Section: Pathology

Original Research Article

BENIGN ADNEXAL NEOPLASMS OF SKIN – ONE YEAR STUDY IN A TERTIARY CARE CENTRE

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Abstract

Background: The cutaneous appendages give rise to a number of neoplasms both benign and malignant. These neoplasms are heterogeneous and are easily misdiagnosed due to the various classifications proposed and a huge number of variants that exists. Benign neoplasms are more common when compared to the malignant neoplasms. The critical diagnosis depends upon the histo-morphology. This study was done to analyse the clinical presentation and the histo-morphological features ofbenign cutaneous adnexal neoplasms in our centre over a period of one year. **Materials and Methods:** The This is a retrospective study conducted for a period of one year from December 2020 to November 2021. It comprises 18 cases of benign cutaneous adnexal neoplasms diagnosed in the Institute of Pathology, Madras Medical College, Rajiv Gandhi Government Hospital, Chennai, Tamilnadu. The benign cutaneous adnexal neoplasms were further classified according to the origin as eccrine, apocrine, hair follicles and sebaceous glands. **Result:** Most of the benign cutaneous adnexal neoplasms were identified in the scalp region. About 44.4% of the neoplasms diagnosed were of eccrine origin, 38.8 % showed hair follicle differentiation, apocrine differentiation in 11.1% and sebaceous gland differentiation was diagnosed in 5.6 % each. Pilomatricoma followed by Nodular Hidradenoma were the most common variants diagnosed. Only 11.1 % concordance was observed between the clinical diagnosis and the histopathological diagnosis. **Conclusion:** Benign cutaneous adnexal neoplasms are quite rare neoplasms that are often clinically misdiagnosed. Histo-morphology is the gold standard for diagnosis of such neoplasms.

INTRODUCTION

Cutaneous adnexal neoplasms are a heterogeneous group of neoplasms that differentiate into the various skin adnexal structures, which includes eccrine, apocrine, hair follicle, sebaceous gland and multi-lineage differentiation.[1] There is a considerable overlap between the various entities of benign cutaneous adnexal neoplasms, yet many of them show remarkable differences in the histo-morphological presentations. These neoplasm accounts to only about 1-2 % of the skin lesions.[2] Most of these neoplasms are unique to the skin, though some have extra-cutaneous counterparts including salivary gland and the breast. Benign cutaneous neoplasms are more common than their malignant counterparts,[3] and they are more common in men. A large number of these cutaneous adnexal neoplasms are associated with syndromes, having an autosomal dominant pattern of inheritance, for example trichilemmomas are seen in Cowdens disease and sebaceous tumours seen in Muir –Torre syndrome.[4] These can also be markers of Birt-Hogg-Dube and Brook – Spiegler syndrome.[5] The etiology or the pathogenesis of these cutaneous adnexal neoplasms is not much dealt with in the literature. Immunosuppression and exposure to ultra violet radiation are proposed as possible factors triggering their development.[6] The most common location is in the head and neck region. The clinical presentation of cutaneous benign adnexal neoplasms includes solitary or multiple papules, nodules and plaques. Cystic changes and pigmented variants seen in many of these neoplasms had led to the diagnostic difficulty. Immunohistochemistry has little value in diagnosing these neoplasms.

This study was done to analyse the clinical presentation and the histo-morphological features of benign cutaneous adnexal neoplasms in our centre over a period of one year.

MATERIALS AND METHODS

This is a retrospective study conducted for a period of one year from December 2020 to November 2021. The cases of benign cutaneous adnexal neoplasms diagnosed in the Institute of Pathology, Madras Medical College, Rajiv Gandhi Government

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Hospital, Chennai, Tamilnadu, during the study period were included in the study. The patient details, clinical diagnosis and the location of the neoplasm were documented. The histo-morphological diagnosis was arrived at using hematoxylin and eosin staining of the excision biopsy specimens. The benign cutaneous adnexal neoplasms were further classified according to the origin as eccrine, apocrine, hair follicles and sebaceous glands.

RESULTS

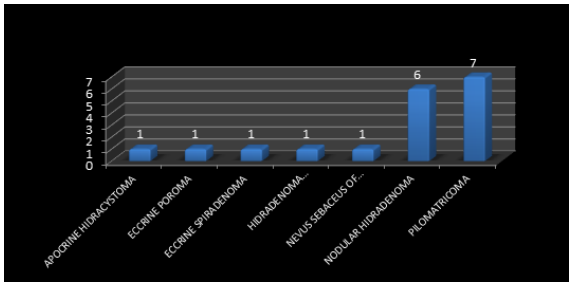

Figure 1: Case distribution of Benign adnexal neoplasms

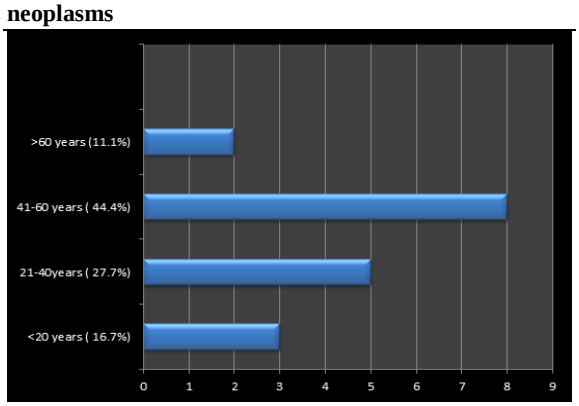

Figure 2: Age group distribution

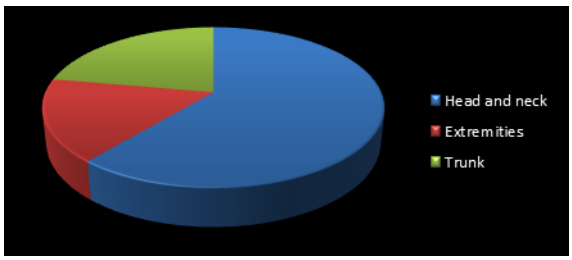

Figure 3: Location specific distribution of the benign adnexal neoplasms:

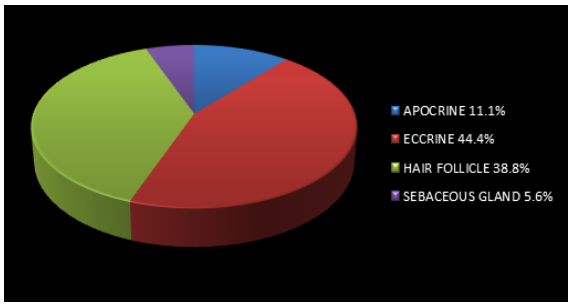

Figure 4: Number of Benign cutaneous adnexal neoplasm versus differentiation.

In the present study a total of 18 benign cutaneous adnexal neoplasms were diagnosed within one year period from December 2020 to November 2021 in the Institute of Pathology [Figure 1] Madras Medical College, Rajiv Gandhi Government Hospital, Chennai. The patients in this study were between 15 to 68 years of age, and most common age group affected was between 41- 60 years (44.4 %) [Figure 2]. Among them male to female ratio was found to be 1:1. Most common location of the benign cutaneous adnexal neoplasm is scalp (38.8%) followed by forearm (11.1%) [Figure 3].

Table 1: Case distribution of benign skin adnexal neoplasms

Diagnosis	No Of Cases
Pilomatricoma	7
Nodular Hidradenoma	6
Apocrine Hidrocystoma	1
Eccrine Poroma	1
Eccrine Spiradenoma	1
Hidradenoma Papilliferum	1
Nevus Sebaceus Of Jadassohn	1
Total	18

Table 2: Comparison with various studies

Study	Year	No of cases	Sweat gland (%)	Hair follicle (%)	Sebaceous gland (%)
Gayathri et al.[12]	2012	29	51.7	37.9	10.3
Pantola et al.[11]	2013	70	60	34.3	5.7
Sharma et al.[10]	2014	56	42.8	35.7	21.4
Pujani et al.[9]	2017	25	56	28	4
Omar AM et al.[13]	2020	18	61.1	33.3	5.6
Present study	2021	18	55.5	38.8	5.6

The eccrine origin was identified in 44.4 % of the benign cutaneous adnexal neoplasms, while hair follicle differentiation comprised about 38.8%, apocrine differentiation in 11.1% and sweat gland differentiation comprised about 5.6 %.

Most of these benign cutaneous adnexal neoplasms were clinically diagnosed to be sebaceous cyst (66.7%) while benign adnexal origin was suspected only in 11.1% of the study population. [Figure 4]

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DISCUSSION

Cutaneous adnexal neoplasms are a group of heterogenous neoplasms that are classified according to the line of differentiation into eccrine, apocrine, hair follicle and sweat gland types. Evidence of more than one lineage could be seen within a single tumor.[7] The basal germinative cells forms a cresentric mass with clusters of mescenchymal cells which develops into the infundibular epidermis, hair follicle, the sweat and sebaceous glands.[8] This common embryology causes the varied differentiation in these neoplasms. The presence of a large list of variants and rare incidence of these neoplasms poses challenges to the correct clinical diagnosis. Even expert pathologists can get confused when it comes to skin adnexal tumours, which arise from hair follicles and sweat glands. Many well-defined entities share characteristics, tumours are frequently only partially sampled, and many cases do not neatly fit into well-established classification schemes. Histopathology becomes the gold standard in diagnosis of benign cutaneous adnexal neoplasms. Hence in this study 18 benign cutaneous adnexal neoplasms were diagnosed within one year study period. Pilomatricoma was the most common diagnosis accounting for about 38.8% (7 out of 18) of the cases. [Table 1]. Eccrine origin was identified in 44.4 % , apocrine differentiation in 11.1% ; while hair follicle differentiation comprised about 38.8 % and sebaceous gland differentiation comprised about 5.6 % of the cases. This was in concordance with studies done by Pujani M et al,[9] in the year 2017, also in studies by Sharma et al,[10] Pantola etal,[11] Radhika et al,[1] Gayathri et al,[12] and Omar AM, et al.[13] [Table 2]

The male to female ratio in our study was 1:1. Studies like Nair et al,[14] found male-to-female ratio of 1:2.3 while Pantola et al,[11] found the ratio of 1.8:1and Omar AM, et al,[13] 1.57:1. The age group ranged from 15 to 68 years. The mean age group was 40.5+/-16.56 years. Most of the patients were between 41 to 60 years of age. (8/18, 44.44%).

Benign cutaneous adnexal neoplasms most commonly occur in the head and neck region. This was also true in our study, about 61.1 percent was diagnosed in the head and neck region, most commonly in scalp 38.8%, followed by fore arm in 11.1 % of cases. The clinical presentation was cysts, nodules and masses.

Diagnostic patterns: Pilomatricoma / calcifying epithelioma of Malherbe (n7, 38.8%), [Figure 5] was the most common diagnosis found in our study. Pilomatricoma accounts to 1 % of skin lesions. Most studies show a female preponderance.[15] This study also shows female preponderance (57.1%) of pilomatricoma cases similar to most other studies.[16] In our study pilomatricoma was seen more commonly in adults over 40 years of age (28.5%). Pilomatricoma occur as single or multiple dermal nodules that are firm to palpation. Microscopically these are well circumscribed cystic neoplasms with smooth borders. They are usually not connected to the epidermis and are composed of monomorphic basophilic cells in the periphery, which keratinize towards the centre forming ghost or mummified cells. The intermediate zone shows small pyknotic basophilic nuclei with pale cytoplasm.Surrounding fibrotic dermis often shows foreign body granulomatous infiltration, focal calcification and metaplastic ossification. BCL2 and Beta catenin expression is seen in the basaloid cells.[17] About 3% of the cases show local recurrence.[18]

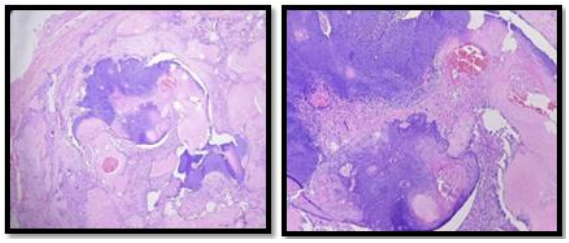

Figure 5: Pilomatricoma

Second common diagnosis in our study was Nodular Hidradenoma/ Eccrine Acrospiroma (n 6, 33.3%), [Figure 6]. These are well circumscribed dermal neoplasms, sometimes extending into subcutaneous tissue and may be connected to one or more pre-existing follicular infundibula. Most of them are solid, some show cystic areas filled with eosinophilic material. Various cell types are identified, clear cell being the most common due to abundant intracellular glycogen. Nucleus is small, round and eccentrically placed. Oncocytic, squamous, mucinous and glandular differentiation can be seen. Clear cell change is a frequent finding in hidradenoma, and when extensive can mimic metastatic renal cell carcinoma. Cystic spaces, basement membrane material, or direct connection to epidermis and/or adnexal structures are all features that support hidradenoma over metastatic renal cell carcinoma. EMA and CEA highlight glandular differentiation. S100, CK and vimentin are positive in nodular hidradenoma. Differential diagnosis includes Tricholemmomas which expand the follicular infundibulum, have peripheral palisading and are surrounded by thick prominent basement membrane. A predominant solid component needs to be differentiated from glomus tumor. Glomus tumor is positive for vimentin alpha smooth muscle actin.[19]

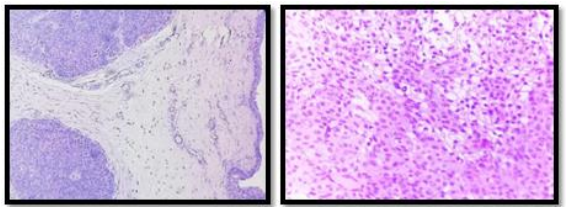

Figure 6: Nodular Hidradenoma

In our study we reported one case of Eccrine Spiradenoma (5.5%), [Figure 7]. They mostly occur

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as solitary subcutaneous nodules associated with pain.[20] These neoplasms have basaloid dermal nodules with smooth borders, edematous stroma showing numerous blood vessels, lymphatics with abundant lymphocytes. Two cell populations are seen, peripheral basaloid dark cell and central pale cells. Basement membrane material are seen around tumor cell islets. Cylindroma and spiradenoma are two morphological variants of the same neoplasm. Cylindroma shows epithelial aggregates of basaloid cells disposed in a jig saw puzzle fashion, with surrounding thick homogenous basement membrane material. Both show immunoreactivity for CEA, S100, alpha Smooth Muscle Actin, CK 8 and 18.[21]

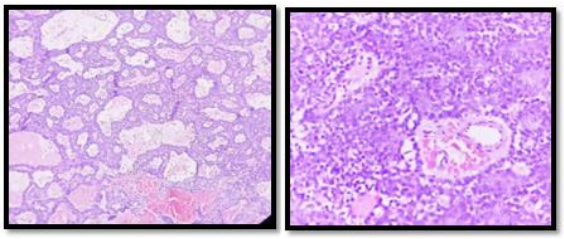

Figure 7: Eccrine Spiradenoma

In our study Apocrine Hidrocystoma (5.5%), [Figure 8] was diagnosed in one patient behind the left auricle. Thoughthe most common location of hidrocystoma is eyelids, cases have also been described in ear, vulva and fingers. The use of reflectance confocal microscopy is helpful in differentiating hidrocystomas from basal cell carcinoma.[22] Multiple Hidrocystoma in eyelids is associated with Schopf-Schulz-Passarge syndromeand Goltz syndrome.[23,24] They clinically present as small, translucent papules on the upper cheek near the eye. Usually they are single cystic lesion lined by tall columnar cells with decapitation secretion, surrounded by myoepithelial cells and basement membrane. Occasional papillary or complex lining is also found. Cyst lumen shows mucin or eosinophilic material. The presence of lipofuschin and the degree of its oxidation differentiates non pigmented from pigmented hidrocystomas.[25] The lining may be eccrine or apocrine, but the distinction between eccrine and apocrine differentiation is not clinically important. EMA and CEA are positive in the luminal cells; S100 positive in the myoepithelial cells.

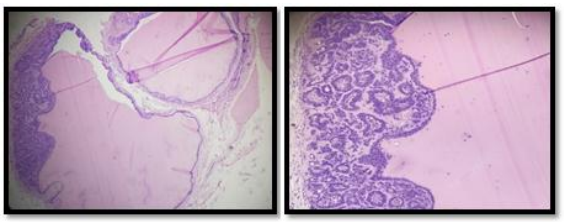

Figure 8: Apocrine Hidrocystoma

We also diagnosed one case of Nevus Sebaceus of Jadassohn (5.5%), [Figure 9]. This is a complex hamartoma involving pilosebacous unit, the epidermis and other adnexal structures, occationally there may be a mescenchymal component. The most common location is scalp, face aound pinna and in the neck.[26] In our study nevus sebaceous was seen in scalp. Nevus sebaceous usually presents clinically as a pebbled, hairless plaque on the face or scalp. It presents at birth and subsequently enlarges over time. A more yellow "greasy" appearance due to enlargement of the sebaceous glands occurs during puberty. Older patients have thicker hyperkeratotic lesion with verrucous surface. Microscopically these neoplasms show enlarged sebaceous gland high up in the dermis with malformed ducts, acanthosis and papillomatosis coupled with markedly diminished or completely absent hair follicles within the centre of the lesion. Surrounding dermis is thickened and show chronic inflammatory cell infiltrates. Normal terminal hair follicles are absent. Nevus sebaceus may harbour other tumors, mostly benign adnexal tumors including trichoblastoma, trichilemmoma, and syringocystadenoma papilliferum. Secondary malignant tumors include basal cell carcinoma, squamous cell carcinoma, and apocrine carcinoma.[27]

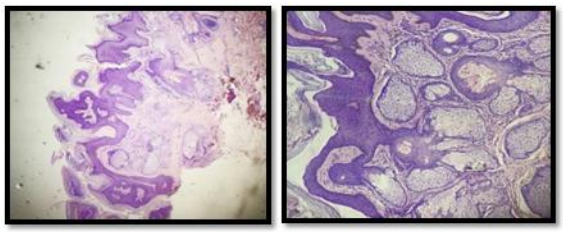

Figure 9: Nevus Sebaceus of Jadassohn

We also diagnosed a case of Eccrine Poroma (5.5%), [Figure 10] in a lesion clinically diagnosed as pyogenic granuloma in scalp in a forty year old female. Poromas are usually found in the extremities, rarely seen in the region of head and neck. These neoplasms present as solitary sessile or pedunculated polyp. It can be reddish or normal skin colour in appearance. It is classically described on the sole or side of the foot. They are composed of basaloid cells called poroid cells and cells with ample eosinophilic cytoplasm called cuticle cells. In classic poroma, the poroid cells connect with the epidermis in the superficial dermis and comprise both solid and cystic areas surrounded by a richly vascular stroma. A range of ductal differentiation is present within the tumor, including small cytoplasmic vacuoles, immature ducts, and more well-developed tubules embedded within the tumor. Poromas have a characteristic pattern of necrosis en masse, usually in the centre of the neoplastic aggregates. Four types of poroma are hidracanthoma simplex (intraepidermal), classic poroma (connected to superficial epidermis infiltrating into superficial dermis), dermal duct tumor (nodules in dermis, not connected to epidermis, no cyst formation), and poroid hidradenoma (dermal nodule with solid and cystic component). CEA is positive in the luminal border of

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the ductal structures and EMA positive in the neoplastic cells. Pigmented poromas display abundant melanin within tumor cells as well as admixed dendritic melanocytes: these can be clinically confused with nodular melanoma.[28]

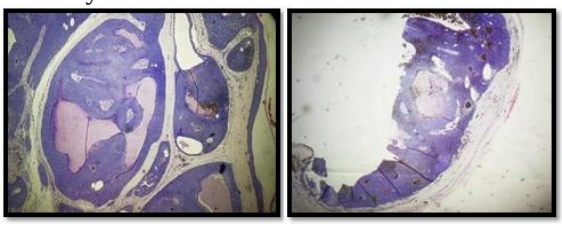

Figure 10: Eccrine Poroma

We diagnosed one interesting case of Hidradenoma Papilleferum (5.5%) [Figure 11], clinically diagnosed in a known case of breast carcinoma as vulval tumor growth. These are solitary skin coloured papules or cystic nodules seen in labia majora of adult female patients. Microscopically they are solid or cystic lesions with maze like papillary pattern lined by peripheral cuboidal myoepithelial cells and luminal columnar cells with decapitation secretion. Surrounding stroma shows retraction clefts. The luminal cells express various cytokeratins and myoepithelial cells express S100, calponin and SMA.[11] Differential diagnosis is syringocysadenoma papilleferum, which shows connection to follicular infundibulum and has stromal plasma cells, while hidradenoma papilleferum is not connected to the follicular infundibulum and lacks plasma cell infiltration.

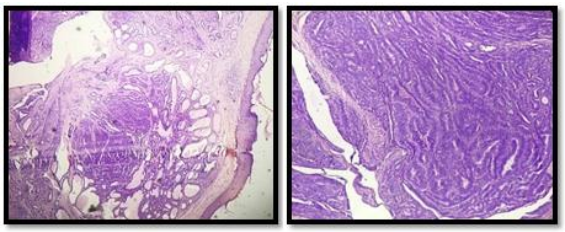

Figure 11: Hidradenoma Papilliferum

CONCLUSION

Cutaneous adnexal neoplasms are a complex group of rare neoplasms that are often misdiagnosed clinically because of the wide variation in presentation and because of the large number of variants. Benign cutaneous adnexal neoplasms are more common than their malignant counterparts. Macroscopic features of each neoplasm are nonspecific. A skin biopsy is essential to make a proper diagnosis. Complete resection forms the best therapeutic approach for benign adnexal neoplasms. Histo-morphology becomes the back bone in the diagnosis of these neoplasms. Immunohistochemistry is not commonly usedin the diagnosis of cutaneous adnexal neoplasms except in a few cases.

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