Basal Cell Carcinoma in Cases with or without Xeroderma Pigmentosum

Dilasma Ghartimagar,[1] Arnab Ghosh,[1] Sushil Ram Shrestha,[2] Sachet Shrestha,[3] Sushma Thapa,[1] Raghavan Narasimhan,[1] OP Talwar [1]

[1]Department of Pathology, Manipal College of Medical Science, Pokhara, Nepal, [2]Department of Pathology, Kanti Children's Hospital, Kathmandu, Nepal, [3]Department of Ophthalmology, Manipal College of Medical Science, Pokhara, Nepal.

ABSTRACT

Introduction: Basal cell carcinoma is the most common form of cancer in humans and comprises the vast majority of skin cancers. It predominantly affects fair-skinned individuals, and its incidence is rapidly increasing. The objective of the study is to identify the epidemiology, its topography and different histological subtypes of basal cell carcinoma in patients with or without Xeroderma Pigmentosum.

Methods: A cross-sectional descriptive study was conducted at Manipal Teaching Hospital, Pokhara from Jan 2009 to Dec 2016. Ethical approval was taken from MEMG/IRC/GA. The study included patients with a confirmed diagnosis of basal cell carcinoma irrespective of their age and sex.

Results: This study showed 77 individuals with 91 biopsies of BCC including 5 cases of Xeroderma Pigmentosum. The predominant histological subtype was nodular with 41 (53.94%) cases, followed by the 14 (18.42%) cases of pigmented and 10 (13.15%) cases baso-squamous subtype. The most frequent sites of involvement were the head and neck, with predominance in the nasal and orbital region. The mean age was 57.68 years but the basal cell carcinoma in cases of Xeroderma Pigmentosum was seen more in younger age groups. There were 43 (55.84 %) male patients and 34 (44.16 %) female patients with a male to female ratio of 1.26:1.

Conclusions: Nodular and pigmented varieties were the most frequent subtypes with nose being the commonest site of involvement. Basal cell carcinomas in cases of Xeroderma Pigmentosum were noted in younger age group with multiple lesions.

Keywords: *basal cell carcinoma; recurrence; topography; xeroderma pigmentosum.*

INTRODUCTION

Basal cell carcinoma (BCC) is the most common skin cancer. It usually occurs in the elderly population and has a higher incidence with increasing age.[1] It is quite rare in the pediatric population and often occurs in the presence of predisposing genetic conditions like Xeroderma Pigmentosum (XP). Etiology for BCC can be multifactorial, but sun exposure appears to play a critical role.[2]

BCC originates from the pluripotent cells in the epidermis and hair follicles. It is a slow growing tumor and may take years to enlarge significantly. It can cause extensive local tissue destruction if the diagnosis is not made on time or left untreated. The mortality rates of this cancer are low.[3]

This study shows the incidence of BCC with or without Xeroderma Pigmentosum, its topographical distribution and histological subtypes along with recurrences of the tumor.

Correspondence: Dr. Dilasma Ghartimagar, Department of Pathology, Manipal College of Medical Science, Pokhara, Nepal. Email: dilasmagm@hotmail.com, Phone: +977-9840603962.

METHODS

A cross-sectional descriptive study was conducted in the Department of Pathology, Manipal Teaching Hospital, Pokhara from Jan 2009 to Dec 2016. Ethical approval was taken from IRC, MCOMS, Pokhara with approval number MEMG/IRC/GA. The study included patients with a confirmed diagnosis of BCC with or without Xeroderma Pigmentosum irrespective of their age and sex. Patients presenting with other skin and adnexal cancers were not included in the study. All specimens were sent to histopathological examination from our hospital and other hospitals within Pokhara valley. Relevant clinical history, duration of the lesion, location and recurrences of the cancer were analyzed. The skin biopsies were routinely fixed with 10% formalin. After fixation, sections were given from the skin lesions including its all four margins and base. The slides were stained with H&E stains and also with special stains wherever required. The data were analyzed using Microsoft Excel and SPSS 21.0 version.

RESULTS

The study included 77 individuals with 91 biopsies of BCC including five cases of XP. The age of the patient ranged from 5 to 82 years with a mean age was 57.68 years. Basal cell carcinoma occurring in cases of XP was seen more in younger age groups. There were 43 (55.84%) male patients and 34 (44.16%) female patients (Figure 1) with a male to female ratio of 1.26:1.

Most cases of BCC were located on the head region with 72 (94.73%) cases. Anatomical distributions of the lesions were as follows: the nose 22 (28.94%) cases, periorbital region 20 (26.31%) cases, cheek 11 (14.47%) cases, ear 8 (10.52%) cases, forehead 5 (6.57%) cases, lip 2 (2.63%) cases, temporal region 1 (1.31%) case and neck 3 (3.94%) cases. The predominant histological subtype was nodular BCC which included 41 (53.94%) cases, followed by 14 (18.42%) cases of pigmented type and 10 (13.15%) cases of baso-squamous subtype (Table 1).

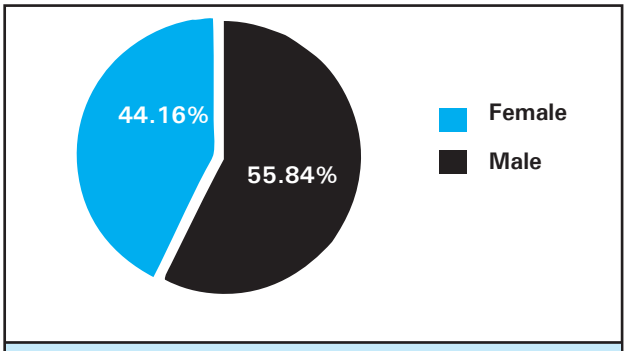

Figure 1. Gender percentages of BCC patients.

Table 1. Basal cell carcinoma cases without Xeroderma Pigmentosum.

	Subtypes of BCC							
Site of involvement	Nodular	Pigmented	Baso-squamous	Adenoid	Cystic degeneration	Superficial	Morphea type	Total
Forehead	3	1	1					5
Nose ala	15		1	1	1			18
Nasolabial fold	1	3						4
Eye lids	9	4	4	2			1	20
Ear pinna	2	2	2	2				8
Temporal region			1					1
Cheek	8	2	1					11
Neck	2						1	3
Chest wall	1							1
Axilla						1		1
Back		1				1		2
Angle of mouth / lip		1		1				2
Total	41	14	10	6	1	2	2	76

There were 4 repeat biopsies in cases of BCC without XP and 10 repeat biopsies in cases of BCC with XP. 61 lesions were smaller than 10mm (67.03%), 24 lesions were between 10 and 20mm (26.37%), and 6 lesions were bigger than 20mm (6.59%) (Figure 2).

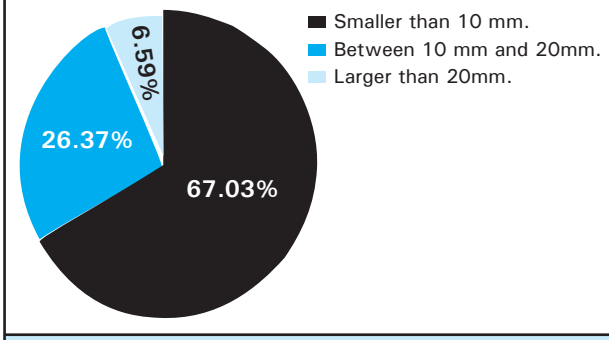

Figure 2. Diameter of BCC lesions.

All 5 cases of XP had multiple lesions in the head and neck region (Table 2). The lesions were excised more than once in 4 cases of XP. Four BCCs (4.3%) required re-excision of the tumor because of involved margins. The surgical bases in all cases were negative for the tumor. During the follow up, we found the recurrence of the tumor in 3 (3.29%) cases and all occurred during the first two years of diagnosis of BCC. The recurrence of the tumor was seen in one each case of left temporal region, right nasolabial fold and left lower eye lid.

Table 2. Basal cell carcinoma cases with Xeroderma Pigmentosum.

Case	Sex	Age at presentation	Total biopsy	Sites of involvement	Diagnosis
1	M	10	3	Right and left ala of nose Left nasolabial fold Left check Angle left eye Left lower eye lid	Keratotic BCC
		10		Nape of neck	Nodular BCC
		19		Left nasolabial fold	Keratotic BCC
2	M	5	4	Nose ulcer Upper lip	Nodular BCC with SCC
		7		Right forehead Left cheek	Nodular BCC
		10		Eyelid	Keratotic BCC
3	F	16	5	Right pina	Nodular BCC
		16		Cheek	Squamoid BCC
		18		Left lower eye lid	Pigmented BCC
		20		Left lower eye lid	Pigmented BCC with squamoid and adenoid area
4	F	17	1	Left eye brow	Nodular BCC
5	M	14	2	Eye, cheek, lip, nose, ear	Nodular BCC
		14		Eye, cheek, lip, nose, ear,	Pigmented BCC
Total			15		

*BCC – Basal cell carcinoma, † XP – Xeroderma Pigmentosum

Table 3. Distribution of Basal cell carcinoma cases according of age and sex.

Age range (Years)	Male	Female	n (%)	CI
<20	4	3	7 (9.09)	(6.42, 16.71)
21-40	1	3	4 (5.19)	(34.96, 41.53)
41-60	18	10	28(36.36)	(48.46, 53.39)
61 -80	17	15	32(41.55)	(68.61, 72.82)
>80	3	3	6 (7.79)	(82.53, 90.12)
Total	43	34	77 (100)	(53.13, 62.22)

Table 4. Comparison of Basal cell carcinoma with or without XP in different age groups.

	Age		Total	P value
	<40yrs n (%)	≥ 40yrs n (%)		
BCC with XP	5 (100)	0 (0)	5	0.001
BCC without XP	4 (5.6)	68 (94.4)	72	
Total	9 (11.7)	68 (88.3)	77	

*BCC – Basal cell carcinoma, † XP – Xeroderma Pigmentosum

DISCUSSION

Basal cell carcinoma is considered as the most common skin malignancy with its increasing incidence worldwide due to increased exposure to UV light and ozone depletion in various parts of the world as a result of environmental and industrial pollution.[2] BCC occurs in 200 to 600 cases per 100,000 individuals in the white population and 3.5 cases per 100,000 individuals in the black population worldwide.[4] Excessive exposure to UV radiation have been found to be major etiologic factors which results in DNA damage which finally increases the risk for BCC.[2,3] In the present study, no predisposing factors other than exposure to sunlight could be identified. Since agriculture is the major source of livelihood of our country, most of the patients had a history of chronic sun exposure. BCC has been linked with various syndromes also like Bazex, Nevoid Basal Cell Carcinoma Syndrome, Rasmussen and Darier's disease because of mutations in Sonic hedgehog pathway.[2,5]

The majority of BCC occur in men, and the ratio of male to female in our study was 1.26:1. In other studies also, there were male predominance.[1,2,6] The higher incidence of BCC in men is probably due to increased occupational exposure to the sun. However, the incidence in women is also increasing because of changing fashions in lifestyle and higher participation of women in the labor market.[1,6]

The mean age of the study was 57.68 years. Several studies have shown that majority of skin cancers are seen in individuals above 50 years or older.[7-10] The older people are more prone to develop BCC, however, they have also been reported in young adults and children.[11] In our study, the maximum number of cases (32, 41.55%) were seen in the age group of 61 to 80 yrs (Table 3).

Up to 80% of all BCCs are found on head and neck with face being the most common site in both genders. These regions are the main sun-exposed areas for the development of skin cancers.[6,12] About 15% develop on the shoulders or trunk.[12] Present study also showed 95.60% cases of BCC in the head and neck region which corroborates well with other findings in the literatures.[6,12-14]

Nodular BCC shows large lobules of basaloid cells with peripheral palisading of nuclei which extends deeper into the dermis.[12] The most common histopathological pattern in our study was nodular BCC which was similar as other studies.[4,6,12,15] Pigmented BCC shows basaloid tumor cells along with melanin pigmentation and this tumor should be differentiated from melanoma clinically.[3] There were 17 cases of pigmented BCCs including 3 cases from XP in the present study which all showed tumor with melanin pigmentation. Baso-squamous carcinoma has both basal and squamous differentiation.[3] Our study showed 10 cases of baso-squamous type. Adenoid BCC shows thin strands of basaloid cell arranged in reticulate pattern.[11] Our study showed 6 cases of adenoid BCC. Other variants like cystic, superficial and morphea type were also noted in the study (Table 1).

Although the results of primary excision are excellent, recurrences can occur. Recurrence rates are higher in the inner canthus, base of the nostril and auricular areas. This may be due to scarcity of tissue, proximity to vital structures and cosmetic region which should be taken into consideration while treating lesions on these locations.[3] We observed recurrence in 3 (3.29%) cases.

Even though majority of BCCs are slow growing and comparatively non-aggressive, a minority have an invasive behaviour with local tissue damage and infrequently, metastasis. Metastasis has been reported only in 0.0028-0.5% of all cases.[12,16,17] The present study did not show any site of metastasis.

BCC in children is unusual, but it can occur in cases of XP, a rare hereditary atuosomal recessive disorder.[18] The incidence of XP is 1:250,000 births in the USA and 1:20, 000 in Japan.[19] XP is characterized by extreme sensitivity to UV radiation and leads to more than 1,000 fold increase risk for the development of cutaneous malignancy which includes basal cell carcinoma, squamous cell carcinoma and malignant melanoma in the sun exposed part.[20] In our study, there were 5 cases of XP which showed BCCs in young age group when compared to the patients of BCC without XP (Table 4). XP cases showed nodular BCC, keratotic BCC, squamoid BCC and pigmented BCC. One case showed nodular BCC along with squamous cell carcinoma at the age of 5years in the head and neck region. Another case showed pigmented BCC with squamoid and adenoid area in the lower eye lid at the age of 20 years.

In normal persons, the body repairs the damaged genetic material (DNA) of skin cells when exposed to UV rays but in persons with XP, the body does not fix the damage due to molecular defects in genes involved in NER.[21]

XP is characterized by dermatological manifestations like severe sunburn, persistent erythema, marked freckle like pigmentation of the skin, dry pigmented skin, keratosis, and neoplasm. Patients of XP with multiple primary lesions develop skin cancer by 8 years of age.[18] In our study, we found BCC in XP with a minimum age of 5 years who had multiple lesions in the head and neck region. These children of XP may present with ocular changes before skin lesions like photophobia, keratitis, atrophy of the skin of the lids and eye tumors.[19] Our study also showed one female with keratitis and keratoconjunctivitis sicca at the age of 16 years and she presented with BCC up to 5 times.

Definitive treatment of XP is not well established, so persons with XP must avoid sun exposure and should wear protective clothing and UV absorbing eye glasses.[21]

The limitation of this study includes the fact that the study was done in only one hospital of the Pokhara valley. It may not represent the entire population, so similar studies with a larger sample size should be conducted in multiple centers which would provide clear picture of the situation.

CONCLUSIONS

Basal cell carcinoma is the most common cutaneous cancer and nose was the commonest site involved followed by the orbital region. Nodular and pigmented varieties were the most frequent subtypes of the present study. Basal cell carcinomas in cases of Xeroderma pigmentosum were noted in younger age group patients with multiple recurrences of lesions in different sites of the body.

ACKNOWLEDGEMENTS

We would like to thank Prof. Dr. Ishwari Sharma Paudel for helping us in data analyzing of this study.

Conflict of Interest: None.

REFERENCES

1. Turan E, Nurdan Yurt, YesilovaY, Turkcu G. Early-onset basal cell carcinoma. Turk J Pediatr. 2013;55:354-6. [Full Text]
2. Demirseren DD, Ceran C, Aksam B, Demirseren ME, Metin A. Basal Cell Carcinoma of the Head and Neck Region: A Retrospective Analysis of Completely Excised 331 Cases. J Skin Cancer. 2014; 2014: 858636. [PMC]
3. Abbas OL, Borman H. Basal Cell Carcinoma: A Single-Center Experience. ISRN Dermatol. 2012;2012:246542. [Full Text]
4. Pinkus H. Premalignant fibroepithelial tumors of skin. AMA Arch Derm Syphilol. 1953;67(6):598-615. [PubMed]
5. Iwasaki JK, Srivastava D, Moy RL, Lin HJ, Kouba DJ. The molecular genetics underlying basal cell carcinoma pathogenesis and links to targeted therapeutics. J Am Acad Dermatol. 2012;66(5):e167-78. [Pub Med]
6. Ferreira FR, Pevide BC, Rodrigues RF, Nascimento LFC, Lira MLDA. Differences in age and topographic distribution of the different histological subtypes of basal cell carcinoma, Taubaté (SP), Brazil. An Bras Dermatol. 2013;88(5):726-30. [PMC]
7. Adinarayan M, Krishnamurthy SP. Clinicopathological evaluation of nonmelanoma skin cancer. Indian J Dermatol. 2011;56:670-2. [Full Text]
8. Yamaguchi Y, Beer JZ, Hearing VJ. Melanin mediated apoptosis of epidermal cells damaged by ultraviolet radiation: factors influencing the incidence of skin cancer. Arch Dermatol Res. 2008 Apr;300 Suppl 1:S43-50. [Pub Med]
9. Malhotra P, Singh A, Ramesh V. Basal cell carcinoma in the North Indian population: clinicopathologic review and immunohistochemical analysis. Indian J Dermatol Venereol Leprol. 2011;77(3):328-30. [Full Text]

10. Noorbala MT, Kafaie P. Analysis of 15 years of skin cancer in central Iran (Yazd). Dermatol Online J. 2007;13(4):1. [PubMed]

11. Saldanha P, Shanthala PR, Upadhaya K. Cutaneous basal cell carcinoma: A morphological spectrum. Arch Med Health Sci. 2015;3(1):24-8. [Full Text]

12. Sreeram S, Lobo FD, Naik R, Khadilkar UN, Kini H, Kini UA. Morphological Spectrum of Basal Cell Carcinoma in Southern Karnataka. J Clin Diagn Res. 2016; 10(6): EC04–EC07. [PubMed | PMC]

13. Mantese SAO, Berbert ALCV, Gomides MDA, Rocha A. Basal cell Carcinoma - Analysis of 300 cases observed in Uberlandia - MG, Brazil. An Bras Dermatol. 2006;81(2):136-42. [Full Text]

14. Ferreira FR, Nascimento LFC, Rodrigues RF, Pevide BDC, Lira MLDA.Skin cancer in Taubate (SP) – Brazil, from 2001 to 2005: A prevalence study. An Bras Dermatol. 2008;88(5):317-22. [Full Text]

15. de Vries E, Louwman M, Bastiaens M, de Gruijl F, Coebergh JW. Rapid and continuous increases in incidence rates of basal cell carcinoma in the southeast Netherlands since 1973. J Invest Dermatol. 2004;123(4):634-8. [PubMed]

16. Chinem VP, Miot HA. Epidemiology of basal cell carcinoma. An Bras Dermatol. 2011;86(2):292-305. [PubMed | Full Text]

17. Shrivastava R, Singh KK, Shrivastava M. Soft tissue metastasis in basal cell carcinoma. Indian J Dermatol. 2007;52(4):206-08. [Full Text]

18. Mulimani SM, Talikoti DG. A child with xeroderma pigmentosum for excision of basal cell carcinoma. Saudi J Anaesth. 2013;7(4):467–9. [Full Text]