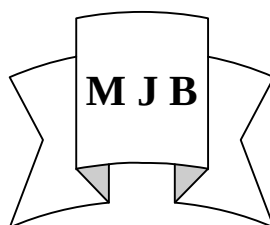


**Non – melanoma skin cancers of the face
A clinical and pathological study**

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Abstract

Non – melanoma skin cancer like basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are not an uncommon skin diseases in Iraqi patients, so this study was conducted to shed light on various clinical and histopathological aspects of these cancers affecting the face, at Hilla city.

A total of 50 patients with non – melanoma skin cancers was seen. Their ages ranged between 10 – 85 years (mean $\pm$ SD, 54.9 ± 16.1 years), while their ages of onset ranged between 7 – 80 years (mean $\pm$ SD, 52.4 ± 15.5 years). The duration of the disease ranged from 1-7 years (mean $\pm$ SD, 2.9 ± 1.5 years). There were 28 males (56 %) and 22 females (44 %) with a sex ratio of 1.3 : 1.

Twenty – nine patients with basal cell carcinomas were seen (58%). Their ages ranged between 30 – 85 years (mean $\pm$ SD 58.4 ± 13.9 years), while their ages of onset between 29 – 80 years (mean $\pm$ SD, 50.7 ± 18.4 years). The duration of the disease ranged between 1-7years (mean $\pm$ SD, 3.4 ± 1.4 years). There were 16 males (55 %) and 13 females (45 %) with a sex ratio of 1.2 : 1. The clinical types of BCCs on the face were : nodulo – ulcerative (38 %), pigmented (14 %), morpheaform (4 %) and cystic (2 %). The sites of involvement of BCCs on the face were : nose (16 %), cheeks (14 %), forehead (12 %), inner canthi of eyes (6 %), upper vermilion lip (4 %), retroauricular (4 %) and inside the auricle of left ear (2 %). The pathological types of BCCs were : nodular (40 %), pigmented (14 %) and morpheaform (4 %). The clinical types of BCCs, the sites of involvement on the face and the pathological features were comparable to what has been reported.

Eighteen patient with squamous cell carcinomas were seen (36 %). Their ages ranged between 10 – 70 years (mean $\pm$ SD, 48 ± 19 years) while their ages of onset between 7 – 68 years (mean $\pm$ SD, 54.6 ± 10.6 years). The duration of the disease ranged between 1 – 3 years (mean $\pm$ SD 1.5 ± 1.6 years). There were 9 males (50 %) and 9 females (50 %) with a sex ratio of 1 : 1. The sites of involvement of SCCs on the face were : cheeks (16 %), lower lip (8 %), upper lip (4 %), forehead (4 %), nose (2 %) and pinna of left ear (2 %). The pathological types of SCCs were : well differentiated (16 %), moderately well differentiated (18 %) and poorly differentiated (2 %). The

clinical, histopathological and sites of involvement were similar to what has been reported. The study presented the first reported case of SCC arising from a scar of localized atrophic discoid lupus erythematosus on the upper lip, in Iraq.

Other non – melanoma skin cancers of the face reported in the study were : basosquamous (2 %), mycosis fungoides (2 %) and kaposi's sarcoma (2 %).

الخلاصة

الاورام السرطانية الجلدية غير الصبغية في منطقة الوجه ، دراسة سريرية ونسجية :

تم دراسة 50 حالة من الاورام السرطانية الجلدية غير الصبغية، تراوح أعمار المرضى ما بين 10 – 85 سنة ، ومدة الإصابة تراوحت ما بين (ونسبة الذكور إلى الإناث بلغت 1.3 : 1 . 1 – 7 سنوات . بلغ عدد الذكور المصابين 28 (56 %) وعدد الإناث 22 (44 %) من العدد الكلي لهذه الاورام الغير الصبغية تم ملاحظة 29 حالة من الاورام السرطانية الجلدية القاعدية تتراوح اعمارهم ما بين 30 – 85 سنة ومدة الإصابة تراوحت ما بين 1 – 7 سنوات. عدد الذكور المصابين 16 (55 %) وعدد الإناث 13 (45 %) ونسبة الذكور إلى الإناث بلغت 1.2 : 1 . تم كذلك ملاحظة 18 حالة من الاورام السرطانية الجلدية الحشفية تراوحت اعمارهم ما بين 10 – 70 سنة ومدة الإصابة ما بين 1 – 3 سنوات. عدد الذكور المصابين 9 (50 %) وعدد الإناث 9 (50 %) ونسبة الذكور إلى الإناث 1 : 1 . تم كذلك تسجيل 3 حالات اخرى من الاورام السرطانية الجلدية غير الصبغية وهي : ورم جلدي مشترك قاعدي وطلائي حشفي ، سرطان الجلد اللمفاوي وسرطان الجلد من نوع كابوسي .

Introduction

Basal cell carcinoma (BCC) is a malignant tumor of skin composed of cells similar to those in the basal area of the epidermis and it's appendages (1) . Although a cancer, BCC is only locally invasive and rarely metastasizes (1 , 2) . Basal cell carcinoma is the most common form of skin cancer (3 , 4) . It crops up most commonly on the faces of the middle aged or elderly (3) . BCC is generally a disorder of white individuals especially those with very fair skin (5) . Men have a significantly higher incidence than women (6) . The male : female ratio is approximately 3 : 2 (5) . The tumor may occur at any age but the incidence of BCC increases markedly after age of 40

years. The incidence in younger people is increasing possibly as a result of increased sun exposure (7) . Eighty – five percent of all BCCs appear on the head and neck region, 25 – 30 % occur on the nose alone, the most common site (7) . nodulo – ulcerative type is the most common type (3) . The typical BCC runs a slow progressive course of peripheral extension which produces the thread – like margin, the nodule with a central depression or the expanding rodent ulcer (1) . Other variants are cystic, cicatricial (morpheic), superficial and pigmented (3) . Lesions of pigmented BCC contain increased brown or black pigment and are seen more commonly in individuals with dark skin (8) . The

characteristic cells of BCC (basalioma) cells have a large oval or elongated nucleus (9). The nuclei resemble those of basal cells of the epidermis but basalioma cells differ from basal cells by having a larger ratio of nucleus to cytoplasm and by not showing intercellular bridges (9). The peripheral cell layer of the tumor masses shows a palisade arrangement of the nuclei (9 , 10).

Squamous cell carcinoma (SCC) is malignant tumor arising from the keratinocytes to of the epidermis (1). SCC does not often arise from healthy looking skin. Commonly there are signs of damage from sun light : solar elastosis of the dermis, hyperkeratosis, irregular pigmentation and telangiectasia of the skin or leuko – keratosis and fissuring of the lip. The first evidence of malignancy is induration. The area may be plague – like, verrucous, tumid or ulcerated, but in all cases, the lesion feels firm when pressed between the finger and thumb. The most common sites for SCC are those most exposed to the sun, they occur on the upper part of the face and especially in males on the lower lip and pinna of ear (1). The incidence increases rapidly with age and sun exposure and is approximately twice as high in men as in women (4). Cutaneous SCC that arise secondary to

inflammatory and degenerative processes (previous x – radiation or thermal injury, chronic ulcers, chronic inflammation or Bowen's disease) have much higher rate of metastasis than those developing in sun – damaged skin (3 , 9).

Squamous cell carcinoma is a true invasive carcinoma of the surface epidermis (9). On histological examination, the tumor consists of irregular masses of epidermal cells that proliferate downwards into the dermis. The invading tumor masses are composed in varying proportions of normal squamous cells and of atypical (anaplastic) squamous cells. Atypicality of squamous cells expresses itself in such changes as : great variation in the size and shape of the cells, hyperplasia and hyperchromasia of the nuclei, absence of intercellular bridges, keratinization of individual cells and the presence of atypical mitotic figures (9). Differentiation in SCC is in the direction of keratinization. Keratinization often takes place in the form of horn pearls which are very characteristic structures composed of concentric layers of squamous cells showing gradually increasing keratinization towards the center (9).

Aim of study :

Non – melanoma skin cancers like BCC and SCC are not an uncommon skin

diseases in Iraqi patients, so the aim of this work was to shed light on various clinical and histopathological aspects of these cancers affecting the face; at Hilla city.

Patients and methods :

A total of 50 patients with in non – melanoma skin cancers were studied in department of dermatology, Merjan teaching hospital during the period from July 2005 to December 2007.

A clinical history was taken from each patient including: name , age , sex , age of onset and duration of disease; symptoms related to the lesion like pain, itching, bleeding and tenderness were recorded; and predisposing medical conditions such as albinism, xeroderma pigmentosa, epidermo dysplasia verruciformis, organ transplantation and any immune compromised state.

A thorough physical examination was performed to determine general health, type of tumor, site on the face and number of lesions. Also by examination, we tried to exclude the presence or absence of lymphadenopathy. Shaving or incisional biopsies were obtained in all patients. The biopsies were kept in 10 % formalin solution and sent for histopathological examination with hematoxylin and eosin staining methods.

Results :

A total of 50 patients with non – melanoma skin cancers (NMSCs) was seen, their ages ranged between 10 – 85 years with a mean $\pm$ standard deviation (SD) of 54.9 ± 16.1 years, while their ages of onset ranged between 7 – 80 years with a mean $\pm$ SD of 52.4 ± 15.5 years. The duration of the disease ranged from 1 – 7 years with a mean $\pm$ SD of 2.9 ± 1.5 years. There were 28 males (56 %) and 22 females (44 %) with a sex ratio of 1.3 : 1. Regarding the age of presentation, the bulk of the patients was between 40 – 80 years of age. Most of the cases were in the 6th decade of life forming about 30 % (**Figure I**).

Regarding the age of onset, most of the cases started in the 6th decade of life forming about 40 % (**Figure II**).

The types and numbers of cases of non – melanoma skin cancers seen in this study were shown in **table (1)** .

Twenty – nine patients with basal cell carcinoma were seen (58 %). Their ages ranged between 30 – 85 years with a mean $\pm$ SD of 58.4 ± 13.9 years, while their ages of onset between 29 – 80 years with a mean $\pm$ SD of 50.7 ± 18.4 years. The duration of the disease ranged between 1 – 7 years with a mean $\pm$ SD of 3.4 ± 1.4 years. There were

16 males (55 %) and 13 females (45 %) with a sex ratio of 1.2 : 1.

Clinical types of BCCs and sites of involvement were shown in **tables (2) and (3)** respectively.

The majority of patients (19) were in the form of nodular and noduloulcerative which was the classical presentation with a pink pearly shaped border, the surface of some was covered with a telangiectatic vessels **figure (1)**. The size of lesions ranged from 0.5 – 3 cm in diameter.

Pigmented BCCs were seen in 7 patients. Clinically, it was the same of nodular type but with black color **figure (2)**. Morphea form or sclerosing BCC was seen in 2 female patients, one on the nasal tip and the other on the right cheek. The lesions were firm yellowish with a waxy surface and ill – defined borders .

Cystic BCC was seen in one patient in left cheek of a 35 years old man as a smooth round pinkish cystic lesion with a telangiectatic vessels on the surface.

Nose, cheeks and forehead were the common sites of involvement of BCC on the face. Two cases of BCC, pigmented and noduloulcerated were seen on the vermilion border of the upper lip and a case of nodular lesion was seen inside the auricle of left ear **figure (3)** .

The histopathological picture was corresponding with the clinical picture **table (4)**. The classical picture was masses of basophilic cells (basalioma cells) invading the dermis with a palisading arrangement of nuclei at the periphery of these masses **figure (4)**.

In pigmented BCC, in addition to tumor masses in the dermis, there was heavy deposition of brown pigment within melanophages surrounding these masses of basophilic cells. In morphea form BCC, small groups of closely packed tumor cells arranged in elongated strands and embedded in a dense fibrous tissue of the dermis .

Eighteen patients with SCCs (36 %) were seen. Their ages ranged between 10 – 70 years with a mean $\pm$ SD of 48 ± 19 years, while their ages of onset between 7 – 68 years with a mean $\pm$ SD of 54.6 ± 10.6 . The duration of disease ranged between 1 – 3 years with a mean $\pm$ SD of 1.5 ± 1.6 years. There were 9 males (50 %) and 9 females (50 %) with a sex ratio of 1 : 1.

Clinically, the patients with SCC presented as a hard indurated plaques or nodules, some were ulcerated. The majority arised from areas damaged by sunlight in actinic keratosis or solar cheilitis of lower lip especially. Cheeks and lower lip were the common sites of involvement **table (5)**.

A 50 years old female patient with an old scar of localized atrophic discoid lupus erythematosus in a butterfly distribution on the face developed SCC on the part of the scar located on the upper lip ⁽¹¹⁾ **figure (5)**).

Two children female patients 10 years old with xeroderma pigmentosa which is a rare autosomal recessive disease in which there is a defect of repair of DNA damage by exposure to sunlight because of deficiency of an endonuclease enzyme which is responsible for this repair of DNA damage. Patient suffer from sever photosensitivity, hypo and hyper pigmentation, early aging process and skin tumors at an early age ⁽¹²⁾. These patients developed SCC on the cheeks and nose **figure (6)**.

In one male patient, SCC presented as a hard circumscribed conical markedly hyperkeratotic lesion on the pinna of the left ear (cutaneous horn).

Pathological types of SCCs were shown in **table(6)**. Nearly all the types may be in the form of well differentiated or moderately well differentiated. The dermis was invaded by masses of squamous epithelial cells, some were large and others were small in size with loss of polarity. Several horn pearls were present in the majority of cases **figure (7)**. Others

contain few horn pearls in addition to individual cell keratinization (dyskeratosis). Well differentiated carcinomas showed marked lymphocytic inflammatory infiltrate surrounding tumor masses. One poorly differentiated SCC showed no evidence of keratinization (no horn pearls or dyskeratosis) with absence of inflammatory infiltrate. There was only atypical tumor cells.

A 60 years old male patient presented with ulcerated lesion on the upper lip with a pearly shaped border. Clinically looking as BCC but on histopathological examination, had features of both BCC and SCC, so this type was called a baso squamous cell carcinoma or metatypical BCC⁽¹⁾. The cells were larger with a larger paler nucleus than in the classic BCC and have a more eosinophilic cytoplasm.

A 55 years old male patient with a hard pinkish ulcerated plaque 2 × 2 cm on the forehead. The patient also had tumid plaques and nodules, some were ulcerated affecting the trunk on the chest and back of 3 years duration. Histopathological examination revealed a diffuse inflammatory infiltrate of lymphocytes in the upper dermis in a band – like, many of the cells were atypical, some infiltrating the epidermis (epidermotropism) forming in

some sites a pauprier microabscesses. So this was a case of mycosis fungoides which is a type of cutaneous T – cell lymphoma.

A 70 years old male patient presented with multiple hard dark brown nodule involving both ears bilaterally symmetrical. These nodules coalesce together forming a cauliflower – like picture **figure (8)**. The patient also had multiple violet nodules and plaques affecting upper and lower limbs with genitalia. The duration of the disease was about 1 year. Histopathology showed proliferation of spindle cells, protruding endothelial cells of capillaries and extravasation of red blood cells. These clinical and pathological pictures consistent with classical Kaposi sarcoma.

In all cases of non – melanoma skin cancers of the face, metastasis to regional lymph nodes was not noticed.

Discussion :

Basal cell carcinoma is the most common form of skin cancer, seen commonly on the faces of the middle age or elderly. Male to female ratio is about 3 : 2 and the incidence increases markedly after age of 40 years (5). In our study, BCC was the commonest type of non – melanoma skin cancers of the face forming about 58 % of the cases. Most BCC cases were between the ages 50 – 80 years. The male to female

ratio was about 1.2 : 1. This finding was comparable to those reported in the literature (3,5).

Noduloulcerative was the commonest type of BCC. Nose, cheeks and forehead were the commonest sites of involvement. The clinical types of BCC and sites of involvement of the face, in the present study were comparable to what has been published (3 , 7). Regarding the sites of BCC in this study, 2 patients with BCC (pigmented and nodulo ulcerative) were seen on the vermilion border of the upper lip. This finding was also comparable to a study of 18 cases of BCC which involved predominantly the vermilion lip which include the vermilion border and the outer mucosal surface of the lip (13). These sites are rarely involved by BCC.

BCC was also seen in sites not exclusively with maximum exposure to sunlight like inner canthus of both eyes, behind the ears and inside the auricle of left ear (6 patients). This may indicate that regional factors perhaps related to the density and type of pilosebaceous follicles are important in determining the distribution of the tumor and distribution of the lesions on the face(1). The histopathological features of different types of BCC were similar to what has been reported (9 , 10).

Squamous cell carcinoma was the next common non – melanoma skin cancers of the face forming about 36 % of cases with an equal male to female ratio 1 : 1. This contradicts to what has been reported in the literature which shows that men are twice affected as women with a sex ratio of 2 : 1. This probably because of a relatively small number of cases was taken during the study period (18 cases).

The clinical, histopathological and sites of involvement of SCC in our study were similar to what has been reported (1 ,3 ,9). The prevalence and distribution of lesions of SCC correlates well with the exposure to ultraviolet radiation. In the presort work, there was a first reported case of SCC arising from a scar of localized atrophic discoid lupus erythematosus on the upper lip, in Iraq (14).

Other non – melanoma skin cancers reported in this study were baso squamous, mycosis fungoides and Kaposi sarcoma (2 %) for each one.

The biological significance of baso squamous carcinoma is that this pathological pattern is associated with a significantly higher incidence of metastatic spread (1).

The finding of hard indurated plaque on the forehead of our patient with mycosis

fungoides was comparable to a previous Iraqi study of 20 patients with mycosis fungoides (1998) in which 3 patients (15 %) with tumor stage, nodular lesions some fungating with ulceration were involving the face.

Ears involvement, bilaterally symmetrical in our patient with kaposi sarcoma was the first reported site of face involvement in Iraqi patients. In a previous Iraqi study, face was also involved and mucosal involvement was detected in 10 % of the cases in the form of macules or papules on the hard palate and ulcerative lesions on the tongue (15).

References :

1. Mackie RM. Epidermal skin tumors. In : champion RH, Burton JL, Burns DA, Breathnach SM, (eds.) Rook / Wilkinson / Ebling Text book of Dermatology. 7thed. Oxford : Blackwell scientific publications ; 2004 : 1036 – 50.
2. Leffell DJ, Fitzgerald DA. Epidermal and appendageal tumors. In : Fitzpatrick's TB, Irwin M , Freedberg , Eisen AZ, Austin KW, Gold smith LA, Katz SI , Thomas SI, Thomas BF, (eds.) Dermatology in General Medicine. 5thed. New York :

- Mc Graw – Hill Brook CO. 1999 : 857 – 63 .
3. Hunter JAA, Savin JA, Dahl MV. Skin tumors. In : Hunter clinical dermatology. 3rded. Oxford : Blackwell scientific publications ; 2003 : 265 – 8 .
4. Habif TP. Premalignant and malignant non – melanoma skin tumors. In : clinical dermatology, A color guide to diagnosis and therapy. 3rd ed. Mosby , 1996 : 649 – 85 .
5. Gloster HM, Brodland DG. The epidemiology of skin cancer. Dermatol Surg. 1996 ; 22 : 217 – 23 .
6. Reizner GT, Chuang TY. BCC in Kauai, Hawaii; the highest documented incidence in the united states. J Am Acad Dermatol . 1993 ; 29 : 184 – 9 .
7. Cox NH. BCC in young adults. Br J Dermatol. 1992 ; 127 : 26 – 9 .
8. Adam IR, Elbert HC, Ratner D. Basal cell carcinoma : current concept. N Engl J Med. 2005 ; 353 : 2262 – 9 .
9. Jaworsky C. Tumors of the epidermal appendages. In : Elder D, Elenitsas R, Jawosky C, Johnson JrB, (eds.) Lever's histopathology of the skin. 8th ed. Philadelphia : Lippincott – Raven publishers , 1997 : 552 – 625.
10. Odom RB, James WD, Berger TC. Epidermal nevi, neoplasms and cysts. In : Richard BO, William DJ, Timothy GB, (eds.) Andrews' diseases of the skin, clinical dermatology . 10th ed. W. B Saunders CO. 2006 : 634 – 83 .
11. Al – Hattab MK, AL – Waiz MM. Discoid lupus erythomatosus in Iraqi patients ; A clinical and histopathological study. Ann Saudi Med. 2004 ; 24 (4) : 289 – 92 .
12. Marks R. Non – melanoma skin cancers. In : Marks R, Ronald H, (eds.) Roxburgh's common skin diseases. 17th ed. Oxford university press, 2003 : 207 – 19 .
13. Silapunt S , Peterson R, Goldberg LH. Basal cell carcinoma on the vermilion lip : A study of 18 cases. J Am Acad Dermatol. 2004 ; 50 : 384 – 7 .
14. Al – Hattab MK, AL – Waiz MM. Squamous cell carcinoma complicating discoid lupus lesions. Medical Journal of Babylon MJB. 2006 ; 3 (1 – 2 July) : 169 – 70 .

15. Al – Waiz MM, E – Sharquie K, Al
– Hamdani GA. An up surge of new
cases of Kaposi sarcoma in Iraqi

patients. Saudi Med J. 2003 ; 24 (2
) : 1425 – 6 .

Figure I : Age of presentation for NMSCs of the face .

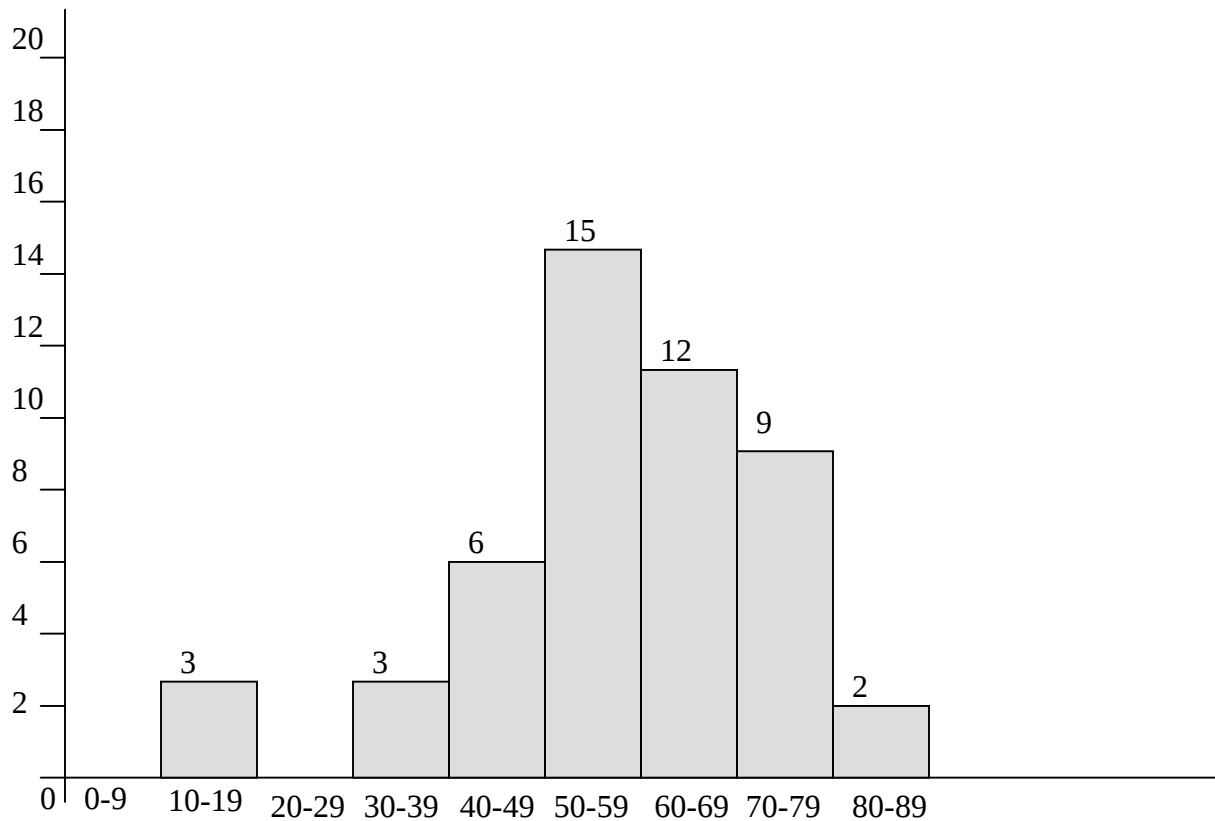


Figure II : Age of onset for NMSCs of the face .

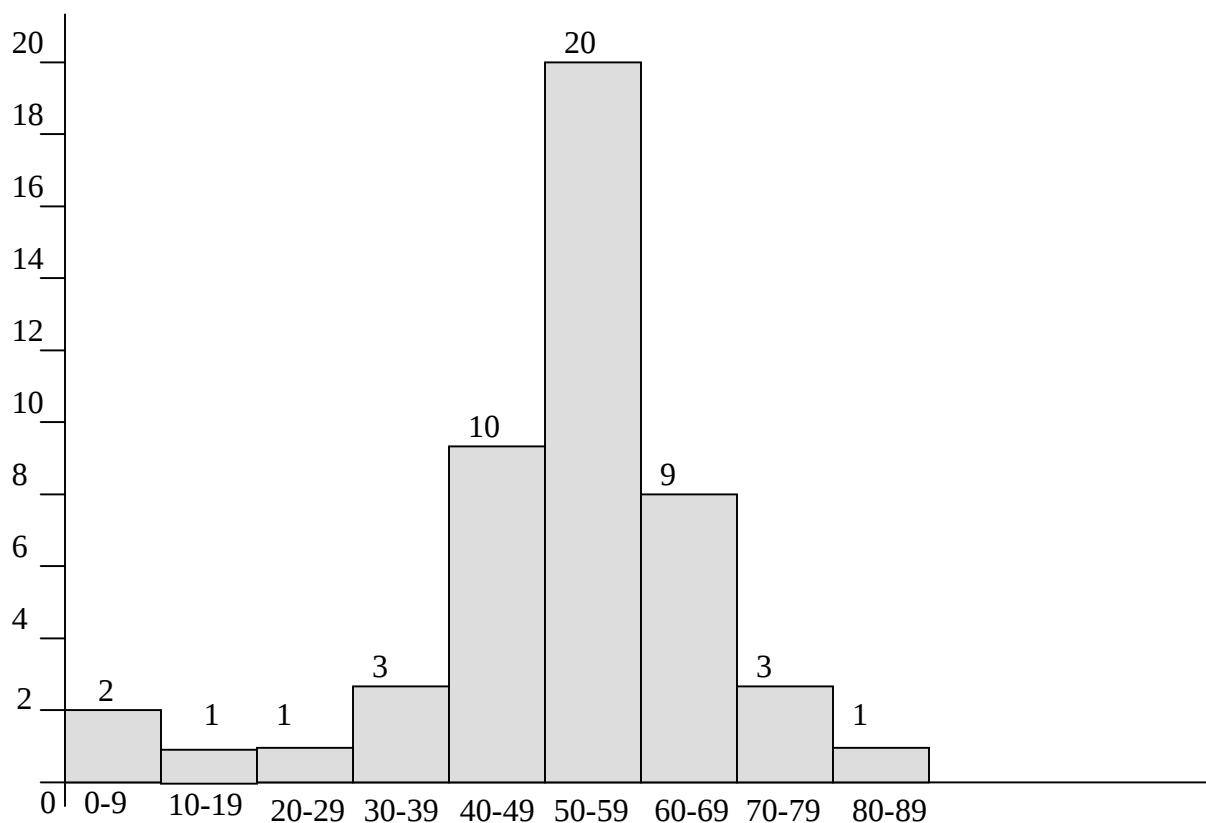


Table 1 : Types of NMSCs of the face :

Type	No. of cases	Percentage
Basal cell carcinoma	29	58 %
Squamous cell carcinoma	18	36 %
Baso squamous carcinoma	1	2 %
Mycosis fungoides	1	2 %
Kaposi sarcoma	1	2 %

Table 2 : Clinical types of BCCs on the face :

Clinical type of BCC	No. of cases	Percentage
Nodulo – ulcerative (rodent ulcer)	19	38 %
Pigmented	7	14%
Morpheaform	2	4%
Cystic	1	2%

Table 3 : Sites of involvement of BCCs on the face :

Site of BCC	No. of cases	Percentage
Nose	8	16%
Cheeks	7	14%
Forehead	6	12%
Inner canthi of eyes	3	6%
Upper vermilion lip	2	4%
Retro auricular	2	4%
Inside auricle of left ear	1	2%

Table 4 : Pathological types of BCC of the face :

Pathology of BCC	No. of cases	Percentage
Nodular	20	40%
Pigmented	7	14%
Morpheaform	2	4%

Table 5 : Sites of involvement of SCCs on the face :

Site of SCC	No. of cases	Percentage
Cheeks	8	16%
Lower lip	4	8%
Upper lip	2	4%
Forehead	2	4%
Nose	1	2%
Pinna of left ear	1	2%

Table 6 : pathological types of SCC of the face :

Pathology of SCC	No. of cases	Percentage
Well differentiated	8	16%
Moderately well differentiated	9	18%
Poorly differentiated	1	2%

**Figure (1) : Nodular BCC involving the nose.**



Figure (2) : Pigmented BCCs involving right cheek and the side of the nose.



Figure (3): Nodular BCC inside the auricle of left ear .



Figure (4): Histopathology of classical BCC showing masses of basophilic cells invading the dermis with peripheral palisading (H & , x40).



Figure (5) : SCC involving the scar of atrophic discoid lupus erythematosus.



Figure (6) : SCC in xeroderma pigmentosa patient.

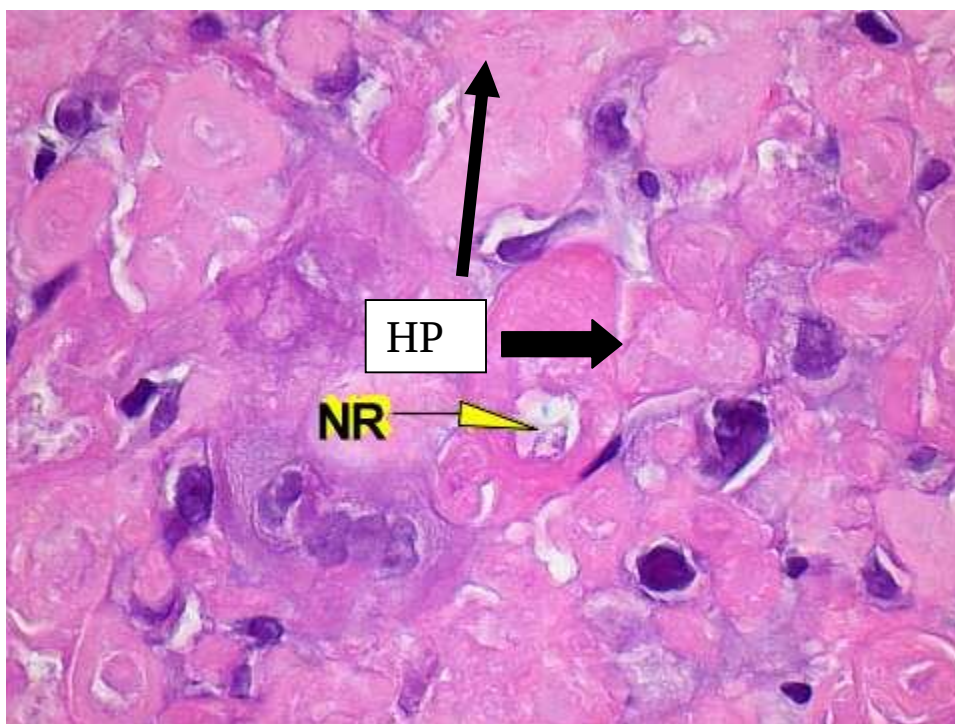


Figure (7): Histopathology of well differentiated SCC showing squamous cells invading the dermis with multiple horn pearls and dyskeratosis (individual cell keratinization) (H & E, x400).

