Spectrum of Cutaneous Appendage Tumors at Aga Khan University Hospital

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Abstract

Objective: To determine the frequency of various types of cutaneous appendage tumors in our practice.

Method: This is a partly retrospective and partly prospective study conducted at the Department of Pathology, Histopathology Section, The Aga Khan University Hospital, Karachi between 1st January 1997 and 31st December 2001.

Results: One hundred sixty six skin appendage tumors were diagnosed during the study period. 87.3%were benign, while 12.6% were malignant. Male female ratio was almost equal. Mean age was 41.72 years. 37.34% showed eccrine differentiation, 14.45% showed apocrine differentiation and 41.56% showed pilosebaceous differentiation, 6.62% exhibited mixed differentiation. The 5 commonest tumors were pilomatricoma, nodular hidradenoma (eccrine acrospiroma), syringocystadenoma papilleferum, eccrine poroma and eccrine spiradenoma. The commonest malignant tumors were porocarcinoma and sebaceous carcinoma. Pilomatricoma were common in children.

Conclusion: Most of our findings roughly correlate with the western published data. However, commonest site for eccrine poromas in our study was head and neck. Also, not a single case of eccrine spiradenoma was seen in the first two decades of life.These findings differ significantly from western data (JPMA 53:427;2003).

Introduction

Neoplasms of cutaneous appendages are rare lesions and since they are so infrequently encountered in practice, they may cause difficulty in diagnosis. These tumors can differentiate in the direction of any of the four types of cutaneous appendages i.e. eccrine sweat glands, apocrine sweat glands, sebaceous glands and hair follicles.[1] Although most of these tumors are benign, it is important to diagnose them accurately since many of such tumors are genetically predetermined and may arise in the form of multiple potentially disfiguring lesions, or may represent sites of predilection for later development of more aggressive tumors, or may themselves be locally aggressive or capable of metastases and may be misdiagnosed as metastatic tumors to the skin.[2] Apart from their rarity, difficulties in diagnosis also result due to their large variety, their frequent differentiation along two or more adnexal lines simultaneously[3] and their complicated nomenclature.[4] The aim of our study was to determine the frequency of various types of cutaneous appendage tumors encountered in our practice, to delineate the spectrum in our setup and to determine the different histological patterns, anatomical Location, site predilection and age and sex incidence. This study was carried out keeping in View that data about cutaneous appendage tumors is almost non-existent in local literature.

Materials and Methods

A partly retrospective and partly prospective study was conducted in the Section of Histopathology, The Aga Khan University Hospital, Karachi (AKUH), to determine the frequency of all skin appendage neoplasms. This study included all cases of adnexal tumors diagnosed during the five-year period i.e., from 1st January 1997 to 31st December 2001. All specimens were also performed. Tumors were analyzed considering histological type, anatomic location, age and sex of the patient. The Histological characterization was done according to the WHO classification system for skin tumors.[5]

Results

A total of 166 neoplasms of skin appendages were diagnosed during the study period. There were 145 (87.34%) benign and 21 (12.65%) malignant tumors. Male patients were 85 (51.20%) while 81(48.79%) were females. The overall age ranged from 5 years to 86 years. The median age was 41 years (mean age 40.19, SD 19.74). The 21 malignant tumors had a mean age of 54 years and a median age of 54 years. All tumors showed a male predominance. Of the 166 tumors, 62(37.34%) were eccrine, 24 (14.45%) were apocrine and 69 (41.56%) showed pilosebaceous differentiation. Eleven tumors (6.62%) which included 4 benign and 7 malignant tumors were diagnosed as mixed appendage tumors without further possible characterization.

Of the 62 tumors with eccrine differentiation, 55(88.70%) were benign, while 7 (11.29%) were malignant. Nodular hidradenoma (eccrine acrospiroma) was the commonest eccrine tumor comprising 45.16% of all eccrine tumors.(Table 1). Of the 24 tumors with apocrine differentiation, 22 (91.66%) were benign, while 2 (8.33%) were malignant. Syringocystadenoma papilliferum was the commonest tumor comprising 50% of all apocrine tumors. (Table 2). Of the 69 tumors with pilosebaceous differentiation, 64 (92.75%) were benign, while 5 (7.24%) were malignant. Pilomatricoma was the commonest pilosebaceous tumor comprising 57.97% of all pilosebaceous tumors (Table 3).

Of the malignant tumours, there were 3 porocarcinomas, 2 in females and one in male, of ages 47, 67 and 73 years and sites, head,

Nodular hidradenoma (eccrine acrospiroma) was the Nodular hidradenoma (eccrine acrospiroma) was the pilomatricomas, eccrine poromas and all the cases of syringocystadenoma papilleferum occurred in the head and neck region; while eccrine spiradenomas were mostly located in the lower limb (77.77%). On the other hand Nodular hidradenomas(eccrine acrospiromas) had a more even distribution in the body and no specific site pre dilection was noted.(Table 6).

All the other common benign tumors in our study like syringoma, chondroid syringoma, cylindroma, trichilemmoma, tricheopithelioma, sebaceous adenoma and proliferating trichilemmal cyst occurred over whelmingly in the head and neck and region, while hidradenoma papilleferum occurred almost exclusively in the anogenital region of adult women.

Discussion

To our knowledge, no significant data regarding neoplasms of cutaneous appendages in the local literature is available. The large majority (87.34%) of tumors in our series were benign. It must be kept in mind, however, that even benign appendage tumors if incompletely excised can recur and evaluation of margins is recommended.[2]

Nodular hidradenoma (eccrine acrospiroma) is relatively primitive in its degree of eccrine differentiation. It is a common tumor without a preferred site predilection and face, scalp, chest, abdomen and limbs are all possible sites.[1,2] In our study too, a similar pattern was seen (Table 6) . Majority of nodular hidradenomas in our series occurred between the ages of 21 and 50 years.

Eccrine poroma is another relatively common tumor, over two thirds of which occur on or near the palms and soles.[1] However, head and neck and trunk may also be involved. It usually affects middle aged persons.[2] In our study, however, the common site for this tumor was the head and neck (50%) followed by the lower limb. The majority of these tumors were seen after the age of 40 years.

Eccrine spiradenoma also is relatively primitive in the degree of eccrine differentiation and has no definite site of predilection, although many occur on the trunk and extremities. It mainly occurs in children and young adults.[1,2] in our study, the large majority (77.77%) were located on the lower extremities. Surprisingly,not a single eccrine spiradenoma in our series was seen in the first two decades of life. The majority were in the fourth and fifth decades . These findings differ significantly from the published data.

Tumors with appocrine differentiation comprised 14.45% of appendage tumors in our study. 91.66% of all apocrine tumors were benign.

Syringocystadenoma papilliferum was the commonest of all tumors with apocrine differentiation comprising 50% of these tumors (Table 2). The histogenesis of this tumor is controversial. It histologically shows apocrine features and although it shows reactivity for apocrine and eccrine markers, there is definite reactivity with gross cystic disease fluid protein, an apocrine marker.[6] More than 75% of cases occur on face or scalp and usually begin in early childhood.[1,2,7]

A study by Morrogi et al reported male female ratio of 3:1 for pilomatricomas.[14] However in our study, 22 cases(55%) occurred in females while 18 (45%) occurred in males.

Other benign adrenal tumors include syringoma, a tumor of well-differentiated eccrine ductular elements and usually occuring as multiple papules on the face of genetically predisposed individuals, women being primarily affected.[2]

Chondroid Syringoma (mixed tumor of the skin) is a relatively common benign tumor and is so named due to a mixture of proliferating ductular eccrine epithelium (similar to Syringoma) and a characteristic Chondroid stromal matrix. It occurs mainly on the head and neck.[2] Ultra structurally, cells within its Chondroid matrix show features of both epithelial and mesenchymal cells raising the possibility that both cell lines may be the neoplastic progeny of pluripotiential which is expressed early in the development of this tumor.[15]

Hidradenoma Papilleferum is a cystic and papillary apocrine neoplasm which characteristically affects women above 30 years of age and occurs mainly in the anogenital region [2] Rarely extragenital sites such as eyelid and external ear canal are affected and again, the tumor consistently occurs in women.[16]

Cylindroma is a benign, histologically primitive adenoma of apocrine differentiation which occurs in two forms: a solitary form on the face or scalp of older adults; and a multiple form which is dominantly inherited and begins in childhood affecting the scalp and over time produces a disfiguring, mutilating turban like growth (turban tumor).[2]

Malignant transformation is a rare complication of cylindroma and may occur in both solitary and multiple forms of this tumor.[17] Malignant cylindroma is more common in the multiple form and is an aggressive carcinoma with a tendency to local destructive growth and metastases.[18]

Trichilemmoma is a relatively common benign tumor, which shows hair follicular infundibular differentiation occurs usually on the face and can be either solitary or multiple. Multiple trichilemmomas occurring on the face represent cutaneous manifestations of the autosomal dominant disorder, cowden's syndrome which is most commonly associated with carcinoma of the breast.[2]

Trichofolliculoma is highly differentiated neoplastic lesion representing proliferatins of actively Trichofolliculoma but is les swell differentiated with absent or abortive trichogenesis, and occurs most commonly on the face adults.[2]

Sebaceous Adenoma is a benign circumscribed neoplasm of sebaceous epithelim composed mainly of mature (lipidized) sebaceous cells and mostly occurs on the face of middle aged and older persons. It may be a component of Muir-Torre Syndrome, which is inherited without well-defined pattern families that are especially, prone to develop colon carcinoma.[19]

Profliferating Trichilemmal cyst or pilar tumor is a benign tumor of pilar differentiation, which is nearly always single with about 90% cases occurring on the scalp.[1] More than 80% cases occur in women,

most of them are elderly.[20] It is composed of variably sized lobules of squamous epithelium and characteristically, the epithelium in the center of the lobules abruptly changes into eosinophitic amorphous keratin.[1] In many areas, the tumor cells show nuclear atypia and individual cell keratinisation thus resembling squamours cell carcinoma but the two can be differentiated by the demarcation of proliferating trichilemmal cyst from surrounding stroma and its abrupt keratinisation.[21] Rarely, malignant transformation occurs which is indicated by rapid increase in size. Microscopically, there are extensive areas of atypia with invasion of surrounding tissue. Metastases can occur, but most of these are regional.[22]

Malignant appendage tumors often resemble their benign counterparts and attention has to be paid to features such as large size, ill defined infiltrative margins, necrosis, nuclear atypia, mitoses including abnormal mitotic figures etc. The presence of these features singly or in combination must raise the suspicion of malignancy in the appendage tumors. Wide excision with careful examination of all surgical margins is recommended with close follow-up for possible distant metastases.[2]

Some malignant appendage tumors present as moderate to poorly differentiated adenocarcinomas, which may resemble metastatic tumors to skin. In such cases, historic features must be combined with complete systemic workup to exclude primary extra cutaneous tumors. Seven such tumors were present in our series. The two commonest malignant tumors in our study were porocarcinoma and sebaceous carcinoma.

Porocarcinoma although may arise denovo usually develops in an eccrine poroma of long standing.[23,24] It mostly occurs on legs and feet of elderly adults without any sex predilection.[1] However, it can occur on head or upper extremities and with metastatic spread, it has a special tendency to produce multiple cutaneous deposits.[2]

Sebaceous carcinoma is a high grade neoplasm and the overwhelming majority occur on the eyelids in association with meibomian glands of the tarsus.[25] It often invades the dermis, underlying skeletal muscle and subcutaneous fibrovascular tissue.[26] It commonly involves the upper eyelid of women.[2] The various clinico- pathologic features that indicate bad prognosis include vascular, lymphatic and orbital invasion, involvement of both upper and lower eyelids, poor differentiation, multicentric origin, duration of symptoms greater than six months, tumor diameter greater than 10 mm, a highly infiltrative pattern and pagetoid invasion of the overlying epithelium of the eyelids. The results of this study will provide a baseline data on skin appendage tumours in our region.

References

1. Elder D, Elenitsas R, Ragsdale BD.Tumors of the Epidermal Appendages. In: Lever's histopathology of the skin. Elder D, Elenitsas R, Jaworsky C, et al. eds. 8th edition Lippincott - Raven Publishers 1997, pp. 747-803.
2. Cutaneous Appendage Tumors. In: Murphy GI, Elder DE. Atlas of Tumor Pathology. Non-melanocytic tumors of the skin. 3rd series Fascicle 1. Armed Forces Institute of Pathology Washington, D.C. 1991, pp. 61-153.
3. Sanchez YE, Requena L, Simon P, et al. Complex adnexal tumor of the primary epithelial germ with distinct patterns of superficial epithelioma with sebaceous differentiation, immature trichoepithelioma and apocrine adenocarcinoma. Am J Dermatopathol 1992;14:245-52.
4. Massa MC, Medenica M. Cutaneous adnexal tumors and cysts; a review. Part 1 tumors with hair follicle differentiation and cysts related to different parts of the hair follicle. Pathol Annu 1985;20:189-233.
5. Heenan PJ, Elder DE , Sobin LH. Histological typing of skin tumors. Berlin Heidelberg: Springer, 1996, p. 3.
6. Mazoujian G, Margolis R. Immunohistochemistry of gross cystic disease fluid protein (GCDFP-15) in 65 benign sweat gland tumors of the skin. Am J Dermatopathol 1988;10:28-35.
7. Marrogi AJ, Wick MR, Dehner LP. Benign cutaneous adnexal tumors in childhood and young adults, excluding pilomatrixoma: review of 28 cases and literature. J Cutan Pathol 1991;18:20-27.
8. Moehlenbeck F. Pilomatrixoma: calcifying epithelioma, Arch Dermatol 1973;108:532-6.
9. Thomas RW, Perkins JA, Ruegemer JL, et al. Surgical excision of pilomatricoma of the head and neck; a retrospective review of 26 cases. ENT J 1999;78:541-8.
10. Singh B, Tolete-Velcek F, Alexis R. Pathological case of the month; pilomatrixoma. Arch Pediatr Adolesc Med 1995;149:551-2.
11. Solanki P, Ramzy I, Durr N, et al. Pilomatrixoma: cytologic features with differential diagnostic considerations. Arch Pathol Lab Med 1987;111:294-7.
12. Lopansri S, Mihm MC, Jr. Pilomatrix Carcinoma or calcifying epitheliocarcinoma of malherbe: a case report and review of literature. Cancer 1980;45:2368-73.
13. Inglefield CJ, Muir IF, Gray ES. Aggressive pilomatricoma in childhood. Ann Plast Surg 1994;33:656-8.
14. Marrogi AJ, Wick MR, Dehner LP. Pilomatrical neoplasms in children and young adults. Am J Dermatopathol 1992;14:87-94.
15. Mills SE. Mixed tumor of the skin a model of divergent differentiation. J Cutan Pathol 1984;11382-6.
16. Santa Cruz DJ, Prioleau PG, Smith ME. Hidradenoma Papilli ferum of the eyelid. Arch Dermatol 1981;117:55-6.
17. Urbanski SJ, From L, Abramovicz A, et al. Metamorphosis of dermal cylindroma: possible relation to malignant transformation J Am Acad Dermatol 1985;12:188-95.
18. Gerretsen AL, Sebastian CJ, Deenstra W, et al. Cutaneous cylindroma with malignant transformation Cancer 1993;72:1618-23.
19. Lynch HT, Lynch PM, Pester J, et al. The cancer family syndrome. Rare cutaneous phenotypic linkage of Torre's syndrome. Arch Intern Med 1981;141:607-11.
20. Brownstein MH, Arluk DJ. Proliferating trichilemmal cyst. Cancer 1981; 48:1207-14.
21. Wilson JE. Proliferating epidermoid cysts. Arch Dermatol 1966;94:9-11.
22. Saida T, Oahara K, Hori Y. Development of a malignant proliferating trichilemmal cyst in a patient with multiple trichilemmal cysts. Dermatol 1983;166:203-8.
23. Gschnait F, Horn F, Lindlbauer R, Eccrine Porocarcinoma. J Cutan Pathol 1980;7:349-53.
24. Mohri S, Chika K, Saito I. A case of porocarcinoma. J Dermatol 1980;7: 431-4.
25. Rao NA, Hidayat AA, Mchean IW, et al. Sebaceous carcinomas of the ocular adnexa: a chinicopathological study of 104 cases with five year follow up data. Hum Pathol 1982;13:113-22.
26. Wick MR, Goellner JR, Wolfe JT III, et al. Adnexal carcinomas of the skin. II. Extraocular sebaceous carcinomas. Cancer 1985;56:1163-72.