



Exploring the Histomorphology of Cutaneous Adnexal Tumors: Insights into Predominant Line of Differentiation and Malignant Tumor Trends

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KEYWORDS

Cutaneous adnexal tumors (CATs), histomorphology, predominant line of differentiation, Malignant tumor trends.

ABSTRACT:

Introduction: Cutaneous adnexal tumors represent a diverse group of neoplasms that differentiate into one or more adnexal structures typically found in normal skin. While the overall incidence of these tumors is low, their diagnosis can be challenging.

Objectives: Our study aims to analyze the histomorphological features of various CATs, focusing on factors such as age, sex, predominant line of differentiation, the frequency of malignant tumors in each variant, and comparison of our findings with those of previous studies.

Methods: This study was conducted from January 2022 to December 2024, involved specimens of wide local excision and edge biopsies received in 10% neutral formalin at the Department of Pathology, MMCRI, Mysore. Specimens were fixed for 24 hours, processed, sectioned, and the slides were subjected to automated haematoxylin and eosin staining. These slides were examined.

Results: 52 cases were diagnosed as CATs, representing 36.5 % of tumors with eccrine gland differentiation, which is the predominant line of differentiation, followed by those showing hair follicle differentiation (32.6%), sebaceous differentiation (21.1%), and apocrine gland differentiation (7.6%). The age range of patients was from 08 to 85 years, with a male-to-female ratio of 1.2:1. Benign tumors (78.8%) were predominant, while 21.1% were malignant. Malignant tumors were frequent in sebaceous differentiation.

Conclusions: Skin adnexal tumors are relatively rare neoplasms. Histopathology is quite essential from a diagnostic point of view. Malignant cases are less common than benign ones. Eccrine tumors are the predominant line of differentiation. Malignant tumors are frequent with Sebaceous differentiation.

1. Introduction

Cutaneous adnexal tumors comprise a rare and heterogeneous group of benign and malignant neoplasms. They arise from undifferentiated multipotent stem cells and exhibit differentiation towards adnexal structures, including hair follicles, sebaceous glands, eccrine glands, and apocrine glands [1-3]. This multifactorial neoplastic transformation is linked to the local tissue microenvironment, epithelial-mesenchymal interactions, activation of certain molecular pathways, and hereditary background [1]. Because of this, CATs can occasionally exhibit many lines of appendageal differentiation, which makes it challenging to accurately

classify these neoplasms. Hence, Histopathological examination is the gold standard in the diagnosis of skin adnexal tumors and precise categorization of these tumors along their phenotypic expression [1]. Adnexal neoplasms manifest as asymptomatic nodules or papules with an unspecific morphology [3]. They exhibit distinctive clinical presentations, manifesting either as solitary lesions or as multiple papules, nodules, or plaques. In syndromic contexts, CATs characteristically multiple in occurrence [4]. The great majority of CATs are benign tumors with little bearing on prognosis [1]. Cutaneous adnexal tumors were referred to as "troublesome tumors," by Cotton D, highlighting the significant challenges encountered in their classification



based solely on clinical evaluation [5]. Certain cutaneous adnexal tumors may serve as cutaneous markers of underlying malignancies. For instance, the presence of multiple trichilemmomas is characteristic of Cowden syndrome, while sebaceous adenomas are frequently associated with Muir-Torre syndrome [6]. The histopathological investigation has the extra benefit of revealing the prevalence of precancerous conditions, which would otherwise go unnoticed during a standard clinical workup or even when advanced technologies like computed tomography are used [3]. In cases where histopathological features are inconclusive, immunohistochemical analysis can serve as a valuable adjunct in establishing a definitive diagnosis [7]. In this study, we examined the histomorphological characteristics of cutaneous adnexal tumors, and their relationship to age, gender, and analyzed the predominant line of differentiation in all the tumors, and evaluated the frequency of malignant tumors in our tertiary care centre. Finally, our observations were juxtaposed with similar previous relevant studies.

2. Objectives

This study aims to evaluate the histomorphological characteristics of diverse cutaneous adnexal tumors (CATs), with emphasis on patient demographics (age and sex), predominant line of differentiation, incidence of malignancy within each subtype, and comparison of findings with previously published data.

3. Methods

This study was conducted for 3 years from January 2022 to December 2024 in the Department of Pathology, Mysore Medical College and Research Institute, Mysore.

Inclusion Criteria

Cases with cutaneous adnexal neoplasms diagnosed by histopathological examination were included in the study.

Exclusion Criteria

Cases with non-neoplastic cutaneous adnexal lesions were excluded.

Methodology

All specimens received in 10% neutral formalin with complete clinical information and clinicopathological parameters that are relevant to our study. These specimens are examined, and a gross description is documented. An adequate bit of tissue is taken from the

lesion, which is subjected to tissue processing in an automated machine. A 4 μ m-thick section was obtained from representative paraffin blocks and stained with Haematoxylin and Eosin (H&E) staining. These stained slides were subjected to histopathological examination.

4. Results

The total number of cases with histopathological diagnosis of cutaneous adnexal neoplasms is 52. The age group ranged from 08 to 85 years, with a mean age of occurrence of 46.5 years (Table 1). The male-to-female ratio is 1.2:1 (Table 2).

TABLE 1: Age-wise distribution of tumors

Age group (in years)	Number of cases
5- 25	9
26- 45	12
46- 65	22
66- 85	9

TABLE 2: Gender-wise distribution of tumors

Gender	Number of cases
Female	24
Male	28

Of these, 41/52 cases (78.8%) were benign, and malignant counterparts comprised 11/52 cases (21.1%) (Table 3).

TABLE 3: Frequency of Benign and Malignant tumors

Benign	Malignant
41	11

Overall neoplasms with eccrine differentiation constitute 36.5 % (21/52), followed by hair follicle differentiation comprising of 32.6% (16/52), 21.1% (10/52), and 7.6% (4/52) of cases with sebaceous differentiation and apocrine differentiation, respectively. One case showed both sebaceous and hair follicle differentiation, diagnosed as sebaceous trichofolliculoma.

In our study, tumors with eccrine differentiation are the predominant subtype of cutaneous adnexal neoplasms (36.5%) (Table 4)



Table 4: Frequency of each line of distribution

Line of distribution	No. of cases	%	No. of benign and malignant cases
Eccrine differentiation	21	36.5	Benign- 18 Malignant- 3
Hair follicle	16	32.6	Benign- 14 Malignant- 2
Apocrine differentiation	4	7.6	Benign- 4 Malignant- 0
Sebaceous differentiation	10	21.1	Benign- 4 Malignant- 6
Sebaceous and Hair follicle differentiation	1	1.9	Benign

Among eccrine cutaneous neoplasms, commonest are hidradenoma seen in 7/21 cases (13.4%), followed by poroma and hidrocystoma in 3/21 cases each (5.7%, 5.7%), syringocystadenoma papilliferum, spiradenoma, eccrine porocarcinoma in 2/21 cases each (3.8%, 3.8%), tubular adenoma, malignant nodular hidradenoma in 1/21 case each (1.9%, 1.9%). (Table 5)

Cutaneous adnexal tumors with hair follicle differentiation: hair follicle differentiation is noted in 16/52 cases (30.7%). The commonest is pilomatricoma in 8/16 cases (15.3%), followed by trichoepithelioma in 3/16 cases (5.7%). Others are trichoadenoma and trichilemmoma. Malignant tumors are Trichilemmal carcinoma and malignant proliferating trichilemmal tumor. (Table 5)

Cutaneous adnexal tumors with sebaceous differentiation: Tumors with sebaceous differentiation is seen in 10/52 cases (19.2%). Malignant tumors are commonest which included 6/10 cases (11.5%), followed by benign tumors, 4/10 cases (7.6%). Among the benign tumors, sebaceous adenoma is the commonest, seen in 3/10 cases (5.7%), followed by nevus sebaceous. (Table 5)

Cutaneous adnexal tumors with apocrine differentiation: Tumors with apocrine differentiation were seen in 4/52 cases (7.6%). All are benign tumors, among which tubular apocrine adenoma and apocrine hidrocystoma are seen in 2/4 cases each (3.8%, 3.8%). (Table 5)

TABLE 5: Various benign and malignant tumors in each line of distribution

Line of distribution	Benign No.	%	Malignant No.	%
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Eccrine differentiation	Hidradenoma 7 (13.4%) Eccrine poroma 3 (5.7%) Eccrine hidrocystoma 3 (5.7%) Syringocystadenoma papilliferum 2 (3.8%) Spiradenoma 2 (3.8%) Tubular adenoma 1 (1.9%)	Eccrine porocarcinoma 2 (3.8%) Malignant nodular hidradenoma 1 (1.9%)
Hair follicle	Pilomatricoma 8 (15.3%) Trichoepithelioma 3 (5.7%) Trichoadenoma 2 (3.8%) Trichilemmoma 1 (1.9%)	Trichilemmal carcinoma 1 (1.9%) Malignant Proliferating trichilemmal tumor 1 (1.9%)
Apocrine differentiation	Tubular apocrine adenoma 2 (3.8%) Apocrine hidrocystoma 2 (3.8%)	-
Sebaceous differentiation	Sebaceous adenoma 3 (5.7%) Nevus sebaceous 1 (1.9%)	Sebaceous carcinoma 6 (11.5%)
Sebaceous and Hair follicle differentiation	Sebaceous trichofolliculoma 1 (1.9%)	-



5. Discussion

Cutaneous adnexal tumors constitute a diverse group of primary skin neoplasms, with their prevalence varying across the human population. Studies on CATs primarily focus on retrospective analyses of epidemiological characteristics. However, they often include a small patient sample and vary in classification criteria [9]. In our study, we analyzed 52 histopathological cases of cutaneous adnexal tumors over 3 years. Martin [1] reported 38 cases within a 2-year period, while Archana [2] documented 55 cases over 5 years. In contrast, Shulbha [3] recorded 105 cases in just one year.

Our study found a higher incidence of skin adnexal tumors in males compared to females with Males to Females ratio of 1.2:1, which aligns with the findings of Satish [8]. In contrast, Archana [2] and Agrawal [12] observed a predominance of female cases.

The age of patients affected by skin adnexal tumors in our study ranged from 8 to 85 years, with a mean age of 38.5 years. In Martin's study, the age range was between 31 and 50 years, with a mean age of 29 years [1]. Most of the cases are seen in the 46- 65 years age group.

In our study, benign lesions accounted for a higher incidence (94.3%) compared to malignant ones (5.7%). Similarly, Archana [2] identified only 2 malignant cases in their 5-year study.

Most cutaneous adnexal tumors typically exhibit benign behaviour, as they originate from undifferentiated pluripotent stem cells. However, factors such as genetics,

local vascularity, and the microenvironment of the epidermis and dermis contribute to the malignant transformation of these tumors [1]. Since incomplete excision can heighten the risk of recurrence and malignancy, it is crucial to ensure that benign tumors are fully excised with wider margins. The diagnosis relies exclusively on histopathological examination, with IHC playing a limited role [13].

Although rare, malignant variants tend to be locally aggressive, have a poor prognosis, and are more prone to metastasizing through lymphatic and hematogenous routes [3].

According to our study, most of the tumors are seen in the eccrine line of differentiation, followed by pilar and sebaceous differentiations. According to reviews of research and literature, tumors with pilar differentiation were often more common than tumors that differentiated from sweat glands and sebaceous glands [3].

In our study, lesions with eccrine differentiation comprised 36.5% of the total burden, similar to study by Samanta M [10]. Among them, hidradenoma is the commonest. They are microscopically characterized by well-circumscribed lesions composed of solid, cystic spaces and hyalinised stroma. Solid components showed polyhedral cells with basophilic cytoplasm and clear cells with eccentric round nuclei. Cystic spaces showed eosinophilic material [15,16]. (Figures 1a and 1b).

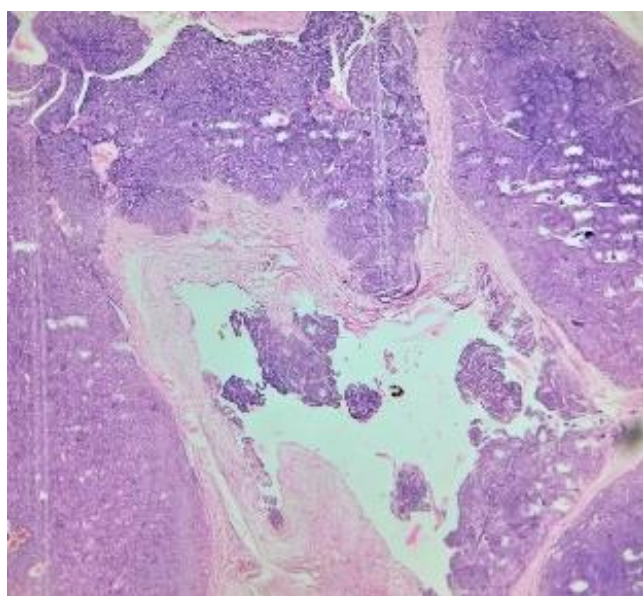


Fig. 1a: Nodular Hidradenoma- solid and cystic spaces

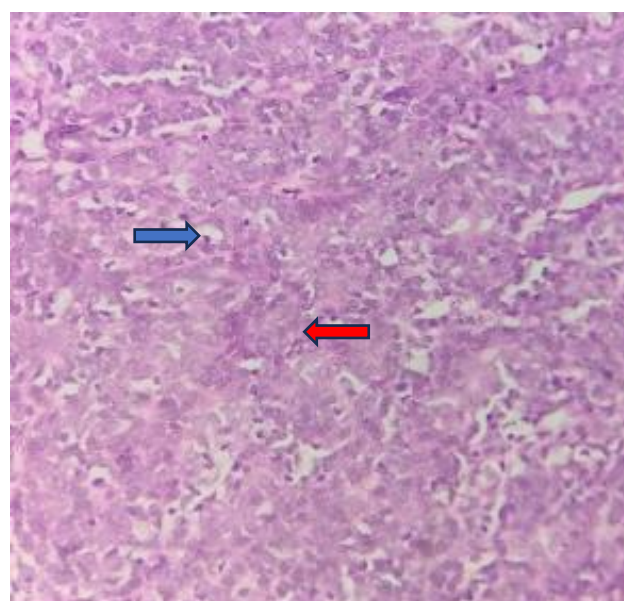


Figure 1b: polyhedral cells (red arrow) and clear cells with eccentric round nuclei (blue arrow)



Porocarcinoma is a malignant tumor of eccrine glands seen in the dermis composed of basaloid cells arranged in solid, nested patterns, and broad anastomosing bands. Cells show moderate nuclear pleomorphism with a high nucleo-cytoplasmic ratio, enlarged vesicular nuclei with

prominent nucleoli, and moderate eosinophilic cytoplasm. Numerous atypical mitotic figures seen. Multiple cysts with eosinophilic secretions. Occasional squamoid differentiation with keratinization seen [15,16]. (Figure 2a and 2b).

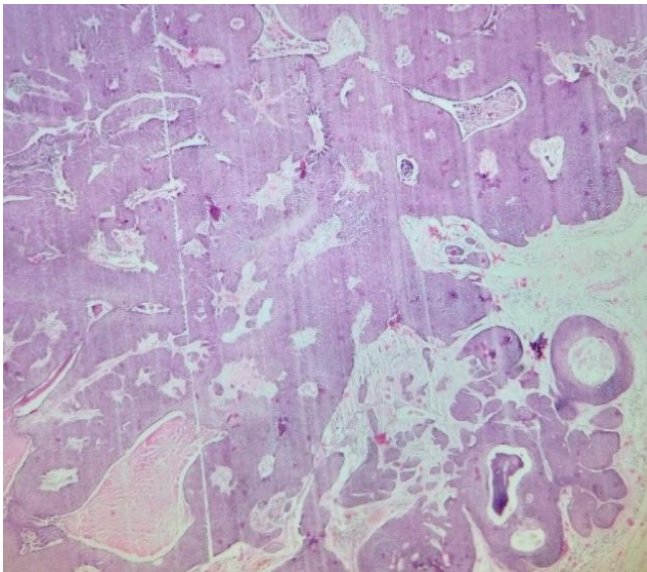


Fig. 2a: Porocarcinoma- solids, nested patterns, and broad anastomosing bands

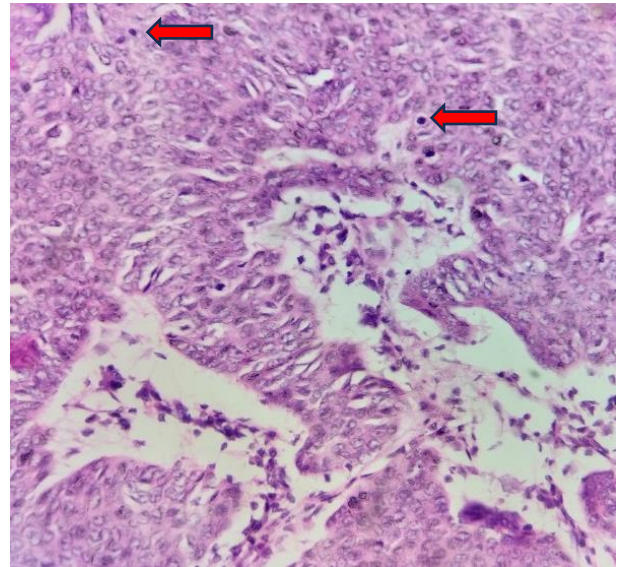


Fig. 2b: Vesicular nuclei with prominent nucleoli and numerous mitotic figures(arrows).

In our study, lesions with hair follicle differentiation are the second most common, comprising 30.7% of the total skin adnexal lesions. The majority of them are benign,

basaloid cells, anucleated ghost cells, multinucleated giant cells, and areas of calcification [15,16]. (Figure 3a and 3b).

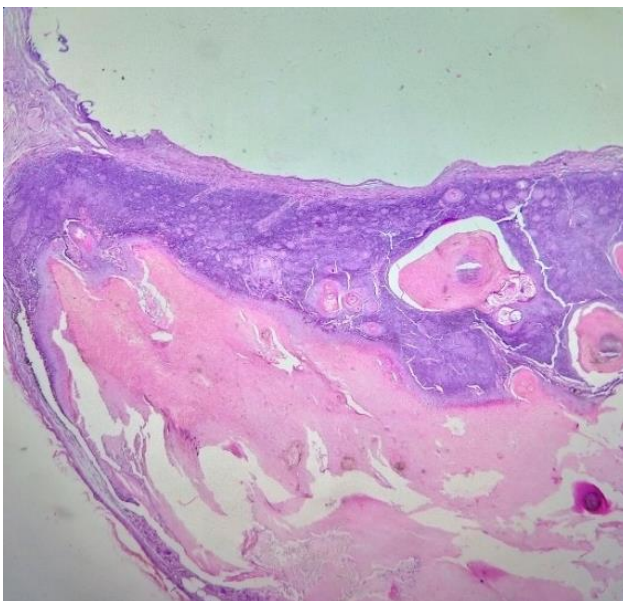


Fig.3a: Pilomatricoma- nests of basaloid cells

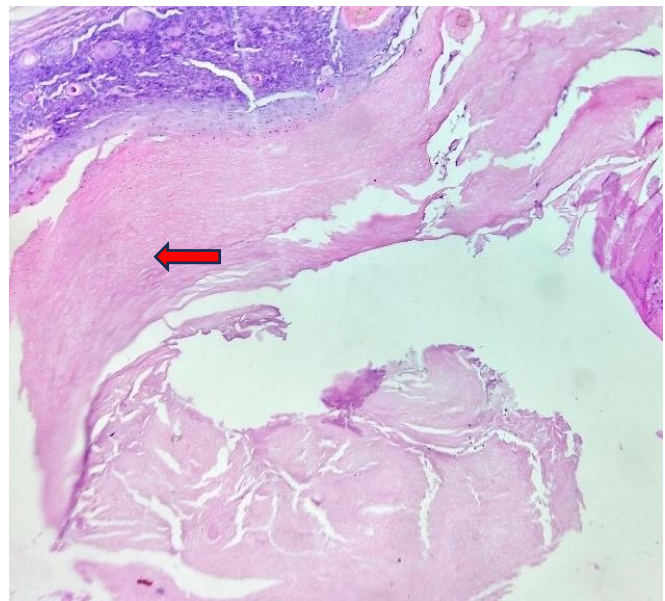


Fig.3b: Anucleated ghost cells(arrow)



Sebaceous gland tumors comprised 19.2% of our study. Malignant tumors are more common than benign. The most common malignant tumors encountered in our study are sebaceous carcinoma, congruous with the study by Kaur [11], Sailendra [13], and Sanapala S [14]. All the cases of sebaceous carcinoma showed neoplastic cells arranged in lobules and nests, infiltrating the entire dermis, separated by thin fibrous septa. These cells show

sebaceous differentiation with anisonucleosis, central nuclei. Also seen are focal necrosis, numerous mitotic figures [15,16]. (Figure 4a and 4b). The most common benign tumor with sebaceous differentiation in our study is sebaceous adenoma.

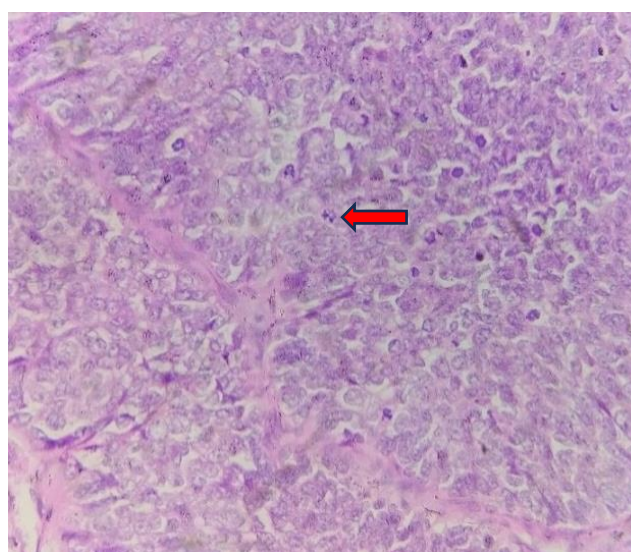
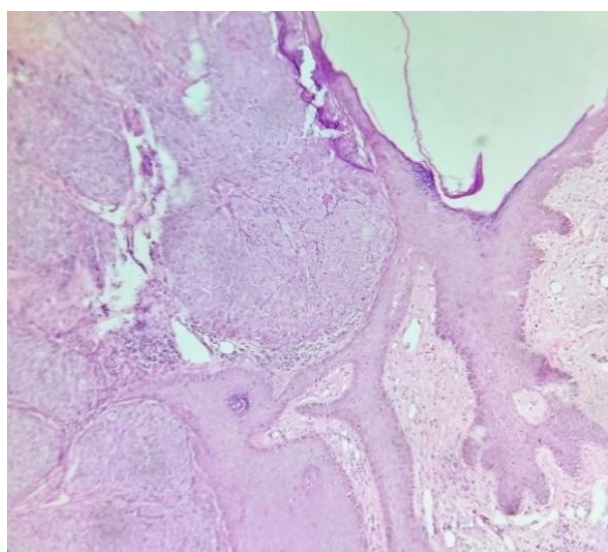


Fig.4a: Sebaceous carcinoma- neoplastic cells arranged in lobules and nests

Fig.4b: sebaceous differentiation with anisonucleosis, central nuclei, few atypical mitotic figures(arrow).

Table 6- Comparative Analysis of Demographic and Histopathological Features of Cutaneous Adnexal Tumors Across Different Studies

Variable	Current study	Martin, et al. [1] (2021)	Archana, et al. [2] (2024)	Sailendra, et al [8] (2020)
Total no. of cases	52	38	55	25
Prevalent age group	46-65	31-50	61-70	41-50
Gender ratio(M:F)	1.2:1	1.2:1	1:1.4	1:1.5
Predominant line of differentiation	Eccrine	Hair follicle	Eccrine	Eccrine
Line of differentiation with most malignant tumors	Sebaceous	-	Eccrine	Sebaceous



Conclusion

To conclude, cutaneous adnexal tumors are most uncommon group of neoplasms. Benign cutaneous adnexal tumors are more frequent than malignant ones. Our study showed a higher incidence of cutaneous adnexal tumors is seen in males compared to females. The predominant line of differentiation is eccrine glands, followed by hair follicle. Malignant tumors are frequent in sebaceous line of differentiation. Most of our findings are in congruence with some previous studies. Due to the difficulty in clinical diagnosis, histopathology remains the gold standard for accurate identification.

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