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Original Article

Clinicopathological Profile of Cutaneous Adnexal Tumors at a Tertiary Care Hospital in Pakistan

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ABSTRACT

Objective: To analyze clinicopathological wise frequency of Cutaneous Adnexal Tumors presenting at a tertiary care hospital, Kharian, Pakistan.

Study Design: Cross-sectional study

Place and Duration of Study: Dermato-pathology department of a tertiary care hospital in Kharian, Pakistan, from Dec 2019 to Nov 2021.

Methodology: The sample was collected from the biopsy specimens with clinical diagnosis indicating cutaneous tumors. Relevant clinical information was obtained from the clinical details submitted by the clinicians. The specimens were examined by a team comprising a dermatologist and a histopathologist. The Cutaneous Adnexal Tumors were classified according to the WHO classification into three groups which included Tumors with Apocrine and Eccrine, Follicular and Sebaceous differentiation. Each group was further divided into Benign and Malignant tumors.

Results: A total of 41 cases with a diagnosis of Cutaneous Adnexal Tumors were encountered during the two years. These comprised 4.8% of the total number of cutaneous tumors. The mean age of patients was 39.98+15.20 years with a range of 11 years to 65 years. 53.7% of Cutaneous Adnexal Tumors were seen in the third and fourth decades of life. General surgeons submitted maximum number of biopsies (n=27, 65.8 %), followed by dermatologists (n=8, 19.5%), plastic surgeons (n=4, 9.8%), and ophthalmologists (n=2, 4.9%). 97.6% of the tumors were benign, and only one was Malignant. Tumors with Follicular Differentiation were among the most commonly presented. Pilomatrixoma was the most common Cutaneous Adnexal Tumor. 65.9% of Cutaneous Adnexal Tumors were seen on the head and neck.

Keywords: Adnexal Tumors, Clinicopathological Spectrum, Cutaneous Adnexal Tumors, Eccrine Differentiation, Follicular Differentiation, Pilomatricoma, Sebaceous Differentiation,

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INTRODUCTION

Adnexal tumors of the skin are a heterogeneous group of rare benign and malignant neoplasms.[1] The tumors are classified according to their line of morphological differentiation along follicular, eccrine, apocrine, and sebaceous lines or a combination of these elements.[2] These tumors have a common origin from undifferentiated pluripotent stem cells, and the genetics and the microenvironment of epidermis or dermis influence the differentiation to a specific tumor subtype.[3]

The components of pilosebaceous apparatus are densely concentrated in the area of head and neck.[4] The scalp has maximum density of hair follicles, and the face, chest, and upper back have maximum density of sebaceous glands. Therefore, the tumors that arise from pilosebaceous units are found predominantly over the head and neck area.[5] In contrast to the pilosebaceous apparatus, the eccrine sweat glands are distributed all over the body. They consist of a double-layered secretory component, which is located deeply in the dermis, and their excretory duct opens directly onto the surface of the skin.[6]

Adnexal tumors commonly occur as solitary lesions, but they may be part of an inherited tumor syndrome.1 Histological evaluation is required for their diagnosis.[7] The Majority of these neoplasms are benign, but for almost each of them, a "malignant" counterpart also has been described. Most of these malignant tumors were thought to develop de novo, while a minority of them result from malignant transformation of a benign precursor.[8] Therefore, recognition of malignant transformation is significant for an accurate diagnosis.[9] Many authors have studied Adnexal tumors worldwide. Skin adnexal tumors are comparatively uncommon lesions. Benign neoplasms are more frequent than malignant neoplasms.[10]

The study was conducted to determine how often skin adnexal tumors occur in the study population and to describe their clinicopathological features,

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including patient demographics, clinical presentation, and microscopic characteristics, based on the histopathological presentations of specimens.

METHODOLOGY

This cross-sectional study was conducted at the Dermatopathology department of a tertiary healthcare hospital in Kharian, Pakistan, from Dec 2019 to Nov 2021. The study was conducted after getting approval from the Institutional Ethical Review Committee (Reference No. 29, dated 21 Nov 2019). The study sample was obtained from the biopsy specimens submitted to the Histopathology department of the Hospital for histopathological diagnosis during the study period.

Inclusion Criteria: Biopsy specimens of both male and female patients, aged 11 to 65 years, with a clinical diagnosis indicating diagnosis of tumors of the skin and subcutaneous tissue were included in the study. Those cases in which no clinical information was provided but a histopathological diagnosis of tumors of the skin and subcutaneous tissue was made were also included in the study.

Exclusion Criteria: Patients under 11 years and more than 65 years of age were not included in the study. The cases of recurrent tumors and duplicate cases were excluded from the study.

Clinical information was gathered from the clinical details of patients submitted by the clinicians, along with the histopathological specimen. Age and gender of the patient, the site of the tumor, type of biopsy performed, and the specialty of the clinician submitting the biopsy specimen were recorded. The biopsy specimens were examined by a team of dermatologists and a histopathologist. The diagnosis for each case was made jointly by both specialists. The cutaneous adnexal tumors were classified according to the WHO classification into three groups, which included Tumors with Apocrine and Eccrine differentiation, Tumors with Follicular differentiation, and Tumors with Sebaceous differentiation. Each group was further divided into Benign and Malignant tumors.

Data was analyzed by using Statistical Package for Social Sciences (SPSS) 22.00. Quantitative data was represented using Mean±SD and qualitative data was represented by using percentage and frequency. Fisher exact test was applied. The p-value < 0.05 was considered significant.

RESULTS

Of the total 851 cases with a diagnosis of tumors of the skin and subcutaneous tissue, 41 cases with a Diagnosis of Cutaneous Adnexal Tumors were included in the study. Cutaneous Adnexal Tumors of skin comprised 4.8% of the total tumors of the skin and subcutaneous tissue. Excision biopsy was the most commonly performed procedure, which was performed in 35(85.4 %) cases. Incisional biopsy was performed in 6(14.6 %) cases.

Table-I: Frequency and Gender Distribution Of Cutaneous Adnexal Tumors (n=41)

Tumor n(%)		Gender		*p*-Value
		Male(n=25)	Female (n=16)	
Tumors Follicular Differentiation (n=25, 61.0%)		16(64%)	9(36%)	
Pilomatricoma	17(41.5%)	10(24.4%)	7(17.1%)	0.300
Trichoepithelioma	3(7.3%)	3(7.3%)	0	0.195
Proliferating Pilar Sheath Tumor	1(2.4%)	0	1(2.4%)	0.160
Trichofolliculoma	1(2.4%)	1(2.4%)	0	0.466
Pilar Sheath Acanthoma	1(2.4%)	1(2.4%)	0	0.466
Naevus Comedonicus	1(2.4%)	1(2.4%)	0	0.466
Malignant Pilomatricoma	1(2.4%)	0	1(2.4%)	0.160
Tumors with Eccrine Differentiation (n=12, 29.3%)				
Hidrocystoma	1(2.4%)	0	1(2.4%)	0.160
Poroma	1(2.4%)	1(2.4%)	0	0.466
Chondoroid Syringoma	2(4.9%)	2(4.9%)	0	0.296
Nodular Hidradenoma	5(12.2%)	2(4.9%)	3(7.3%)	0.193
Atypical Nodular Hidradenoma	2(4.9%)	2(4.9%)	0	0.266
Cylindroma	1(2.4%)	0	1(2.4%)	0.466
Tumors with Apocrine Differentiation (n=3, 7.3%)				
Hidradenoma Papilliferum	1(2.4%)	1(2.4%)	1(2.4%)	0.466
Syringocystadenoma Paplliferum	2(4.9%)	(4.9%)	0	0.296
Tumors with Sebaceous Differentiation (n=1, 2.4%)				
Sebaceous Adenoma	1(2.4%)	0	1(2.4%)	0.466

Of the 41 specimens included, 8(19.5%) were sent by dermatologists and 33(80.5%) by non-dermatologists. General surgeons performed maximum number of excisions 27(65.8 %) followed by dermatologists (n=8, 19.5%), plastic surgeons 4(9.8%), and ophthalmologists 2(4.9%). 27(65.9 %) specimens belonged to male patients and 14(34.1%) to female patients. The Male: Female ratio was approximately

Table-II: Decade-Wise Frequency of Cutaneous Adnexal Tumors (n=41)

Tumor Differentiation		Age Decade (%)						Total
		Second Decade	Third Decade	Fourth Decade	Fifth Decade	Sixth Decade	Seventh Decade	
Tumors with Follicular Differentiation	Pilomatricoma	2(4.9%)	5(12.2%)	5(12.2%)	1(2.4%)	1(2.4%)	3(7.3%)	17(41.5%)
	Trichoepithelioma	1(2.4%)	0	0	2(4.9%)	0	0	3(7.3%)
	Proliferating Pilar Sheath Tumor	0	0	0	0	1(2.4%)	0	1(2.4%)
	Trichofolliculoma	0	0	1(2.4%)	0	0	0	1(2.4%)
	Pilar Sheath Acanthoma	0	0	0	1(2.4%)	0	0	1(2.4%)
	Naevus Comedonicus	0	0	0	1(2.4%)	0	0	1(2.4%)
	Malignant Pilomatricoma	0	0	0	0	0	1	1(2.4%)
Tumors with Eccrine Differentiation	Hidrocystoma	0	1(2.4%)	0	0	0	0	1(2.4%)
	Poroma	0	0	1(2.4%)	0	0	0	1(2.4%)
	Chondroid Syringoma	0	1(2.4%)	0	0	0	1(2.4%)	2(4.9%)
	Nodular Hidradenoma	0	1(2.4%)	0	1(2.4%)	1(2.4%)	2(4.9%)	5(12.2%)
	Atypical Nodular Hidradenoma	0	0	2(4.9%)	0	0	0	2(4.9%)
	Cylindroma	0	0	1(2.4%)	0	0	0	1(2.4%)
Tumors with Apocrine Differentiation	Hidradenoma Papilliferum	0	0	1(2.4%)	0	0	0	1(2.4%)
	Syringocystadenoma Paplliferum	0	1(2.4%)	1(2.4%)	0	0	0	2(4.9%)
Tumors with Sebaceous Differentiation	Sebaceous Adenoma	0	1	0	0	0	0	1
	Total	3(7.3%)	10(24.4%)	12(29.3%)	6(14.6%)	3(7.3%)	7(17.1%)	41

Table-III: Frequencies of Cutaneous Adnexal Tumors According to Site (n=41)

Tumor Differentiation	Tumors	Body Region				Total 41
		Head and Neck 27(65.9%)	Upper Extremities 6(14.6%)	Trunk 2(4.9%)	Lower Extremities 6(14.6%)	
Tumors with Follicular Differentiation	Pilomatricoma	12 (29.3%)	2(4.9%)	0	3(7.3%)	17(41.5%)
	Trichoepithelioma	3 (7.3%)	0	0	0	3(7.3%)
	Proliferating Trichilemmal Tumor	0	0	1(2.4%)	0	1(2.4%)
	Trichofolliculoma	1(2.4%)	0	0	0	1(2.4%)
	Pilar Sheath Acanthoma	1(2.4%)	0	0	0	1(2.4%)
	Naevus Comedonicus	0	0	1(2.4%)	0	1(2.4%)
	Malignant Pilomatricoma	1(2.4%)	0	0	0	1(2.4%)
	Region-wise Total	18(72.0 %)	2(8.0 %)	2(8.0 %)	3(12.0 %)	25(61.0%)
Tumors with Eccrine Differentiation	Hidrocystoma	0	1(2.4%)	0	0	1(2.4%)
	Poroma	0	0	0	1(2.4%)	1(2.4%)
	Chondroid Syringoma	2(4.9%)	0	0	0	2(4.9%)
	Nodular Hidradenoma	2(4.9%)	2(4.9%)	0	1(2.4%)	5(12.2%)
	Atypical Nodular Hidradenoma	2(4.9%)	0	0	0	2(4.9%)
	Cylindroma	1(2.4%)	0	0	0	1(2.4%)
	Region-wise Total	7(58.3 %)	3(25.0%)	0	2(16.6 %)	12(29.3%)
Tumors with Apocrine Differentiation	Hidradenoma Papilliferum	0	1(2.4%)	0	0	1(2.4%)
	Syringocystadenoma Paplliferum	1(2.4%)	0	0	1(2.4%)	2(4.9%)
	Total For The Region	1(33.3%)	1(33.3%)		1(33.3%)	3(7.3%)
Tumors with Sebaceous Differentiation	Sebaceous Adenoma	1(2.4%)	0	0	0	1(2.4%)
	Region-wise Total	1(100%)	0	0	0	1(2.4%)

2:1 (1.93:1). The mean age of patients was 39.98+15.20 years. The mean age of male patients was 39.44+14.102 years, and that of female patients was 41.00+17.66 with a range of 11 years to 65 years. 97.6% of the tumors were benign, and only one tumor was Malignant. Tumors with Follicular Differentiation were most commonly encountered, followed by Tumors with Eccrine Differentiation and Tumors with Apocrine Differentiation. Only one case of Tumor with Sebaceous Differentiation was seen. Pilomatricoma was the most common cutaneous adnexal tumor, diagnosed in 41.5% of cases, followed by nodular hidradenoma, diagnosed in 12.2% of cases (Table-I). 53.7% of Cutaneous Adnexal Tumors were seen in the third and fourth decades of life (Table-II). 65.9% of Cutaneous Adnexal Tumors were observed on the head and neck region, and 14.6% were found on the lower extremities. The face was the most common site affected by these tumors, with 53.7% of cases, followed by the scalp, which was involved in 27.3% of cases. The distribution of each type of Cutaneous Adnexal Tumors by body region is summarized in Table-III.

DISCUSSION

The study findings established that keeping mean age of patients was 39.98+15.20 years with a range of.[11] years to 65 years was not significant in identifying the presentation of these skin tumors. It also proves that tumors with Follicular Differentiation were among the most commonly presented. Pilomatrixoma was the most common Cutaneous Adnexal Tumor. 65.9% of Cutaneous Adnexal Tumors were seen on the head and neck, and 53.7% of Cutaneous Adnexal Tumors were seen in the third and fourth decades of life.

Cutaneous adnexal tumors are traditionally classified into follicular, eccrine, apocrine, and sebaceous types on the basis of their line of differentiation towards normal adnexal structures of the skin.[11] Clinical diagnoses of these tumors are not easy, as they all present clinically as non-descript, flesh colored, solitary or multiple papules or nodules.[12] Although clinical morphology and specific site or age predilections may help in the differential diagnosis, histopathologic evaluation is always required for their diagnosis.

Studies conducted by Yaqoob *et al.,*[13] and Samaila *et al.,*[14] have reported lower mean age, while the study contributions of Aslan *et al.,*[15] reported a higher mean age. This study's findings have found no significant difference in the mean age of male and female patients. Thus, determining that age-wise frequency has shown variation in the worldwide population.

Cutaneous adnexal tumors are relatively rare, accounting for 4.8% of the skin tumors diagnosed at the study setting. The findings of this study were aligned with those of Kamyab *et al.,*[16], who reported a lower frequency. Sarkar *et al.,*[17], however, noted a very high prevalence, with cutaneous adnexal tumors making up 14.7% of skin tumors. The true prevalence of cutaneous adnexal tumors might be higher than reported because many of these tumors are often asymptomatic, show slow growth, and do not cause patient discomfort. Some tumors, such as syringomas, are diagnosed clinically and treated with destructive methods like electrodessication and therefore are not submitted for histopathological evaluation.

Saleem J *et al.,* have reported a higher frequency of male cases. In benign adnexal skin tumors, sweat gland tumors were the most prevalent class, in which hidradenoma and poroma were the most frequent subtypes. Hair follicle origin was the second most prevalent class of tumors, with pilomatricoma being the most frequent.[18] According to Sharma *et al.,* and Reddy *et al.,* cutaneous adnexal tumors comprise a wide spectrum of tumors occurring in all age groups. Malignant tumors are rare and common in older age groups. Histopathological examination is the gold standard in distinguishing between the different subtypes.[19,20]

Of the 41 specimens included, 8(19.5%) were sent by dermatologists, and 33(80.5%) by non-dermatologists. 65,8% of the biopsy specimens were sent by general surgeons. The clinical diagnosis provided by the clinicians may assist pathologists in establishing a histopathological diagnosis.[21] General surgeons did not include any clinical notes except for 'growth for histopathology. It has been reported that general surgeons perform most of the excisions of cutaneous tumors in our population and submit the specimens without sufficient clinical information.[22]

The majority (97.6%) of the Cutaneous adnexal tumors were benign. This was in concordance with previous studies. The frequency of benign tumors previously reported ranged from 80.4% to 99.4%. Tumors with Follicular Differentiation were most common, followed by tumors with sweat gland differentiation and tumors with sebaceous differentiation.[23]

The findings of this study were aligned with the literature. Since a limited number of cases were reported by most of the authors, the exact frequency of tumors of different appendages may not be evident.

LIMITATION OF STUDY

This study was a single-center study comprising a limited number of cases. Studies with larger sample sizes are further required to have a better visibility of the clinicopathological profile of Cutaneous Adnexal Tumors in the Pakistani population to establish a feasible treatment plan.

CONCLUSION

Cutaneous adnexal tumors have been conclusively considered as rare lesions that frequently present with non-specific papules or nodules, making clinical diagnosis challenging. The majority are benign; however, their varied morphology necessitates histopathological confirmation for accurate classification. This study reinforces the significant role of microscopic evaluation in distinguishing tumor subtypes and guiding appropriate management. Early recognition and precise diagnosis are essential to ensure optimal patient outcomes.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AH & AQ: Data acquisition, data analysis, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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