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Original Article

Histomorphological patterns of skin adnexal tumors with an insight into molecular updates- A single institutional study

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ABSTRACT

Background: Skin adnexal tumors are a spectrum of benign and malignant tumors that differentiate toward or arise from the adnexal unit of the skin. These rare tumors pose a challenge in diagnosis, and often, a discrepancy is seen between clinical and histopathological diagnosis.

Materials and Methods: This single institutional study was carried out among 36 patients who presented with swelling. An initial diagnosis was considered based on the clinical history followed by histopathological examination.

Results: Among the 36 patients, only 4 had malignant tumors. Among them, 3 had sebaceous differentiation, and 1 had apocrine and eccrine differentiation. Among the benign, 14 had follicular differentiation, 12 had apocrine and eccrine differentiation, and 6 had sebaceous differentiation. The clinic-pathological correlation was 65%.

Conclusions: An accurate diagnosis is not possible with just the clinical features. Histopathologic examination is considered the gold standard for diagnosis and categorization.

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INTRODUCTION

Skin adnexal tumors (SAT) encompass a wide spectrum of skin tumors that originate from or show differentiation towards adnexal structures, such as pilosebaceous unit, eccrine and apocrine glands.[1] These tumors may include hyperplasia, hamartomatous lesions, benign, and malignant tumors. These tumors arise from multipotent stem cells that are present within the epidermis or its appendages. During neoplastic transformation, these tumors due to an aberration may express one or more lines of appendageal differentiation of varying degrees.[1]

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Common sites where dermal tumors are seen are the head, neck, trunk, and extremities. They are classified according to appendageal differentiation.[2,3] These tumors are mostly benign in nature.[4,5] They are usually found as solitary, sporadic lesions. However, certain types of multiple tumors may be an indication of some underlying genetic syndromes. e.g., trichilemmomas are commonly seen in Cowden's syndrome and sebaceous tumors in Muir Torre syndrome.[4,5]

Every benign SAT has a malignant counterpart. These malignant tumors, though rare, have poor clinical outcomes, tend to recur, and show lymph node metastasis.[6] Hence, the categorization of the tumor as benign or malignant is vital for therapeutic and prognostic purposes.[4]

Skin adnexal tumors were termed "troublesome tumors" and posed a challenge in clinching an accurate diagnosis.[7] Their variable histomorphological patterns make it difficult to classify these tumors.[8] Though clinical features such as anatomic location, number, and pattern of distribution provide clues to the diagnosis, histopathology remains the gold standard in the confirmation of the diagnosis.[9]

This study was carried out among 36 SAT patients in a single institution to record and compare their clinical history and histopathologic diagnosis and study the histomorphological patterns and differentiation and assess the clinicopathological correlation of diagnosis.

MATERIALS AND METHODS

This descriptive study was carried out over a period of two years between March 2019 to March 2021, in the Department of Pathology, at a teaching medical college. All the various types of skin adnexal tumor cases presented to the Department of Pathology were included in the study. The clinical notes of all 36 cases were reviewed and retrieved from the histopathology requisition form, and the following details were analyzed: age, gender, site of involvement, and clinical diagnosis. Only histopathologically diagnosed skin appendageal tumors were included in the study & the skin epidermal tumors were excluded. Formalin-fixed, paraffin-embedded tissue sections stained with hematoxylin and eosin were retrieved & studied. The tumors were classified according to the origin of various adnexa. The present study was approved by the institutional ethical committee. Data were analyzed using Microsoft Excel and the results were expressed in frequency and percentage.

RESULTS

In the present study, benign adnexal tumors constituted 88.9% of cases, and malignant adnexal tumors constituted 11.1% of cases(Table 1). Hair follicular tumors constituted the largest group involving 40% of cases, followed by apocrine and eccrine tumors involving 37% of cases, and lastly, sebaceous tumors involving 23% of cases. Tumors were seen in all age groups ranging from 3 to 80 years. Pilomatricoma was the commonest tumor, observed in 23% of cases. Sebaceous carcinoma was the most common malignant tumour, observed in 6% of cases. The clinico-pathological correlation of diagnosis was 65%.

Table 1: Histopathological differentiation among study participants

	Follicular differentiation (n,%)	Apocrine & eccrine differentiation (n,%)	Sebaceous differentiation (n,%)
Benign	Pilomatricoma (8;23%)	Poroma (fig.1; n=2; 6%)	Sebaceous hyperplasia (1;3%)
	Trichoblastoma (1;3%)	Hidradenoma (4;11%)	Sebaceous adenoma (3;9%)
	Trichoadenoma (fig.2; n=1; 3%)	Spiradenoma (1;3%)	Nevussebaceous of Jadassohn (2;6%)
	Trichoepithelioma (fig. 3; n= 2;6%)	Syringocystadenoma papilliferum (2;6%)	
	Proliferating trichilemmal cyst (2;6%)	Combined lesion (Syringocystadenoma papilliferum & Tubular apocrine adenoma) (fig.4; n= 2; 6%)	
		Chondroid syringoma(Mixed tumour of skin) (fig.5; n=1;3%)	
Malignant		Porocarcinoma (1;3%)	Sebaceous carcinoma (3;6%)
Total	14 (40%)	13(37 %)	9 (23%)

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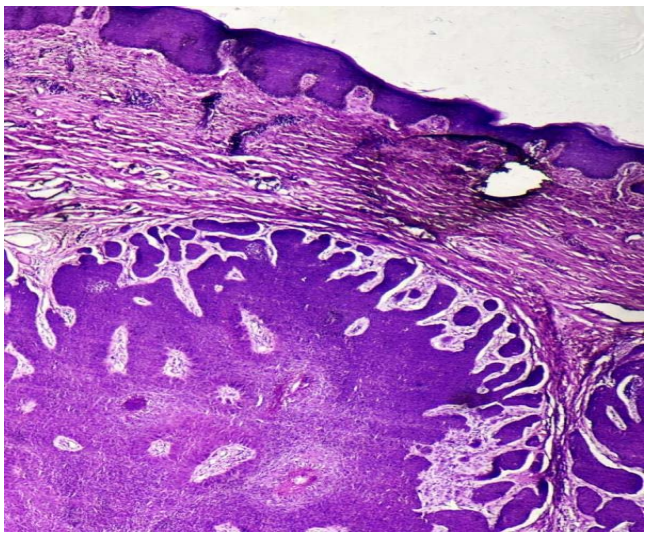


Figure 1: *Poroma; Dermal-based tumour with epidermal connection(HE stain, x100)*

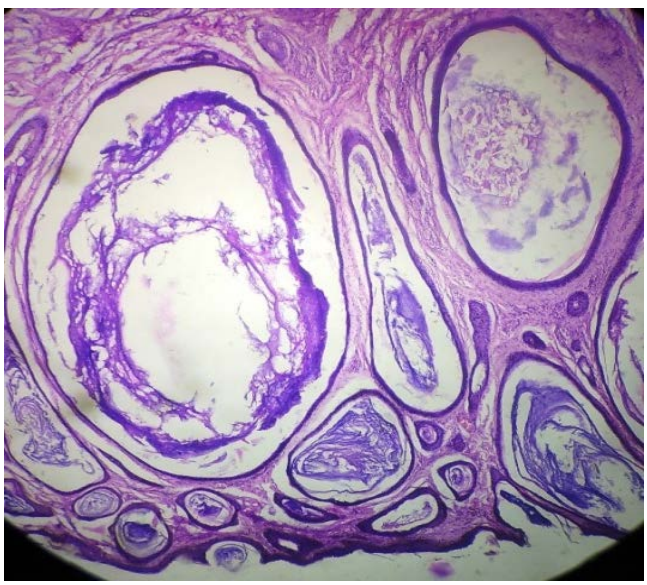
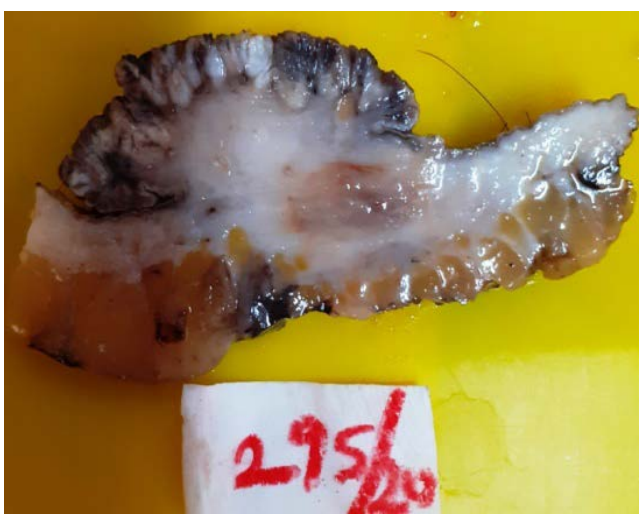
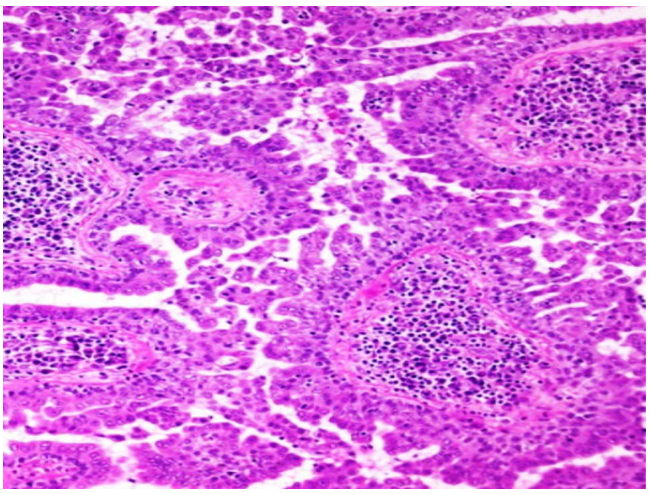


Figure 2: *Trichoadenoma; Dermal tumor composed of numerous cysts, lined by squamous epithelium (HE stain, x100)*



3A)



3B)

Figure 3A: *Gross-Skin colored nodule* ***3B:*** *Microscopy of Syringocystadenoma papilliferum. The epidermis is thrown into papillary projections lined by bilayered epithelium. Decapitation secretion of luminal cells is noted focally with stromal plasma cells. (HE stain, x100)*

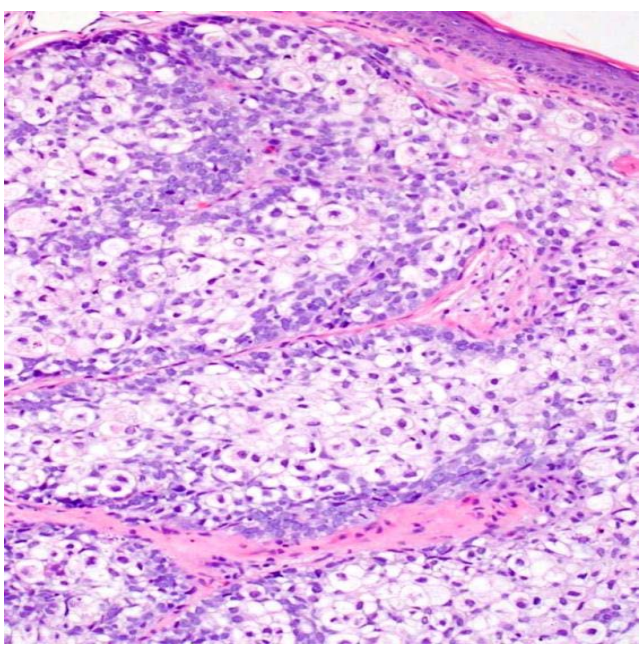


Figure 4: *Sebaceous carcinoma. The tumoris composed ofcells arranged in papillary patterns, nests & sheets with focal areas showing sebaceous differentiation (HE stain, x100)*

DISCUSSION

Many works of literature report that benign tumors occur more commonly than malignant tumors. In the present study, benign adnexal tumors constituted 88.9% of cases, and malignant adnexal tumors constituted 11.1% of cases. This is similar to the findings of Radhika et al.[8], Reddy et al.[10], and Samaila[11]. They reported 77.14%, 69.41%, and 88.5% benign and 29.63%, 30.59%, and 11.5% malignant tumors, respectively. Also, Radhika et al.[8] and Samalia[11] observed that sweat glands tumors are the most common followed by

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sebaceous glands tumors, and lastly, tumors of hair follicles. In the present study, it is observed that hair follicular tumors were the most common involving 40% of cases, followed by apocrine and eccrine tumors involving 37% of cases, and lastly, sebaceous tumors involving 23% of cases. This might be due to a relatively small sample size.

Kanwalpreet et al.[1], Song et al.[12], and Alsaad et al.[5], in their studies, observed that pilomatrixoma was the most common benign tumor. This is similar to the present study, where pilomatrixoma was the most common tumor, observed in 23% of cases. However, Radhika et al. reported that the most common benign tumor was nodular hidradenoma.[8]

Sebaceous carcinoma was the most common malignant tumor reported in the present study, observed in 6% of cases. This is in tandem with many studies that reported sebaceous carcinoma was the most common malignant adnexal tumor.[13,14,15,16] However, Samaila reports that sweat gland carcinoma is the most common skin adnexal malignancy.[11]

These show the varied nature of the tumors. SATs need to be diagnosed and classified according to differentiation to understand the pathology and nature of the disease. Bernard Ackerman was the first to emphasize the importance of architectural features in distinguishing between benign and malignant tumors. He observed that benign tumors are vertically oriented and symmetrical with uniform epithelial cells; they show dense fibrotic stroma, and there is an absence of atypia, necrosis, and mitosis. Malignant tumors show asymmetry, nuclear pleomorphism, necrosis, and increased mitosis.[1]

The diagnosis of adnexal tumors is difficult and cannot be arrived at with just the clinical features alone. The usual presentation of flesh-colored nodules, papules, and disfiguring lesions such as ulcers may be mistaken for keratinous cysts.[4,2,3,8,17] Histopathology remains the gold standard for the diagnosis of SATs. Special stains such as periodic acid Schiff, mucicarmine, alcian blue, and reticulin may help in arriving at a definitive diagnosis.[4,2]

Most adnexal tumors are diagnosed histopathologically. However, few adnexal tumors have diagnostic challenges. In this regard, immunohistochemistry can be utilized. BCL-2 positivity is diffuse in basal cell carcinoma; whereas basal positivity is seen in desmoplastic trichoepithelioma (DT). CD34 positivity is seen in desmoplastic trichelomma whereas CD34 negativity is seen in basal cell carcinoma. Microcytic adnexal carcinoma (MAC) can be differentiated from other sclerosing adnexal tumors(morphea-like BCC and desmoplastic trichoepithelioma) by showing positivity for CK 7 and BCL-2. Syringoma and desmoplastic trichoepithelioma and be differentiated by CEA positivity and involucrin negativity in the former and vice versa. Most primary cutaneous adnexal tumors express p63, CK 5/6 & D2-40, whereas cutaneous metastasis from visceral adenocarcinomas shows negativity for these markers. Immunohistochemical staining for androgen receptors is specific for sebaceous lesions as compared to basal cell carcinomas, squamous cell carcinomas, and clear cell acanthomas. Epithelial membrane antigen (EMA), anti-BCA-255 (BRST-1), and CAM 5.2 can help distinguish sebaceous carcinoma from basal cell carcinoma and squamous cell carcinoma.[18]

CONCLUSIONS

The present study concludes that histopathologic examination is the gold standard for the diagnosis and categorization of SATs. This study reaffirms that an accurate diagnosis cannot be arrived at with just the clinical features. Under microscopy, these tumors show complex histomorphology due to the variety of tissue elements, patterns, and metaplastic transformations involved, which also makes the diagnosis difficult. Hence, histopathologic examination remains the gold standard. Also, most of these tumors are benign, and hence, timely diagnosis and appropriate treatment can prove to be curative in most cases.

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