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A Retrospective Study of Morphology and Histology of Cutaneous Appendageal Tumors from Northern India

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ABSTRACT
Skin adnexal tumors are a group of skin tumors which differentiate towards hair follicles, sebaceous glands, eccrine and apocrine sweat glands. These tumors are uncommon in routine practice and usually cause diagnostic problems. The aim of this study was to determine the incidence of skin adnexal tumors, its correlation with age group and sex and to study detail histopathological character of each tumor by light microscopy. A prospective and retrospective study was conducted on 50 cases for four years period in department of pathology, ASCCOMS, Jammu. Among the all types of skin appendageal tumors diagnosed 94% were benign and 6% were malignant. Maximum benign tumor cases were seen in age group of 26-50 years and maximum malignant cases were seen in age group 51-75 years. Tumors were observed most frequently on the scalp in both the sexes. As per histopathological types of the benign skin appendageal tumors, benign follicular tumor was seen in 23 cases (46%), benign eccrine tumor in 20 cases (40%), benign apocrine in 3 cases (6%) and benign sebaceous tumor in one case(2%). As per histopathological types of malignant tumors, 2 cases of eccrine poracarcinoma and a case of sebaceous carcinoma were seen. The incidence of appendageal skin tumors is relatively uncommon. Histopathological study of clinically suspected cases of skin appendageal tumor is a need of an hour.

INTRODUCTION

The skin is the complex structure and largest organ of the body. The sebaceous and other glands of the skin, are collectively called adnexal structures, they are found in the dermis and adjacent subcutaneous tissue. In general, tumors are not derived directly from mature cells, rather, originate from multipotent stem cells present within the epidermis or its appendageal structures. Such cells, when undergoing neoplastic transformation, may aberrantly express one or more lines of appendageal differentiation to various degrees. The large majority of skin appendageal tumors (SAT) differentiate only along one appendageal line and these results in the formation of reasonably distinct types[1]. There are literally hundreds of neoplasms that can arise from cutaneous appendages and they are known since long. They are basically classified into four groups, tumors with differentiation towards hairs follicles, sebaceous glands, eccrine or apocrine sweat glands[2,3].

Most SAT are benign, and local complete surgical excision is curative. However, diagnosing some of these tumors has important implications, as they might be markers for syndromes associated with internal malignancies, such as trichelemmomas in cowden disease and sebaceous tumors in Muir-Torre syndrome[4,5]. Malignant tumors are rare compared to benign counterparts. Clinically, the distinction between benign and malignant neoplasm is rather more difficult to define when they appear in skin and histopathological examination is frequently required to establish a definitive diagnosis. Diagnosis of any tumours can be done by correlating clinical features and histological features, which can be supported by histochemistry, imm-unohistochemistry and electron microscopy[6]. This study was therefore undertaken to analyze adnexal tumors of the skin for their morphological and histological features.

MATERIALS AND METHODS

The material of the present study included all the skin appendageal tumors submitted for histopathological examination in the Department of Pathology, Acharya Shri Chander College of Medical Sciences and Hospital, Jammu. The duration of study was of four years from. One year study was prospective and rests were retrospective study. The study protocol was approved by an institutional ethical committee before commencing the study. In retrospective study all the histopathological reports of skin appendageal tumors were reviewed and Haematoxylin and Eosin (H and E) stained slides of every case were examined. Further sections were cut from paraffin blocks wherever needed. Clinical information provided in the requisition form was taken into consideration and recorded. In prospective study, the clinical information of the patients was obtained from histopathological requisition forms and relevant deficient information was pursued from clinical case sheets and the concerned clinician. All relevant information was recorded and analyzed.

The specimens received during prospective study were fixed in 10% buffered formalin overnight. After fixation, specimens were examined grossly and three dimensional measurements of the specimen were taken. The external surface was examined for the kind of lesion, color, consistency and presence of ulceration. In case of cystic lesions, nature of cyst and its contents were recorded. Sections from the tumor, overlying skin and resection margins were taken. The selected representative parts of the tissue were processed. For histological examination, representative tissue sections were stained with Hematoxylin and Eosin. Where necessary, relevant sections were stained with PAS and final confirmation of the diagnosis was done. A detailed microscopic examination was carried out and recorded and tumors were categorized as per widely accepted, Lever's Classification of Skin Appendageal tumors. The statistical analysis was done and the results were expressed as percentages.

RESULTS AND DISCUSSIONS

In the present study, benign SAT was 94% (47/50) and malignant tumors were 6% (3/50). The male to female ration was 1.17:1.Tumours was observed in all age groups ranging from 10-80 years. However, the highest incidence was observed in the age group of 26-50 years (50%, 25/50) followed by age groups of 10-25 years (24%, 12/50) and 51-75 years (24%, 12/50) and > 75 years (2%, 1/50) respectively. In our study we observed maximum numbers of tumors on head and neck region (70%) followed by 22% on trunk and upper limb and 8% on abdomen and lower limb. Amongst head and neck region 31.42% SAT were located on the scalp followed by on face (22.85%), on eyelid and neck(14.28) each, on cheek(8.57%)and on forehead(5.71%) (Table 1). Amongst the benign SATs the most common tumor was follicular tumor (48.93 %23/47) followed by eccrine tumor (42.55 % 20/47), apocrine tumor (6.4% 3/47) and sebaceous tumor(2.12 % 1/47) respectively. Whereas amongst the three malignant tumors two were of malignant eccrine tumor and one was that of malignant sebaceous tumor.

According to distribution of histopathological types of diagnosed benign follicular tumors, pilomatricoma was 56.52%, trichoepithelioma was 13.04%, trichofolloculoma was 8.7%, trichoadenoma was 8.7% and proliferating trichilemmal tumor was 13.04% respectively. Amongst benign eccrine tumors, eccrine hidradenoma/ eccrine acrospiroma was 25%, eccrine cylindroma was 20%, eccrine poroma was 15% and 10% each of eccrine spiradenoma, eccrine hidrocytoma, syringoma and chondroid syringoma

Table 1: The distribution of various tumours depending upon their site

Site involved	No. of cases	Percentage of Cases
Head and Neck	(35)	70
Scalp	11	
Face	8	
Eyelid	5	
Neck	5	
Cheek	3	
Forehead	2	
Nose	1	
Trunk and upper limb	(11)	22
Chest	1	
Areola	1	
Axilla	1	
Arm	5	
Forearm	1	
Palm	1	
Fingers	1	
Abdomen and lower limb	(4)	8
Laiba	1	
Thigh	2	
Sole of foot	1	

Table 2: Distribution of histopathological types diagnosed Benign SAT according to sex and age group categories

Age groups (years)	Sex	Histopathological type of diagnosed Benign SAT				
		Follicular tumor	Eccrine tumor	Sebaceous tumour	Apocrine tumor	Total
< 25 years	Male	7	0	0	1	8
	Female	2	1	0	1	4
26-50 years	Male	5	6	0	0	11
	Female	4	8	1	1	14
51-70 years	Male	2	4	0	0	6
	Female	2	1	0	0	3
>70 years	Male	1	0	0	0	1
	Female	0	0	0	0	0

respectively. Distribution of histopathological types diagnosed Benign SAT according to sex and age group categories is shown in (Table 2). Distribution of Histopathological type of diagnosed Benign SAT according to site of origin and age group categories is shown in (Table 3). As per distribution of histopathological types of diagnosed malignant SAT, age group 51-70 years, 01 male and 01 female were diagnosed with malignant eccrine tumor, 01 female was diagnosed with malignant sebaceous tumor. Malignant eccrine tumor was that of eccrine porocarcinoma and malignant sebaceous tumor was that of sebaceous carcinoma. Appendageal tumors are relatively rare[7] and only 0.08% of patients attending the outpatient department were found to be suffering from it in our study. Importance of diagnosing appendageal tumors lies in the fact that in some instances the presence of these tumors may lead to the recognition of a genetic syndrome, like Muir-Torre syndrome associated with sebaceous tumors, Cowden's symdrome with trichilemmomas, etc[8]. It is currently believed that appendageal tumors are derived from cells that have the ability to differentiate toward any of the appendages. In many lesions, the differentiation is uniform and the tumor can be recognized and categorized based on its resemblance to a normal appendage or part of it. In other cases, the pleuripotent cell may differentiate toward more than one type of appendage giving rise to a tumor that contains element of two or more appendage in varying degree of maturation[2]. Various studies had been done showing these combined characteristics of appendageal tumors[9]. In our study, though such combined nature was not detected. Various studies done showed the mean age for adnexal tumors is of 41.72 and 33 years[10-12]. The mean age for adnexal tumors in this study was 39.04year, which is consistent with other studies. In the present study male to female ration was 1.17:1. Similar findings were obtained by other workers[13]. This in contrast to the study conducted by Saha *et al.,*[7] who reported that females (65.21%) outnumbered males (34.78%). In the present study 94% cases were benign and only 6 % cases were malignant. Similarly other workers also reported almost same incidence as benign 96% and malignant cases as 4%[14]. Pilomatricoma was the commonest (56.52%) benign follicular tumor seen in this study whereas trichoepithelioma was diagnosed in 13% of the cases, whereas other workers observed 27% and 3% cases of trichoepithelioma and pilomatricoma respectively[15]. The case of pilomatricoma(calcifying epithelioma of Malherbe) was characterized by a sharply demarcated tumor island composed of 2 types of cells, one basophilic with elongated nuclei and the other with eosinophilic cytoplasm and a central unstained area in the region of the nucleus, known as shadow cells. Recent studies show that pilomatricoma shows mutation of the ß catenin gene, which in turn may affect cell-to-cell adhesion. Pilomatricoma may rarely lead to carcinoma, and metastases can occur

Table 3: Distribution of Histopathological type of diagnosed Benign SAT according to site of origin and age group categories

		Age group (years)				
Benign tumour	**Site of tumour**	**<25**	**26-50**	**51-75**	**>75**	**Total**
Benign	Forearm	0	1	0	0	
	1					
follicular	Neck	0	2	0	0	2
Tumour	Arm	3	0	0	0	3
	Eyelid	0	0	1	1	2
	Scalp	2	3	3	0	8
	Face	4	2	0	0	6
Benign	Neck	0	3	0	0	3
Eccrine	Arm	0	0	2	0	2
Tumour	Eyelid	1	1	0	0	2
	Scalp	0	2	0	0	2
	Face	0	2	1	0	1
	Forehead	0	1	0	0	2
	Cheek	0	0	1	0	3
	Palm	0	1	0	0	1
Benign	Areola	0	1	0	0	1
Sebaceous tumour						
Benign	Scalp	1	0	0	0	1
Apocrine	Face	1	0	0	0	1
Tumour	Laiba	0	1	0	0	1

especially to the lungs[16]. In our study, all cases of trichoepithelioma were distributed around nose suggesting that trichoepithelioma remains the primary differential diagnosis of appendageal tumor centered around nose. Trichoepithelioma was found to be solitary only in two cases. The tumor was characterized by multiple horn cysts and islands of basophilic tumour masses with peripheral palisading of the nuclei. The basaloid cells are hair germinative cells, and the horn cysts are attempts at follicular canal formation. It may be difficult to differentiate it from basal cell carcinoma (BCC) histopathologically. Papillary mesenchymal bodies are fibroblastic aggregates, which represent abortive abortive attempts to form the papillary mesenchyme, are not seen in BCC.

Nodular hidradenoma/eccrine acrospiroma was the commonest (25%) benign eccrine tumour seen in the present study whereas syringoma was diagnosed in 10% of the cases. Other worker in their study reported eccrine acrospiroma and eccrine syringofibroadenoma 50% and 10% respectively[14]. The case of nodular hidradenoma was characterized by lobulated tumour masses in the dermis with eosinophilic hyalinized stroma and lumina and cyst. The tumour masses showed 2 types of cells. One cell type was rounded or fusiform with round nucleus and basophilic cytoplasm, while the other cell was round with small dark nuclei and clear cytoplasm. The clear cytoplasm is due to deposition of glycogen and hence the alternate terminology, clear cell hidradenoma[17]. Syringoma was characterized histopathologically by the presence of cystic ductal structures lined by 2 layers of cells. Some of the ducts showed a comma-like tail of epithelial cells at one end. Enzyme histochemical studies show syringoma to be rich in eccrine enzymes like succinic dehydrogenase, phosphorylase and leucineaminopeptidase[12].

The two cases of eccrine spiradenoma in our study were painful tumors, as mentioned in literature, and characterized histopatholgically by multiple lobules of tumor epithelial cells separated by a fibrous stroma[18]. The tumor cells were arranged in cordlike structures containing small epithelial cells with dark nuclei in the periphery and large epithelial cells with pale nuclei in the centre. The hyaline material seen in the stroma, as described in literature, was also present in our cases[19]. Syringocystadenoma papilliferum was the only benign apocrine tumor seen in this study. Among two subjects of syringocystadenoma papilliferum, one arose from nevus sebaceous and one developed de novo. This is quite expected because de novo variant of Syringocystadenoma papilliferum is much less common[9]. Childhood presentations can occur in Syringocystadenoma papilliferum but is reported to be very rare. The long duration of the tumor before presentation (12.25±8.95 years) can be explained by the fact that in our study population most cases were preceded by a pre-existing nevoid condition. The case of Syringocystadenoma papilliferum showed a cystic invagination with numerous papillary projections in the lower part lined by two layers of cells. Positive immune-reactivity with gross cystic disease fluid protein-15 (GCDEP-15) is seen, indicating tumor of apocrine origin[6]. Recent study show loss of heterozygosity at chromosome 9q22 in cases of Syringocystadenoma papilliferum[20].

The case of cylindroma was characterized by multiple islands of tumor cells lined at the periphery by small cells with dark nuclei with palisading and the centre containing large cells with light staining nuclei. The tumor was surrounded by a hyaline sheath and there were hyaline droplets found in the tumor islands. Rarely malignant transformation can occur in cylindroma[21]. Eccrine porocarcinoma was the only

malignant eccrine malignant tumor seen in the study. Among the two eccrine porocarcinomas one was seen on the thigh of the adult female and another in adult male on sole of foot. This is quite expected because the tumor favors extremities, mostly legs and feet, commonly present in adults of either sex. The eccrine porocarcinoma showed large islands and nest of tumor cells extending from epidermis into the dermis. The tumor cells showed large hypercromatic nuclei with moderate nuclear atypia. Many mitotic figures and necrosis was also seen. At places squamous differentiation was seen. Sebaceous carcinoma was the only malignant tumor (33.3%, 1/3) seen on the eyelid of adult female in our study. Whereas other workers reported 11.8% incidence of sebaceous carcinoma in their study[22]. The ocular type of sebaceous carcinoma most frequently occurs on the eyelids. Extra ocular sebaceous carcinoma has been reported on the head and neck region and occasionally on vulva and penis. The sebaceous carcinoma showed tumor cells arranged in irregular lobules. Tumor cells showed marked atypia, conspicuous nucleoli and foamy cytoplasm. Frequent mitosis was seen under microscope.

CONCLUSION

Appendageal skin tumors are relatively uncommon and the incidence of benign skin adnexal tumors is more as compared to the malignant ones. Maximum benign tumors were seen in 26-50 years group and most of the malignant tumors occur in age group o 51-75 years. SATs can occur anywhere in the body however scalp, face and neck constitutes the most common site in both sexes. Clinically, the distinction between benign and malignant neoplasm is rather more difficult to define when they appear in skin. Majority of the tumors can be classified into different group and subgroups on the basis of light microscopy alone. Histopathological examination is the gold standard in the diagnosis of SATs.

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