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ORIGINAL ARTICLE

Adnexal Skin Tumors; A Histopathological Review of 64 Cases

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ABSTRACT

Background:
Most adnexal tumors are benign and do not carry a risk of recurrence, however, according to the histological origin, these tumors show histological overlapping, therefore, are usually misdiagnosed clinically and often further workup for conformation is required.
Objective: To highlight the spectrum of histopathological features of adnexal skin tumors and to categorize these tumors histologically according to World Health Organization (WHO) classification.
Materials and Methods: This was a retrospective cross-sectional study, carried out in Al- Najaf center of histopathology, Najaf, Iraq. It included sixty-four registered cases of adnexal skin tumors diagnosed between January 2020 and August 2024 at our center. Histopathological examination was performed using tissue sections that fixed with formalin and embedded by paraffin , the hematoxylin and eosin used in staining of these sections. Clinical data and provisional diagnoses were reported from the archive of pathology unit. Histopathological reexamination of these tumors concerning on cell differentiation was carried out for all cases.
Results: A total of 64 biopsies of skin tumors were diagnosed as adnexal tumors. The studied group composed of 25 males and 39 females (Male: Female ratio was 1:1.56). Among cases, (23.4%) at the 6th age group. Head and neck are the most affected sites (64%), followed by extremities (18.8%) and then trunk (17.2%). Benign and malignant tumors contributed for (71.9%) and (28.1%), respectively. Sweat gland differentiation contributed for (57.8%), hair follicle differentiation (39.1%) and sebaceous differentiation accounted for (3.1%). Hidradenoma was most common benign adnexal tumor followed by pilomatrixoma.
Conclusion: we find through the histopathological review of adnexal skin tumors emphasized that these tumors are rare and have a wide spectrum of morphology and workup including IHC study is essential for confirmation of the diagnosis.

Keywords: *Adnexal Skin Tumors, Morphology Histopathological evaluation*

1. INTRODUCTION

The adnexa are epidermal apparatus of the skin and consisting of hair follicles, sebaceous and sweat glands. Rather than the mature cells located in within the epidermis or appendageal structures, tumors of these adnexa arise from multipotent stem cells (1-3). It has been evident that neoplastic transformation of these elements may give rise to one or more differentiation lines of appendageal apparatus with different histological type (4-5).

According to their origin, they may differentiate to a wide variety of tumors with evident of histological overlapping. So, they are usually misdiagnosed clinically and often further workup for conformation is required (6-7). The histological classification of these tumors is notably complex due to their shared origin, which results in overlapping histological features both within this group and with surface epidermal-type tumors (8-11). Accurate identification of their origin is crucial for determining the optimal management approach (12-13). Most of benign tumors do not carry a risk of recurrence, however, they may serve as markers for clinical syndromes linked to internal cancers, such as Cowden syndrome (14). The counterpart malignant adnexal tumors are rare and heterogeneous in their histological presentation. These are aggressive neoplasms with a propensity for nodal involvement and distant metastases, resulting in poor clinical outcomes (15-19). Consequently, diagnosing malignancy in adnexal tumors is crucial for treatment and prognosis considerations (20). Bernard Ackerman was the first to underscore the significance of architectural characteristics in differentiating between benign and malignant tumors. He has elucidated that benign tumors exhibit well-defined orientation and histological symmetry with homogeneous epithelial cells, dense fibrotic stroma devoid of atypia, necrosis, and mitotic activity, whereas malignant tumors display heterogeneous histological characteristics with asymmetry and all aforementioned traits (21).

Depending on histological differentiation bases, adnexal tumors can be divided into 3 major groups with their characteristic features (15). Sebaceous glands tumors are characterized by vacuolated sebocytes. Sweat glands tumors are more frequent and composed of two types (eccrine and/or apocrine), characterized by ducts formation ranging from small to large dilated cystic spaces. The last entity are the hair follicles tumors. They are usually difficult to be recognized in histopathological evaluation as they represent a diverse histological group with

wide morphological overlapping (22). As a role in histological examination of adnexal tumors, ruling out sebaceous proliferations is of priority, followed by sweat glands. The last step in histopathology is to consider the possibility of hair follicle tumors.

The prevalence of adnexal skin tumors is 1-2% worldwide. In Iraq, according to cancer registry of 2023, malignant skin tumors in general have formed 3.5% and 3.5/100,000 population, skin appendage carcinoma had formed 2.3% of all malignant skin tumors.

Therefore, in this context, the objective of our study was to highlight the pathological variety and spectrum of adnexal tumors of the skin in respect to age, sex, location and histopathological pattern in our setting.

2. METHODOLOGY

This was a cross-sectional retrospective observational study carried in Al- Najaf center of histopathology, Najaf, Iraq. It included sixty-four cases of adnexal skin tumors diagnosed between January 2020 and August 2024 at our center. Histopathological examination was performed using tissue sections that fixed with formalin and embedded by paraffin, the hematoxylin and eosin used in staining of these sections. Clinical data included the age, sex and site of tumor were extracted from the archive of pathology in this center. Also, clinical provisional diagnoses were reported. Histopathological reexamination of these tumors concerning on cell differentiation was carried out for all these cases. The data analysis plan included using the SPSS software. Parametric and non-parametric statistical tests were applied according to the type of variables to assess the relationship between histopathological results and clinical at a level of significance of 0.05.

3. RESULTS

During the studied period, a total of 64 biopsies of skin tumors were diagnosed as adnexal tumors during three years. Twenty-five patients (39.0%) were males and 39 patients (61.0%) were females. Male to female ratio was 1:1.56, with a significant difference between both gender in regard to the frequency of tumor, (P. value<0.05). Patients' age ranged between 6 and 77 years and majority of patients at the age between the third and sixth decade, however, most of these tumors (23.4%) were reported in patients at the age group 51-60 years, followed by age group 41-50 (20.3%), while less frequently presented tumors were seen in

other age groups as follow; 9 cases (14.1%) in age group 21-30, 7 cases (10.9%) in each age group 11-20 and 61-70 years, 6 cases (9.4%) in age group31-40 years, 4 cases (6.3%) in age group 71-80 years and lastly 3 cases (4.7%) in age group 1-10 years. Nonetheless, no significant difference in the frequency of tumors across all age groups, (P. value >0.05). The distribution of the tumors according to the site of their location showed that head and neck were the most affected sites (41 out of 64 cases) forming 64.1%, followed by extremities (12 cases) forming 18.8% and then trunk (11 cases) forming 17.2%. The origin of differentiation, was categorized into the following; sweat gland tumors which contributed for 57.8% of all tumor, hair follicle tumors (39.1%) and sebaceous glands tumors (3.1%). All aforementioned findings are summarized in (**Table 1**).

In regard to the gender distribution of adnexal tumor in general, it has been found that sweat gland tumors were more frequently reported in females than males; (56.8%) vs. 43.2%, respectively. Hair follicle tumors were also reported in both genders; they formed 72.0% in females and 28.0% in males, however, no significant differences were found in the distribution of these two tumors across both genders. In contrast to both sweat glands tumors and hair follicles tumors, sebaceous glands tumors were less frequently reported in this study and interestingly found in male gender only. They formed 3.1% of the total adnexal tumors. A part from sebaceous glands tumors, there was no significant difference among these adnexal tumors in regard to their frequency and gender distribution (p value>0.05), (**Table 2**).

Histopathological evaluation of all submitted cases in this study revealed that benign tumors were significantly the most frequent histological type, accounted for (46 out of 64 cases), and represented (71.9%), while the malignant tumors were less frequent, contributed for 28.1% (18/64) cases, (P. value <0.05) (**Figure 1**).

From other point of view, benign adnexal skin tumors were significantly, (P. value<0.05), more frequently diagnosed in females (32 vs 14 cases), while malignant tumors were more frequently diagnosed in males (11 vs. 7 cases). Distribution of adnexal skin tumors according to age showed that these tumors were more frequently diagnosed in patients at earlier age groups (50 years and younger), (38/64), , (**Table 3**).

Additionally, benign tumors were the more frequently diagnosed among cases aged 50 years and below, they formed 86.8% of patients in this age group, while 13.2% of cases in this age

group had malignant tumors. Malignant tumors were more frequently diagnosed in patients older than 50 years, compared to those younger than 50 years; 50% vs. 13.2%, respectively. The difference in the proportional distribution of benign and malignant tumors across the age groups was statistically significant, (P. value<0.05), (**Table 3**).

Regarding the distribution of the site of adnexal skin tumors, head and neck sites were the more frequent in benign than malignant tumors, 75.6% vs. 24.4%, respectively, with significant difference (P. value <0.05). Trunk site was more frequently associated with benign tumors (63.6%) in contrast to malignant tumors (36.4%), furthermore, extremities sites were also found to be more frequently reported in benign tumors rather than malignant (66.7%) vs. 33.3%, respectively, (P. value<0.05), (**Table 3**).

In regard to histopathological types of skin tumors, the results revealed that hidradenoma was the most frequent type of benign tumos17(37%), followed by pilomatricoma 11(23.9%). While sweat gland carcinoma was the most frequent type of malignant adnexial tumors 8(44.4%).

By comparing the tumor types across gender, hidradenoma was more frequent among females; 11 (28.2%) cases, compared to 6 (24%) cases among males. Pilomatricoma tumors were also more frequent among females compared to males; where they reported in 8(20.5%) and 3 (12%), respectively. The trichoblastoma was found in 3 (7.7%) females and 1(4.0%) male. While other types showed variable frequency between both genders. In contrast, malignant adnexal tumors Sweat gland carcinoma, was more frequent in males with 5(20.0%) compared 3(7.7%) to in females. While other tumors showed variable frequency between both genders. The findings are shown in (**Table 4 & Table 5**) and (**Figures 2, 3, 4 & 5**).

Table 1. Demographic features of the studied 64 cases of adnexal skin tumors

Characteristic feature	No.	%	P. value
Gender			
Male	25	39.1	<0.05
Female	39	60.9	
Male: female ratio	1:1.56		
Age(year)			
1 - 10	3	4.7	>0.05
11 - 20	7	10.9	
21 - 30	9	14.1	
31 - 40	6	9.4	
41 - 50	13	20.3	
51 - 60	15	23.4	
61 - 70	7	10.9	
71 - 80	4	6.3	
Site			
Head and neck	41	64.1	<0.05
Extremities	12	18.8	
Trunk	11	17.2	
Histopathology			
Benign	46	71.9	<0.05
Malignant	18	28.1	
Origin of differentiation			
Sweat gland	37	57.8	<0.05
Hair follicles	25	39.1	
Sebaceous gland	2	3.1	

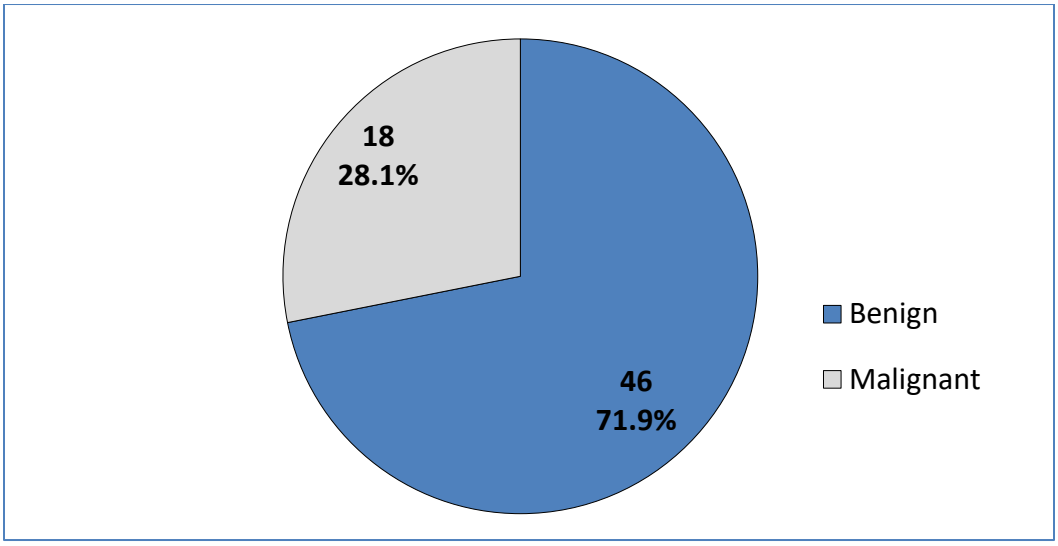

Figure 1. Distribution of adnexal skin tumors according to the type

Table 2. Distribution frequency of adnexal skin tumors according to gender.

Gender	Sweat glands		Sebaceous glands		Hair follicles		P. value
	No.	%	No.	%	No.	%	
Male (n=25)	16	43.2	2	8.0	7	28.0	<.0.05
Female (n=39)	21	56.8	0	0.0	18	72.0	> 0.05
Total	37	57.8	2	3.1	25	39.1	> 0.05
Male: female ratio	1.0: 1.3		2.0: 0.0		1.0: 2.6		> 0.05

Table 3. Distribution of benign and malignant adnexal skin tumors according to gender, age and site of tumor

Variable		Type of tumor				Total	P. value
		Benign		Malignant			
		No.	%	No.	%		
Gender	Male	14	56.0	11	44.0	25	<0.05
	Female	32	82.1	7	17.9	39	
Age (years)	≤ 50	33	86.8	5	13.2	38	<0.05
	> 50	13	50.0	13	50.0	26	
Site of tumor	Head & neck	31	75.6	10	24.4	41	<0.05
	Trunk	7	63.6	4	36.4	11	
	Extremities	8	66.7	4	33.3	12	

Table 4. Cross-tabulation for the relationship between gender and histopathological types of Benign adnexial skin tumors

Benign tumors (n=46)	Gender				Total (n=64)	
	Male (n=25)		Female (n=39)			
	No.	%	No.	%	No.	%
Hidradenoma	6	24	11	28.2	17	37
Pilomatricoma	3	12	8	20.5	11	23.9
Trichoblastoma	1	4	3	7.7	4	8.7
Proliferative pilar cyst	1	4	2	5.1	3	6.5
Chondroid syringma	0	0	3	7.7	3	6.5
Trichofolliculoma	0	0	2	5.1	2	4.3
Sebaceoma	1	4	0	0	1	2.2
Syringocystadenoma Papilliferum	1	4	0	0	1	2.2
Spiradenoma	0	0	1	2.6	1	2.2
Syringoma	0	0	1	2.6	1	2.2
Sebaceous adenoma	1	4	0	0	1	2.2
Trichelmmoma	0	0	1	2.6	1	2.2
P. value <0.05 significant						

Table 5. Cross-tabulation for the relationship between gender and histopathological types of Malignant adnexial skin tumors

Malignant tumors (n=18)	Gender				Total (n=64)	
	Male (n=25)		Female (n=39)			
	No.	%	No.	%	No.	%
Sweat gland carcinoma	5	20	3	7.7	8	44.4
Porocarcinoma	2	8	1	2.6	3	16.7
Malignant adnexal	2	8	0	0	2	11.1
Malignant pilar tumor	0	0	2	5.1	2	11.1
Trichilemmal carcinoma	1	4	0	0	1	5.6
Digital papillary ad.	0	0	1	2.6	1	5.6
Pilomatrix carcinoma	1	4	0	0	1	5.6
P. value <0.05 significant						

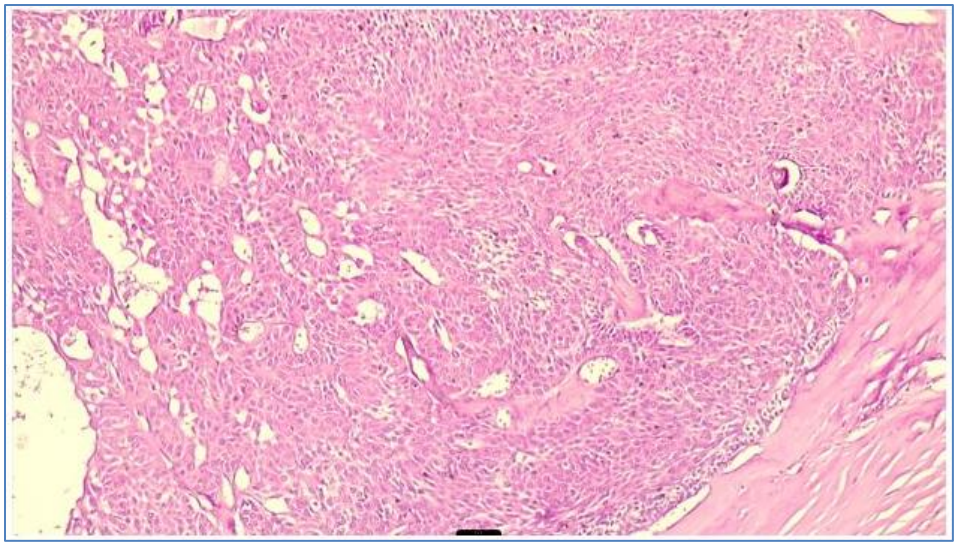

Figure 2: *Hidradenoma is well circumscribes dermal mass showing both cystic & solid components. The cells polyhedral basophilic cells with hyalinized stroma. There are foci of glycogen containing clear cells with eccentric nucleus (as pointed by the arrow). At 4x H&E magnification.*

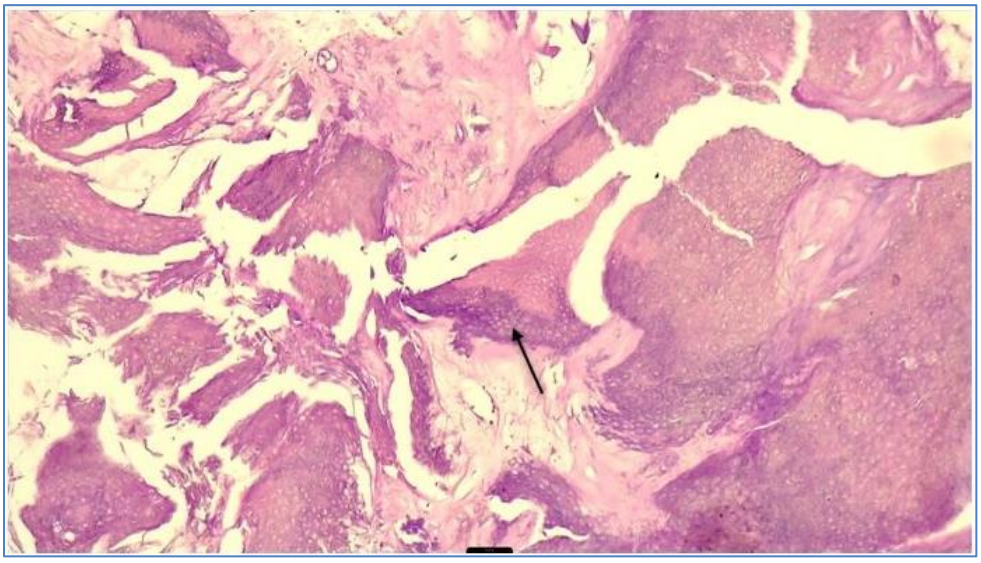

Figure 3: *pilomatricomas showing lobulated dermal mass with eosinophilic shadow cells with central pallor indicating ghost nucleus as pointed by the arrow). At 4x H&E magnification.*

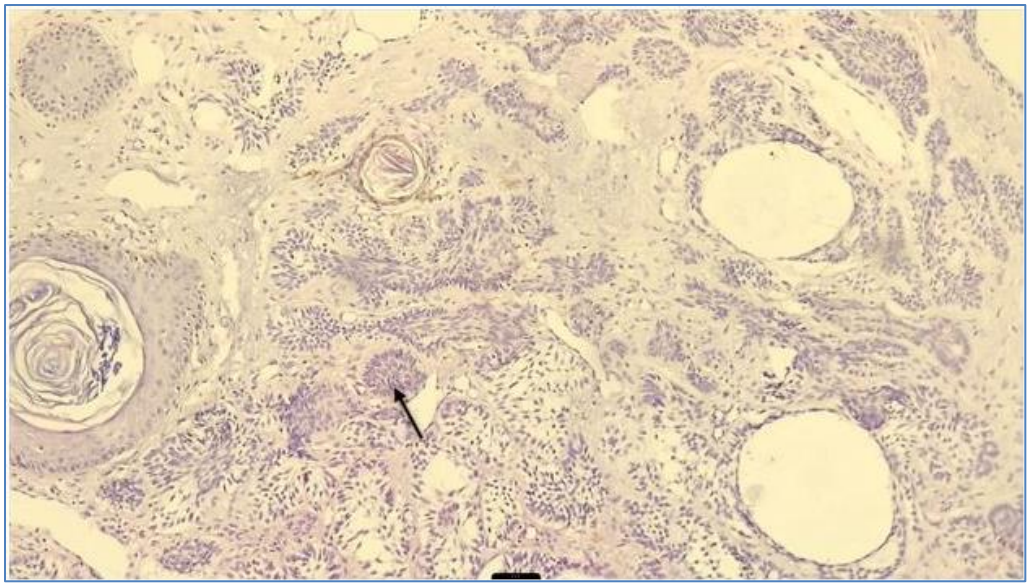

Figure 4: *Trichoblastoma. well circumscribed dermal base tumor. Composed of the basaloid epithelial cells with peripheral palisading. Note the keratin cyst and papillary mesenchymal body (as pointed by the arrow). At 4x H&E magnification.*

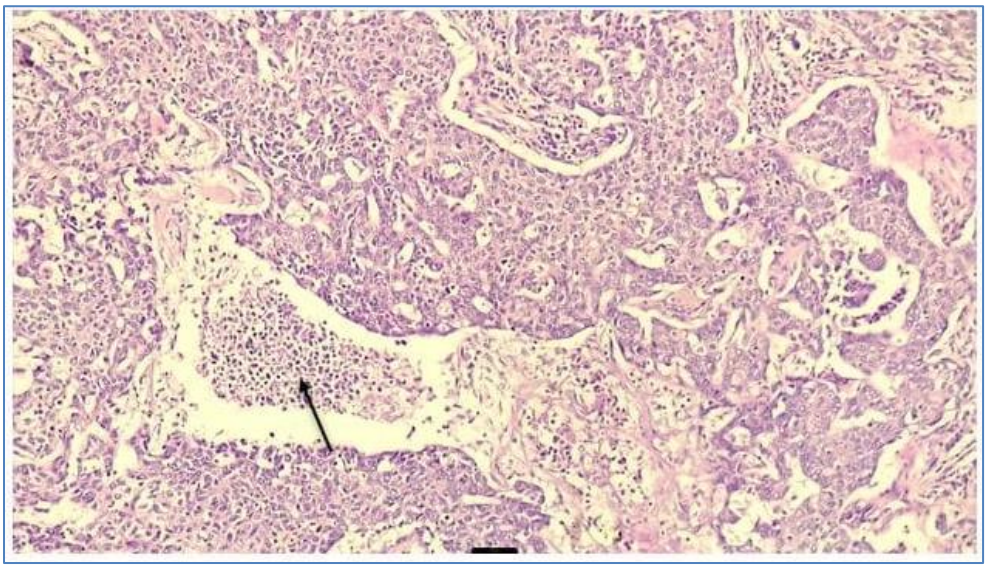

Figure 5: *Sweat gland carcinoma showing cribriform and high nuclear features with foci of necrosis (as pointed by the arrow). At 4x H&E magnification.*

4. DISCUSSION

Adnexal tumors include a wide range of skin epithelial tumors encompassing both benign and malignant neoplasms that exhibit differentiation towards sweat glands, sebaceous glands, and hair follicles (5). The present study agreed that reported in previous studies and the evidenced predominance of females among cases with adnexal skin tumors compared to males, the male to female ratio was one to 1.56; close to our finding, Pujani M et al. (23), reported predominance of females. Conversely, Sharma et al. reported a ratio of (1.07:1) (24). The most frequently affected age group in this study is the sixth decade of life (51-60 years). This result is similar to that reported by Sharma et al (24). Adnexal tumors are often located in the head and neck, trunk, and extremities. In our investigation, the predominant site was the head and neck (64.1%), followed by the extremities (18.8%) and trunk (17.2%), consistent with the findings of Pujani et al. (23), Sharma et al. (24), and Samaila et al. (25). This is due to the region's abundance of pilosebaceous units and both apocrine and eccrine glands, creating a conducive environment for the formation of adnexial skin tumors (25). The percent of benign cases was (71.9%) while malignant was (28.1%) which are semi-similar to those reported by other studies; Sharma et al (24), Samaila et al (25) Viswanathan et al (26) and Kaur et al (21). The predominant tumors in our study were those with sweat gland differentiation (57.8%), followed by tumors of follicular differentiation (39.1%) and sebaceous tumors (3.1%). This finding was not different from other observation documented by Pujani et al (23) and Sharma et al (24). In contrast to that reported by Kaur et al (21), they concluded that almost 39.1% of tumors were of follicular origin , 37.3% of sweat gland origin, and almost 23.6% of sebaceous gland origin. Moreover, Samaila et al (25) documented that sweat gland tumors formed 78.8%, sebaceous gland (13.5%) and hair follicle 4 (7.7%), which disagreed with our results.

The hidradenoma was the most common histological type in our study followed by pilomatricoma (26.6%). In the study of Pujani et al (23) and Sharma et al (24) show the same results, but it's disagreed with the study of Kaur et al (21), who showed pilomatricoma was the most common type followed by hidradenoma. On microscopical examination, , Hideradenoma shows mid-sized round cells tend to have hydropic changes organized into nodules as seen with light microscopy. Histopathologically, most tumors are classified as solid, although some cystic tumors have been described (27). Pilomatricoma is a distinctly defined

dermal tumor marked by islands of epithelial cells that contain ghost cells in their center and are bordered by basaloid cells. At lower levels of magnification, these ghost cells may be misinterpreted as necrotic tissue, however, upon higher magnification, they are seen to be eosinophilic cells with empty nuclear spaces (25, 27-29). The difference in several studies compared to ours is likely due to the small sample size in our study which was limited by the duration of the study and the infrequent nature of the disease under investigation. Thus, we suggest further studies with larger sample sizes and greater numbers of resection specimens in order to refine classification.

5. CONCLUSIONS

According to the results of this study, adnexal skin tumors are rare tumors more commonly seen in females. Benign tumors are more frequent than malignant. The most common reported differentiation among these tumors was Sweat gland tumor. The second commonest one was follicular then sebaceous tumors. The most frequent site of tumors located in the head and neck, due to due to the high density of pilosebaceous and glandular structure. Hidradenoma is the most common histological type, followed by pilomatricoma. Because of the clinical overlapping between these tumors, careful histological and immunohistochemical study is required to confirm the final diagnosis.

Ethical Approval:

All ethical issues were approved by the authors. Data collection and patient's enrollment were in accordance with Declaration of Helsinki of World Medical Association, 2013 for the ethical principles of researches involving human.

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