Study of the Frequency and the Histo-Pathological Characteristics of Skin Tumors and Tumor-Like Conditions

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ABSTRACT:

BACKGROUND:

Skin tumors and tumor like conditions constitute an important part of the work of the dermatopathologist. The incidence, the clinical and pathological characteristics differ in different countries due to genetic and environmental factors.

AIM OF THE STUDY:

To evaluate the rates of skin tumors and tumor like conditions and to study the histopathological characteristics of 3 important malignant neoplasms (basal cell carcinoma, squamous cell carcinoma and malignant melanoma).

PATIENTS AND METHODS:

The study is a cross-sectional retrospective study. It was conducted at the Histopathology Department, Teaching Laboratories, Baghdad Medical City during the period extending from the beginning of January 2018 till the end of December 2020. It included all skin biopsies sent from different departments. It included 243(37.97%) skin tumors and tumor-like conditions from 640 skin biopsies.

RESULTS:

Females were more commonly affected than males with a female to male ratio of (1.19:1). Malignant tumors (67.48%)) were more common than benign tumors (32.51%). The most common malignant tumor was basal cell carcinoma)(16.87%), followed by direct invasion by cancer (15.64%), then squamous cell carcinoma (9.87%). The most common benign tumors were intradermal nevus (3.7%), skin tag (3.7%%)and seborrheic keratosis (3.29%).

CONCLUSION:

Skin tumors and tumor like conditions constitute an important part of the work of the dermatopathologists. Malignant neoplasms were more frequently encountered than benign neoplasms in our laboratory. Basal cell carcinoma, direct local invasion by cancer and squamous cell carcinoma were the most frequently reported.

KEYWORDS: benign tumors, malignant tumors, Basal cell carcinoma, squamous cell carcinoma, malignant melanoma.

INTRODUCTION:

Skin tumors can arise in the epidermis, the dermis and the subcutis. They can be presented clinically as nodules, plaques or cysts [(1)]. Some are diagnosed by their clinical features whereas the others require histopathological examination of a biopsy specimen [(2)]. Most of the skin tumors are benign, however malignant tumors like basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and malignant melanoma have a special importance. BCC is the most common malignancy in humans [(3)] and especially affects light skinned individuals.

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SCC can arise from skin damaged by chronic inflammation, scarring and more importantly actinic keratosis [(4)]. Malignant melanoma is a highly malignant neoplasm that can metastasize early [(5)]. The incidence is rising all over the world [(6)]. Skin can be the site of metastasis of malignant tumors and can be affected by lymphoma. The diagnosis and evaluation of skin tumors constitute an important part of the work of dermatopathologist [(7)]. In addition to routine hematoxilin and eosin stain, special stains and immunohistochemical stains are sometimes needed [(8)]. The incidence of skin tumors and their clinic- pathological characteristics differ from country to country [(3)] .

This could be due to racial and genetic factors, in addition environmental factors such as exposure to sunlight and carcinogens are also important [9]. The present study is designed to evaluate the rate of skin tumors in a referral teaching laboratory in Baghdad, in addition to the study of pathological characteristics of the most frequent malignant neoplasms.

PATIENTS AND METHODS:

The study is a cross-sectional retrospective study. It was conducted at the Histopathology Department, Teaching laboratories, Baghdad Medical City during the period extending from the beginning of January 2018 till the end of December 2020. It included all skin biopsies sent from different departments to the Histopathology Department. It included 243(37.97%) skin tumors and tumor-like conditions from a total of 640 skin biopsies. The biopsies were stained with hematoxylin and eosin. Immunohistochemical stains were performed when needed.

The pathological reports concerning biopsies of various skin lesions were collected and cases of skin tumors and tumor-like conditions were recorded and analyzed using SPSS system (statistical package of social sciences) and Excel 2010 programs. Data including age, gender, site, and diagnosis were retrieved from electronic pathologic records. Various pathological features were studied. Frequencies, percentages, means and standard deviation were calculated. Tables and charts were constructed according to information obtained from the reports.

RESULTS:

Females (132) (54.32%) were more commonly affected than males (111 case) (45.67%) with a female to male ratio of (1.19:1). The minimum age for all patients was 1 year and the maximum was 92 years with a mean 52.32 years.

Malignant tumors (164 cases) (67.48%) were more common than benign lesions (79 cases) (32.51%).

The most common skin tumor was basal cell carcinoma (41 cases) (16.87%) (table 1) followed by direct invasion of the skin by malignancy (38 cases) (15.64%); 35 cases were from breast cancer, 2 from thyroid cancer and one the origin was not mentioned, then invasive squamous cell carcinoma (24 cases)(9.87%), lymphoma whether T or B cell (excluding mycosis fungoides)(11 cases), intradermal nevus, mycosis fungoides and skin tag (9 cases for each), Kaposi sarcoma and seborrheic keratosis (each one 8 cases), epidermal cyst (7 cases), neurofibroma and SCC in-situ (each of them 6 cases), metastasis to the skin (6 cases); 1 from the stomach, the other 5 the origin was not mentioned, malignant melanoma and benign skin adnexal tumors (each 5 cases), dermatofibroma, dermoid cyst, leukemia and Paget disease of nipple (4 cases for each), dermatofibrosarcoma protuberans, keratoacanthoma and nevus sebaceous (3 cases for each), angiokeratoma, pilar (trichelimmal) cyst and plasma cell tumor (2 cases for each). One case was recorded for each of the following; compound melanocytic nevus, cutaneous mastocytosis, coexistence of epidermal cyst with glomus tumor, extrammary Paget disease (table 1), lymphoproliferative disorder, poorly differentiated tumor and coexistence of skin tag with benign skin adnexal tumor. Under the heading of others, one case was recorded for each of the following; hemangioma, cavernous hemangioma, pyogenic granuloma, epithelioid hemangioendothelioma, hamartoma, skin horn, traumatic neuroma, leiomyoma, congenital nevus, infantile digital fibromatosis, fibromatosis, lymphangioma/lymphangectesia, and digital fibrokeratoma. We excluded lipomas whether subcutaneous or intramuscular.

Site of the tumors

The most common site of involvement was head and neck, followed by breast, then lower limb, then trunk, hands and feet and upper limb (figure 1), the site of individual tumors is shown in table 2

Histopathological features of basal cell carcinoma :

The most common feature was ulceration (8 cases, 19.5%), followed by pigmentation and basosquamous differentiation (3 cases for each, 7.31%), nodular type (2 cases, 4.87%), adenocytic, nodulocystic, adenoid, focal adenoid and focal squamous differentiation (1 case for each, 2.43%). The histological type was not mentioned in 2 cases. (table 3)

Regarding the surgical margin; 12 lesions were completely excised while 21 lesions were incompletely excised**.** The surgical margin status was not mentioned in 8 lesions.

Histopathological features of squamous cell carcinoma :

Regarding the histological type; 5 tumors (16.67 %) were well differentiated, 2 (6.67 %) were moderately differentiated and one (3.33%) was poorly differentiated.

Carcinoma in situ was seen in 7 lesions (23.33%), 4 lesions had focal invasion. The following features were seen in 2 cases for each: ulceration, verrocous and focal areas of SCC in keratoacanthoma, while acantholytic and focal basaloid differentiation were seen in one case for each. The histological type was not mentioned in (3 lesions,10%). Table 4.

Table 1: Demographics of Skin Tumors.

Diagnosis	Number (%)	Gender		Age (years)			
		Female	Male	Minimum	Maximum	Mean	Standard deviation
1- BCC	41(16.87%)	18	23	39	92	66	14
2- Direct invasion	38(15.64%)	34	4	24	86	55	15
3- SCC	24 (9.88%)	7	17	28	70	54	14
4- Lymphoma	11 (4.53%)	1	10	36	73	63	11
5- Intradermal nevus	9 (3.7%)	7	2	11	69	38	17
6-Mycosis fungoides	9 (3.7%)	5	4	35	56	46	7
7-Skin tag	9 (3.7%)	4	5	1	70	37	20
8-Kaposi sarcoma	8 (3.3%)	1	7	35	82	61	19
9-Seborrheic keratosis	8 (3.3%)	5	3	42	74	57	11
10-Epidermal cyst	7 (2.88%)	2	5	10	62	31	20
11-Metastasis	6 (2.47%)	5	1	25	68	51	15
12-SCC in situ	6 (2.47%)	2	4	50	61	58	4
13-Neurofibroma	6 (2.47%)	3	3	18	76	48	25
14-Malignant melanoma	5(2.06%)	4	1	27	70	59	18
15-Skin adnexal tumor	5 (2.06%)	4	1	27	71	46	18
16-Dermatofibroma	4 (1.65%)	1	3	27	61	40	15
17-Dermoid cyst	4 (1.65%)	3	1	6	40	25	15
18-Leukemia	4 (1.65%)	3	1	23	67	52	25
19-Paget disease of nipple	4 (1.65%)	4	0	40	69	52	15
20-DFSP	3 (1.23%)	2	1	50	74	63	12
21-Keratoacanthoma	3 (1.23%)	0	3	35	50	43	11
22-Nevus sebaceous	3 (1.23%)	2	1	13	21	18	5
23-Angiokeratoma	2 (0.82%)	2	0	55	65	60	7
24-Pilar cyst	2 (0.82%)	2	0	52	76	64	17
25-Plasma cell tumor	2 (0.82%)	2	0	55	55	55	0
26-Compound nevus	1(0.41%)	0	1	23	23	23	
27-Cutaneous mastocytosis	1(0.41%)	1	0	44	44	44	
28-Epidermal cyst + glomus tumor	1(0.41%)	1	0	35	35	35	
29-Extramamary Paget disease	1(0.41%)	1	0	28	28	28	
30-ymphoproliferative disorder	1(0.41%)	0	1	68	68	68	
31-Poorly differentiated tumor	1(0.41%)	0	1	64	64	64	
32-Skin tag + skin adnexial tumor	1(0.41%)	0	1	20	20	20	
33- Others	13 (5.35%)	6	7	8	75	44	24

Table 2: Site of individual tumors.

Diagnosis	head and neck	trunk	breast	upper limb	lower limb	hands and feet	not applicable	Total
Angiokeratoma	0	0	0	0	0	1	1	2
BCC	24	3	0	1	0	0	13	41
Compound melanocytic nevus	0	0	0	0	0	0	1	1
Cutaneous mastocytosis	0	1	0	0	0	0	0	1
Dermatofibroma	1	0	0	0	2	0	1	4
Dermoid cyst	2	0	0	2	0	0	0	4
DFSP	1	1	0	0	0	0	1	3
Epidermal cyst	3	1	0	0	1	0	2	7
Epidermal cyst + glomus tumor	0	0	0	0	0	1	0	1
Extramamary paget disease	0	0	0	0	1	0	0	1
Intradermal nevus	4	0	0	0	1	0	4	9
Direct Invasion	3	0	35	0	0	0	0	38
Kaposi sarcoma	0	0	0	0	3	3	2	8
Keratoacanthoma	2	0	0	1	0	0	0	3
Leukemia	0	0	0	0	2	2	0	4
Lymphoma	3	2	0	0	0	1	5	11
Lymphoproliferative disorder	0	1	0	0	0	0	0	1
Malignant melanoma	1	1	0	0	0	3	0	5
Metastasis	2	3	0	0	0	0	1	6
Mycosis fungoides	2	2	0	0	1	0	4	9
Neurofibroma	3	0	0	0	0	0	3	6
Nevus sebaceous	3	0	0	0	0	0	0	3
Others	4	2	0	1	2	2	2	13
Paget disease of nipple	0	0	4	0	0	0	0	4
Pilar cyst	2	0	0	0	0	0	0	2
Plasma cell tumor	0	1	0	0	1	0	0	2
Poorly differentiated tumor	0	0	0	0	1	0	0	1
SCC	6	1	0	0	9	4	4	24
SCC in situ	1	1	1	0	2	0	1	6
Seborrheic keratosis	2	1	2	0	2	0	1	8
Skin adnexial tumor	1	0	0	2	1	0	1	5
Skin tag	1	0	0	0	4	2	2	9
Skin tag + skin adnexial tumor	0	0	0	0	1	0	0	1

Regarding the surgical margin, the lesion was completely excised in (5 cases, 20.83%) and incompletely excised in (7 case, 29.61%). The surgical margin status was not mentioned in 12 cases, 50%.

Histopathological features of malignant melanoma:

The most common finding was frequent mitotic figures (4 lesions), next were melanin pigmentation and ulceration (3 lesions for each), the lesion was primary, secondary, composed of epithelioid cells and completely excised (2 cases for each). One lesion was recorded for each of the following features; mixed spindle and epithelioid cells composition, necrosis, hemorrhage, Pagetoid spread, giant cell reaction, desmoplastic reaction, chronic lymphocytic infilterate, invasion of adjacent organs and being incompletely excised. (table 5).

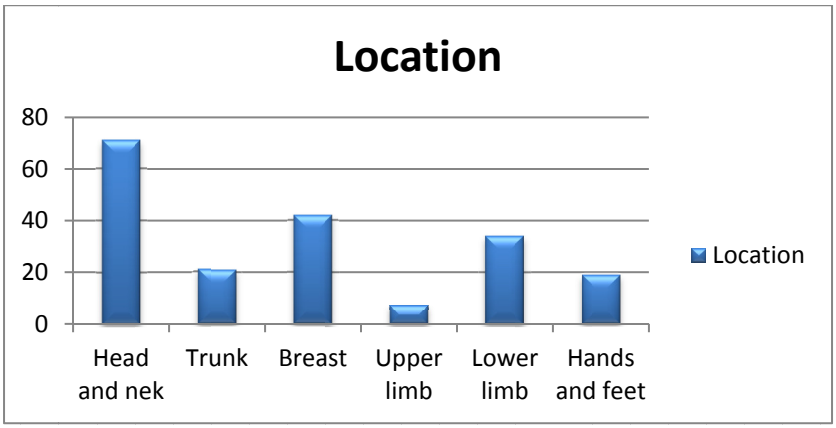

Figure 1: Site of all the tumors.

Table 3: Histopathological types of basal cell carcinoma.

Type	Frequency	Percent %
Nodular	2	4.87 %
Pigmented	3	7.31 %
Ulcerated	8	19.51 %
Adenocystic	1	2.43 %
Basosquamous	3	7.31 %
Nodulocystic	1	2.43 %
Focal adenoid differentiation	1	2.43 %
Focal squamous differentiation	1	2.43 %
Adenoid	1	2.43 %
Not mentioned	20	48.78 %
Total	41	100 %

Table 4: Histological types of squamous cell carcinoma.

Type	Frequency	Percent %
Well differentiated	5	16.67 %
Moderately differentiated	2	6.67 %
Poorly differentiated	1	3.33 %
Carcinoma in situ	7	23.33 %
Focal invasion	4	13.33 %
Ulcerated	2	6.67 %
Focal area of SCC in keratoacanthoma	2	6.67 %
Verrocous	2	6.67 %
Acantholytic	1	3.33 %
Focal basaloid differentiation	1	3.33 %
Not mentioned	3	10 %
Total	30	100 %

Table 5: Histopathological features of malignant melanoma

Characteristics	Number
Primary	2
Secondary	2
Epithelioid cell	2
Mixed cell	1
Melanin pigmentation	3
Mitosis	4
Ulceration	3
Necrosis	1
Hemorrhage	1
Breslow thickness	1 case
Clark level	1 case
Pagetoid spread	1
Giant cell reaction	1
Desmoplastic reaction and chronic lymphocytic infiltrate	1

DISCUSSION:

A wide range of tumors, benign as well as malignant, are encountered in clinical practice [10]. The prevalence of skin malignancy is on rise in many countries [11]. With increased UV irradiation resulting from thinning of the ozone layer, skin malignancy incidence rates have been predicted to increase in the future unless, as is hoped, human behaviour to reduce sun exposure can offset these predicted rises [6,12].

Accurate identification of skin lesions is vital in ensuring malignancies are not missed and that they are treated early to avoid morbidity and mortality [13]. Skin biopsy is essential to assist the dermatologists to reach a definitive diagnosis of skin tumors and guide patient management. [1]

In the present study, a review of all pathology sections examined at the Histopathology Department, Teaching Laboratories, Baghdad

Medical City during a 3 year period extending from the beginning of January 2018 till the end of December 2020. Skin tumors and tumor-like condition were recorded and analyzed. All biopsies were stained by hematoxylin and eosin and immunohistochemistry was performed as needed.

Gender

In the present study, more females were seen. The female to male ratio was 1.19:1. Pappala et al[21] also found more females with a female to male ratio (1.56:1). Narhire et al [14] found more benign tumors in females with a female to male ratio of 1.2:1, Sherpa et al [7] found more benign tumors in females with a female to male ratio of 1.2:1.

While Uplaonkar et al [15] conducted a study in India during 5 years from January 2012 to December 2016 and found more males affected with a female to male ratio 0.97:1. Also Alwunais et al [9] determined the pattern of skin malignancies in Dammam Medical Complex, Dammam, Kingdom of Saudi Arabia from June 2008 and May 2014 found more males with a female to male ratio 0.68:1, Al-Hasnawi et al [16] who searched the records of the Ministry of Health of Iraq during the period 2000-2004 reported a 0.81:1 ratio.

Ratio of skin tumors and tumor like conditions from the total number of skin **biopsies** in the present study was 37.97% (243 from 640), while Sherpa et al [7] found a ratio 52.2 % (214 from 410)

Ratio of malignant and benign tumors

In the present study, the ratio of malignant tumors was 67.48% (164 cases out of 234 specimens), while the benign tumor constituted 32.52% (79 out of 234 specimens). Samanta et al [2] found the percentage of malignant tumors was 55.77% (29 cases out of 52 cases) during a five-year-study in India, while benign tumors constituted 44.23% , Uplaonkar et al [15] found 47.82% malignant (33 cases out of 69 cases), while benign tumors constituted 52.17%. Narhire et al [14] found malignant tumors percentage 30.55% (11 out of 36 cases), while benign tumors constituted 69.45%. Sherpa et al [7] recorded 18**.**22 % malignant tumors (39 cases out of 214 specimen) while benign tumors constituted 81.77%, Pappala et al [21] found that malignant tumors percentage was 6.52% (3 out of 46 cases), while benign tumors constituted 93.48% . The difference in the percentages of the benign and malignant neoplasms may be related to geographical factors in addition to the referral policy. Our Laboratory is a referral laboratory for a tertiary care center this may explain the high percentage of malignant neoplasms seen in the present study.

Type of malignant tumor

The most common malignant tumor in the present study was BCC (16.87%) and was more common in males with a mean age of 66 years, next was direct invasion of the skin by secondary neoplasm which was more common in females with a mean age of 55 years, next was SCC (9.87%) which was more in males with a mean age of 54 years, then malignant melanoma which was more common in females with a mean age of 59 years.

Al Hasnawi et al [16] also reported that BCC was the most common skin tumor. It constituted 43% of the total number of skin cancers. Next was SCC (35%) and malignant melanoma 6%. The percentage of skin cancers from the total number of cancers was 4.04% (2585 from 63923). Uplaonkar et al [15] also reported that the most common was BCC (11.59%), followed by SCC (5.79%), then malignant melanoma (7.24%). This finding was also reported by Alwuanais et al [9] who reported BCC (26%), followed by SCC (22.2%), then dermatofibrosarcoma protuberans (18.5%). On the other hand Sherpa et al [7] reported that SCC was the most common malignant skin tumor (50%), followed by BCC (16.6%), then verrocous carcinoma (2.8%) with 50-60 years age range. Pappala et al [21] reported that the most common was SCC (4.34%) followed by malignant melanoma (2.17%) and the most common age range was 50-60 years for SCC and 60-70 years for melanoma, **Sa**manta et al [2] reported that the most common tumor was SCC (48.27%), followed by BCC (24.13%), then verrucous carcinoma (10.34%), Narhire et al [14] reported the most common was SCC (45.5%) , followed by basaloid carcinoma (18.1%). Differences in the type of malignant neoplasm may be related to different environmental as well as genetic factors in different locations.

Type of benign tumors

In the present study, the most common was intradermal nevus (3.7%) with the mean age 38 years and skin tags (3.7%) with mean age 37 years, then seborrheic keratosis (3.29%) with mean age 57 years. Samanta et al [2] also reported the most common was intradermal nevus (5.77%), followed

by congenital neuronevus (3.84%), then compound nevus (3.84%).

While Pappala et al [21] reported the most common was squamous papilloma (19.56%) seen from 11-64 years, followed by skin tags (13.06%) seen in first 3 decades, then verruca vulgaris (10.86%) seen in 2 to 5th decade. Sherpa P.et al [7] reported the most common was squamous papilloma (14.3%), followed by seborrheic keratosis (8.6%), then verruca vulgaris (7.4%). Narhire et al [14] reported the most common was verruca (16%), followed by compound nevus (12%), then pilomatricoma (12%).

Uplaonkar et al [15] reported the most common was squamous papilloma (8.7%) from 45-65 years, followed by skin tag (2.9%) from 35-50 years, then adenoacanthoma (2.9%) from 35-40 years.

Site of skin tumors

In the present study, the most common site for BCC was the head and neck region (9.88%), while for direct invasion it is breast (14.4%), for SCC it was lower limb (3.7%).

Alwuanais et al [9] found the most common site for BCC was the head and neck, for SCC and dermatofibrosarcoma protuberans was the trunk, Uplaonkar et al [15] reported head and neck was the most common site for BCC and lower limb for SCC. Narhire et al [14] and Sherpa et al [7] stated that the most common site for BCC was the head and neck

Histopathological Features

The histopathological features of BCC vary according to the subtype. In general, malignant cells have large nuclei and basophilic cytoplasm. They are usually arranged in palisade and surrounded by stromal retraction. The following histological types are recognized; pigmented, nodular, superficial and morpheaform, in addition there is basosquamous overlap variety. [1]

In the present study, the most important feature of BCC was the ulceration (19.5%). The histological type was not mentioned in all the reports. Pigmentation was mentioned in 7.3% of lesions while the nodular variant was reported in 4.87%. Scrivener et al [17] described the different histological patterns of BCC and related them to the site.

SCC is diagnosed when atypical keratinocytes invade the basement membrane into the dermis; otherwise it is considered carcinoma in situ which has a better prognosis. Grading of SCC depends on many factors; one of them is the degree of differentiation from well to moderately to poorly differentiated [4].

In the present study, the most common SCC was in situ (23%). Focal invasion was detected in 13%.

The SCC was well differentiated in 16.67%. This indicates the good prognosis in our patients as compared to other studies [18].

Malignant melanoma is the most serious cutaneous malignancy. The most important histological features to be reported are the type of the tumor; lentigo maligna, superficial spreading, nodular or acral lentiginous melanoma. In addition to the Breslaw thickness and Clarke level, it is also important to mention whether the melanoma is primary or secondary. [19, 20]

In the present study 2 cases were mentioned to be secondary malignant melanoma. Breslaw thickness was mentioned in one case and Clarke level was mentioned in the other case.

CONCLUSION:

Skin tumors and tumor like conditions constitute an important part of the work of the dermatopathologists. Malignant neoplasms were more frequently encountered than benign neoplasms in our laboratory. Basal cell carcinoma, direct local invasion by cancer and squamous cell carcinoma were the most frequently reported.

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