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Histological Subtype of Renal Cell Tumors at Urology Department of Teaching Hospital Hassan 2, Morocco

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Abstract:-
Purpose: The aim of this study is the analysis of the anatomopathological aspects of renal tumors in our center.
Materials and methods this is a retrospective study of 108 cases of renal tumors collected from the Department of Urology CHU HASSAN II FES and Department of Anatomy - Pathology CHU HASSAN II FES over 10 years from 2009 to 2019.

Results There were 108 patients, 65 men, and 43 women, the median age was 59 years with a range of age between 30 years and 85 years. Most of our patients had presented urologic signs at the time of the diagnosis, which was dominated by low back pain (47%) and hematuria (22%). The left kidney was affected in 56.3% of cases and the right kidney in 42.7% of cases. The average height is 7 cm with extremes of 2 and 9.5. Tumors of heterogeneous appearance represent the majority of cases with a percentage of 52.4% of which 40% is encapsulated and 12% without capsule, buff-yellow tumors is 22.3% with the presence of capsule in 17.4%, whitish 20% of which 19.4% are encapsulated. Histologically, papillary carcinoma was found in 17.5% of cases and chromophobic cell carcinoma was noted in 10.9% of cases. Low-grade mucinous tubular spindle cell carcinoma and angiomyolipoma were reported in our study (2.7%), (4.6%), carcinosarcoma in 2.78% of cases, carcinoid tumor in 0, 93% of cases, and oncocytoma 1.58%. For histo-prognostic factors, Fuhrman's grade 2 was the most frequently revealed in 44% of cases followed by grade 3 in 33%. For the pTNM classification, the stage pT2 was predominant followed by pT1, lymph node involvement was found in 13% of cases and metastases in 12%. The outcome was favorable in 81% and unfavorable in 19%.

Keywords:- *Renal Cell Carcinoma, Subtypes of Renal Cell Carcinoma, Immunohistochemistry of Renal Cell Carcinoma, Staging, Classification of Renal Cell Carcinoma.*

I. INTRODUCTION

1.1Epidemiology

According to the Globocan, kidney cancer is still ranked in the top 10 tumors worldwide, the incidence is constantly growing with more than 270,000 new cases diagnosed each year and mortality of more than 116,000 cases due to this cancer[1]. Renal carcinoma alone accounts for 3% of the death rate in 2021 in the USA[2]. The prevalence of renal carcinoma is also higher than in men compared to women[3]. In Morocco like in others North Africa country the incidence remains important and more than 4 716 news cases have been diagnosed in Morocco in 2020 during pandemic Covid-19[1]. The diagnosis age is between 60 and 70 years of age[3]. Solid kidney neoplasms are renal cell carcinomas that represent about 90% of all types of kidney cancer.

1.2Diagnosis

Cardiovascular diseases, chronic tobacco use, overweight, and end-stage renal cystic diseases are the factors that contribute to the development of renal carcinoma. Exposure to trichloroethylene may lead to the development of renal carcinoma. [4, 5]. People with BMI >30kg/m2 represent 50% of people with a kidney tumor and this risk increases by 20-35% for each 5 kg/m2 BMI gain. Thus obesity is the primary cause of the occurrence of diseases with high malignancy potential [6, 7].

Renal carcinoma has a genetic component, the probability of occurrence is 3% in families with a history of renal carcinoma [8]. Other syndromes are associated with the occurrence of renal carcinoma. von Hippel-Lindau disease is the cause of clear cell kidney tumors. [9].

Mass screening for renal carcinoma is not recommended. In cases of hereditary disease, a screening can be done within the patient's family, to treat new cases early. [10]. There are family syndromes identified for clear cell renal carcinoma. This suggests that genetic testing is increasingly being offered to detect these syndromes[8].

Above fifty percent of patients with RCC are asymptomatic and are diagnosed during CT-scan performing for other diseases. The classical triad of renal tumor is less and less found in clinical practice. It is increasingly appearing at an advanced stage of the disease. Varicocele now appears as a warning sign of a kidney tumor. Before a varicocele of sudden occurrence, not disappearing at rest and localizing right, we should also look for a probable kidney tumor associated[11]. Paraneoplastic syndrome is also an indicator of metastatic localization; it is accompanied by cardiovascular disorders, ionic disorders, weight loss, and an infectious syndrome[12].

A complimentary assessment is required in the face of the suspicion of renal carcinoma, the blood count, a biochemical assessment because certain biological parameters are included in the prognostic classification of renal tumors. An abdominal CT scan is used in the diagnostic arm to also assess the existence of a probable tumor extension. When the CT scan is insufficient, MRI can be used to better appreciate the stage of the tumor and better detect vascular invasion [13].

CT is the reference study for the classification of renal tumors, it is performed with contrast injection times if there is no contraindication. Cerebral CT and MRI are not indicated in routine practice[14,15]. CT image of kidney cancer can reveal the morphological and enhanced features of kidney tumor. The consistency between the CT stage and the pathological stage is high and can be applied as a forecasting method for pathological staging [16]. Abdominal MRI Can be performed when abdominal CT with contrast injection is not allowed in a patient. PET scan is not yet routinely used for renal tumor assessment. Its use is still experimental[17]. The renal biopsy is indicated to determine the histopathology type of the renal tumor, it allows to evaluate the malignancy potential of the tumor. Moreover, this biopsy is indicated before any ablative treatment of the kidney or before the initiation of systemic treatment in metastatic renal tumors. This is a key study in the management of renal tumors. Only the nephrectomy part can give the final classification of the renal tumor and the final diagnosis.

1.3Classification

The WHO ISUP classification dates from 2013 and is the most recent classification of renal tumors. It distinguishes 5 new epithelial tumors: tubular renal cell carcinoma (RCC), secondary renal cysts associated with renal cell tumors, clear-cell (tubular) papillary tumors, MiT family translocation RCC (in particular t(6;11) BCR), and BCR associated with the hereditary BCR syndrome of leiogenesis. Modifications have been made in already existing entities: Multicystic clear-cell CCR (formerly called multilocular cystic CCR) is newly included as a sub-category of clear-cell CCR with low malignant potential [19]. Clear-cell papillary renal cell carcinoma (ccpRCC) is the most common form of renal cell carcinoma (RCC)[21].

1.4Prognostic factors

For renal tumors, six factors were retained by IMDC and Heng's score. Karnofsky's performance status, the time between diagnosis and start of treatment, hemoglobin level, corrected calcemia were already taken into account in the MSKCC score[22]. All factors are included in the groups as follows: anatomical, histological, clinical, and molecular factors. The TNM classification includes prognostic elements, tumor size, vascular invasion, collector systems, adrenal gland involvement, extension beyond the renal capsule or Gerota fascia, and lymph node involvement. Histologically, prognostic factors include tumor grade, histological subtype, sarcomatoid or rhabdoid lesions, and microvascular involvement [23].

II. MATERIALS AND METHODS

This study group contains 108 cases of renal tumors. All cases were retrieved from the electronic database of our Departments of Urology and the division of Pathology in academic hospital Hassan II, Fès, Morocco, between 2009 and 2019 (10 years). Pathology study macroscopic, microscopic, and immunohistochemical data of renal tumors were analyzed. Analysis was performed on parts of total nephrectomy, partial nephrectomy, and renal biopsy. Immunohistochemical analysis was performed. The study of the samples has passed through the following steps: fixation, dehydration, inclusion in paraffin, cooling, making the cuts, rehydration, and coloring by Hematein-Eosine-Safran. The antibodies used were Vimentin, Ck7, C10, C117, EMA, and CK. Pronostic factors were determined by the Fuhrman grade, pathology TNM staging, Sarcomatoïd component, vascular invasion, invasion of the adrenal gland.

III. RESULTS

The average age of the patients was 59 years and the extremes were between 30 and 85 years. In our series, we had 43 women (40%) and 65 men (60%). The distribution of tumors by histological type was as follows: 64 patients of clear cell renal cell carcinoma, 19 patients of papillary renal cell carcinoma, 11 patients of chromophobe RCC (ChRCC), 3 cases of Renal cell carcinosarcoma, 3 patients of Mucinous tubular and spindle cell carcinomas, 2 patients of renal oncocytoma (RO), 5 cases of angiomyolipoma and 1 case of carcinoid tumor. Almost 90% of the tumors found were malignant tumors.

Concerning the mode of the revelation of tumors is found the low back pain as the most common sign that is found in 60% of cases, hematuria is noted in 32% of cases, impaired general condition was found in 25%, in 20% the discovery was an incidental and abdominal mass in 7% of cases. The tumor was located on the left in 56% of patients, on the right side in 43% of cases, and bilaterally in 1% of cases.

Anatomopathological data, for macroscopic aspect the average size of the tumor is 7 cm with extremes of 2 and 9,5cm. Tumors of heterogeneous appearance represent the majority of cases with a percentage of 52% of which 38% is encapsulated and 14% without capsule. The buff-yellow tumors are 22% with the presence of capsules in 17%, the whitish 21% of which 19% are encapsulated.

Clear cell carcinomas (ccRCC) are the most common 59%, followed by clear-cell papillary RCC (CCPRCC) and chromophobe RCC (ChRCC) representing respectively 17.59% and 10.19%, the other types are rare **(figure 1).**

Immunohistochemical antibodies are not used systematically. In our series Clear cell renal cell carcinomas are positive for antibodies anti-cytokeratin, anti-cytokeratin 7, anti-vimentin, anti-EMA, and anti CD 10, for papillary renal cell carcinoma, tumor cells express antibody anti-cytokeratin, anti-cytokeratin 7, anti-vimentin, anti-EMA and anti CD 10, chromophobes renal cells carcinoma are negative for vimentin and CD10, positive for CK7, CK, and EMA, oncocytic cells attach only anti-cytokeratin antibodies, mucinous tubular carcinoma and low-grade fusiform cells fixed antibodies against cytokeratin, anti-cytokeratin 7 and anti-vimentin **(table 1).**

Concerning Histoprognostic Factors, Grade 2 of Fuhrman is most common in 45% of cases, followed by Grade 3 with a percentage of 33%, then Score 4 in 13%, and finally Grade 5 with 9% of cases.

Concerning the pathology TNM staging, the T2 stage is the majority with 45% of cases, T1 represents 37%, T3 is 15%, T4 is 4% of cases.

In our series the majority of cases represented neither ganglionic involvement 77% nor metastasis 75%, on the other hand, we had ganglionic involvement in 11% of cases and metastasis in 12%, a sarcomatoid component was found in 10% of cases, the vascular invasion was found in only 8% of cases and the adrenal gland was not invaded in 98% of cases.

The trend was favorable in 81% and unfavorable in 19%.

IV. DISCUSSIONS

Renal cell carcinoma is common cancer that accounts for 3% of adult cancers, affects men most often than women with a sex ratio of 2, the third urological cancer in men after those of the prostate and bladder, However, its impact varies geographically, being higher in Europe, North America and Australia, and lower in China, Japan, and Africa. It is a cancer of late-onset and discovery, the average age of onset is 65 years, according to the series PEYROMAURE [24] the average age is 61 years, while it is 59.6 years in the series of POISSON [25], and 64.4 years in the series of BENSALEH [26], against 61.8 years in the series of HETET [27].

Kidney cancer mainly affects older subjects with male predominance. The sex ratio is two. In the series of PEYROMAURE [24] and POISSON [25], patients were divided into 68% male versus 32% female, a ratio of two men to one woman. In the BENSALEH series [26], patients were divided into 65% male and 35% female. In the HETET series [27] men represented 78%, for 22% women. In our series, patients are divided into 63 men (62%) and 39 women (38%), which is similar to the data from the other series.

The classic clinical triad associated with RCC consists of flank pain, hematuria, and palpable abdominal mass is rarely present, it is often associated with an advanced stage. The discovery is incidental by an ultrasound or CT scan, or the presence of one or two of these symptoms, the most common of which are hematuria and pain [12]. Hematuria in the PEYROMAURE series [24] is found in 15% of patients, in the POISSON series [25], in 33% of the cases in our series had hematuria at the time of diagnosis whether it was isolated or associated with other symptoms, which is consistent with the results of the literature. For low back pain, 32.4% of our patients had low back pain, in the series of POISSON [25] it represented 29.1%. For abdominal mass, this mode of revelation has become increasingly rare and found in only 2 to 5% of cases, testifying to a tumor already evolved, in the series of POISSON [25], the lumbar mass, was found in 9,7% of cases and in our series the lumbar mass with a large kidney was found in 6.4%.

The incidental found, at present, the majority of RCCs are found incidentally from abdominal ultrasound or computer tomography examinations. Some studies have found RCC is diagnosed incidentally over 50% of the time[29, 30].In the PEYROMAURE series [24], involving 230 kidney cancer patients, the discovery of 75% of these tumors was incidental, in the POISSON series [25], involving 810 patients more than one tumor in two was found incidentally.

Radical nephrectomy is recommended for patients with stage I (T1a, T1b), Stage II, Stage III, Stage IV, if a tumor indicates increased oncologic potential (larger tumor size, infiltrative growth pattern, aggressive histology on RMB, etc.)[32, 33] in our series we found that most cases benefited from a nephrectomy enlarged by a percentage of 76.7%, as well as the average size of the discovery is 7cm, this shows that the discovery of kidney cancer has become at least late in our country, 6.7cm for PEYROMAURE series [24] and 6.1cm for POISSON series [25]. There are several histological types of kidney cancer, the most common being Clear cell carcinomas (ccRCC) which accounts for more than 85% of all kidney cancers, and the 9th most common cancer in developed countries, while papillary tumors are the second most common group of renal tumors.

The most widely accepted factors independently affecting prognosis in patients with RCC are TNM stage, Fuhrman grade, tumor size, and patient performance status. Among these factors, the use of tumor grade and subtype is

recommended by the EAU guidelines. The most frequent histological type of renal cell carcinoma is clear.

Cell renal cell carcinoma (ccRCC), with a prevalence of 75% of all primary kidney cancers[10].In our series, the histological study confirmed the predominance of kidney clear cell carcinoma (ccRCC) in 58.33% of cases, which is consistent with literature data. Papillary renal cell carcinoma was found in 17.5% of cases, this type of kidney tumor comprises approximately 10% of all RCCs according to literature series[10], and Chromophobe renal cell carcinoma was noted in 10,9% of cases, the Papillary renal cell carcinoma was found in 3rd position after carcinoma with Chromophobe renal cell carcinoma, mucinous tubular renal cell carcinoma with low grade 2 fusiform cells,7% and angiomyolipoma 4.6% and these are rare tumors according to the literature [35]. Other rare histological types have been described in our series as carcinosarcoma in 2.78% of cases, carcinoid tumor in 0.93% of cases, and Renal oncocytoma in 1.58%.

For the immunohistochemistry (IHC) study antibodies such as cytokeratin (CK), cytokeratin 7 (CK7), Vimentin, and CD10 were the most incriminated in our study, Renal clear cell carcinoma and Renal papillary carcinoma are positive for all antibodies cited before, chromophobe carcinomas are negative for vimentin and CD10, positive for CK and CK7. The oncocytoma cells only fixed the anti-Kck.

Comparing with other series, Into clear-cell carcinoma, cytokeratin 7 (CK7) was negative or occasionally focal positive, but it was not found to be diffusely positive [36], In papillary RCC type I, CK7 is constantly positive, while CD10 is negative. CD10 and EMA were stained along compressed luminal borders between papillary tracts, or a “clubbing sign” in typical papillary fronds (30), ChRCC is primarily characterized by CK7 positivity or being generally diffuse or occasionally patchy. KIM proposed the following profile: Renal clear cell carcinoma is positive for CD10, negative for CK7, tubulo-papillary carcinoma is positive for both, chromophobe carcinoma is positive for CK7 but negative for CD10, oncocytomas did not fix either AC anti-CD10 or AC anti CK7, and this is consistent with our study [24].

Pathological staging is the essential tool for assessing the prognosis of a patient with a kidney tumor. Patients diagnosed with stage I or stage II disease have a high 5-year survival rate of 80% to 90%(28). Two common prognostic factors noted in our study are the pTNM stage and the nuclear grade of Fuhrman, in our series the Fuhrman grade 2 is most common in 45% of cases. For the pTNM classification, the pT2 stage is the majority followed by pT1, lymph node involvement was found in 13% of cases and metastases in 12%.

It should be noted that although the TNM classification and histological criteria such as nuclear grade remain the basis of prognostic systems in localized kidney cancer, it is not the same in metastatic kidney cancer whose prognosis is based on the degree of metastatic progression that involves biological and molecular variables.

V. CONCLUSION

Kidney cancer is the 3rd urological cancer with a sex ratio of two men to a woman, its absolute incidence is increasing due to the improvement of diagnostic means, in 85% of cases, it is a tumor with clear cells. The final diagnosis of these tumors is histological, but sometimes the use of cytogenetics and molecular biology is indispensable. The improvement of its prognosis depends mainly on the tumor stage. Kidney cancer has benefited nowadays from advances in radiological explorations, genetics, and management through the concordance between histology, immuno-phenotyping, and histochemical and molecular genetics, which helped with diagnosis and prognosis.

Author contributions:

The authors contributed equally to preparing the manuscript.

Conflict of interest statement:

The authors declare there are no conflicts of interest regarding the publication of this article.

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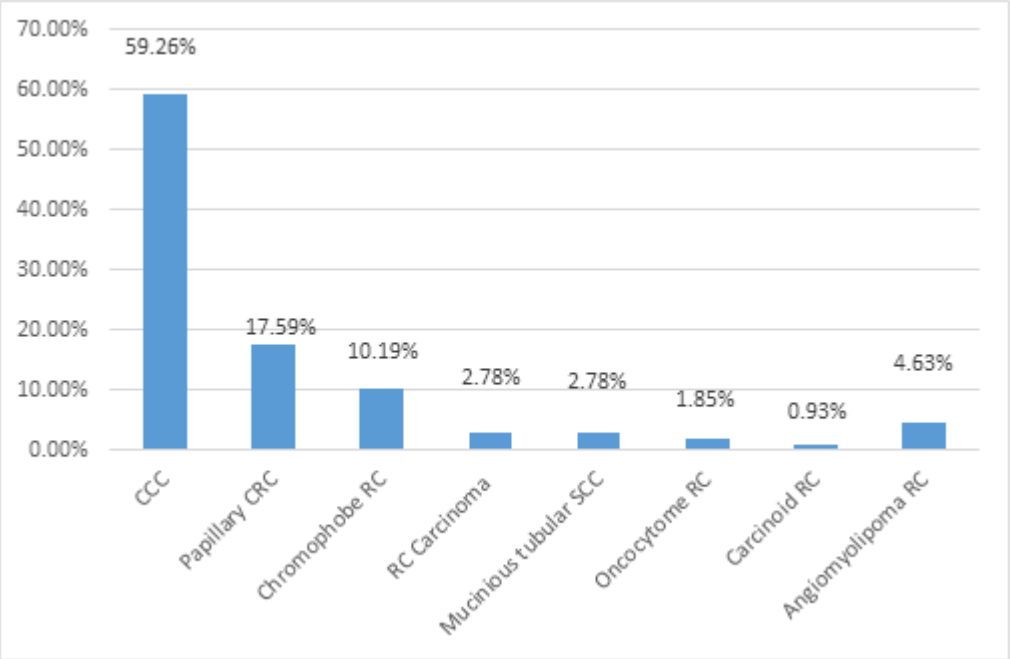

Figure 1*Distribution according to histological aspects*

Table 1*, immunohistochemistry (IHC) aspects*

AC / Type	Vimentin	CK	CK7	CD10	EMA
CCC	+	+	+	+	+
Papillary CRC	+	+	+	+	+
Chromophobe RC	-	+	+	-	+
Oncocytome RC	-	+	-	-	-
Mucinious tubular SCC	-	+	+	-	-
Carcinoid RC	-	+	+	+	-
Angiomyolipoma	-	-	-	-	-