Original Article

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Skin Adnexal Tumors: A Histopathological Study of 60 Cases at a Tertiary Care Centre

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ABSTRACT

Background: Skin adnexal tumors(SATs) are one of the most challenging areas of dermatopathology.SAT encompasses a large and a diverse group of benign and malignant neoplasms which exhibit morphological differentiation towards one of the different types of adnexal epithelium present in normal skin.The aim of this study is to study the spectrum and microscopic features of skin adnexal tumors.

Methods: A cross-sectional, descriptive study was conducted over a period of 5 years in the Department of Pathology,VIMSAR,Burla. Formalin fixed, paraffin embedded tissue sections were stained with hematoxylin and eosin stain for histopathological analysis.

Result: Out of total 60 cases diagnosed as adnexal neoplasm27(45%) tumors were with sweat gland differentiation followed by tumors with sebaceous differentiation 19(31.66%) and follicular differentiation14(23.33%). The age ranged from 11 years to 75 years and male to female ratio was 1.7:1.Mostof the tumors(78.33%) were benign while only 21.66% were malignant. Eccrine poroma was the most common benign tumor while sebaceous carcinoma was the most common malignant tumor.

Conclusion: Architectural features are of great importance in differentiating benign tumors from malignant tumors in histopathology.

Keywords: *Adnexal, Differentiation, Histopathology, Skin*

Introduction

Skin adnexal tumors (SATs) are the tumors arising from the appendages of the skin such as sweat glands, sebaceous glands and hair follicles. They are often difficult to diagnose clinically and histopathology usually provides diagnostic confirmation. SATs are a heterogeneous group of skin tumors usually found as solitary, sporadic lesions with mostly benign behaviour; however, certain specific types of tumors may be an indication of some complex genetic syndromes like Cowden's syndrome and Muir Torre syndrome.[1,2] These tumors are derived from multipotent undifferentiated cells present within the epidermis or its appendageal structures and the histologic features of the tumor are related to the activation of molecular pathways responsible for forming the mature adnexal structure.[1]This study was undertaken to analyze the spectrum and histopathological profile of adnexal tumors of the skin.

Material and Methods

The present study was a cross-sectional, descriptive study conducted over a period of 5 years (October 2012 – October2017) in the Department of Pathology, VIMSAR, Burla. Approval from institutional ethical committee was taken for the study. Patients with suspected skin adnexal tumors attending the out patients department of dermatology were recruited for the study. Demographic and clinical details of patients were documented. The excised specimens were fixed in 10% formalin, properly processed and stained using hematoxylin and eosin (H&E) stain and subjected for microscopic evaluation. Immunohistochemistry (IHC) was performed as and when required. All the slides were reviewed, diagnosed and classified as SATs arising from sebaceous glands, hair follicles or sweat glands. Necessary statistical analysis was done using Microsoft Office Excel 2007. The concordance of clinical and histopathological diagnoses was accessed.

Results

A total of 60 patients (38 males and 22 females) with SATs were evaluated. The male to female ratio was 1.7 : 1. Out of 60 cases, 47(78.33%) were benign while only 13(21.66%) were malignant SATs. The sweat gland tumors accounted for 27(45%) cases, sebaceous gland tumors 19(31.66%) cases and hair follicle tumors 14(23.33%) cases according to direction of differentiation (Table 1). Among the benign SATs, eccrine poroma constituted 10(16.66%) cases, sebaceous adenoma 9(15%) cases, syringoma and pilomatricoma 7(11.66%) cases each, nodular hidradenoma and trichoepithelioma 3(5%) cases each whereas, eccrine spiradenoma, sebaceoma, proliferating trichilemmal tumor and trichoblastoma constituted 2(3.33%) cases each (Table 1). Among malignant SATs, sebaceous carcinoma constituted 8(13.33%) cases whereas malignant poroma

& malignant nodular hidradenoma 2(3.33%) each and adenoid cystic carcinoma constituted only 1(1.66%) case (Table 1). Clinical diagnosis was discordant with histopathological diagnosis in 8 cases. The age group wise distribution of SATs is depicted in (Table 2) and the site wise distribution is shown in (Table 3). The size of tumors (maximum dimension) was less than 1.5cm in 42(70%) cases, between 1.6cm to 2.5cm in 9(15%) cases, between 2.6cm to 4cm in 7(11.66%) cases and more than 4cm in 2(3.33%) cases.

Table 1: Proportions of various skin adnexal tumors according to direction of differentiation (n=60).

Category	Direction Of Differentiation	Types of skin adnexal tumors		Number Of Cases with percentage
I	Sweat Gland	Benign	Eccrine Poroma	10 (16.66%)
			Syringoma	7 (11.66%)
			Nodular Hidradenoma	3 (5%)
			Eccrine Spiradenoma	2 (3.33%)
		Malignant	Malignant Poroma	2 (3.33%)
			Malignant Nodular Hidradenoma	2 (3.33%)
			Adenoid Cystic Carcinoma	1 (1.66%)
		Total		**27 (45%)**
II	Sebaceous Gland	Benign	Sebaceous Adenoma	9 (15%)
			Sebaceoma	2 (3.33%)
		Malignant	Sebaceous Carcinoma	8 (13.33%)
		Total		**19 (31.66%)**
III	Hair Follicle	Benign	Pilomatricoma	7 (11.66%)
			Trichoepithelioma	3 (5%)
			Proliferating Trichilemmal Tumor	2 (3.33%)
			Trichoblastoma	2 (3.33%)
		Total		**14 (23.33%)**
	Total			60

Table 2: Age group wise distribution of skin adnexal tumors (n=60).

Sl No.	Age Group (in years)	Number of Cases with percentage
1	11 – 20	08(13.33%)
2	21 – 30	15(25%)
3	31 – 40	06(10%)
4	41 – 50	09(15%)
5	51 -60	08(13.33%)
6	61 – 70	11(18.33%)
7	71 -80	03(5%)
	Total	**60**

Table 3: Site distribution of skin adnexal tumors (n=60).

Sl No.	Site Of Tumor	Number of Cases with percentage
1	Scalp	17(28.33%)
2	Face	10(16.67%)
3	Neck	09(15%)
4	Trunk	12 (20%)
5	Upper Limb	05 (8.33%)
6	Lower Limb	07 (11.66%)
	Total	**60**

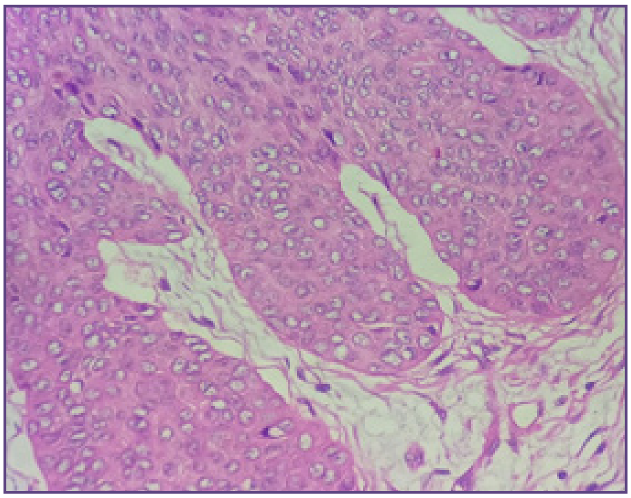

Fig. 1: Eccrine Poroma - Lobules of basaloid cells in lower portion of epidermis extending towards the dermis (H&E, 100X).

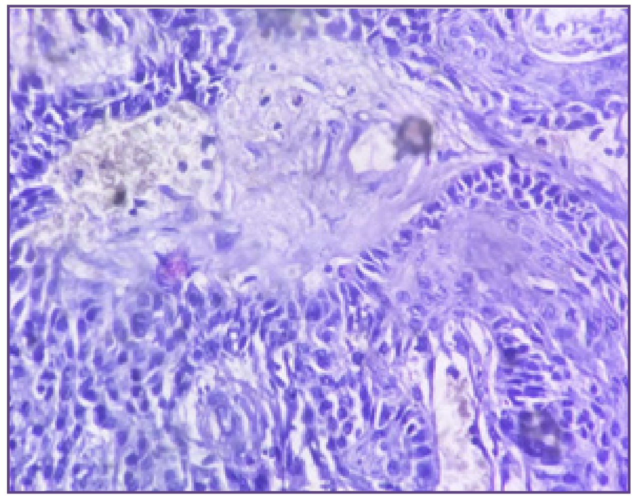

Fig. 2: Nodular Hidradenoma – Epithelial lobules comprising of clear cells and polygonal cells (H&E, 400X).

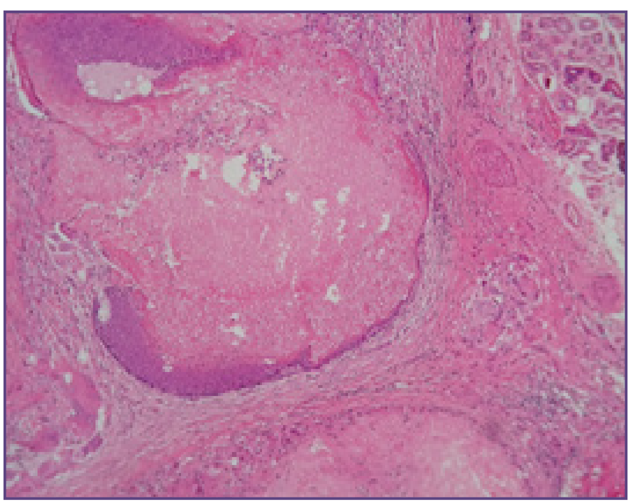

Fig. 3: Pilomatricoma – Islands of tumor cells having both basophilic cells and shadow cells (H& E, 100X).

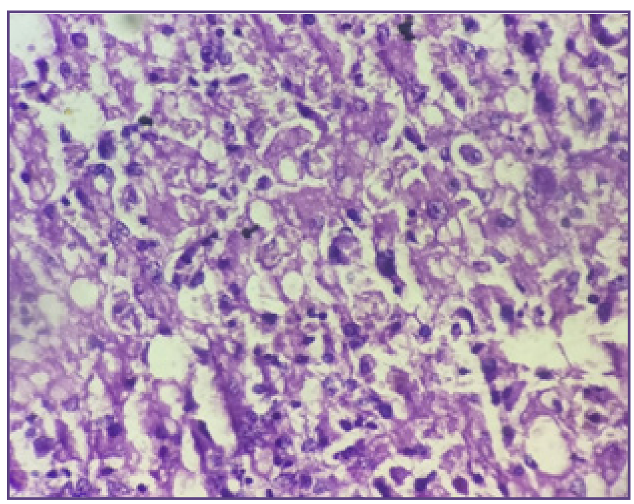

Fig. 4: Sebaceous Carcinoma – Cytologic atypia, mitotic activity and focal sebaceous cells with foamy cytoplasm (H&E, 400X).

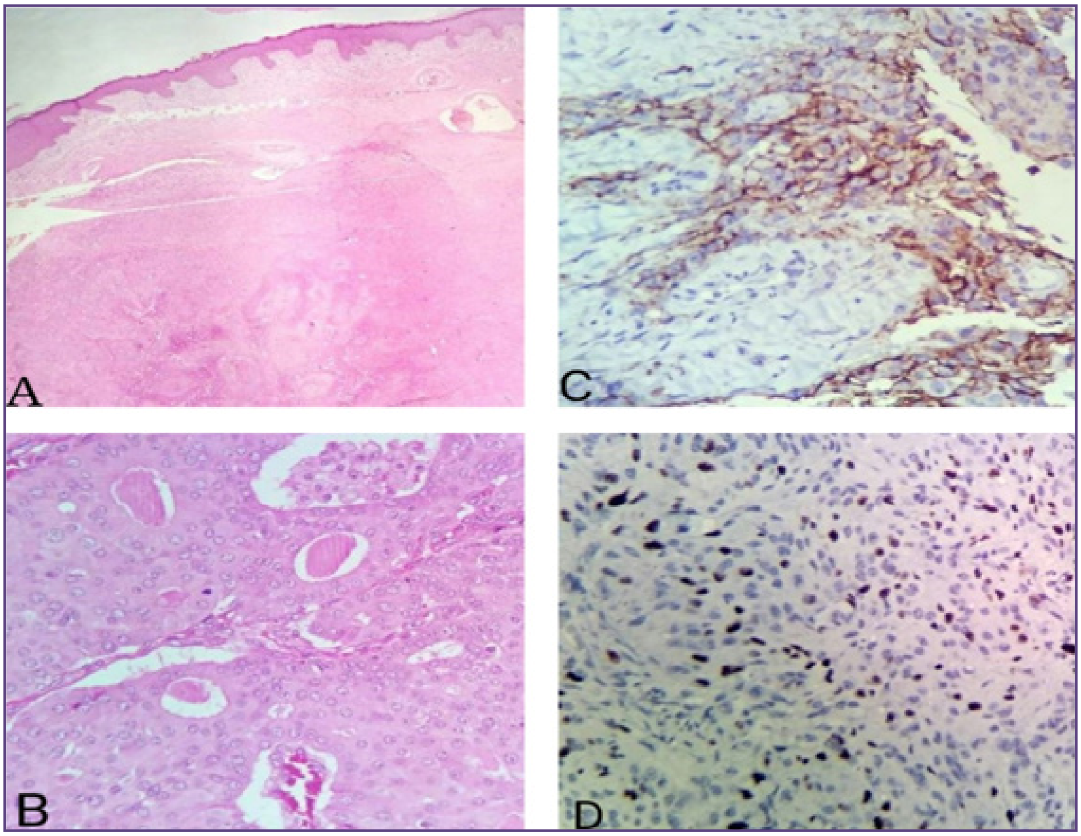

Fig. 5: Malignant Nodular Hidradenoma (A)Tumor cells arranged in invasive nodular pattern with prominent cystic spaces (H&E, 40X). (B) Atypical epithelial cells arranged in sheets (H&E, 400X). (C)Immunohistochemistry showing EMA positivity(IHC,400X). (D)Immunohistochemistryshowing Ki 67 >14%(IHC,400X).

Discussion

The large majority of SATs differentiate only along one adnexal line and this results in the formation of reasonably distinct types whose stucture, cytochemistry and immunohistochemistry can be correlated with those of the corresponding adnexa or even a subdivision thereof.[3] The diagnosis of adnexal tumour poses great difficulties owing to a variety of reasons namely, the enormous types of tumors with their variants, the occurrence of multiple lines of differentiation in a single tumor as well as the complicated nomenclature. Adnexal tumors originate from multipotent undifferentiated stem cells which have the capability to differentiate along particular pathways, may be multiple.[1,2] In the present study, the most frequent line of differentiation encountered was sweat gland differentiation(45%), followed by sebaceous differentiation (31.66%) and the least frequent being hair follicle differentiation (23.33%). With regards to the line of differentiation of adnexal tumors, our findings are consistent with many other studies like Samaila *et al*.[4], Saha *et al*.[5] , Jindal *et al*. [6] , Gayathri *et al*.[7], Radhika *et al*. [8], Pentola *et al*.[9] and Sharma *et al*.[10] In this study, the proportion of adnexal tumors with sebaceous differentiation is comparatively more (31.66%) than the above mentioned studies.[4,5,6,7,8,9,10].

The male to female ratio of the patients was found to be 1.7:1 which was comparable to that of Pantola *et al*.[9] (1.8:1) . However, Saha *et al*.[5] found female preponderance in their study (male to female ratio was 8:15).

In the Indian population, the overall incidence of SATs is very low as documented by several studies.[5,6,7,8,9] The location of SATs varies with the histological types. By far, head and neck region is the most common location where adnexal tumors are frequently encountered, the other sites being axilla, trunk, legs etc. In the present study, the site of predilection was head and neck in 36(60%) cases, followed by extremities (20%) and trunk (20%). The predominance of adnexal tumors in head and neck region is a well documented fact supported by most of the series in literature.[4,5,8,10] This is due to the fact that this region is rich in pilosebaceous units, apocrine as well as eccrine glands, thereby providing a fertile environment for the development of adnexal tumors.

Most of the tumors in our study (70%) were <1.5cm in maximum dimension. Very rarely, the size of these tumors exceeded 4cm in diameter. Jindal *et al*.[6] also observed 76% of SATs to be <2cm in size. Eccrine poroma was the most commonly encountered benign SAT in our study with a total number of 10(16.66%) cases. Samaila *et al*.[4] also found eccrine poroma (32.7%) to be the most common benign SAT. However, Saha *et al*.[5] and Nair PS[11] found syringoma to be the most common SAT of head and neck region whereas Kaur *et al*.[12], El Ochi *et al*.[13] and Rajalakshmi *et al*.[14] found pilomatricoma to be the most common benign SAT. Among the malignant SATs sebaceous carcinoma was the commonest neoplasm 8(13.33%) in our study. This finding was consistent with Sharma *et al*.[10] and Kaur *et a.l*[12] However, Samaila *et al*.[4] and Radhika *et al*.[8] found sweat gland carcinoma to be the most common malignant SAT.

Microscopically, eccrine poroma showed broad anastomosing bands of epithelial cells extending from epidermis to dermis having uniform cuboidal cells with round deeply basophilic nucleus (Figure 1). Syringoma showed numerous small ducts lined by two rows of epithelial cells and embedded in fibrous stroma. Some of these ducts have small, comma-like tails of epithelial cells, giving tadpole appearance. Nodular hidradenoma showed capsulated, well circumscribed epithelial lobules in the dermis, having two populations of cells; polyhedral cells with rounded nucleus & slightly basophilic cytoplasm and round cells with small dark nucleus & clear cytoplasm (Figure2).Eccrine spiradenoma showed lobules of epithelial cells in dermis consisting of peripheral small dark nuclei and central larger pale nuclei. Microscopically, pilomatricoma showed islands of basophilic and shadow cells in the lower dermis. The basophilic cells are arranged in the periphery or on one side of tumor islands; the shadow cells have distinct border and a central unstained area as a shadow of lost nucleus (Figure 3).Trichoepithelioma showed horn cysts and tumor islands consisting of basophilic cells arranged in lace like or adenoid pattern or solid aggregates. The tumor islands also exhibit peripheral palisading of their cells but lack retraction artifact typical of basal cell carcinoma. Trichoblastoma showed large islands of basaloid cells showing peripheral palisading in the dermis dispersed in a delicate fibrotic stroma without any connection with the epidermis. Due to presence of symmetry, circumscription with smooth margin, follicular pattern of lesional cells, lack of retraction artifact, lack of stromal edema & lymphocytes it was precluded from the diagnosis basal cell carcinoma .Proliferating trichilemmal tumor presented as large elevated lobular mass with ulceration on scalp resembling squamous cell carcinoma. Microscopically, it showed multiple variably sized lobules of squamous epithelium showing abrupt keratinisation. These tumors differ from squamous cell carcinoma by a rather sharp demarcation from surrounding stroma as well as an abrupt mode of keratinisation and absence of extensive area of severe atypia. Sebaceous carcinoma, in our study were exclusively from meibomian gland origin. It occurs most frequently on the eyelids as observed in our study. The tumor is composed of irregular lobular formations of sebaceous cells as well as undifferentiated cells with moderate to marked nuclear pleomorphism (Figure 4).We came across a single rare case of adenoid cystic carcinoma showing cribriform pattern of growth and fibrous stroma histologically. The neoplastic basaloid cells are arranged in variably sized, smooth contoured islands comprising small uniform basaloid cells punctured by round rigid spaces, giving rise to Swiss cheese appearance. The lack of epidermal connection and absence of peripheral palisading of neoplastic cells and the presence of PAS positive material and perineural space invasion favour the diagnosis of adenoid cystic carcinoma over adenoid BCC.[15]Malignant eccrine poroma showed polygonal cells arranged in cords, lobules and cribriform pattern having large hyperchromatic irregular shaped nuclei extending to dermis along with presence of mitosis and necrosis. The rarity of these lesion cannot be overemphasized; one large laboratory identified only 5 such lesions in a group of 750,000cases over an 8 year period.[16]

Malignant nodular hidradenoma presented as a large scalp swelling with clinical diagnosis of Cock's peculiar tumor. Microscopy it showed a grenz zone between epidermis and dermis, tumor cells arranged in nodular pattern, prominent cystic spaces, high cellularity, marked cytologic atypia, clear cytoplasm, nuclear anaplasia, mitosis4/10HPF, necrosis (Figure 5A & 5B). IHC showed epithelial membrane antigen (EMA) reactivity in tubular structures and Ki67>14% suggesting high proliferative index (Figure 5C & 5D). IHC has little, if any role in differentiating between the various types of adnexal tumors. Carcinoembryonic antigen positivity indicates a ductal differentiation, cytokeratin indicates follicular differentiation while sebaceous differentiation is suggested by EMA positivity. IHC may play an important role in distinguishing primary adnexal cutaneous carcinoma from metastatic carcinoma. p63 and CK5/6 positivity favour a primary cutaneous adnexal carcinoma over a metastatic carcinoma.[1,2]

Conclusion

SATs are rare neoplasm with benign tumor being far more common. Majority of tumors can be classified into different subgroups on the basis of light microscopy alone. The commonest variant are those of sweat gland origin;

which is also reflected in our study. Most tumors are asymptomatic and often difficult to diagnose clinically. So the clinician mostly rely upon the histopathology for diagnosis of SATs.

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