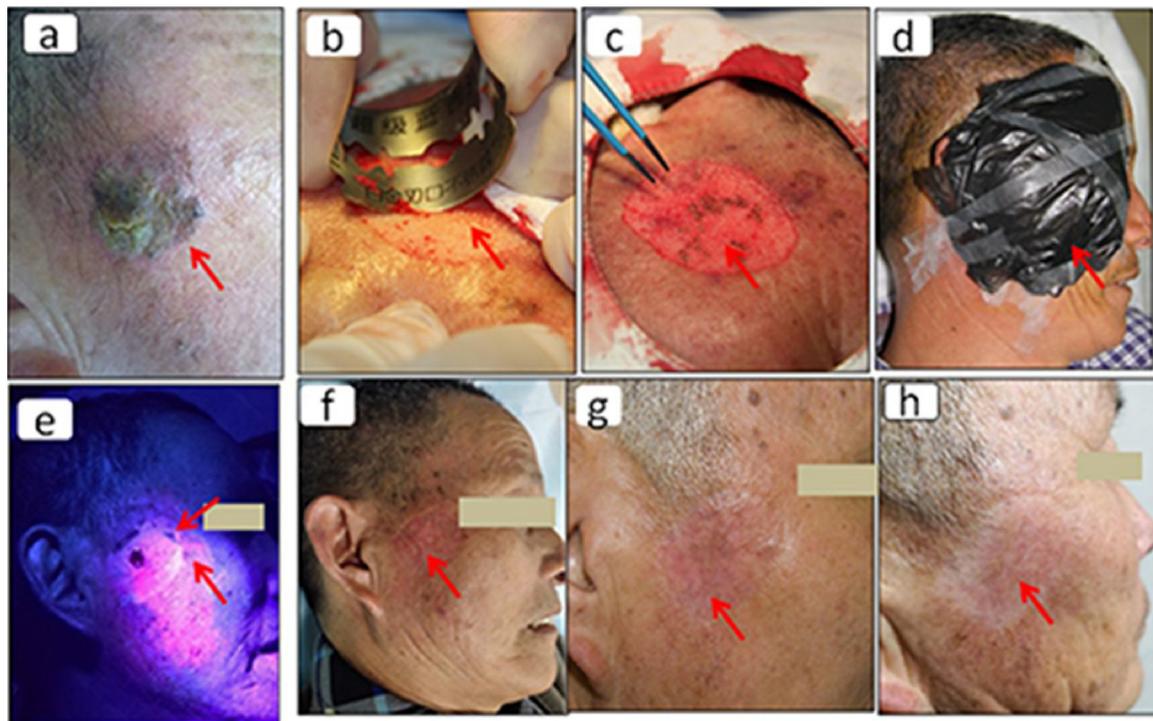


Fig. 1. Representative clinical pictures from one patient. (a) At baseline; (b) During simple shaving; (c) After simple shaving; (d) Light free incubation; (e) During the 3rd PDT illumination; (f) After treatment 12 weeks; (g) After 6 months treatment; h: After 12 months treatment.

immediately performed after shaving. Briefly, we topically treated with 20% 5-aminolaevulinic acid (5-ALA) cream (Shanghai Fudan-Zhangjiang Bio-Pharmaceutical Co. Ltd, Shanghai, China). After light free incubation for 3 h, the lesions then were irradiated with 633 nm red-light at 80 mW/cm² for 20 min. The ALA-PDT procedure was repeated 3 times at 1-week intervals.

3.3. Follow-up

Follow-up was conducted by combining outpatient visits with telephone inquiries. All of patients finished more than 12 months follow-up.

3.4. Statistical analysis

SPSS 17.0 for Windows was used. Statistical analysis was performed using the Paired sample's t test, and the significance level was $p < 0.05$.

4. Results

At treatment 12 weeks, 100% of BD lesions have shown complete clinical response and good cosmetic outcomes (Fig. 1f). After 6 months follow-up, all patients had excellent cosmetic outcomes (Fig. 1g). Meanwhile, the skin histopathological (Fig. 2c-d) showed no histopathological changes of Bowen disease. After 12 months follow-up, the patients' cosmetic outcomes (Fig. 1h) were better than at 6 months follow-up. The scores of satisfactions with treatment (0–10 points, the higher the score is, the more satisfied with the treatment effect is) ranges from 8 to 9 points (Table 1), indicated that patients are quite satisfied with the treatment effects. The mean values of DLQI before and 12 months after operation were 21.20 ± 2.348 and 4.70 ± 2.058 , respectively. There was a significant difference between the two DLQI ($t = 25.909, p = 0.000 < 0.001$), indicated that the quality of life was remarkably improved. In addition, the main adverse event was pain. Pain was assessed by visual analogue scale (VAS), ranging from 0 (no pain) to 10 (unbearable pain). In the current study, the average score of 3.1 points, indicated that the pain was mainly mild. The average healing time was 10.4 days.

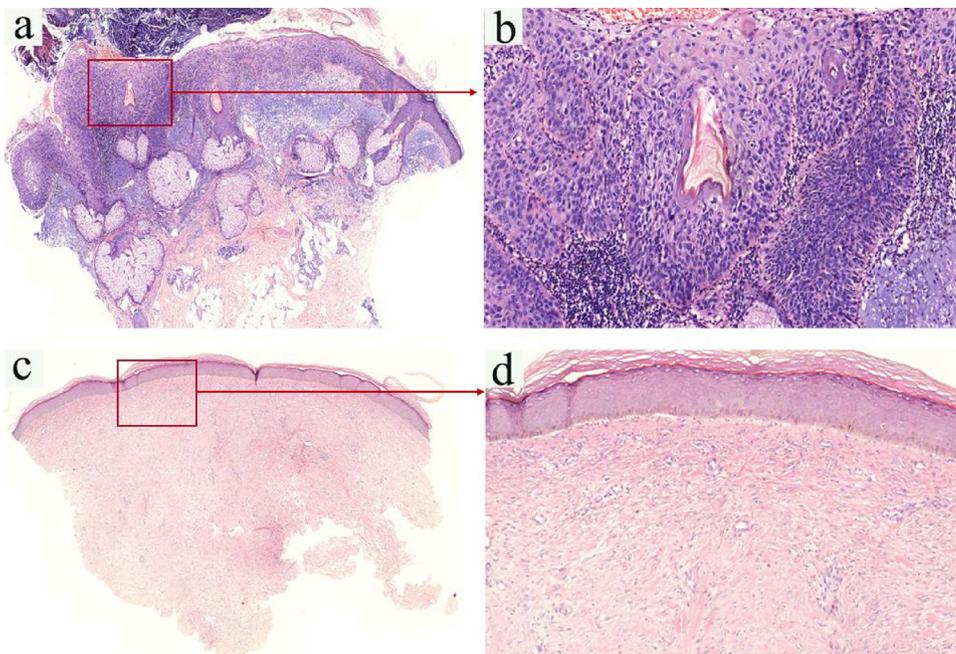


Fig. 2. Representative histopathological images: (a, b) Initial histopathological image: the whole layer of the stratum spinosum cell is disordered, and the cell size and shape are different, showing a mitotic image. The superficial dermal collagen fibers are basophilic and dense lymphocytes infiltrate. The diagnosis of Bowen disease was made; (c, d) At 6 months follow-up, the pictures of histopathology have showed the hypertrophy of scars and no histopathological changes of Bowen disease. The original magnification $\times 50$ (a, c); $\times 200$ (b, d), respectively.

5. Conclusion

PDT is an effective and less invasive therapy. And the latest PDT guidelines [7] has pointed out that PDT is suitable for the treatment of nonhyperkeratotic AK, superficial BCC and SCC *in situ*. However, the response rate of some diseases to PDT is not high, and some auxiliary measures are needed, for example Plantar Warts [8] nodular BCC [6] and squamous cell carcinoma [9]. We have considered that the reason may be related to the limited penetration ability of PDT. In line with that, the research [10] has indicated that the treatment depth of PDT was less than 6 mm.

In order to overcome PDT penetration limitation, we used the method of simple shaving combined with PDT to treat for BD. We have speculated that this method removed the stratum corneum, increased the penetration ability of photosensitizer, and directly reduced the lesion thickness, thus indirectly and efficiently increased the depth of PDT penetration. The experiences of treating these 10 patients showed that simple shaving combined with PDT has remarkable therapeutic effect on refractory BD, and has the advantages of faster healing, fewer scars and good cosmetic outcome. We recommend the method of simple shaving combined with PDT to treat for refractory BD, which is characterized with multiple lesions, difficult-to-remove parts such as face and neck, or large area. In addition, this method might be simple to operate due to no requirement for high level surgeons. Otherwise, it should easy to obtain operating equipment, and could be carried out well in grass-roots hospitals.

In the future, we need to compare the therapeutic difference between PDT alone and combination with PDT by multicenter clinical centers, and further confirm the worth of our combination therapy. Long-term follow-up of patients is needed in order to monitor true outcomes.

Author role

Each author can access to the data. All authors contributed to the manuscript.

Funding

This research received no external funding.

Conflicts of interest

None of the authors has any conflict of interest to be disclosed.

Acknowledgment

This study was supported by the National Natural Science Foundation of China (grant number 81430075).

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