# RENAL TUMORES

<table>
<thead>
<tr>
<th>GENERAL PATIENTS</th>
<th>PATIENTS WITH BHD SYNDROME</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Clear-cell renal carcinoma (75%)</td>
<td>• Chromophobe carcinoma (34%)</td>
</tr>
<tr>
<td>• Papillary renal carcinoma (15%)</td>
<td>• Renal oncocytooma (5%)</td>
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<tr>
<td>• Renal oncocytooma (5%)</td>
<td>• Hybrid tumors between chromophobe carcinoma and renal oncocytooma (50%)</td>
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<tr>
<td>• Chromophobe carcinoma (5%)</td>
<td>• Clear-cell renal carcinoma (9%)</td>
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<td>• Papillary renal carcinoma (2%)</td>
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</tbody>
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Hereditary leiomyomas, renal cell carcinoma and fumarate hydratase deficiency
Hereditary leiomyomatosis and renal cell carcinoma syndrome (HLRCC)

- Cutaneous and uterine leiomyomas, and renal cell carcinoma
- Cutaneous lesions appear in young adults, increase in number with age
- Segmental leiomyomas are a marker for HLRCC
- Uterine leiomyomas appear in affected women, from their twenties to middle age
- The renal cell carcinomas include papillary, tubulo-papillary and collecting duct neoplasms, and often behave aggressively
Hereditary leiomyomatosis and renal cell carcinoma syndrome (HLRCC)

- Enzymatic testing in skin fibroblasts
- Molecular genetic testing
Carney’s complex
Carney’s complex

- Autosomal dominant condition
- Angiomyxomas, epithelioid blue nevi, and mucosal lentigines
- Endocrine abnormalities, including neoplasms
- CNC1 gene located on chromosome 17q22-24 and the CNC2 gene mapped to 2p16 are considered responsible
- CNC1 gene, also known as the PRKAR1A gene, is a tumor suppressor gene that the type 1A regulatory subunit of c-AMP-dependent protein kinase A.
Carney’s complex, cont’d

• Superficial angiomyxoma
• Unlike banal cutaneous myxomas, those of Carney’s complex often feature the induction of hair follicular structures from the overlying epidermis, in the form of rudimentary follicular bulbs and papillae.
• Especially in external ear canal
• Atrial myxoma
Pigmented epithelioid melanocytoma

- Is it distinct from epithelioid blue nevus of Carney complex and from “animal type melanoma”?
- Protein kinase regulatory subunit R1α loss a possible marker for sporadic PEM
- Many cases with sentinel nodal involvement, few with distant metastases (Zembowicz, USCAP 2009)
Basal cell nevus syndrome
Basal cell nevus syndrome

- The basal cell nevus syndrome (BCNS) is due to mutations in the patched or PTCH1 gene.
- This gene encodes a transmembrane protein that is part of the sonic hedgehog pathway, normally inhibiting smoothened (SMO) and thus slowing down GLI1 translocation to the cell nucleus.
- Sporadic BCCs can have mutations in PTCH1 that render it ineffective, or mutations in SMO; either can result in increased GLI1 translocation. GLI1 translocation, in turn causes proliferation and inhibits differentiation. PTCH1 is also mutated in trichoepitheliomas, and PTCH1 knock-out mice develop trichoblastomas- hence, mutation is necessary but not sufficient for the formation of BCC in many cases.
Basal cell nevus syndrome (BCNS, Gorlin-Goltz Syndrome)

- Mutation in patched gene (ptchd)
- Basal cell carcinomas at early age
- Palmar pits
- Odontogenic keratocysts
- Infundibulocystic BCCs in clinically normal skin
- Anti-ptchd therapy in clinical trials (e.g. GDC-0449)
Infundibular differentiation

- Cystic lesions lined by epithelium similar to follicular infundibulum
- Basal layer, several layers of keratinocytes, a granular layer, and a cornified layer composed of laminated or basket-weave corneocytes
Cutaneous keratocysts of nevoid basal cell carcinoma syndrome

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Four cysts were removed from two unrelated patients with nevoid basal cell carcinoma syndrome. Multiple sections from each cyst were studied. Two cysts showed histologic features similar to keratocysts that occur in the jaws of patients with this syndrome. The cysts were lined by a festooned epithelium consisting of two to five layers of squamous cells that formed keratin without the presence of a granular cell layer. One cyst contained some lanugo hair and a small bud of follicular epithelium. This cyst was therefore similar to cutaneous steatocysts but did not have an identifiable sebaceous component. The second cyst was devoid of hair and adnexal structures and was indistinguishable from a jaw keratocyst. Two other cysts were typical epidermoid (infundibular) cysts. Although speculative, it is likely that some cutaneous cysts in patients with nevoid basal cell carcinoma syndrome are identical to jaw keratocysts and may be another cutaneous marker for this disease complex. (J AM ACAD DERMATOL 14:572-576, 1986.)
Ultraviolet and ionizing radiation enhance the growth of BCCs and trichoblastomas in patched heterozygous knockout mice

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Brooke’s syndrome
Brooke’s syndrome

• Aka Brooke-Spiegler syndrome, hereditary cylindromatosis, multiple familial trichoepithelioma
• Susceptibility to trichoepitheliomas, cylindromas, spiradenomas, pure or in combination
• Most lesions on head/neck
Brooke’s syndrome, cont’d

- Predilection for face, scalp
- Entire scalp can be involved in cylindromatosis
- Rarely, cylindrocarcinomas, spiradenocarcinomas, trichoblastic carcinomas
Brooke’s syndrome, cont’d

- Familial cylindromatosis mapped to 16q12-16q13
- CYLD, a tumor suppressor gene identified in this locus, and then found in sporadic cylindromas
- CYLD interacts with NF-kB signalling pathway
Basaloid follicular hamartoma

Clinical features

- Clinical variants: Systematized, multiple, localized and linear.
- Generalized forms are familiar with autosomal dominant inheritance.
- Generalized variants may be associated with hypotrichosis and myasthenia gravis.
- In all clinical variants: Small papular lesions centered in hair follicles.
LOCALIZED BASALOID FOLLICULAR HAMARTOMA
Basaloid follicular hamartoma

**Histopathologic features**

- Individual hair follicles are replaced by strands and branching cords of undifferentiated basaloid cells.
- Anastomosing basaloid cords
- Scant fibrous stroma
- **Histopathologic differential diagnosis**: Infundibulocystic BCC, trichoepithelioma and Pinkus fibroepithelioma: BFH has less stroma and interfollicular dermis is not involved.
That's all Folks!
The Art of Warner Bros. Animation
By Pete Schneider
Introduction by Ken Steinberg