

## Adnexa Cutis: Demystifying the plethora of Pilosebaceous and Sweat gland neoplasms

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### Abstract

**Background:** The neoplasms of the adnexa cutis arising from the pluripotent stem cell show differentiation towards one of the four adnexal cell lines i.e. follicular, sebaceous, eccrine and apocrine type. Categorizing these neoplasms into specific cell line differentiation and into benign or malignant is important, as malignant adnexal neoplasms are associated with a number of uncommon genetic syndromes and have an aggressive outcome. This study was conducted to primarily categorize these neoplasms based on their histological differentiation.

**Methods:** Fifty-five cases of adnexa cutis that were reported over a four-year period were classified based on their histopathological differentiation and association with clinical parameters.

**Results:** Thirty-three cases (60%) showed pilosebaceous differentiation with pilomatricoma being the commonest benign neoplasm. Twenty two cases (40%) showed eccrine differentiation. The most common malignant adnexal tumor was sebaceous carcinoma. (3 cases – 5.4%).

**Conclusion:** All clinically suspected nodular/papular lesions should be subjected for histopathological examination and classified by differentiation to accurately determine the biologic behavior of the neoplasm.

**Key Words:** Adnexa Cutis, Neoplasm.

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internal malignancies. The histogenesis of these neoplasms is attributed to a pluripotent stem cell resident in the epidermis with divergent differentiation into any of the four lines.<sup>3,4</sup> These heterogenous and complex patterns can be histomorphologically demystified which enable diagnosis and prognostication in these patients. The aim of the study is to categorize these neoplasms based on their histological differentiation patterns and their association with clinical parameters.

### Introduction

The skin, or the human integument is a dynamically complex organ system of the human body comprising of the mutually dependent epidermal and dermal layers. Whilst lesions of the epidermis are exhaustively studied, lesions of the epidermal appendages (Latin: *Adnexa cutis*) relatively remain a clinical and diagnostic obscurity. The adnexa cutis is composed of the pilosebaceous unit which includes the hair follicles and sebaceous glands, while the sweat glands can exhibit either eccrine or apocrine differentiation. Neoplasms arising from these appendages present as clinically insignificant papules or nodules which may either show an indolent benign course or an aggressive malignant outcome. It is imperative to accurately identify these lesions in the backdrop of their rarity and significantly so in their almost certain co-existence with uncommon genetic syndromes such as the Birt-Hogg-Dube' syndrome, Brooke-Spiegler syndrome, Cowden syndrome and Muir-Torre syndrome.<sup>1,2</sup> These neoplasms of the adnexa cutis can be hallmarks in the early diagnosis of these syndromes as well as a harbinger of

### Materials and Methods

A cross-sectional study was conducted, wherein 55 cases of neoplasms of adnexa cutis reported over a four-year period in the department of pathology were studied. Case files were retrieved and clinicopathological details collected. Hematoxylin and eosin stained slides from representative areas of all neoplasms were subjected to systematic examination and special stains including immunohistochemistry were done wherever necessary to arrive at a final diagnosis. The neoplasms were histologically categorized into neoplasms of follicular differentiation, sebaceous differentiation eccrine and apocrine differentiation. Descriptive statistics were employed and results tabulated.

### Results

A total of 55 tumors of the adnexa cutis retrieved over a four year period, were included for the study. Twenty-eight tumors (50.9%) were seen in males and the rest were seen in females (27 cases, 49.1%). These tumors were seen in a wide age group ranging from 2 to 65 years. Mean age of the adnexal tumor was 32 years.

Head and neck region showed the maximum number of cases. Forty-nine cases (89%) were of benign nature and 6 cases (11%) were malignant. The lesions were categorized as those arising from pilosebaceous unit i.e. showing follicular and sebaceous differentiation; and those arising from sweat glands i.e. showing eccrine/apocrine differentiation. Table 1 shows proportion of tumors of adnexa cutis showing pilosebaceous unit and sweat gland differentiation.

**Table 1: Tumors of pilosebaceous unit and sweat gland differentiation**

Tumor	No of cases	%
<b>Tumors of adnexa cutis</b>	<b>55</b>	<b>100</b>
<b><u>Tumors of Pilosebaceous unit</u></b>	<b>33</b>	<b>60</b>
<b><i>Tumors with follicular differentiation</i></b>	<b>30</b>	<b>54.6</b>
Benign	30	54.6
Pilomatricoma	26	47.3
Trichofolliculoma	02	3.6
Desmoplastic Trichoepithelioma.	01	1.8
Trichilemmoma	01	1.8
Malignant	00	00
<b><i>Tumors with sebaceous differentiation</i></b>	<b>03</b>	<b>5.4</b>
Benign	00	00
Malignant	03	5.4
Sebaceous carcinoma	03	5.4
<b><u>Tumors of Sweat gland differentiation</u></b>	<b>22</b>	<b>40</b>
<b><i>Tumors of eccrine differentiation</i></b>	<b>14</b>	<b>25.5</b>
Benign	11	20
Eccrine poroma	05	9.0
Nodular Hidradenoma	03	5.4
Eccrine syringoma	02	3.6
Eccrine Spiradenoma	01	1.8
Malignant	03	5.4
Eccrine porocarcinoma	01	1.8
Malignant chondroid syringoma	01	1.8
Malignant hidradenocarcinoma	01	1.8
<b><i>Tumors of apocrine differentiation</i></b>	<b>08</b>	<b>14.6</b>
Benign	08	14.6
Syringocystadenoma papilliferum	05	9.0
Apocrine cylindroma	02	3.6
Hidradenoma papilliferum	01	1.8
Malignant	00	00

Among the various tumors of adnexa cutis, 60% (33 cases) of them were of pilosebaceous differentiation (follicular – 30cases and sebaceous – 3 cases). Of the benign tumours with follicular differentiation, pilomatricoma was the commonest (27 cases; 47.3%). No malignant cases of follicular differentiation were seen in our study. In contrast, all the tumors showing sebaceous differentiation were malignant (sebaceous carcinoma – 3 cases; 5.4%).

Tumors of sweat gland differentiation accounted for 40% of all tumors of adnexa cutis, with eccrine poroma being the most common benign tumor of eccrine differentiation. One case each of eccrine porocarcinoma, malignant chondroid syringoma and malignant hidradenocarcinoma was also seen in the category of tumors of eccrine differentiation. Eight tumors (14.6%) of apocrine differentiation were encountered in our study, all of which were benign with

syringocystadenoma papilliferum being the commonest one.

### Discussion

The skin adnexa or adnexa cutis, is composed of different types of adnexal epithelium seen in pilosebaceous unit and sweat glands. Tumors arising from these adnexal epithelium show morphological differentiation towards follicular, sebaceous, eccrine or apocrine cells even though they arise from a pluripotent stem cell.<sup>3,4</sup> Differentiation of these neoplasms into one of the above mentioned cell line makes it amenable for rendering a specific nomenclature to it although it may be difficult to do so accurately in some cases.

Tumors of adnexa cutis are uncommon neoplasms, a fact exemplified by the relatively small number of cases encountered in studies by various authors who reviewed the histopathological cases in their institution for years. Sharma A et al<sup>5</sup> reviewed 56 cases over a 7-

year period, Nair PS<sup>6</sup> studied 33 cases over a 3-year period, Saha A et al<sup>7</sup> studied 23 cases over a period of one year. Studies conducted by Samaila<sup>8</sup> and Tirumalae R et al<sup>9</sup> documented 52 and 68 cases over a period of 16 years and 13 years respectively. The present study yielded a sample size of 52 cases over a period of 4 years. These data clearly speaks about the rarity of these neoplasms in particular.

Cutaneous adnexal tumors are seen to occur over a wide age group. The present study had patients' age ranging from 2 to 65 years of age, with a mean age of 32 years. Studies conducted by Saha A et al,<sup>7</sup> Samaila<sup>8</sup> and Kamyab-Hesari K et al<sup>10</sup> have shown almost similar mean age distribution. In contrast, study by Sharma A et al<sup>5</sup> shows a higher age of presentation of adnexal tumors (51-60 yrs). Gender wise, the present study had a slight male predominance (1.1:1). Most of the studies have documented a female predominance. One possible explanation given to female predominance is that females present to the clinic more often due to cosmetic reasons. However at present, the trend appears to be similar in males too.

Most of these skin adnexal tumors present as papular or nodular lesions which are generally asymptomatic and cannot be diagnosed solely based on clinical grounds. However, depending on their anatomic location, number, distribution and duration of the lesions, a provisional diagnosis of tumor of the adnexa cutis can be contemplated.<sup>11</sup>

In the present study, tumors with follicular differentiation accounted for 54.6% of all tumors of adnexa cutis. Tumors with eccrine, apocrine and sebaceous differentiation accounted for 25.5%, 14.6% and 5.4% respectively. Benign cases constituted about 49 cases (89%), the rest were malignant. Studies conducted by Saha A et al<sup>7</sup>, Samaila<sup>8</sup> and Kamyab-Hesari k et al<sup>10</sup> have all shown a very high prevalence of benign tumors. The commonest benign tumor encountered in the present study was pilomatricoma (26 cases, 47.3%), a tumor of follicular differentiation; followed by eccrine poroma (5 cases, 9%) and syringocystadenoma papilliferum (5 cases, 9%).

The most common malignant tumor encountered was sebaceous carcinoma (3cases, 5.4%). Studies conducted by other authors show varied frequency of occurrence of different benign and malignant neoplasms. In a study by Kamyab-Hesari k et al,<sup>10</sup> the most prevalent single tumor type was of sebaceous differentiation (52.7%), the most common benign tumor being sebaceous nevus and the commonest malignancy was sebaceous carcinoma. Samaila<sup>8</sup> documented sweat gland tumors (78.8%) to be the predominant type, with eccrine acrospiroma being the commonest benign tumor in their study. Syringoma (40%) was the commonest tumor encountered in a study by Saha A et al<sup>7</sup> and Nair PS<sup>6</sup>. Sharma A<sup>5</sup> documented clear cell hidradenoma, a sweat gland tumor to be the commonest type along with pilomatricoma in the benign category. The role of

adnexal tumors in cutaneous syndromes has to be highlighted. In our study, the case of malignant chondroid syringoma was seen in a patient documented to have xeroderma pigmentosa. This co-occurrence is hitherto not reported.

Histopathological examination is the gold standard in diagnosis of tumours of adnexa cutis. Of late immunohistochemistry is in use for differentiation among various adnexal cell lines. One such marker is CD 117, a stem cell indicator, which shows strong positivity in tumors of eccrine/apocrine differentiation.<sup>12</sup> However due to cost-benefit ratio, immunohistochemistry is not used routinely for diagnosis of tumors of the adnexa cutis in most centres.

### Conclusion

All clinically suspected lesion should undergo histopathological examination and a systematic approach in evaluation is mandatory to categorise the neoplasm into one of the four appendage lines. It is also imperative to accurately determine the biologic behavior of these neoplasms as benign or malignant as it is implicated in their prognostication and histopathology is the most cost-effective tool to do so.

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