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Original Article

Pathology Section

Histomorphological Pattern of Analysis of Skin Adnexal Tumours- A Retrospective Study

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ABSTRACT

Introduction: Skin adnexal tumours are relatively uncommon in routine practice. They pose a diagnostic challenge to pathologists, due to their overlapping features and multiple lines of differentiation. Morphological assessment is crucial to subtype these lesions accurately.

Aim: To study skin adnexal tumours based on their histomorphology and clinical profile.

Materials and Methods: This was a retrospective, descriptive study conducted from January 2016 to December 2019 on 52 cases, done at BGS Global Institute of Medical Sciences, Bengaluru, Karnataka, India. All benign and malignant skin adnexal tumours were included in the study. Microscopic findings were studied by two pathologists. Based on histomorphological analysis, tumours were classified as per recent World Health Organisation (WHO) guidelines.

Results: A total of 52 cases were studied. Of the 52 cases, 45 (87%) cases were benign and 7 (13%) cases were malignant. The most common benign adnexal tumour was Pilomatricoma and the most common malignant tumour was Sebaceous Carcinoma. The most common site of presentation was the head and neck, followed by lower limb and trunk.

Conclusion: Skin adnexal tumours are subtyped based on the predominant morphological component. Benign adnexal tumours are more common compared to malignant adnexal tumours. Histopathological assessment is the mainstay in evaluating skin adnexal tumours.

Keywords: Appendageal neoplasms, Cylindroma, Histopathology, Nodular hidradenoma, Pilomatricoma

INTRODUCTION

Skin adnexal neoplasms present with unique challenges owing to their limited occurrence, overlapping features, myriad ways of differentiation and complicated nomenclature [1]. They often appear as sporadic, solitary lesions; however, presence of multiple lesions may indicate an underlying complex genetic syndrome. Rarely, adnexal tumours are seen in association with internal malignancies [2]. Skin adnexal tumours often present with indistinctive clinical features and hence diagnosis of these lesions largely rests on histopathological assessment [3]. Adnexal tumours are uncommon. There is paucity of cross-sectional studies focusing on prevalence of these tumours in our population [3]. Hence, the study was conducted with the aim to determine the occurrence as well as the histomorphological spectrum of skin adnexal neoplasms, focusing on the overlapping and confounding features.

MATERIALS AND METHODS

This retrospective study comprised of skin biopsies from patients received in the Department of Pathology, BGSGIMS, Bengaluru.Skin biopsy reports from January 2016 to December 2019 were reviewed and 52 cases diagnosed as skin adnexal tumours were studied. The approval was obtained from the Institutional Ethics Committee prior to the study IEC number: BGSGIMS/IEC/FEB2020/20

Inclusion criteria: All benign and malignant skin adnexal tumours were included in the study.

Exclusion criteria: All non neoplastic lesions were excluded.

Patients' clinical details such as age, sex and site of lesion were documented. The tissue was fixed in 10% formalin and 3-5 µ thick sections were stained with haematoxylin-eosin. Serial sectioning, step deeper, reverse embedding along with special stains such as Periodic Acid Schiff (PAS) stain and alcian blue were done wherever necessary. Microscopic findings were reviewed and tumours were classified according to the recent WHO classification [4]. Relative frequency of various lesions along with age and site distribution of the lesions was analysed.

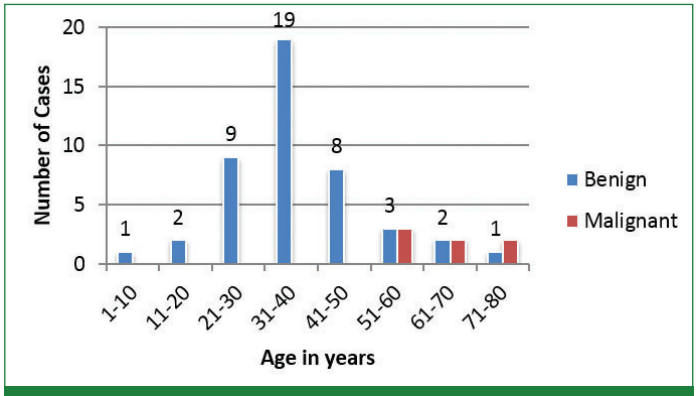
STATISTICAL ANALYSIS

The collected data were entered and analysed using Microsoft excel. The data were expressed in percentages (%).

RESULTS

A total of 52 cases were studied. The median age at presentation was 39 years; and the range was from 7-74 years. Male to female patient ratio was 1.47:1. Of the 52 cases, 45 (87%) cases were benign and 7 (13%) cases were malignant. The age group most commonly affected was 31-40 years with 19 cases [Table/Fig-1]. Malignant tumours were seen in the older age group between 51-80 years.

Adnexal tumours are broadly classified into sweat gland, follicular and sebaceous gland tumours. [Table/Fig-2] shows distribution of benign adnexal tumours (n=45). Benign sweat gland tumours accounted to 53% (24/45) of the cases, benign follicular tumours 36% (16/45) of the cases and benign sebaceous gland tumours accounted to 11% (5/45) of the cases. [Table/Fig-3] shows the distribution of malignant adnexal tumours in the study. [Table/Fig-4] shows the most common site of presentation which was the head and neck, including face and scalp; followed by lower limb and trunk.



[Table/Fig-1]: Age wise distribution of benign and malignant adnexal tumours

Sweat gland tumours	Number of cases	Follicular tumours	Number of cases	Sebaceous gland tumours	Number of cases
Nodular hidradenoma	6	Pilomatricoma	7	Sebaceous hyperplasia	2
Eccrine poroma	4	Trichoepithelioma	3	Sebaceous adenoma	2
Chondroidsyringoma	4	Proliferating trichilemmal cyst	3	Sebaceoma	1
Syringocystadenoma papilliferum	2	Trichoblastoma	1		
Apocrine hydrocystoma	2	Trichofolliculoma	1		
Hidradenoma papilliferum	2	Trichoadenoma	1		
Eccrine spiradenoma	2				
Cylindroma	1				
Tubular adenoma	1				
Total	24 (53%)		16 (36%)		5 (11%)

[Table/Fig-2]: Distribution of benign adnexal tumours

Malignant tumour	Number of cases
Sebaceous carcinoma	2
Porocarcinoma	1
Malignant adnexal tumour (eccrine/ apocrine)	1
Mucinous eccrine adenocarcinoma	1
Malignant spiradenoma	1
Trichilemmal carcinoma	1
Total	7

[Table/Fig-3]: Distribution of malignant adnexal tumours

Site	Follicular	Sebaceous gland	Sweat gland	Total (n, %)
Head and neck	14	6	10	30, 57.69%
Upper limb	0	0	2	2, 3.85%
Trunk	2	1	10	13, 25.00%
Lower limb	1	0	6	7, 13.46%
Total	17	7	28	52, 100.00%

[Table/Fig-4]: Distribution of adnexal tumours based on site

DISCUSSION

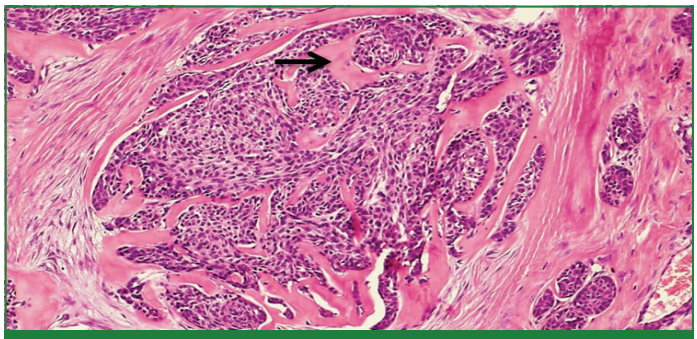
Skin adnexal neoplasms are a diverse group of tumours with morphological differentiation towards one of the three types of adnexa; hair follicles, sebaceous and sweat glands. Often, adnexal tumours exhibit more than one line of differentiation (hybrid tumours) and this is attributed to their common embryology. Basal germinative cells together with clusters of mesenchymal cells that congregate beneath them form the infundibular epidermis, sebaceous glands, apocrine glands, and hair follicles. Eccrine glands however, are distinctly separate from the sebaceous-follicular-apocrine unit [5].

An accurate histopathological assessment of skin adnexal tumours requires complete and relevant history. The gross specimens should be extensively sampled, and the sections should include tumoural and grossly uninvolved surrounding tissue. All resected margins should be painted and submitted to assess for complete excision [5]. Though anatomic location, number, distribution can provide a clue to the type of tumour, it is only histopathology which is the gold standard in the diagnosis of skin adnexal tumours [6]. The presence of cells with abundant vacuolated cytoplasm and small central nucleus is indicative of sebaceous differentiation. The presence of proliferation of basaloid follicular cells, nuclear palisading and papillary mesenchymal cells indicate follicular differentiation. Other clues to follicular differentiation are presence of matricial shadow cells, and if tumour is attached to normal follicular structures. Apocrine cells have abundant eosinophilic cytoplasm and eccentric, basally located nuclei along with presence of decapitation secretion [5].

Benign adnexal tumours are symmetrical lesions and have a V shape, smooth borders, Clefting between compressed fibrous tissue and stroma and absence of necrosis. Malignant tumours on the other hand show asymmetry, clefts between tumour cells and stroma, increased mitosis and necrosis [7]. The incidence of benign tumours is more as compared to malignant cases. In the present study, 87% of tumours were benign (n=45) and 13% were malignant (n=7), which was similar to studies done by Rajesh Nataraj AP et al., Vani D et al., and Sharma A et al., [8-10].

Of the benign adnexal tumours, sweat gland tumours (53%) were most common followed by hair follicle tumours (36%) and sebaceous tumours (11%) [Table/Fig-2]. This observation is similar to studies done by Radhika K et al., and Samaila MOA, [11,12]. However, Kamyab-Hesari K et al., found sebaceous tumours to be the most common type in their study [3]. The most common site of involvement was head and neck followed by trunk and then lower limb [Table/Fig-4]; similar to studies done by Sharma A et al., and Samaila MOA [10,12]. Predilection to the head and neck region could be attributed to the rich distribution of sweat glands and pilosebaceous apparatus, in this location [3].

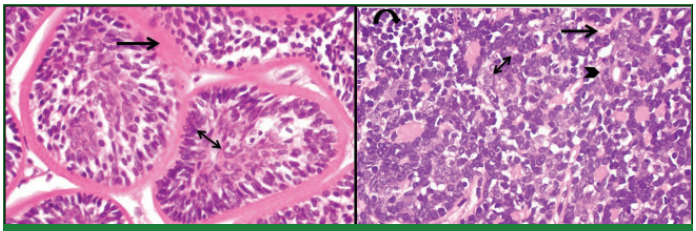
Nodular hidradenomas [Table/Fig-5] are well-circumscribed, deep seated, dermal based tumours and can be composed of solid areas, cystic areas or both. Solid areas are composed of varying proportion of clear cells, poroid cells, squamous cells and rarely mucinous cells. Intervening stroma is often primarily hyalinised [13]. Solid, clear cell hidradenomas are close differentials for Trichilemmoma. In such cases, presence of peripheral palisading of tumour cells in trichilemmoma may be helpful in differentiating it from Hidradenoma [1].



[Table/Fig-5]: Hidradenoma: well-circumscribed nodules composed of poroid cells. Stroma is prominently hyalinised (arrow). (H&E, X200)

Cylindroma and eccrine spiradenoma are two closely related sweat gland tumours. They are both composed of same types of cells but they are arranged in different patterns [14]. Spiradenomas often present as painful nodules in the body above the waist region where as vast majority of cylindromas occur in the head and neck region, most commonly in the scalp [14]. Spiradenomas can have cylindroma like areas but spiradenomas are usually encapsulated, and their stroma has prominent blood vessels. Tumour lobules of trichoblastoma mimic the lobules in cylindroma. While lobules in cylindroma are surrounded by thick basement membrane, lobules in trichoblastoma are surrounded by a fibrotic stroma [13]. There were two cases of eccrine spiradenoma and one case of cylindroma in the present study [Table/Fig-6]. PAS stain was done to highlight the

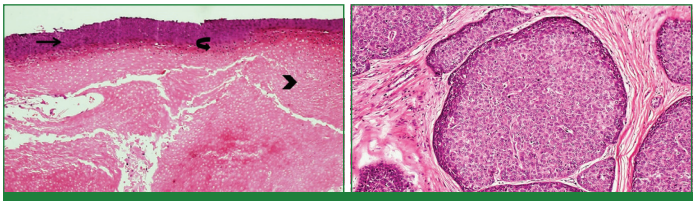
pink basement membrane like material in the cases of spiradenoma and cylindroma.



[Table/Fig-6]: (Left) Cylindroma and (Right) Spiradenoma: Both have two cell population- small basaloid cells and larger ovoid cells with vesicular nucleus (double side arrows), pink basement membrane like material (arrows), and sweat ducts (arrowhead). Spiradenomas are sprinkled with lymphocytes (curved arrow). (H&E, X400)

Pilomatricoma was the most common (n=7) tumour in the present study. Similar findings have been reported by Pujani M et al., and Sharma A et al., [2,10]; while nodular hidradenoma has been reported as most common tumour in other studies [9,11]. Pilomatricoma presents as a well-circumscribed dermal to subcutaneous tumour with a mixture of basaloid and shadow cells. Basaloid cells with variable thickness make up the periphery, and they contiguously transform into pale, eosinophilic, shadow cells [Table/Fig-7] [13]. Wall of trichilemmal cysts may sometimes have basophilic cells which pose diagnostic confusion. Presence of palisading pattern of basaloid cells and absence of shadow cells in trichilemmal cysts will help differentiating it from pilomatricoma [1].

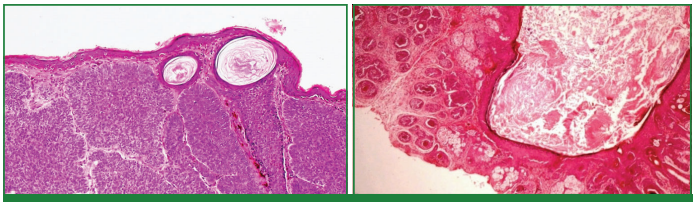
Trichoblastoma is a benign tumour of follicular epithelium and clinically presents as a solitary, well-circumscribed lesion that occurs in the deep dermis and subcutaneous tissue. It consists of nests of basaloid epithelial cells that exhibit peripheral palisading [Table/Fig-8]. The surrounding stroma is fibrotic [5]. It is very important to differentiate trichoblastoma from basal cell carcinoma. Mucinous/myxoid stroma with mucin-filled clefting artifact dividing the tumour nests from the stroma would usually favour basal cell carcinoma over trichoblastoma. The presence of a dense, cellular fibrous stroma, papillary mesenchymal bodies and lack of connection to epidermis, favour a diagnosis of trichoblastoma over basal cell carcinoma [14].



[Table/Fig-7]: Pilomatricoma showing two cell types: Basaloid cells (arrow) and shadow cells (arrowhead). Transitional cells (curved arrow) with pyknotic nuclei (prior to becoming shadow cells) also seen (H&E, X400); **[Table/Fig-8]:** Trichoblastoma shows a lobular basaloid proliferation with a cellular fibrotic stroma (H&E, X200)

Trichoepitheliomas are well-circumscribed, symmetric lesions with or without connection to the epidermis. It is composed of nests of uniform basaloid cells with peripheral palisading surrounded by dense fibrous stroma [13]. Artefactual retraction is uncommon. Small horn cysts with keratin are usually present. This study had reported three cases of trichoepithelioma [Table/Fig-9]. Certain histologic features and immunohistochemical markers may aid in differentiating trichoepithelioma from its close mimic, basal cell carcinoma. The presence of well-formed horn cysts, papillary mesenchymal bodies and lack of high degree atypia and mitosis favour a diagnosis of trichoepithelioma over a basal cell carcinoma. Immunohistochemical markers such as Bcl2, CD 34 and CD 10 may be helpful [1].

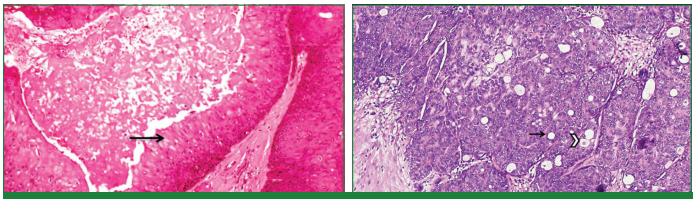
Trichofolliculomas are benign tumours that present as small papules, usually on the face of an adult [11]. Histologically, it presents as an invaginated cyst [Table/Fig-10] lined by keratinising stratified squamous epithelium. The central cystic space is filled with keratin debris. Numerous primitive follicles that communicate with the central cystic space radiate around the periphery of the tumour [13].



[Table/Fig-9]: Trichoepithelioma: Lobules of basaloid cells with peripheral palisading surrounded by fibrous stroma. Horn cysts with keratin seen (H&E, X200); **[Table/Fig-10]:** Trichofolliculoma- Invaginated cystic tumour lined by stratified squamous epithelium with keratin debris in the cystic space. Radiating around the central cystic space are numerous primitive follicles that connect with the central lumen. (H&E, X100)

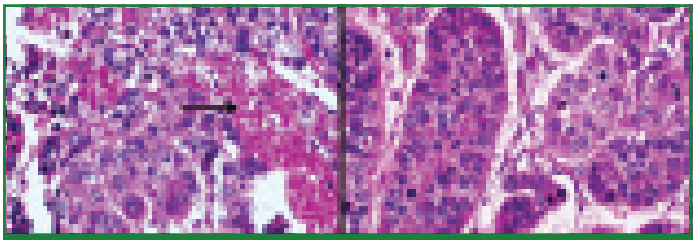
Proliferating trichilemmal cyst/tumour [Table/Fig-11] is a benign lesion, commonly occurring on the scalps of elderly women. It presents as a well-defined lobulated, solid and cystic mass of proliferating well-differentiating squamous epithelium, surrounded by thick basement membrane. Epithelium in the centre of the lobules shows abrupt trichilemmal keratinisation. Some nuclear atypia and mitotic activity may be seen which pose confusion with the more ominous squamous cell carcinoma. However, sharp circumscription, absence of invasion and absence of severe atypia permits differentiation from squamous cell carcinoma [1].

Sebaceous tumours accounted to 11% of all cases in the study. Sebaceous proliferations are characterised by vacuolated, bubbly, mature sebocytes that are present in varying proportions [14]. Based on the percentage of basaloid component, they are characterised as sebaceous adenoma (basaloid component less than 50%) and sebaceoma (basaloid component more than 50%) [Table/Fig-12] [15].



[Table/Fig-11]: Proliferating Trichilemmal cyst/tumour shows bland squamous keratinocytes with abundant eosinophilic cytoplasm surrounding keratin filled spaces. Intervening granular layer is absent (H&E, X 200); **[Table/Fig-12]:** Sebaceoma: proliferation of basaloid cells punctuated by bland appearing multivacuolated clear cells (arrowhead) and several small ducts (arrow) (H&E, X 200)

In the present study, seven cases of malignant adnexal tumours were reported. Malignant adnexal tumours present as asymmetrical lesions with irregular arrangement of neoplastic cells, infiltrating borders, nuclear atypia, significantly increased mitotic activity and abundant necrosis [Table/Fig-13] [4]. It is important to look for these features because tumours with malignant behaviour have important prognostic and therapeutic implication [16].



[Table/Fig-13]: (Left) Malignant adnexal tumours show cytological atypia, necrosis (arrow) and (Right) abundant mitosis (H& E, X400)

Adnexal tumours sometimes display a mixture of eccrine, apocrine, sebaceous and pilar differentiation. The diagnosis of these mixed lesions relies on predominant morphological component. If no component is predominant, terminologies such as “combined adnexal tumours of the skin” or “benign adnexal tumour of mixed lineage” can be used [15].

Limitation(s)

This study was limited by its sample size. Large scale, cross-sectional studies of skin adnexal tumours in our population are lacking and could be done.

CONCLUSION(S)

Skin adnexal tumours are rare lesions, and pathologists can recognise only a limited number of frequently encountered tumours. To add to the existing problem, many well-described entities have overlapping features, and many cases do not fit neatly into well-established classification schemes. Most malignant tumours are seen in older age group (51-80 years of age) while benign tumours are seen in all age groups. Adnexal tumours with sweat gland differentiation are the most common tumours in the present study. Head and neck region is the most common site for skin adnexal tumours though it can occur anywhere in the body.

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