same time, of discarding those that show a poor contribution to the grading results. Different types of features can be included. These can be of pure histomorphological type or they can be related to proliferation or morphometrical analysis.

Conclusions

Epithelial tumors of the adult kidney, in particular ROC, represent a variety of neoplasms that can be classified according to morphology and genotype. There is evidence to indicate that tumor stage is one of the most important prognostic factors, irrespective of tumor subtype. The problem of a more objective nuclear grading is still open. The use of diagnostic decision support systems offers the possibility of a flexible approach to this problem while still using morphological criteria.

Papillary (chromophil) renal cell carcinoma

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Papillary reff~l cell carcinoma (ROC), a well-established subtype of RCC, is the second most common carcinoma arising from the renal tubular epithelium and comprises 10-15% of cases in surgical series (1). To be considered a papillary renal cell carcinoma, at least 75% of the tumor is required to be composed of a papillary or tubulopapillary histology with fibrovascular cores (2). These tumors also have characteristic immunohistochemical and genetic features that separate them from other RCCs. However, the term papillary does not encompass all the morphological variations of this neoplasm. Many tumors have wide areas of tubular architecture, or they may be composed of solid sheets of cells without true papillae, but otherwise resemble papillary RCC. This last category has been called the solid variant of papillary HOC (3). For these reasons, the name chromophil RCC was proposed in the Mainz classification (4) to describe the neoplasm. This name signifies that the definition is not based solely on the papillary architecture.

Papillary RCC shows predominance in males of approximately 2:1. The age range is wide, from early adulthood to old age, the average being between 55 and 60 years.

Grossly, it is a well-circumscribed, globular, brown or tan tumor. Hemorrhage and necrosis are frequent. The cut surface is frequently granular and friable. The tumor may appear cystic. Commonly, there is a thick rim of dense fibrous tissue that forms a pseudocapsule in the larger tumors. Calcifications may be present. In surgical pathology, the mean tumor size is 7 cm (2, 5). Bilaterality it is observed in 4.8% and multifocality in 38.7% of the patients (2). Compared with nonpapillary RCCs, papillary RCCs are more common in end-stage kidney disease, are more frequently multifocal and are more often associated with adenomas.

Microscopically, the diagnosis of the neoplasm is based on architectural and cytoplasmic features. More than 90% of papillary RCCs have predominantly papillary or tubulopapillary architecture. The papillae consist of delicate fibrovascular cores covered by a single layer of carcinoma cells. The pattern of papillae is variable, ranging from complicated branching to parallel arrays of long papillae. This last appearance has been termed the trabecular pattern (6). The papillae may contain foamy macrophages and/or psammoma bodies or may be wide and sclerotic (6). The tubular architecture consists of small tubules lined by a single layer of cells similar to those covering the papillae. Rarely, papillary RCC is composed of solid sheets of cells with distinct micronodules that resemble abortive papillae or form ill-defined tubules. These are solid variants of papillary RCC (3). The cells of papillary RCC are classified into type 1 and type 2 (5). Type 1 cells are small, with pale cytoplasm and small oval nuclei with inconspicuous nucleoli. Type 2 cells are large, with abundant eosinophilic cytoplasm and large spherical nuclei with prominent nucleoli. These cells show pseudostratification. Tumors made up of type 2 cells are larger, more common in patients younger than 40 years and are more frequently stage 3 or 4 than tumors made up of type 1 cells (5). Papillary RCC is generally considered a non-mucin-producing tumor. However, this statement is not absolute. The neoplasm may present acid-mucin secretion. We have demonstrated that this mucin secretion can be either cytoplasmic or luminal (7). This observation has a practical value in the differential diagnosis of intrarenal or extrarenal tumors. Trisomy of chromosomes 3q, 7, 8, 12, 16, 17 and 20 and loss of the Y-chromosome are the most consistent genetic alterations (8) in papillary RCC.

The main differential diagnosis of papillary RCC includes papillary renal cell adenoma, metanephric adenoma and collecting duct carcinoma. The diagnostic criteria for papillary adenoma of the kidney comprise: i) papillary, tubular, or tubulopapillary architecture; ii) a diameter less than or equal to 5 mm; iii) histological nonresemblance to clear cell, chromophobe or collecting duct RCC; and iv) cytogenetic abnormalities limited to ±7,+17, and —Y (9). Metanephric adenoma is a rare neoplasm composed of tubular or tubulopapillary structures and glomeruloid bodies of small cuboidal cells. Cytogenetically, the tumor may show normal karyotype or gain of chromosomes 7 and 17 and loss of the Y-chromosome. This supports the hypothesis that the tumor is related to papillary renal adenoma and to RCC. Collecting duct carcinoma diffusely infiltrates the kidney, elicits a desmoplastic stromal reaction and acute inflammation presents frequent figures of vascular invasion and shows reactivity for CK19, 3413E12 and UEA-1 (10).

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Chromophobe renal cell carcinoma (differential diagnosis with clearlgranular cell carcinoma and oncocytoma)

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Chromophobe carcinomas were first described in humans in 1985. Reports in the literature have described an incidence of 5-9% in surgical series. The late discovery is related to its close phenotypical similarity to conventional clear cell carcinoma on the one hand and to oncocytic adenoma on the other hand. Below is a description of the morphological findings.

Gross features

Depending on size, chromophobe renal cell tumors consist ot one or more solid tumor nodules with a slightly lobulated surface. In unfixed conditions, the cut surface appears homogeneously orange and turns beige or sandy after formalin fixation. The uniform pale cut surface may be interspersed with a few hemorrhages. Lack of necrosis is a very characteristic gross feature. While most well-differentiated chromophobe carcinomas present a pale cut surface, a slight brown colored cut surface is usually associated with moderate to less differentiated chromophobe carcinoma.

Microscopic features

In general, two different cell types can be described. The basic chromophobe cell type is characterized by large polygonal cells with a transparent, slightly reticulated cytoplasm with prominent cell membranes leading to a plant cell-like appearance. The diagnostic hallmark is the lack of cytoplasmic coloring with routine dyes but a diffuse cytoplasmic staining reaction with Hale's iron colloid stain, which is a pathognomonic teature of this special tumor type only. Electron microscopically, the cytoplasm is crowded by loose glycogen deposits and numerous, sometimes invaginated and studded vesicles, 150-300 nm in diameter, resembling those of the intercalated cells type B of the cortical collecting duct. The second cell type in chromophobe renal cell carcinoma is also characterized by an increased cytoplasmic eosinophilia or granularity, due to an augmentation of mitochondria. Both cell types can occur singly or in combination within a given tumor. A characteristic feature is the phenomenon of the lining up of huge, pale cells around blood vessels. When combined, well-differentiated tumors show condensed, shrunken and hyperchromatic nuclei, which become more atypical with increasing grade of malignancy or dedifferentiation respectively. Mitotic figures are very rare while double nuclei and multinucleated cells are very common. In general, the growth pattern is solid and compact, sometimes cribritorm associated with focal scarring and sclerosing phenomena, associated with deposition of psammoma-like calcitications. Tumor infiltration by inflammatory cells is uncommon.

Immunohistochemistry

Chromophobe carcinomas do not coexpress keratins and vimentin unlike the conventional clear cell and papillary carcinoma. As there

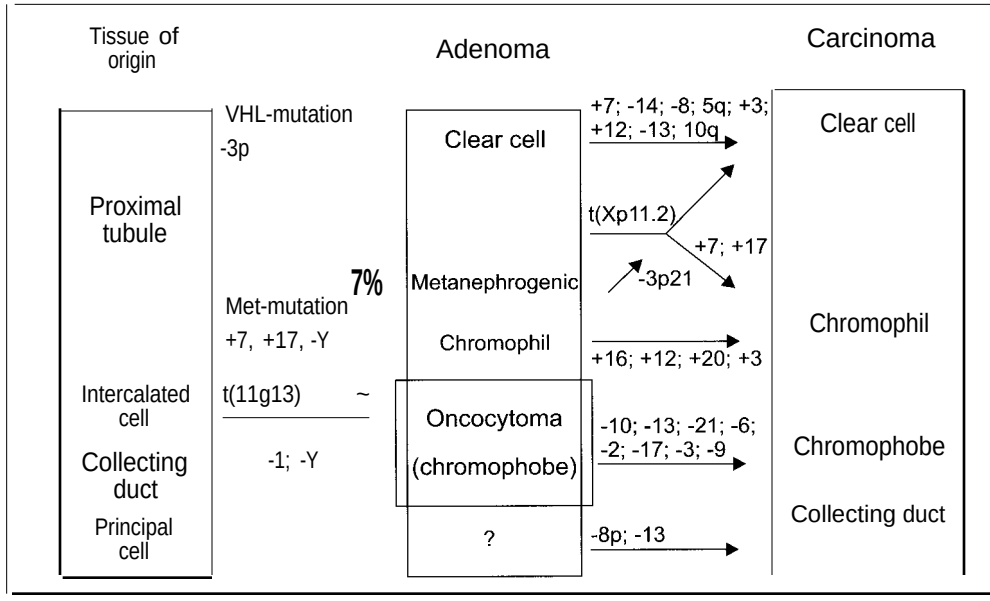

Figure 1. Cytogenetics of epithelial renal cell tumors.