What is new on adnexal neoplasms

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Carney complex is an autosomal dominant disease which characteristically presents with multiple myxomas, mucocutaneous melanocytic lesions (lentigo, epithelioid blue nevi and café au lait spots), and several nonendocrine and endocrine tumors affecting various organs. A mutation in the PRKAR1 gene (also known as CNC1 gene) located on chromosome 17q22-24 is found in most cases. In some cases there is a second mutation in the CNC2 gene, mapped to 2p16.

The most common cutaneous lesions in Carney complex are cutaneous myxomas. Histopathologically, these lesions are fairly well-circumscribed neoplasms characterized by a proliferation of scattered polygonal, stellate, plump and/or spindled cells embedded in a prominent mucinous matrix. Occasionally, epithelial components has been identified which may resemble cutaneous adnexal tumors.

Kazalov et al, have described several cutaneous adnexal type lesions in patients with Carney. They refer to these lesions as trichofolliculoma-like, trichodiscoma-like and infundibular cysts and they believe that they may represent genuine adnexal lesions with prominent myxoid stroma.

Brooke-Spiegler syndrome (BSS) is an inherited autosomal dominant disorder characterized by the presence of multiple adnexal cutaneous neoplasms including spiradenoma, cylindroma and trichoepithelioma. A variant of this syndrome is the multiple familial trichoepitheliomas (MFT) syndrome in which patients present with trichoepitheliomas only. Both syndromes are caused by a mutation of the CYLD gene which is located on chromosome 16.
Grossman et al. published the largest published series of BSS patients, including its MFT variant. Molecular genetic analysis revealed a large spectrum of germline and somatic CYLD mutations, consisting of nearly all types of sequence alterations (small insertions, deletions, duplications and substitutions), in addition to frequent LOH as a somatic event. The most common germline mutation was c.1112C>A in exon 9 which was found in 6 patients (3 with classical BSS and 3 with the MFT phenotype) from 5 families. This mutation has also often been reported in literature. Four recurrent germline CYLD mutations (c.2272C>T, c.2291delAACTA, c.2299A>T and c.2806C>T) were found in more than one family in their cohort, whereas other germline CYLD mutations were family specific.

Adipophilin in sebaceous neoplasms:

The group from MD Anderson Center in Houston, Texas reported the use of adipophilin in the diagnosis of neoplasms with pale cell differentiation.

Adipophilin is a recently described antibody which reacts against proteins associated with lipid droplets and are part of the perilipin family. Adipophilin is reported to be expressed in cells of lactating mammary epithelium, adrenal cortex, male reproductive system (Sertoli and Leydig cells), steatotic hepatocytes in alcoholic cirrhosis, and liposarcomas. However, mature adipocytes of fibroadipose tissue do not stain with this antibody.
In this study the authors found this antibody to be very useful in sebaceous carcinomas. In this particular neoplasm there was a vesicular staining with this antibody, but it did also stained sebocytes of normal sebaceous glands, as well as sebaceous adenomas. It can also stains xanthomatous lesions and metastatic renal cell carcinomas. This antibody is very useful in discriminating poorly differentiated sebaceous carcinomas, from basal cell carcinomas or squamous cell carcinomas with pale cell differentiation, especially in small specimens from the area around the eyes, giving their clinical implications.

Calretinin is a calcium-binding protein member of the EF-hand family. The presence of calretinin has been demonstrated in certain stages of the cellular cycle of a wide variety of normal and neoplastic tissues. In normal skin, calretinin is expressed in the innermost cell layer of the outer root sheath in anagen hair follicles, the duct of sebaceous glands, the secretory portion of the eccrine glands. It is also expressed in pilar cysts, in trichilemmomas/inverted follicular keratosis, tumors of the follicular infundibulum and basal cell carcinomas.

Sweat glands of the human skin are classified into eccrine and apocrine glands, although sweat as such is only produced by eccrine glands. From histological, immunohistochemical and ultrastructural points of view, eccrine and apocrine units have in common the cytology and structure of their excretory duct, which consists of a double layer of basophilic cuboidal cells, with a luminal cuticle and a peripheral basement membrane. Concerning differentiation, a lesion is considered as showing eccrine or apocrine differentiation when such proliferation reproduces with greater or lesser success,
depending on the degree of differentiation, any of the structures of normal eccrine or apocrine units. However, to date, clear-cut histopathologic criteria for eccrine differentiation are lacking. In a study performed by Requena et al, they found that calretinin may be a useful marker to differentiate, apocrine from eccrine neoplasms. As such, they found that this protein is not expressed in all the putative apocrine neoplasms, including syringocystadenoma papilliferum, hidrocystoma, spiradenomas, apocrine mixed tumors, while it was positive in eccrine mixed tumors.

PAX8 is a transcription factor which plays a role in the development of the Mullerian system. It is used to discriminate between ovarian and breast carcinomas. It is also positive in renal cell carcinomas, however, there can be some variability in the staining within the same neoplasm. This marker can be used to distinguish metastatic ovarian carcinomas from adnexal carcinomas.

Recently Kazakov and his group published a series of 50 cases of cutaneous mixed tumor, eccrine variant. These neoplasms are characteristically present with a biphasic pattern. An epithelial component composed of small tubules lined by a single layer of epithelial cells embedded in a myxoid and sometimes cartilaginous stroma. The authors also identified variations in the epithelial component including prominent cribriform areas, clear cell change, pseudorosette structures, osseous metaplasia, and physaliphorous-like cells.

A retrospective study from the Duke Eye Medical center on lesions of the lacrimal caruncle was published recently in the AJDP. The authors identified fifty-nine lesions of
the caruncle. The most common lesions were nevi (40.7%) were the most common lesions encountered, followed by squamous papillomas (8.5%) and three oncocytomas were identified (5.1%). They also found a few malignant and borderline lesions. This paper emphasizes the presence of oncocytomas and discuss their clinical, histological, immunohistochemical features as well as the differential diagnosis.

In a study of sebaceous neoplasms, it was found that sebaceous carcinomas are associated with a strong nuclear p53 staining compared with benign sebaceous lesions, most notably for periocular carcinomas. Importantly, nuclear mismatch repair protein expression was intact in all lesions showing p53 alterations, suggesting that p53 dysfunction may represent a divergent pathway in the molecular pathogenesis of these tumors.
References


