Original Article

Management of Pre-malignant and Malignant Non-melanoma Skin Cancers: A Study from a Tertiary Care Hospital of North India

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Abstract

Introduction: The incidence of non-melanoma skin cancers (NMSCs) is increasing over the last few decades. This necessitates an early diagnosis which is nowadays aided by dermoscopy. Once diagnosed early, the treatment armamentarium is diverse and includes both topical and surgical modalities. **Objective:** Our aim was to diagnose pre-malignant and malignant NMSCs at an early stage and treat them as per the standard protocol. **Materials and Materials:** Out of 136 patients of pre-malignant and malignant tumors enrolled, 100 were taken up for treatment. These were then classified into various subtypes on the basis of clinical examination and dermoscopy. The selected patients were subjected to topical treatment or surgical modalities, wide local excision or flap excision, based on the type of tumor and its size. **Results:** The pre-malignant group included actinic keratoses, Bowen's disease, and keratoacanthoma, whereas the malignant group included undifferentiated squamous cell carcinoma (SCC), differentiated SCC, pigmented basal cell carcinoma (BCC), nodulo-ulcerative BCC, and superficial BCC. Actinic keratoses, superficial BCCs, and five cases of keratoacanthoma were treated with topical therapies with a resolution of 90% in 86.8% cases. All the remaining cases (62 in number) were treated with conventional and flap surgery with 88% and 89.1% clearance rates, respectively, with complications in only 7 patients. **Conclusion:** A prompt identification of NMSCs can enable selection of the appropriate treatment modality for a specific lesion and thus reduce their associated morbidity and mortality.

Keywords: Dermoscopy, malignant, pre-malignant

Introduction

Malignancies are on the rise globally and skin cancers are no exception. The incidence of cutaneous malignancies has been increasing over the last few decades.[1] India too is witnessing a sharp upsurge in their incidence. Non-melanoma skin cancers (NMSCs) form one of the two major groups of cutaneous malignancies and the other being cutaneous melanoma. Excluding mucosal tumors, NMSCs broadly include basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).[2]

The precursor lesions of NMSCs include actinic keratoses, Bowen's disease, and keratoacanthoma in addition to some uncommon variants.[3] All three have a considerable malignant potential, with a tendency to transform into invasive SCC.[4] If treated early, the risk is negated, resulting in considerable reduction in morbidity and mortality.

However, the diagnosis becomes challenging at times and can be eased by performing dermoscopy. The latter has emerged as a novel tool in recent years in the identification of various pre-malignant and malignant cutaneous tumors. Each one of these lesions has a characteristic dermoscopic appearance enabling easy screening and thus early treatment.

The treatment options are multiple for both the groups. Topical therapy is reserved for smaller, superficial, low-risk

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Access this article online

Quick Response Code:

Website: www.jcasonline.com

DOI: 10.4103/JCAS.JCAS_241_20

How to cite this article: Bhat YJ, Zeerak S, Rasool F, Akhtar S, Shah IH, Yaseen A. Management of pre-malignant and malignant non-melanoma skin cancers: A study from a Tertiary Care Hospital of North India. J Cutan Aesthet Surg 2022;15:118-23.

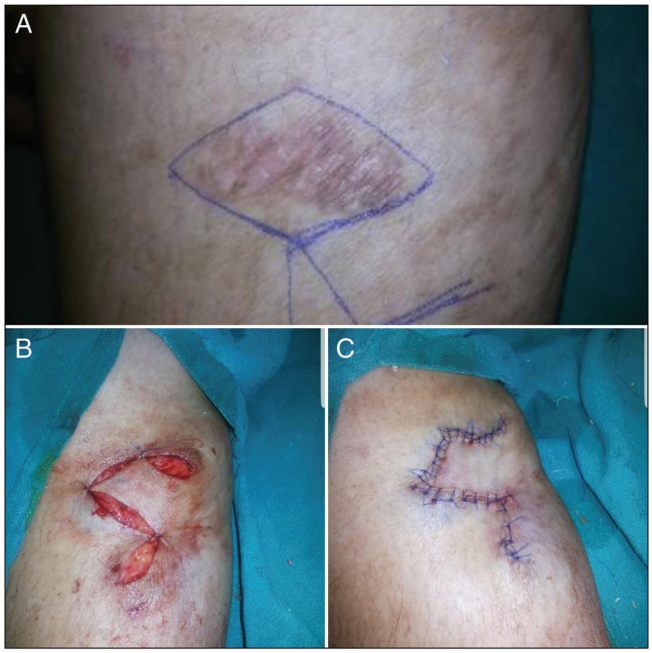

Figure 1: Bowen's disease—Part 1. (A) Clinical image of Bowen's disease on the thigh. (B) Closure of excised area by the flap method. (C) Sutured site

tumors.[5] Surgery is the mainstay of treatment for all types of NMSCs. It includes Mohs micrographic surgery which is the best modality for larger tumors (> 2 cm), for invasive histologic subtypes, and for tumors at locations with higher risk of recurrence. Conventional/standard surgical excision is preferred for well-defined, smaller, nodular pre-malignant, and malignant tumors.[6] In large lesions and those at lax sites, reconstruction with local or distant flaps also constitutes an important surgical option.[7]

Owing to the increasing incidence of these tumors in our valley in the last few years and the emerging role of dermoscopy in their diagnosis, we undertook this study on the screening and treatment of various NMSCs.

Materials and Methods

This was a prospective hospital-based study conducted on patients attending the outpatient department of a tertiary care hospital, for a period of 2 years from August 2017 to July 2019. During this period, 136 patients presenting with clinical features of pre-malignant or malignant non-melanoma skin tumors were taken up for the study.

All the patients were subjected to a detailed history, general physical, and systemic examination. This was followed by a detailed cutaneous examination to ascertain the clinical variant. Dermoscopy was then done in all the cases to confirm the diagnosis, differentiate pre-malignant from malignant tumors in doubtful cases, and ease their sub-categorization. Histopathology of the biopsied specimen was additionally done (punch, edge, or elliptical or of the entire specimen after excision) to validate the diagnosis. Relevant investigations (hemogram, bleeding and clotting time, blood sugar) were done in patients who needed surgical intervention.

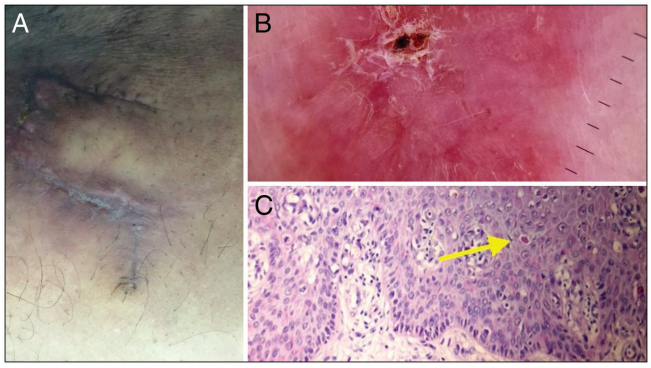

Figure 2: Bowen's disease—Part 2. (A) Excised site in the same patient (collage 1) at day 21 with scar tissue formation. (B) Dermoscopy of Bowen's disease showing brown globules, glomerular and dot vessels in clusters, surrounded by a white halo and surface scales. (C) Histopathological image of the excised Bowen's tumor with dysplastic keratinocytes with multinucleation

After proper stratification, the following treatment modalities were employed:

1. *Topical treatment*: imiquimod 5% or 5-fluorouracil for actinic keratoses and superficial BCCs;
2. Intralesional injection of methotrexate for keratoacanthomas (in those cases with co-morbidities or those reluctant for surgery);
3. *Surgical intervention*:
   a) *Simple/conventional excision*: wide local excision for BCCs (as most of them were low risk) and remaining cases of keratoacanthoma;
   b) Flap excision for Bowen's disease and SCCs.

In both types of excision, the extent of margins excised was done in accordance with the guidelines of the European Dermatology Forum and British Association of Dermatology. They, respectively, recommend 3–4 or 4–5 mm peripheral margins for low-risk BCCs (<2 cm in diameter) and 5–10 mm or greater than 5 mm peripheral margins for high-risk BCCs.[8]

In flap excision, the area to be excised was marked in a rhomboidal fashion with each side equal and the angles marked as 60° and 120°. A V-shaped flap was marked starting from a point adjacent to the angle of 120°, with both limbs of the flap also being equal and forming an angle of 60°. The lesion was then excised and the flap was undermined in the subcutaneous plane. This was followed by transposition of the flap over the rhomboidal defect in such a manner that the "V" of the flap was approximated with the diagonally opposite side to create least tension, in accordance with the conventional Limberg's flap.[9] Closure was done in the deeper layers and then in the skin using vicryl and prolene, respectively. The wound was properly dressed and a drain was placed in some selected patients.

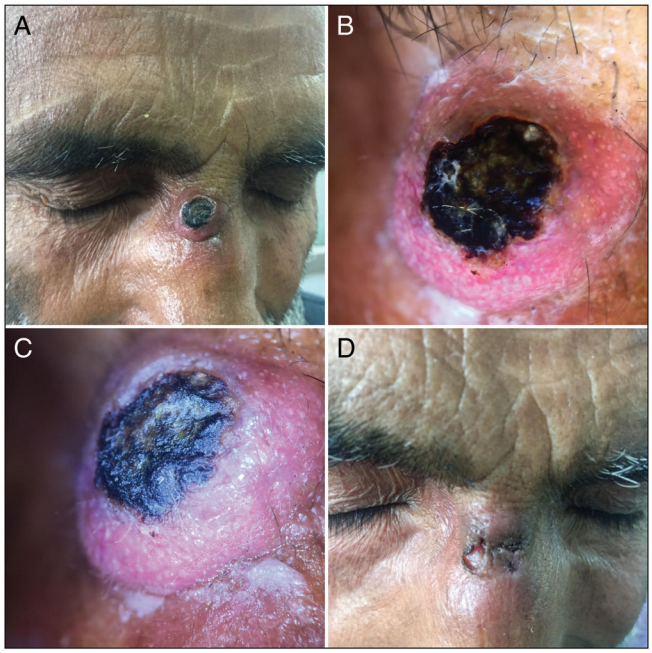

Figure 3: Keratoacanthoma. (A) Clinical image of keratoacanthoma on the nose. (B and C) Polarized and non-polarized dermoscopy of the tumor showing keratic crust, white pearls, blood spots, and atypical vessels. (D) Resolved keratoacanthoma after three doses of intra-lesional methotrexate

In non-operated patients, response to treatment was assessed at biweekly intervals for a period of 3 months or till the lesions resolved and then at 3-monthly intervals for a period of 1 year.

In operated cases, the patients were followed for any post-operative complications till the wound healed and then at 3-monthly intervals for 1 year.

Results

Of the 136 cases, 36 tumors were not amenable to standard dermatological treatment (either due to large size or atypical location—nasolabial fold, medial or lateral canthi, etc.) and were thus referred to plastic surgery department for further management. The remaining 100 cases were enrolled in our study.

A total of 100 cases of pre-malignant and malignant tumors were enrolled. The age of the patients ranged from 45 to 80 years with a mean age of 58.6 years. Males outnumbered females accounting for 68 (68%) cases, whereas the latter were just 32 (32%) in number with a male: female ratio of 2.1:1.

After proper clinical examination and dermoscopy, the tumors were classified into two broad groups: pre-malignant and malignant. The pre-malignant group accounted for 63% of the cases and included actinic keratoses (29%), Bowen's disease (19%) [Figures 1A-C and 2A], and keratoacanthoma (15%) [Figure 3A]. The remaining 37% cases were malignant in nature and included

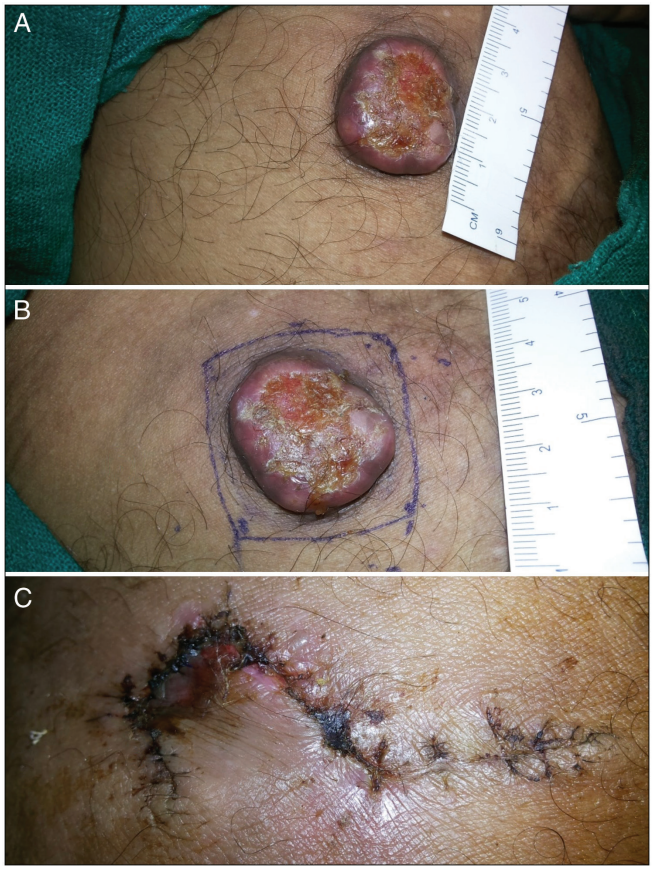

Figure 4: SCC—Part 1. (A) SCC on the thigh of a patient. (B) The same lesion marked for excision. (C) Seventh post-operative day of the same patient

undifferentiated SCCs (10%), differentiated SCCs (8%) [Figure 4A-C], pigmented BCCs (8%), nodulo-ulcerative BCCs (7%), and superficial BCCs (4%). Taken together, actinic keratosis was the most common lesion (29%), followed by Bowen's disease (19%), BCCs (19%), SCCs (18%), and keratoacanthoma (15%) [Table 1].

Face was the most common site (42 cases), followed by the thigh and leg (31 cases), hand and forearm (15 cases), abdomen (7 cases), back (3 cases), and neck (2 cases).

The dermoscopic features seen in these various tumors are summarized in Table 2 [Figures 2B, 3B, 3C, 5A, and 6B].

Out of these, actinic keratoses and superficial BCCs were treated with topical therapies (either with imiquimod 5% or 5-fluorouracil 1% cream along with frequent sunscreen application) [Figure 7A and B]. Half of the patients received imiquimod and half received 5-FU. Imiquimod 5% was applied on alternate days and then washed after 8–10 h. 5-Fluorouracil 1% cream was also given in the same manner. Both were given for a period of 3 months or till clinical resolution (>90% reduction in size) was achieved, which ever was earlier. Selection of patients for these topical

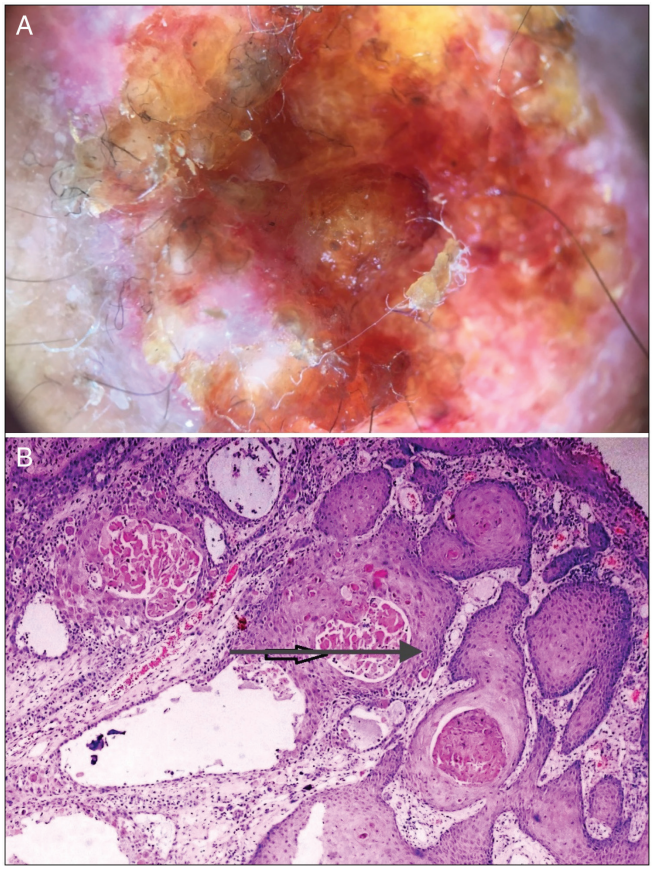

Figure 5: SCC—Part 2. (A) Dermoscopy of SCC depicting yellowish areas of keratin at the periphery and reddish-brown areas in the center representing ulceration. (B) Histopathology of the excised lesion showing well-differentiated pattern with keratin pearls

modalities was done on an alternate basis (i.e., imiquimod to one patient and 5-FU to the second and so on).

Five cases of keratoacanthoma were subjected to intralesional methotrexate (I/L MTX), 15 mg/mL, administered as 2–3 weekly injections of 1 mL each for a total of three doses [Table 1 and Figure 3D]. Thus 38 cases were treated by non-surgical modalities.

Pigmented BCCs (8 cases), nodulo-ulcerative BCCs (7 cases), and operable keratoacanthomas (10 in number) were subjected to conventional excision, making a total of 25 cases. Larger lesions such as Bowen's disease (all being >3 cm) which were 19 in number and all SCCs (18 cases) were subjected to rhomboidal flap surgery (37 in total).

In the 38 non-operated cases, 33 (86.8%) resolved by 90% at the end of 1 year. The remaining non-operated cases resolved partially and were subjected to regular follow-up after 1 year also. The unresolved cases were subjected to alternative treatment options. A few side effects such as intense erythema, bulla formation, crusting, and hypopigmentation were seen in eight patients in the first few weeks of treatment [Table 3].

In the 62 operated patients (conventional and flap), the results were very good. Fifty-five patients (22 from the conventional excision group and 33 from the flap surgery group) showed complete clearance with no immediate or delayed post-operative complications and no relapse at the end of 1 year [Figures 2C, 5B, and 6C]. However, in seven patients, complications were seen. These included localized soft-tissue infection in three cases (resolved with antibiotics) and one case each of dehiscence (resutured), delayed healing, retention of suture material, and incomplete excision (diagnosed after histopathology and re-excised) [Table 3].

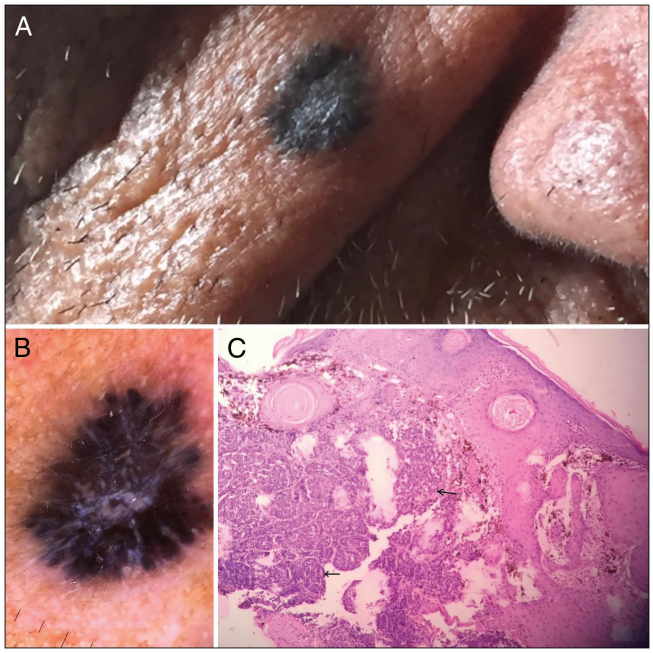

Figure 6: BCC. (A) Pigmented BCC on the cheek of an elderly man. (B) Dermoscopy depicting bluish gray ovoid areas and some maple leaf-like areas. C) Histopathology of the same case showing basaloid cells, artefactual separation of cells, and myxoid stroma

Discussion

NMSCs are not usually life-threatening but can lead to significant morbidity due to local extension. Some of them like SCCs show greater propensity for metastasis, thus resulting in considerable morbidity and mortality.[10] Hence, prompt identification of the tumor followed by proper staging and treatment is highly important for favorable outcome. This necessitates a proper local and systemic examination followed by a dermoscopic examination of the lesion (to confirm the type of the tumor), before proceeding to its definitive management.

In our study, the mean age of the patients was 58.6 years which was comparable to other studies. In a study on skin cancers from Punjab, the mean age of the patients was 62 years.[11] This is in accordance with a late onset of NMSCs seen in majority of the patients worldwide. The gender distribution of our cases (M: F ratio of 2.1:1) was comparable to a study from North India wherein the ratio was 1.8:1.[12]

The pre-malignant tumors (63%) were more common than the malignant tumors (37%) and among the pre-malignant ones, actinic keratosis was the commonest. Similar results were obtained in a study by Sajad *et al.*[13]

Topical therapy and I/L MTX yielded substantial results (90% resolution in 86.8% cases) in the cases enrolled. Between the two topicals, imiquimod gave better results with less cutaneous side effects. Our results were similar to studies wherein substantial resolution was noted in the patients, following topical imiquimod application.[14] Comparable results were observed by Annest *et al.*,[15] who found a 92% resolution rate with I/L MTX. This could be due to suitable patient selection (pre-malignant lesions and superficial BCCs) in our study and the reference study.

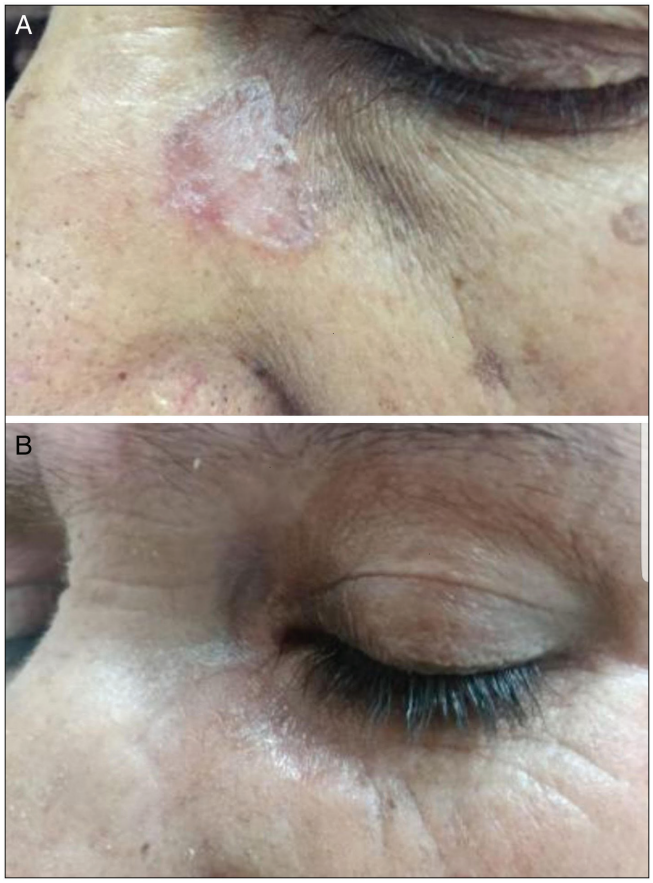

Figure 7: (A) Superficial BCC on the face. (B) After treatment with imiquimod

Wide local excision is one of the preferred modalities for smaller NMSCs, especially at centers in which Mohs surgery is not feasible. The overall recurrence rate is estimated at <2% at 5 years following complete excision in multiple studies.[16,17] In a study by Bisson *et al.*,[18] complete clearance was achieved in 93% of the cases. In our study, we obtained a comparable clearance rate of 88% following wide local excision with no relapse at 1 year. In three patients, incomplete excision was demonstrated after histopathology of the excised tumor. Such patients were subjected to re-excision.

Local flap surgery is the standard surgical modality for large lesions in which simple closure is not possible. Moreover, it provides a cosmetic effect as the donor tissue provides a similar color, texture, and thickness to the recipient area (being adjacent to it) and has higher survival rate when compared with a skin graft.[19]

Among the multiple variants of flaps, we preferred the rhomboidal flap (a subtype of Limberg's flap), being well suited for large defects on the trunk and limbs. Numerous studies have demonstrated the safety and versatility of this flap in many areas of the body.[20] In a study by Divya *et al.*,[21] 8 out of 12 cases (66.7%) operated by the rhomboidal flap method showed excellent results. Our study too yielded substantial results wherein 89.1% of the cases were operated successfully with no complications or sequelae.

Conclusion

So non-melanoma skin tumors should be promptly identified and subtyped by clinical examination, dermoscopy, and histopathology (depending on the case). This will help the clinician to delineate the treatment modality (medical or surgical) specific to each case and eventually reduce the long-term morbidity and mortality due to these tumors. Inability to perform skin grafts and other types of flap surgeries were the limitations of this surgery.

Financial support and sponsorship

Nil.

Table 1: Clinico-dermoscopic classification of cases with treatment modality employed

S. no.	Type of lesion	Frequency (%)	Treatment option employed
1.	Actinic keratoses	29 (29%)	Topical treatment
2.	Bowen's disease	19 (19%)	Rhomboidal flap excision
3.	Keratoacanthoma	15 (15%)	5 cases—I/L MTX 10 cases—conventional surgery
4.	Undifferentiated SCC	10 (10%)	Rhomboidal flap excision
5.	Differentiated SCC	8 (8%)	Rhomboidal flap excision
6.	Pigmented BCC	8 (8%)	Conventional surgery
7.	Nodulo-ulcerative BCC	7 (8%)	Conventional surgery
8.	Superficial BCC	4 (4%)	Topical treatment

Table 2: Dermoscopic features of the pre-malignant and malignant tumors

S. no.	Cutaneous tumor type	Dermoscopic features
1.	Actinic keratoses	Pink/red pseudonetwork and erythema around hair follicles Linear or wavy vessels around hair follicles Hair follicle openings filled with yellowish keratotic plugs
2.	Bowen's disease	Brown globules, glomerular and dot vessels in clusters, surrounded by a white halo and surface scales with few white rosettes
3.	Keratoacanthoma	Keratin crust or scale, white circles and pearls Blood spots, glomerular, linear irregular, hairpin, and atypical vessels
4.	Undifferentiated SCC	Pink areas seen centrally and in irregular spatial arrangements. Larger number of vessel types with irregular, bizarre vessel forms in irregular arrangements; vessels without a white halo
5.	Differentiated SCC	Pink areas distributed evenly around the periphery of the lesion Dot, glomerular, and hairpin vessels and fewer numbers of vessel types; vessels with a white halo
6.	Pigmented BCC	Blue-gray ovoid nests, maple leaf like structures, whitish-blue veil, ulcerations, spoke wheel patterns
7.	Ulcero-nodular BCC	Ulceration, arborizing vessels, blue gray globules and white areas
8.	Superficial BCC	Blue-gray globules, in-focus dots, chrysalis-like structures, concentric globules, and fine telangiectasia

Table 3: Outcome of cases

S. no.	Treatment modality	Frequency of cases operated	Resolution/ clearance	Complications	Frequency of complications
1.	Non-surgical treatment	38	33 (86.8%)	Intense erythema, bullae formation, crusting, and hypopigmentation	8
2.	Conventional excision	25	22 (88%)	Incomplete excision	1
				Delayed healing	1
				Retention of suture material	1
3.	Flap excision	37	33 (89.1%)	Dehiscence	1
				Localized soft-tissue infection	3

Conflicts of interest

There are no conflicts of interest.

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