



International Journal of Surgery Science

E-ISSN: 2616-3470
P-ISSN: 2616-3462
© Surgery Science
www.surgeryscience.com
2019; 3(4): 383-387
Received: 09-08-2019
Accepted: 12-09-2019

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Clinicopathological and surgical management of skin cancer: Experience from high altitude region of Ladakh

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DOI: <https://doi.org/10.33545/surgery.2019.v3.i4g.273>

Abstract

The Ladakhi population pay a heavy price for living in this beautiful place, as the high altitude sunlight with increased ultraviolet radiation predisposes them to various skin conditions including malignancy. Skin cancers are relatively uncommon malignancies, however recent studies have shown an increase in the number of skin cancer all over the world. We also noticed progressive increase in number of patient presenting with suspicious skin lesion in recent years. Like in rest of India we noticed all three form of skin cancer-basal cell carcinoma, squamous cell carcinoma and malignant melanoma. Being a surface malignancy, it can be diagnosed even in peripheral set up like our and could be managed in our remote set up with potential cure. Our aim was to study the clinical and clinicopathological profile of the skin cancer patient from Ladakh.

Keywords: High altitude, ultraviolet radiation, Ladakh, skin cancer

Introduction

The climate of Ladakh is so harsh that you can get frostbite and sunburn at the same time', so goes the saying in Ladakhi. Ladakh is a high altitude mountainous terrain located in the northern most part of India. It is located at the height of 3500 metres above sea level, way above the altitude of 2700 metres above sea level considered as a working definition of high altitude^[1]. The low quantity of oxygen in the rarefied atmosphere, very low humidity, extreme subzero temperature in winter, high velocity wind and increased exposure to ultraviolet radiation in sunlight predisposed the inhabitant to wide spectrum of skin lesion including skin malignancy. Very little has been written about the skin related maladies in high altitude region of India which include the western Kashmir, higher reaches of Uttarakhand and Arunachal Pradesh and Ladakh. Most of the studies about high altitude and malignant skin condition come from western countries. With this study we hope to throw some light on high altitude and skin malignancy in Indian scenario.

In Indian, skin cancer constitute 1-2% of all the diagnosed cancer^[2]. Though national survey and cross country data are not available, various cancer registry in India are showing a cumulative increase in the incidence of skin cancer over past decade^[3]. As per national cancer registry programme, the incidence of skin cancer in India is less than western countries but because of large population and limited study, the estimated number of cases is considered to be significant^[4].

Broadly speaking, the malignant disease of skin is classified into a) basal cell carcinoma. b) Squamous cell carcinoma. c.) malignant melanoma. World over BCC is the most common malignancy of skin. Most of the studies in India however show Squamous cell carcinoma to be the most common skin cancer^[5]. Various recent studies have shown an emerging increasing trend of basal cell carcinoma in Indian population also^[3].

The incidence of non melanotic skin cancer is inversely proportional to the degree of pigment in the skin presumably due to protective effect of melanin on ultraviolet induced skin damage^[6, 7]. Also the disease is commoner in fairer skin people as quoted in almost all the study.

However whether the data published so far in Indian context of skin malignancy is also applicable to Ladakhi population need to be seen as, Ladakh is geographically, genetically and racially distinct from population in Indian Subcontinent. And our study is an effort to demonstrate this variability.

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Material and Method

It is a retrospective study carried out on local of Ladakh who were treated by us for suspicious skin lesion at district hospital Leh and sub-district hospital Nubra between the Year June 2017 to June 2019. A total of 35 patients were included. These Patients data were analysed including their history, clinical examination and baseline investigation done. Special investigation like USG and CECT had been done only in few indicated cases. Most of the cases were operated at Leh and Nubra and the tissues were sent to laboratories of repute in Delhi as the facility of histopathological examination was not available. Few cases were referred to higher centre for oncological consultation

Result and Discussion

The number of patients included in the study is 35 and all the patient included were natives of Ladakh.

Contrary to the only study published regarding the overall skin related maladies in high altitude Ladakh in Indian journal of dermatology by Singh et al, who reported very low or no case of skin cancer in Ladakh, our study showed an appreciable number of skin cancer in local population [8].

Like in rest of india where squamous cell carcinoma is the most common skin malignancy histologically, contributing to 55.8% of all skin cancer followed by melanoma and basal cell carcinoma at 26.1% and 18.1% respectively [9]. Our study also showed that squamous cell carcinoma was the commonest at 48.57% followed by basal cell carcinoma at 34.28% and melanoma was rarer at 14.28% (table no. 3) We also witnessed certain rare variant of skin cancer like adnexal tumor of scalp, spindle cell variant of squamous cell carcinoma and actinic Cheilitis with squamous cell carcinoma in situ.

Adnexal neoplasms of skin are very rare skin tumor. It constitutes 1-2% of all the skin cancer [10]. It exhibit morphological differentiation towards one of the different types of adnexal epithelium present in the normal skin like Pilosebaceous unit, eccrine and apocrine glands. Most important cause suggested for malignant adnexal skin cancer is ultraviolet radiation [11].

Another rare variant of skin cancer that was observed here was actinic cheilitis [12, 13]. Actinic cheilitis is a premalignant condition of skin which occurs due to prolonged exposure to UVB radiation. This condition if not treated at time progress to squamous cell carcinoma of lip. In our study we saw all spectrums of actinic cheilitis. With actinic cheilitis with co-existing squamous cell carcinoma at one hand and frank squamous cell carcinoma of lip on the other hand. Incidentally the entire three patients were working as porter with Indian army at extreme high altitude of siachen glacier the highest battle field in the world. This finding further consolidated the fact that all form of skin cancer could be attributed to ultraviolet exposure and added on in this case by high albedo effect [14] due to snow covered ground throughout the year, thus shortening the duration between exposure and appearance of symptoms. Singh et al also echoed similar observation with high incidence among locals [8].

Another rare form of squamous cell carcinoma observed in our study was spindle cell variant of squamous cell carcinoma of hand and leg. It was first described by Martin and Stewart in 1935 [15]. It occurs on area with high level of sun exposure, but it is also seen in patient with history of radiation. The radiation induced spindle cell variant of SCC is very aggressive but the one which arise de novo behave like the conventional squamous cell carcinoma. They present like a nodule with or without bleeding and ulceration. Histopathologically spindle cell SCC composed of atypical spindle cells arranged in whorled pattern

[15].

Most of the patient with carcinoma of skin were in their sixties and seventies [16] (table 1) as seen in all the studies published earlier worldwide. Some also reporting epidemic like increase in the number of cases with increased life expectancy especially in western world.

The youngest patient noted in our study was a 37 year old local who had actinic Cheilitis with squamous cell carcinoma in situ and the oldest noted in the study was an old man of 86 years who had Kerato Acanthoma of face.

As far as sex distribution was concerned the condition was commoner in male patient than female. The sex ratio observed in our scenario was 55.5%: 44.4% [16, 17] (table 2)

The duration of symptoms (table 4) suggest that none of the patient was aware that the presenting lesion could have malignant potential so the delay in reporting to the hospital. In fact most of the patients were not aware of an entity called skin cancer. Most of the patient presented on an average beyond 6 months after appearance of lesion. In cases of squamous cell carcinoma arising over area of chronic inflammation and post burn scar the underlying lesion was present for several months with duration as long as 16-18 months [18]. The delayed presentation happened due to lack of pain and disability and poor access to the healthcare professional. And in most of the cases there is history of application of ointment application, purchased over the counter and in many there is history of consulting local *amchi* (traditional doctors) or faith healers.

Most of the patient belonged to lower socioeconomic strata with only 7 (20%) out 35 patients belonging to middle class [19].

Risk factor common to all was that they all lived in high altitude Ladakh. All of them had fair skin and none used protective agent like sunscreen, hat or goggles [20, 21]. Unfortunately none knew about the risk of prolonged exposure to sunlight. Some of the other risk factor observed was chronic non healing wound [22] and poor personal hygiene and presence of congenital nevus in two patients [22]. None of the patient gives any history of exposure to carcinogenic chemicals [23] except fertilizer as use of pesticide and insecticide is very minimum in rural Ladakh.

The malignancy of skin has varied clinical presentation (table 4). Gross appearance of lesion varied widely (table 5). The most common lesion noted in our study was an ulcerative lesion (25.71%) followed by nodular 14.285%, noduloulcerative 14.28% and skin induration 14.28%. The basal cell carcinoma group had additional features like pigmentation, keratinisation, scabbing and indurations.

Squamous cell carcinoma presented as nonhealing ulcer, especially over chronic wound and scars. It also showed associated symptoms included pain, itching, serosanguinous discharge with scabbing and lymphadenopathy.

While a case of malignant melanoma presented with history of rapid increase in size and induration of the congenital pigmented nevus of scalp, two of the other case both acral lentiginous melanoma who presented very late with lymph node metastasis and systemic metastasis. Another female (Lentigo Maligna melanoma) also showed rapid increases in the size of pigmented macule over face, the lesion covering almost the entire upper cheek, but refused treatment. One case showed a large melanocytic lesion which showed rapid increase over last two year period.

As depicted in table 6 Most of the lesion suspicious of malignancy developed over the sun exposed area of head and neck especially over the face 48.57% comparable to other study [24]. In our study BCC over rare site like popliteal fossa, shoulder and arm were also seen.

SCC the most frequent type of skin cancer occurred over sun exposed and damaged areas like lip and hand. In our study 3 patient of scc had associated chronic wound and inflammation especially burn scar thus proving that SCC arise from long standing wounds.

Two cases of rare variant of scc (spindle cell variant) was seen in the palm and ankle. In the spindle cell variant of squamous cell carcinoma the keratinocytes infiltrate into the dermis as single cell with elongated nuclei, not as a cohesive nest or island and there are no/minimal sign of keratinisation of squamous cell carcinoma [15]. This condition occur in elderly individual with

history of significant sun exposure like rest of the skin cancer Most of the skin cancers were managed at district and subdistrict hospital with good results [table 9]. Only three cases, two cases of advanced melanoma and one case of advanced squamous cell carcinoma of penis was refered to tertiary care centre for surgical oncological consultation.

Most of the wound after wide local excision were closed primarily however reconstruction needed in some cases were dealt by split thickness skin grafting and fasciocutaneous flaps (table 8).

Table 1: Age distribution of patients (n=35)

S No	Age (years)	Nos	Percentage (%)
1.	0-9	0	0
2.	10-19	0	0
3.	20-29	0	0
4.	30-39	5	13
5.	40-49	4	11.1
6.	50-59	6	16.6
7.	60-69	8	30.55
8.	70-79	9	22.22
9.	80-89	3	8.3
10.	90-99	0	0

Age wise distribution of the patient included in the study with malignancy of skin showed 52.77% of all the patient were in the age group of 60-79%. While 27. 7% of the patient belonged to the age group of 40- 59%. The oldest patient was 86 years old with kerato acanthoma and the youngest was a 37 years old local who worked as a porter in Siachen glacier, who had actinic cheilitis with squamous cell carcinoma in situ.

Table 2: Sex distribution of patients (n=35)

S No	Items	Nos	Percentage (%)
1.	Number of male patients	20	55.5
2.	Number of female patients	15	44.4

Of all the patient studied 20 (55.5%) were male and 15 (44.4%) were female showing male preponderance in the incidence of disease.

Table 3: Histopathological diagnosis of patients

S No	items	No of patients	Percentage (%)
1.	Basal cell carcinoma	12	34.28%
2.	Squamon cell carcinoma	17	48.57%
3.	Malignant malenoma	05	14.28
4.	Adnexal tumor	01	2.85%
		35	

Out of 35 patient maximum number of lesion 48.57% was found to be squamous cell carcinoma as seen in rest of india which was followed by basal cell carcinoma 34.28%.Five out of 35 patient had malignant melanoma constituting 14.28% of all the cases. One patient was found to have adnexal tumor.

Table 4: Symptoms of skin malignancy site and duration of symptom

S No	Site	Duration	Characteristics of lesion ± pigmentation
1.	Rt Cheek	5-8 months	Noduloulcerative lesion with pigmentation
2.	Rt Cheek	9-11 months	Nodulo ulcerative lesion without pigmentation
3.	Lower lip	9 months	Non healing ulcer
4.	Chin	5-6 months	Indurated ulcer
5.	Scalp	2 -4 months	Indurated lesion with brownish pigmentation
6.	Lt leg	7-8 months	Verrocous lesion
7.	Upper lip	1-2 year	Indurated lesion with blackish pigmentation
8.	Left ear	5-6 months	Ulcerative lesion
9.	Nose rt ala	8-9 months	Ulcerative lesion with crusting and pigmentation
10.	Rt nasolabial fold	6 months	Nodular lseion
11.	Rt leg	2 year	Chronic eczematous lesion with discharge with deep seated ulcer.
12.	Rt popliteal fossa	5-6 year	non healing ulcer over post burn scar
13.	Scalp	Recurrent swelling after 6 month	Soft tissue painless swelling

		of excision	
14.	Leg rt	Approx 1 year	Large brown black noduloulcertaive lesion with inguinal lymphadenopathy
15.	Nape of neck	13 months	Soft tissue swelling
16.	Glans penis	16 months	Ulcerative lesion with discharge
17.	Glans penis	18 months	Fungating growth penis with inguinal lymphadenopathy
18.	Lower lip	6 months	Erythematous scaly plaque like lesion
19.	Tip of noise	12 months	Noduloulcerative lesion without pigmentation
20.	Eyelid	6 month	Nodular lesion with keratin horn
21.	Cheek infront of ear	1 year	Nodular swelling keratin horn
22.	Shoulder	1 year	Non healing ulcer with brownish black pigmentation and crusting
23.	Upper trunk	13 months	Plaque like lesion crusting and ulceration
24.	Tip of nos e	14 month	Ulcer with rolled out everted edges
25.	Rt forearm	1 year	Plaque like lesion with scaling
26.	Lt leg	8 month	Painless soft tissue swelling
27.	Rt big toe	2 year approx	Subungual nodular lesion with pigmentation and inguinal lymphadenopathy and liver metastasis
28.	Face Lt cheek	2-3 years	Progressive increase in the size of pre-existing macular lesion
29.	Lower lip	2 -3 months	Erthematous lesion with ulceration amd scaling
30.	Face over the right eyebrow	6-9 months	Pigmented nodular lesion
31.	Left forehead	8 months	Nodular lesion
32.	Trunk upper	10 months	Indurated ulcerative lesion
33.	Sole	8-9 months	Ulcerative lesion over burn scar
34.	Left forearm	17 months	Indurated lesion with keatinization
35.	Nape of the neck	9 months	Papule wilth central erosions

Table 5: Gross appearance of the presenting lesion

S. No	Item	Nos	Percentage (%)
1.	Ulcerative lesion	9	25.71%
2.	naevi	2	5.71
3.	papule	1	2.8
4.	plaque	3	8.57
5.	Verrucous growth	2	5.7
6.	Noduloulcerative lesion	5	14.28
7.	nodular	5	14.28
8.	Soft tissue swelling	3	8.57
9.	Skin induration	5	8.57

Gross appearance of the lesion were varied ranging from ulcerative lesion in 25% followed by nodular 14.28%, noduloulcerative in 14.28% lesion and indurated skin lesion with erythema.8.57% had soft tissue swelling and plaque like lesion. Malignancy Arised from pre-existing Naevi and Verrucous growth in 5.71% individual.

Table 6: Anatomical distribution of lesion

S No	Anatomical location of the lesion	Number of patients	Percentage (%)
1	Face	17	48.57%
2	Scalp	2	5.71%
3	Neck	2	5.71%
4	Upper limb	2	5.71%
5	Lower limb	7	20%
6	Penis	2	5.71%
7	Chest wall	2	5.71%
8	Trunk	1	2.8%

Anatomical distribution of lesion show that the most common site of lesion is definitely the face as it is the exposed part of the body. Face constituted 48,5% of all the site in the body for occurrence of malignancy, followed by lower limb where 20% of all the lesion occurred. Lesion was equally distributed (5.71%) over scalp, neck, upper limb, penis and chest wall. least common site of lesion was the trunk.

Table 7: Types of surgery performed

S No	Type of surgery performed	Number of patient	Percentage (%)
1	Wide local excision	30	85.71%
2	Amputation of limb	2	5.71%
3	Partial amputation of penis	1	2.85%
4	Total amputation of penis with lymph node dissection	1	2.85%
5	Refusal of treatment	1	2.85%

Most of the lesion were amenable to wide local excision Two of the patients with malignant melanoma underwent amputation at higher centre. One patient with ulcerative lesion of glans penis, underwent excision biopsy which was suggestive of squamous cell carcinoma, he later underwent partial penectomy. Prophylactic Lymph Node dissection was not carried out as it was not palpable. One patient with fungating growth with bilateral inguinal lymph node metastasis was also referred to a higher centre for further management.

Table 8: Wound coverage after excision of lesion

Item	Numbers	Percentage (%)
Primary closure	20	42.85%
Flap cover	7	20%
Split skin grafting	7	20%

Most of the defects (42.85%) after excision were closed by primary closure. 7 patients out of 35 (20%) required local fascio cutaneous flap to cover the defect and in 7 patients(20%) defect after excision mainly over limbs were covered by split skin grafting.

Table 9: Place of management of the patients.

Item	Nos	Percentage (%)
Number of patient managed at Leh and Nubra	31	88.57%
Number of patient refered to higher centre	3	8.51%

All the 35 patient studied were locals. They were diagnosed of their illness at our centres and 31 (88.57%) out of 35 patient were given definitive treatment in our hospital However the tissue excised were send to laboratory outside Leh for histopathological examination One patient after being diagnosed refused any intervention. Three out of 35 patients (8.51%) had to be referred to higher centre to tertiary care centre for advanced investigation and oncosurgical reference.

Conclusion

In the first of its kind, our study on skin malignancy and high altitude proved beyond doubt that the people of Ladakh are definitely at high risk of developing skin malignancy both nonmelanomatous and melanoma. Due to lack of a proper cancer data registry system in place percentage of skin cancer could not be defined but, sheer number of case point toward a relatively increased incidence. This could be attributed to the only persistent risk factor common to all the cases i.e prolonged exposure to sunlight. However the uneducated people has to be made aware of the entity

Called' skin cancer 'and ways of preventing it, as exposure to the sun cannot be avoided as sitting in glass room for warmth of the sun especially during the cold winter months is a way of life. Because pain is very late symptom of the disease, patient try various off the counter ointment, faith healer etc before presenting to the hospital. Also number of the cases had chronic non healing wound especially post burn which were not managed by proper health worker due to poor access to it. Since skin malignancies are surface malignancy, no advance technology like CECT, MRI etc are needed to diagnose it. If the clinician even at remote places like ours are aware of these entity these lesions could very well be diagnosed at peripheral set and could be managed without incurring economic burden to the patient of going to big cities.

Acknowledgment: Our sincere thanks to all the patients who gave their consent to be part this study.

Funding: none.

Conflict of Interest: None.

Ethical approval not required.

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