

**HISTOMORPHOLOGICAL SPECTRUM OF PRIMARY CUTANEOUS ADNEXAL NEOPLASMS IN A TERTIARY CARE HOSPITAL**

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ABSTRACT **Background:** Skin Adnexal Tumors (SATs) are relatively rare and pose diagnostic challenges. SATs comprise benign and malignant tumors that differentiate or arise from adnexal structures. **Aim & Objectives:** 1. To study the various histomorphological patterns of cutaneous adnexal neoplasms 2. To determine the incidence of various cutaneous skin adnexal neoplasms in varying age groups, sexes, and sites **Materials & Methodology:** This retrospective descriptive study was undertaken in the Department of Pathology, VIMS from April 2021 to April 2023 over 2 years. Formalin-fixed, paraffin-embedded sections were stained with Hematoxylin and Eosin for histopathological examinations. Special stains like Periodic acid Schiff (PAS) and Alcian blue were used whenever required. **Results:** Out of 2060 biopsies, a total of 51 cases were diagnosed as skin adnexal tumors. The mean age was 45 years and the overall male-to-female ratio was 1:1.3. The commonest age group affected was 40-49 years. Scalp (55%, 28/51) and forearm (14%, 7/51) were the most commonly affected sites. The commonest tumors were benign 94% (48/51) and 6% (3/51) were malignant adnexal tumors. Hair follicle tumors constituted the largest group (59%, 30/51) cases followed by sweat gland tumors (38%, 19/51) cases and sebaceous gland tumors (4%, 2/51) cases. Proliferating Pilar Cysts (37%, 19/51) and Nodular hidradenoma (12%, 6/51) were the commonest benign adnexal tumors. Sebaceous carcinoma was the most common malignant adnexal tumor followed by Porocarcinoma. **Conclusion:** Skin adnexal tumors are categorized based on predominant morphological differentiation. Benign adnexal tumors are more common than malignant adnexal tumors. Detection of skin adnexal tumors (SATs) is evaluated mainly by morphological features studied through histopathological examination as they present indistinctive clinical features.

KEYWORDS : Skin Adnexal Tumors, Histopathology, Pilar Tumor, Nodular Hidradenoma

INTRODUCTION:

SATs are a spectrum of neoplasms that originate or show differentiation towards skin appendageal structures namely hair follicles, sweat glands (eccrine glands and apocrine glands), and sebaceous glands. Since they are multipotent in origin, they differentiate towards more than one line of appendage differentiation rendering diagnostic difficulty¹

Hence, morphologically they are classified based on a predominant component of differentiation of appendageal structures¹

SATs are relatively uncommon and their exact incidence is unclear.⁵

Most of the SATs are benign and don't provide a significant change in managing the benign tumor except for the excision of the tumor. However, some of the tumors are indicators of internal malignancy i.e. Cowden Syndrome due to PTEN mutation consists of mucocutaneous lesions like facial trichilemmoma, acral keratoses, & oral mucosal papillomatous lesions and serves as a marker for breast cancer, endometrial carcinoma, and thyroid carcinoma; Muir-Torre syndrome is a clinical variant of lynch syndrome, presents as cutaneous sebaceous neoplasms like sebaceous adenoma, sebaceoma & sebaceous carcinoma²

On the other hand, malignant tumors need to be differentiated from metastatic cutaneous tumors. Hence establishing a diagnosis of malignancy in SAT is important for therapeutic and prognostic purposes.

Furthermore, overlap in their morphological features and their heterogeneous patterns of differentiation renders diagnostic difficulty⁴

Adnexal neoplasms have a wide pathological variety and complicated nomenclature. Clinical presentation of adnexal tumors is very non-specific and is often missed.⁷

Hence, Histopathological diagnosis serves as a mainstay for the diagnosis as they are clinically indistinguishable⁵

Aims And Objectives:

- To study the various histomorphological patterns of cutaneous adnexal neoplasms and to differentiate from mimickers like

squamous cell carcinoma and basal cell carcinoma

- To determine the incidence of various cutaneous skin adnexal neoplasms in varying age groups, sexes, and sites

Materials & Methodology:

This was a retrospective descriptive study conducted in the Department of Pathology, VIMS from April 2021 to April 2023 over 2 years among the patients who presented with subcutaneous or cutaneous mass with clinical suspicion of skin adnexal tumors

Inclusion Criteria:

All incisional and excisional skin biopsies from patients having suspicious skin adnexal tumors, irrespective of age and sex

Exclusion Criteria:

Patients who were clinically diagnosed with epidermal tumors

Incisional and excisional skin biopsies were taken and sent in 10% formalin to the Department of Pathology for histopathological examination. All formalin-fixed paraffin-embedded sections were stained with hematoxylin and eosin stain. Special stains like Periodic acid Schiff (PAS) and Alcian blue were done whenever required.

RESULTS:

Out of a total of 2060 skin biopsies, 51 skin adnexal tumors were diagnosed encompassing 2.4%. The age ranged between 16 and 91 years with male to female ratio of 1:1.3. Mean age was 45 years. Females were 29 cases comprising 58% of cases while males were 22 cases, accounting for 42% (Figure. 1).

Most of the cases were benign 94% (48/51) and the remaining few cases were malignant 6% (3/41) (Figure.2). The most commonly affected age group was 40-49 years (14/51) followed by 30-39 years (12/51) (Figure 3).

The most common affected site was the scalp 55% (28/51), followed by the forearm 14% (7/51) and the least common affected site was the thigh 2% (1/51) (Table 1)

Tumors with hair follicular differentiation constituted the largest group 59% (30/51), followed by tumors with sweat gland differentiation

38% (19/51) { eccrine and apocrine } and tumors with sebaceous differentiation accounting for 4% (2/51) has been summarized in Figure 4.

The most common overall tumor was the Pilar tumor 37% (19/51), followed by Nodular hidradenoma 12%(6/51) and Pilomatricoma 10% (5/51). The most common overall malignant tumor was Sebaceous carcinoma at 4%(2/51) and also one case of Porocarcinoma was reported and has been summarized in Table 2

The most common tumor with apocrine origin was Apocrine Hidrocystoma 8% (4 / 51) followed by Syringocystadenoma papilliferum 4%(2 / 51). The most common tumor with eccrine origin was Nodular hidradenoma 12% (6/51) followed by Eccrine spiradenoma 6%(3/51). The most common tumor with hair follicular origin was Pilar Tumor 37% (19/51) followed by Pilomatricoma 10%(5/51). [Table 2]

One case(1/51, 2%) of Porocarcinoma with follicular differentiation and 2 cases (2/51, 4%) of Sebaceous carcinoma were the malignant cases reported has been summarised in Table 2.

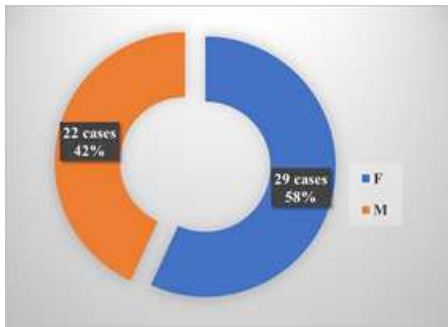


Figure 1: Pie chart showing the Sex-wise distribution of Skin Adnexal Tumor

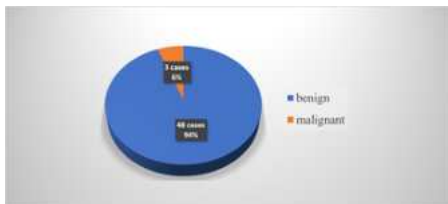


Figure 2: Pie chart showing the Nature-wise distribution of Skin Adnexal Tumor

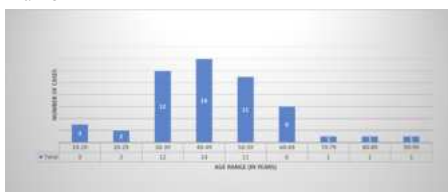


Figure 3: Bar diagram showing the Age-wise distribution of Skin Adnexal Tumor

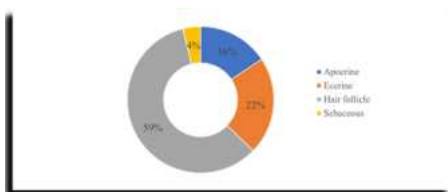


Figure 4: Pie chart showing the Histopathological spectrum of Skin Adnexal Tumor

Table 1:Site-wise distribution of Skin Adnexal Tumors

SITES OF TUMORS	NUMBER OF CASES	%
• Arm	5	10
• Back	4	8
• Eyelid	3	6
• Face	1	2
• Forearm	7	14

• Forearm	7	14
• Jaw	2	4
• Scalp	28	55
• Thigh	1	2
Grand Total	51	100

Table 2: Spectrum of Skin Adnexal Tumors

HISTOLOGICAL TYPE	NO. OF CASES	PERCENTAGE
BENIGN :		
1.APOCRINE:		
• Apocrine hidrocystoma	4	8
• Cyclindroma	1	2
• Hidradenoma Papilleferum	1	2
• Syringocystadenoma papilleferum	2	4
2.ECCRINE:		
• Syringoma	1	3
• Nodular Hidradenoma	6	12
• Eccrine Spiradenoma	3	6
3.FOLLICULAR:		
• Pilomatricoma	5	10
• Trichofolliculoma	1	2
• Trichoepithelioma	2	4
• Proliferating trichilemmal cyst (Pilar tumor)	19	37
• Trichilemmoma	3	6
MALIGNANT:		
• Sebaceous carcinoma	2	4
• Porocarcinoma	1	2
Grand Total	51	100

DISCUSSION:

Though anatomic location can provide a hint to the type of tumor, histopathology is the gold standard in the diagnosis of skin adnexal tumors⁶

Skin adnexal tumors are classified as tumors with apocrine and eccrine differentiation, tumors with follicular differentiation, tumors with sebaceous differentiation, and site-specific appendage tumors.⁹

Proliferating pilar Cyst/tumor (Proliferating trichilemmal Cyst/Tumor) is the most common adnexal tumor in the present study comprising 37% of cases (19/51). It shows a dermal cyst lined by squamous epithelium and shows abrupt keratinization without a granular layer (keratin material present in the center of the cyst) [Figure 6]

Pilomatricoma (Pilomatricoma, Calcifying Epithelioma of Malherbe) is the third most common adnexal tumor in the present study (10%, 5/51) arising from the outer root sheath cell of the hair follicle. It is seen in the head and neck. It presents as a deep-seated skin-colored nodule. On microscopy, it shows a well-circumscribed tumor in the lower dermis arranged as irregular-shaped islands separated by an intervening stroma and composed of peripheral basophilic cells and centrally located eosinophilic anucleated shadow cells.

Trichilemmoma (6%,3/51) arises from the bulb region of the hair follicle. It presents as a solitary wart or dome-shaped lesion on the face and neck of elderly individuals. The microscopic sections show a well-circumscribed growth showing lobules of clear cells with a thin peripheral rim of palisading columnar cells on a prominent basement membrane.

Trichofolliculoma (2%,1/51) is seen among adults typically on the face. It appears as a single or multiple nodules with a central pore having a tuft of fine hairs. The histopathological section shows one or more cystically dilated hair follicles filled with keratinous material and hair shafts from which many abortive follicles radiate into the cellular stroma.

Trichoepithelioma (4%,2/51) is a dermal tumor consisting of horn cysts of varying sizes, and baseloid epithelial cells arranged in the nest. Now, it is considered to be a subtype/variant of trichoblastoma.

Nodular Hidradenoma is the second most common adnexal tumor in this study (12%, 6/51). It is seen in any age group and the most common affected sites are the trunk and limbs. Clinically, It presents as a solitary, firm nodule. On microscopy, it shows a circumscribed, multilobular dermal tumor with both cystic and solid areas. Tumour cells include round to polygonal cells with amphophilic cytoplasm with a predominance of clear cells surrounded by fibrotic and hyalinized stroma. Both ductal and glandular components are seen in

solid areas while cystic spaces are filled with eosinophilic material [Figure 5]

Syringoma(3%,1/51) is a benign neoplastic lesion of eccrine sweat ducts that is mostly seen among females. It presents as asymptomatic firm papules predominantly in the periorbital region. On microscopy, it shows a well-circumscribed dermal tumor composed of tumor cells arranged in ducts, cords, tubules, and cysts surrounded by dense sclerotic stroma. The ducts are lined by two layers of the cuboidal epithelium with a tadpole or comma-like extension.

Eccrine Spiradenoma(6%,3/51) shows circumscribed dermal nodules with a biphasic cell population comprising peripheral small basaloid cells and central clear cells arranged in solid nests and trabecula admixed with heavy lymphocytic infiltrate.

There is a collection of hyalinized material seen within the tumor islands or in the surrounding areas.

Syringocystadenoma papilliferum (4%,2/51) appears as a nodule or papule and is seen mostly on the face. ⁸ Microscopically, it shows the papillary architecture of infiltrating tumor cells, which exhibit loss of polarity, atypia, frequent mitosis, and disordered proliferation adjacent to its in-situ component. [Figure 7]

Cylindroma (2%,1/51) is a benign tumor arising from sweat glands usually seen in the adult. The site of predilection is the head and neck regions. Both lesions appear as single or multiple nodules.⁸ The microscopic features reveal a circumscribed dermal tumor composed of irregular basaloid cell islands arranged in a jigsaw pattern.

Cell nests are surrounded by a thick hyaline sheath. Cells at the periphery show peripheral palisading and have hyperchromatic nuclei.

Apocrine hidrocystoma (8%,4/51) shows a dermal cystic tumor lined by a double layer of epithelial cells, outer flattened myoepithelial cells, and inner tall columnar cells with decapitating secretion.

Hidradenoma papilliferum (2%,1/51) is a benign apocrine tumor arising from an anogenital area. It is usually seen among females as a solitary papule or nodule. It is a well-circumscribed cystic lesion with decapitation secretion in its lumen and is lined by peripheral cuboidal myoepithelial cells and inner columnar epithelial cells.

Sebaceous carcinoma is the most common malignant skin adnexal tumor accounting for 4% (2/51) seen in elderly individuals with the usual site being the periorbital region. It is characterized by irregular lobules of atypical polygonal cells with abundant vacuolated cytoplasm, vesicular nuclei, prominent nucleoli, variable mitosis, and infiltrative borders surrounded by a fibrovascular stroma. [Figure 8]

Porocarcinoma is seen in the elderly age group and usually presents as an ulceroproliferative growth on the scalp. This is a malignant neoplasm of poroid and cuticular cells. On histopathology, it shows a tumor with infiltrative borders showing marked nuclear pleomorphism, atypical mitosis, and necrosis. [Figure 9]

In the study by Omar and Osman, observed that the most common were benign (94.4%) which was in tandem with other studies and our study^{3,4,6,7,10,11}. However, tumor with sweat gland differentiation was the largest group affected whereas tumor with follicular differentiation was the most commonly affected in the present study¹⁰

In the study by Kaur et al, tumors with follicular differentiation were the most common group, which was in concordance with the present study³

There was slight female preponderance with an overall male-to-female ratio of 1:1.3 in our present study, whereas there was a mild male preponderance with a male: female ratio of 1.07:1 in the study by Sharma et al¹¹

In the study by Manjunath et al, the most common benign adnexal tumor was Pilomatricoma and the most common malignant tumor was Sebaceous Carcinoma.⁶

In the present study, proliferating trichilemmal cysts and nodular hidradenoma were the most common tumors.

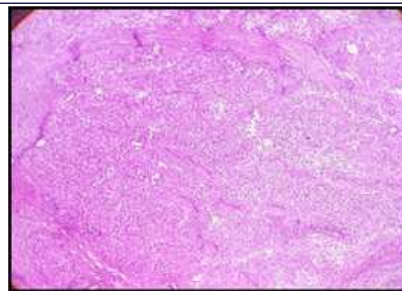


Figure 5 (H&E)(100X): Nodular Hidradenoma showing tumor cells consisting of clear polygonal cells with hyalinized stroma



Figure 6 (H&E)(100X): Pilar Tumor showing stratified squamous epithelium (granular layer) containing keratin

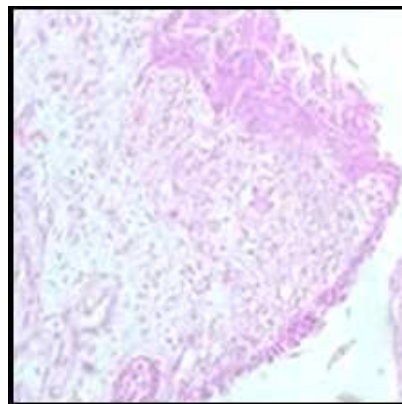


Figure 7 (H&E)(100X): Syringocystadenoma papilliferum showing broad villous projections of the epidermis which contains plasma cells

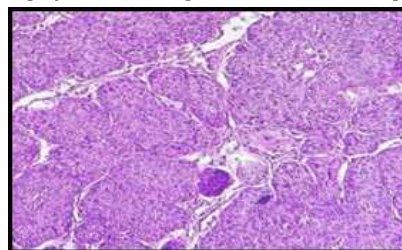


Figure 8 (H&E) (100X): Sebaceous carcinoma showing irregular lobules of sebaceous cells

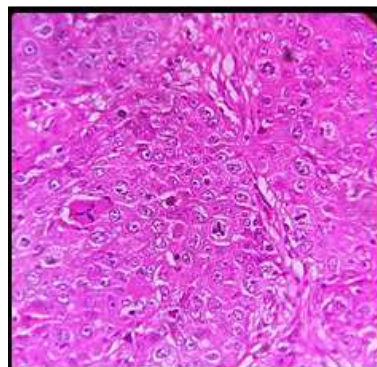


Figure 9 (H&E)(100X): Porocarcinoma showing duct with marked nuclear atypia and atypical mitosis

Limitation Of The Study:

This study was limited by its sample size. In addition, immunohistochemical staining for enzymes like succinic dehydrogenase, alkaline phosphatase, indoxyl esterase, and acid phosphatase was not available in our laboratory and hence not performed.

CONCLUSION :

Histopathology is the gold standard in aiding the diagnosis of skin adnexal tumors and plays a crucial role in differentiating benign and malignant skin adnexal tumors due to its therapeutic and prognostic implications.

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Conflicts of interest: There are no conflicts of interest

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Key Messages:

Histomorphological Spectrum Of Primary Cutaneous Adnexal Neoplasms In A Tertiary Care Hospital

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