Clinicopathological Features of Renal Cell Carcinoma: A Retrospective Statistical Multicentre -Study

Thesis

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ABSTRACT

Introduction:

Renal cell carcinoma (RCC) represents about 1% to 3% of visceral cancers and account for 85% of renal cancers in adults. The median age is 55 years and male predominance is 2: 1. The incidence of RCC is progressively increasing, and it is predictable that this trend will be maintained in the next years. Renal cell carcinomas are classified morphologically into many variants according to the current World Health Organization (W.H.O) 2004 Classification. These variants include clear cell, papillary, chromophobe , collecting duct carcinoma of Bellini ,unclassified carcinoma and other variants**.**

Material & methods:

-Data on age and gender of patients diagnosed to have RCC (in the last 5 years) together with the histopathologic criteria of the tumors were collected from the documented files in the Pathology department, Kasr El Einy Hospital and other private centers.

-The slides were revised and reclassified according to the most recent staging and grading systems , and statistical analysis was done for clinicopathological correlation.

Results:

From the collected 118 cases, most common type was clear cell variant, being 60 cases (50.8%). There was a male predominance, 72 cases (61%).Mean age was 55.2 years. Most cases were diagnosed at an early stage where 44 cases were T1 (37.3%), and predominance was for cases with low nuclear grade, representing 93 cases of the total (78.8 %).

Key words: Renal cell carcinoma-registry

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LIST OF ABBREVIATIONS

ACKD: Acquired cystic kidney disease

AFIP: Armed Forces Institute of Pathology

BHD: Birt-Hogg-Dub*é* syndrome

BMI: Body mass index

CGH: Comparative genomic hybridization

EMA: Epithilial membrane antigen

FH: Fumarate hydratase

FISH: Fluorescent insitu hybridisation

GST: Glutathione S-transferase

HLRCC: Hereditary leiomyomatosis and renal cell cancer

HPRC: Hereditary papillary renal carcinoma

IARC: International Agency for Research on Cancer

PRCC: Papillary renal cell carcinoma

RCC: Renal cell carcinoma

VHL: Von Hippel-Lindau

WHO: World health organization

INTRODUCTION

Renal cell epithelial neoplasms are defined as those which arise from the epithelium of the renal tubules. This name is not ideal- since there are many other interesting renal cells (Juxtaglomerular, for example)- but widely accepted **(Eble,1998a).**

Almost every major pathological type of neoplasm has been documented in the kidneys of adults, but most tumors are carcinomas **(Farrow, 1989).**

Renal cell carcinomas represent about 1% to 3% of visceral cancers and account for 85% of renal cancers in adults. There are 30,000 new cases per year and 12,000 deaths from the disease in the United States. The median age is 55 years and male predominance is 2: 1 **(McLaughlin & Lipworth, 2000).**

The incidence of RCC is progressively increasing, and it is predictable that this trend will be maintained in the next years. Overall mortality (due to any cause, as tendency to metastasize widely) associated with RCC is higher in the first five years after diagnosis **(Santos *et al.*, 2006).**

Two decades ago, there was a tendency to lump all renal neoplasms thought to be of epithelial origin (except urothelial carcinoma of the renal pelvis) occurring in adults regardless of the morphology. The discoveries of the past two decades have proven that a variety of well defined neoplasms with characteristic patterns of genetic abnormality were contained within what previously had been simply as “renal cell neoplasms” **(Eble, 1998b).**

More progress has been made in the histogenesis of renal cell carcinoma. In the nineteenth century, the predominant theory of oncogenesis held that neoplasms arose from heterotopic embryonic tissue

that attempted to recapitulate mature organs at abnormal sites. Under the influence of this concept, **Grawitz** in **1883** proposed the term hypernephroma to describe the histogenesis renal carcinomas from heterotopic adrenal rests in the kidneys **(Farrow, 1989).**

Tremendous advances have been made in the understanding of renal epithelial neoplasms. Renal carcinoma was most often categorized on the basis of the character of the cytoplasm as clear and granular cell types. The detailed morphologic studies done have delineated the major morphologic types of the renal neoplasia and their histogenetic relationship to various segments of the renal tubular system. Cytogenetic and molecular genetic studies have shown that the morphological classification correlates with patterns of genetic abnormality particular to clear cell renal carcinoma, papillary renal cell carcinoma, chromophobe renal cell carcinoma and collecting duct carcinoma **(Thoenes *et al.*, 1986)**.

So renal cell carcinomas are classified morphologically into many variants according to the current World Health Organization (WHO) Classification. These variants include clear cell (conventional), papillary, chromophobe, collecting duct carcinoma of Bellini, unclassified carcinoma and other variants **(Cheville *et al.*, 2003)**

Prognostic factors other than tumor type include; tumor stage, grade, age, gender, renal capsule involvement, renal vein invasion, and exta-renal spread **(Moch *et al.*, 2000)**.

The prognosis may differ among several variants. For example chromophobe renal cell carcinoma was found to have a significantly better prognosis than clear cell carcinoma (**Delahunt *et al.*, 2007)**.

Over the past 2 decades, a greater understanding of the basic biology and genetics of kidney cancer has occurred. Surgical techniques have also evolved, and technological advances have made possible new methods of

managing renal tumors. The most extensively used system to provide prognostic information for renal cell carcinoma (RCC) is currently the Tumor, Nodes, Metastasis (TNM) staging system. **(Lam *et al.*, 2008)**

Emerging data over the last few years has questioned whether further revisions are needed and if improvements can be made with the introduction of new, more accurate and predictive prognostic factors. The recent discovery of molecular tumor biomarkers are expected to revolutionize the staging of RCC and potentially lead to the development of new therapies based on molecular targeting **(Lam *et al.*, 2008).**

AIM OF THE STUDY

-Registeration of all diagnosed cases of RCC in the last 5 years (2004-2008), collected from the Pathology department, Faculty of medicine, Cairo University, Kasr El Einy Hospital as well as from other private centres.

-Study of the most important clinicopathological features of renal cell carcinoma.

-Morphological classification of the cases according to the WHO system 2004 will be revised.

-The application of the most recently recommended staging (TNM) and grading systems of RCC (Fuhrman Nuclear grading system)

- Correlation between clinicopathological features of renal cell carcinoma and other personal data such as age and gender.

REVIEW OF LITERATURE

CLASSIFICATION OF RENAL CELL EPITHELIAL NEOPLASMS

The histogenesis and classification of renal epithelial tumors has been the subject of considerable controversy and change over many decades. Renal cell carcinoma was most often categorized on the basis of the character of the cytoplasm as clear cell and granular cell types. Tumors composed of mixtures of the two were regarded as common, as were tumors that fit imperfectly into either category. A number of studies explored the prognostic significance of these categories, but the results were inconclusive **(Medeiros and Weiss, 1990).**

As the modern classification of renal epithelial malignancies has been clarified and advanced with information gained from cytogenetic and molecular studies, several uncommon variants of renal cell carcinoma have been separated from the more common clear and granular carcinomas **(Medeiros and Weiss, 1990)**.

In **1979, Klein and Valensi** drew attention to a morphologically homogeneous subgroup of renal cell carcinoma with abundant finely granular eosinophilic cytoplasm, which had a remarkably good prognosis. Today, these tumors are recognized as the benign renal oncocytoma **(Chao *et al*., 2002)**.

In **1981, Mostofi and his colleagues** proposed the **WHO** system which categorized tumors on the basis of cell type (clear, granular, oncocytic, spindle, and mixed), architecture (tubular, papillary, solid, cystic, sarcomatoid) and presumed site of origin i.e., proximal versus distal tubules.

In **1985, Thoenes and his colleagues** reported the first human case of a morphologically distinct subtype of renal cell carcinoma, which they called the chromophobe type, that was originally discovered by Bannasch in experimentally induced tumors in rats before in 1974.As the classic type of chromophobe renal cell carcinoma was extracted from the clear cell end of the spectrum, it was soon recognized that there is an eosinophilic variant that emerged from the granular cell end of the spectrum. A bit later, it was recognized that some renal cell carcinomas emerged from the granular end of the spectrum as well, for example collecting duct variant. **(Rumpelt *et al*., 1991).**

In **1986, Thoenes and colleagues** proposed the **Mainz classification** of renal cell neoplasms, based on morphologic, histochemical and electron microscopic features, which recognized these new entities, as well as chromophil renal cell carcinoma (which also is known as papillary renal cell carcinoma because it usually has a predominantly papillary architecture). The basic tumor cell types; included clear, chromophil (basophilic, eosinophilic, duophilic), chromophobe, oncocytic, and spindle shaped/ pleomorphic, and subsequently included categories of collecting duct carcinoma and mixed tumors. The **Mainz classification** was based on morphological criteria, but subsequent genetic studies have confirmed its validity by showing characteristic genetic abnormalities in the groups **(Kovacs, 1993).**

In **1994, Murphy and his colleagues** classified renal epithelial neoplasms into clear cell, papillary, granular, chromophobe cell, sarcomatoid, and collecting duct types.

In **1998, Eble** proposed the **Classification of Renal Cell Neoplasms** at the Urologic Pathology Subspecialty Conference at Boston, which best