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Case Report

Open radical nephrectomy for early treatment of renal cell carcinoma: a case report and review

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ABSTRACT

We report the case of a 46-year-old male with no previous medical background. He complained of abdominal right-sided flank pain, spreading to ipsilateral flank, thermal hikes, hematuria, and positive giordano. The ultrasound found a 5 x 5 cm mass located in right kidney upper pole, which did not compromised renal capsule and presented a fresh bruise, suggesting a malignant tumor. Radical nephrectomy was satisfactory performed; sending the whole kidney to pathology and the patient was discharged within 72 hours. The histopathologic report concluded a conventional clear cell renal cell carcinoma tumor (5.5 x 4.8 cm) Fuhrman grade II, limited to the renal parenchyma. We concluded that the best treatment for this type of cancer is the radical nephrectomy even though you lose a part of the renal function. Radical nephrectomy guarantees the extraction of the whole tumor and avoids dissemination, one of the most common complications.

Keywords: Renal tumor, Surgical treatment, Radical nephrectomy

INTRODUCTION

Renal cell carcinoma is the most common kidney cancer (Table 1), accounting for approximately 2-3% of all cancers (third most common malignancy in genitourinary tract cause) and 90 to 95% of malignant neoplasms arising from the kidney. It is more frequent in males (2: 1) with its peak incidence between 50 and 70 years and in residents of western countries (the lowest rates are found in Asian countries).[1-3] In the last years, there has been an increase in diagnosis of these cases of 2% per year in the world, mainly due to advances in diagnostic radiology abdominal studies.[4,5] Smoking is the principal of many environmental factors, demonstrated with an increase in renal cell carcinoma in smokers (1.7 times higher compared to the general population and the risk decrease after a longer period of 10 years without smoking). Other risk factors are hypertension, treatment with estrogen, obesity (rising by 24% the risk in men and 34% in females for every 5 kg/m^2), use of antidepressants and analgesic chronically, and having a history of kidney cancer in a first-degree.[6] Despite this increased incidence, in Denmark and Sweden there has been a steady decline in the incidencie.[7] It is reported in literature that the incidence increases in patients with tuberous sclerosis, cystic kidney disease and patients undergoing

hemodialysis.[8,9] Sporadic presentation is predominantly (95%), although familial forms have been reported (4%) as in von Hippel-Lindau, autosomal dominant disease that 30% of patients develop clear cell carcinoma.[10,11]

The European Union reported in 2006, 63 300 new cases and a mortality rate of 41.7%, while in 2008 the United States reported 54,390 new cases.[7,12] In South Korea the incidence of renal cell carcinoma it increased from 3 per 100,000 in 1999 to 5.2 per 100 000 in 2010.[5] In Mexico, kidney cancer accounts for 1.5% of all malignancies. There is information by histopathological malignancy record in 2003, that supports that up to 30% of patients present with metastatic disease at diagnosis, being in 20-30% of patients developed later.[13]

Like any other malignancy, tumor characteristics, prognostic factors including specific signs and symptoms related to the tumor and laboratory examinations: pathological stage, size, nuclear grade and histological type should be determined.[14] The most common histological types are: clear cell in 80 to 90%, papillary15%, and chromophobe tumor 4-5% Bellini duct or collecting duct.[15]

Table 1: Types of renal cell carcinoma.

Type of carcinoma	Histological features	Genetic basis or tumor markers
Clear cell carcinoma	Consists primarily of cells containing clear cytoplasm due to its content of glycogen and lipid are dissolved during histological processing, although in some cells predominates a eosinophilic cytoplasm because they contain a greater portion of mitochondria. The growth pattern may be tubular, solid and cystic. Nuclei are rounded and depend on the degree of differentiation.	Identified by the specific deletion of chromosome 3p and the mutation in the VHL gene. Other changes are duplication of chromosome 5q22 and deletion of chromosome 6q, 8p, 9p and 14q.
Chromophobe cell carcinoma	Larger cell size, polyhedral appearance, good delimitation of cytoplasm and abundant pale lattice cytoplasm by the presence of vesicles. Due to the characteristics, used staining Hale. This cell can be clear or eosinophilic cytoplasm, depending more mitochondria it contains. Growth generally occurs in solid sheets.	Genetic feature is the loss combination chromosomes 1, 2, 6, 10, 13 and 17.
Papillary or chromophilic carcinoma (CRp)	Most contain small cells with scant cytoplasm. Predominant papillary growth pattern, although there may be tubular and solid papillary provisions. The necrotic areas are frequent. CRP can be divided into two distinct subtypes: type 1 with small cells and pale cytoplasm and type 2 with large cells and eosinophilic cytoplasm, the latter with a worse prognosis.	The most consistent genetic alterations are trisomies of chromosomes 3q, 7, 8, 12, 16, 17 and loss of Y-chromosome.
Distal collecting duct carcinoma (Bellini)	Presenting cells with high nuclear grade, eosinophilic cytoplasm and cell "boot tack." It is a very rare type, which often debuts at an advanced stage of disease. Up to 40% of patients have metastatic spread at the time of initial presentation and most die within the first 1-3 years after primary diagnosis. Survival was 48% at 5 years and 14% at 10 years.	By cytogenetic analysis it has been associated with the deletion of chromosomes 1q, 6p, 14, 15 and 22.
Sarcomatoid renal carcinoma	It represents a high degree of processing different types of kidney cancer, without being a different histological type. The changes sarcomatoideos take it with a worse prognosis.	Sarcomatoid transformation occurs more commonly associated with clear cell tumors and tumors chromophobe
Renal medullary carcinoma	Clear cells cytoplasm and eosinophilic with grotesque nuclei. Reticular cell grownth and adenoid cystic is usual in this neoplasia.	Translocation t (3; 8) (p21; q24) or monosomy of chromosome 11 (gene beta-globin). HER 2 / neu negative and positive VEGF and HIF.

Pathophysiology

The pathophysiology of this tumor has been linked to VHL gene mutations. This gene encodes a tumor suppressor protein which regulates HIFα levels (hypoxia induced factor). At high levels of HIFα is associated with increased angiogenesis because it regulates the secretion of vascular endothelial growth factor (VEGF) and platelets derived growth factor B chain (PDGF-B) which generates higher tumor development.[16] Some risk factors

that have great influence on the development of kidney cancer include smoking, renal failure, obesity, hypertension, NSAID use, eating habits, among others. Belonging to an urban population has been considered as a risk factor.[17] There is evidence that a principal compound in the smoke cigarette, the BPDE (benzo-alpha-pyrene diol epoxide) produces mutations on chromosome 3p21.3 related to tumorigenesis of several neoplasms, including renal carcinoma.[18] In renal cell carcinoma, hematuria occurs in 40 to 60% of patients, the flank pain in 35 to 40% and the presence of a palpable mass appears in 25 to 50% of cases.[19,20] Between 20% and 30% of malignant kidney tumors have already metastasized at diagnosis and about 20% of cases, metastasis is the first manifestation of the disease.[4] The most common sites of metastasis of renal cancer are: lung, liver and bone. Less frequently is the presence of skin metastases.[21-23] Computed tomography is known as the gold standard for the evaluation of renal cell carcinoma because it provides information about the tumor and its spread to adjacent structures. Through the levels of RHAMM and CD44s can distinguish between subtypes oncocytoma and renal cell carcinoma. They are also potential predictors of metastasis.[24]

Surgical treatment for renal cell carcinoma

Surgery has an important role in oncology, because it is the only treatment that guarantees the total or partial tissue removal which is immersed in the malignant tumor and lymph nodes associated. Histological examination of the surgical specimen enables an evaluation of the tumor, its total or partial removal and forecasting same influences plan to continue with local or systemic treatments.[25] Since 1969 to date, the gold standard treatment is to perform a radical nephrectomy, although more and more often a partial nephrectomy is performed with the intention of preserving organ function, despite having similar results reported in the literature.

Surgery is still the main treatment, especially for a disease limited to the organ, with a selective role in advanced and metastatic disease[4], with low chances of survival without support of this therapeutic practice. Even patients in advanced stages, removing the kidney tumor can improve prognosis as it may indicate the removal of the tumor parenchyma surrounding or the entire kidney, denominating partial and radical nephrectomy respectively (Table 2), and the possibility of affecting the perirenal fat or adrenal gland even in more advanced stages.

In the radical nephrectomy is completely removed the kidney with his perirenal fat and the corresponding adrenal gland, which is removed for consideration by the treating physician about the possibility of being involved in or affected by cancer according to the predominant localization the renal parenchyma, especially when the tumor is present in the upper pole of the kidney. In recent years, it is preferred to use laparoscopic techniques to perform nephrectomy because of the benefits that provides for the recovery of the patient, complications and hospitalization expenses, this technique is not considered an option to large tumors, such as greater than 10cm wide, and those involving the renal veins.[26] Radical nephrectomy involves the risk of chronic kidney failure, increasing the risk of hospitalization (10%), cardiovascular events (40%), metabolic disorders and death (20%).[27]

Table 2: Comparative characteristics between open and laparoscopic radical nephrectomy.

Characteristics	Open radical nephrectomy	Laparoscopic radical nephrectomy
Age	56.9 (35-97 years)	55.6 (41-71 years)
Kidney affected	Right	Right
Tumor size	Average: 81.5 mm Rank : 35-140 mm	Average: 56.7 Rank: 30-120 mm
Tumor location	Upper pole renal	Lower pole renal
Surgical time	148.2 min Average (60-130 min)	177.2 min Average :(115-295 min)
Postoperative bleeding	925 ml aprox. Average: 100 - 3200 ml	762 ml Average: 50-3000 ml
Intraoperative complications	Surgical bed hemorrhage Vena cava lesion Pleural injury	Bleeding hilum Vena cava lesion Bleeding and injury polar vessel
Deaths perioperative	Any	Any
Hospital stay	Three days Rank: 2-7 days	2.4 days Rank : 2-4 days
Pathological stage	pT3 stage	pT1 stage
Benefits		Rapid patient recovery Minor analgesics uses Covalently short period
Against	Pain at home High complications Surgical wound infection	High costs of surgery Long learning curve
Surgical margins	Positive edges	Negative edges

Partial nephrectomy is the procedure in which only part of the renal parenchyma is removed affected by cancer, leaving intact the remaining part of the body with the

benefit of the patient to keep the largest possible share of their functional renal parenchyma, why is called nephron-sparing surgery.

Data on the incidence of de novo chronic kidney disease and accelerated after nephrectomy for cancer are poor.[28] Although smaller tumors is increasingly managed with biopsy, minimally invasive procedures and monitoring, partial nephrectomy is used in treating early stages of renal cancer, tumors frequently used for only amplitude less than 4 cm., which is not used in those cases where the tumor is too large, it is located in the central portion of the body, its presentation is in multiple lesions and metastasis to lymph nodes and surrounding structures andcases in which in addition are proceed to a regional lymphadenectomy, adrenalectomy or other organs. One in four patients is diagnosed with metastases presence in lung, bone, brain and liver.

Studies have shown that long-term results are about the same in cases of partial nephrectomy compared to radical nephrectomy cases. Currently it has another technological benefit applied to the surgical area as the use of a robotic interface (Da Vinci system) in which through a panel robotic arms for carrying the surgical procedure are controlled by providing greater precision and handling compared with laparoscopic or conventional techniques; however it is important to stress the importance of the skill and experience of the surgeon are primary factors for the success of therapy in all its forms.[29]

Current guidelines suggested by the American Urological Association and the European Association of Urology for the management of stage T1 recommend conservative surgery for all cases, which is based on the demonstration of equivalence oncological partial nephrectomy compared to radical procedure and prognosis of chronic kidney disease after radical procedure.[4,30]

Currently there are studies like Sun et al that it has opted for partial nephrectomy to reduce the risk of developing chronic kidney disease and ensure an increase in patient survival. It further suggests that a partial nephrectomy is associated with a decrease in mortality and a low rate of decline in renal function postoperatively, compared with radical nephrectomy.[4,28] Decreased renal functional capacity could lead to renal retention acid load contributing to the presentation of metabolic acidosis.[27] As for other forms of treatment, it has questioned the effectiveness of interventional radiology techniques based on histological findings that suggest the failure of ablation to eliminate malignant cells or to achieve the same tumor-free margins and surgical procedures.[25]

CASE REPORT

A 46 year old male with no previous medical background, started with abdominal pain localized in the right flank, spreading to ipsilateral flank, thermal hikes and hematuria. A physical examination with positive Giordano and right flank pain. Ultrasound reports a mass located in right kidney upper pole of 5x5 cm, which is complemented by CT urography (Figure 1), reporting a 5x5x3 cm tumor lesion without compromised renal capsule and fresh bruise, suggestive performed of malignant tumor of origin. Radical nephrectomy, with right approach on lumbotomy with cutting-incision of skin and muscle, reaching the retroperitoneum and performing radical nephrectomy with ligation of the ureter, renal artery and vein with an approximate bleeding of 300 cc, with satisfactory and discharge at 72 hours evolution (Figure 2). The patient has evolved satisfactorily, rejoining their work and daily activities.

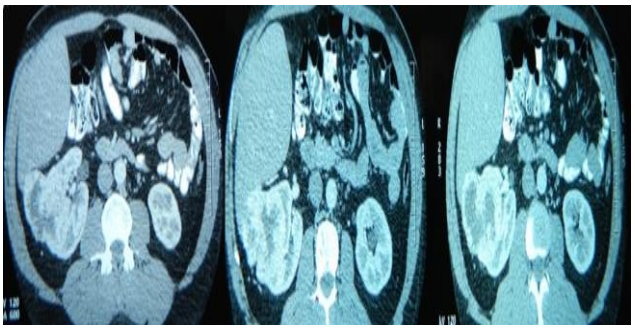

Figure 1: Computed tomography, single phase, axial section, in which 5x5x3 cm tumor lesion is observed without compromised renal capsule and recent hematoma, suggestive of malignant tumor.

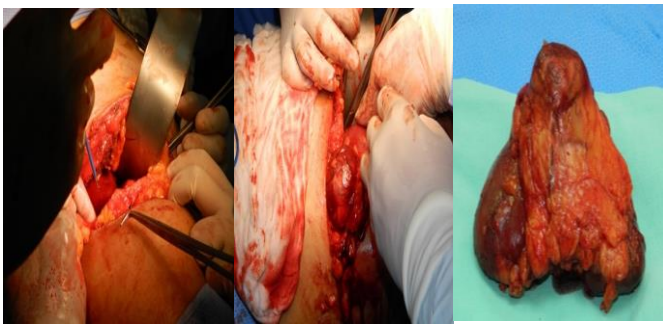

Figure 2: Radical nephrectomy with approach on right lumbotomy cutting-incision of skin and muscle, reaching the retroperitoneum and performing radical nephrectomy with ligation of the ureter, renal artery and vein.

Histopathology report

Microscopic description

Cuts of a kidney tumor characterized by cells that had clear appearance solid mantles or nests are separated by an abundant proliferation of vessels that are interconnected giving rise to a sinusoidal appearance is observed. Nuclei were round to irregular with some areas of presence of apparent nucleoli. Neoplasia was located in the renal parenchyma and the capsule did not infiltrated perinephric fat. The cuts showed some non-

neoplastic kidney glomeruli and areas with abundant erythrocytes with chronic inflammation. Thus concluding a conventional renal clear cell carcinoma 5.5x4.8 cm Fuhrman grade II, limited to the renal parenchyma. Congestion and focal chronic inflammation (Figure 3).

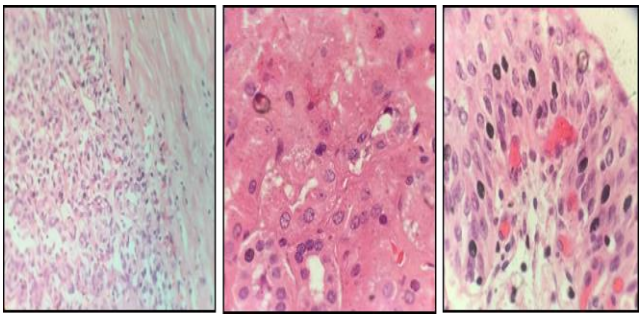

Figure 3: Histopathology of renal tumor, the cells have clear appearance which is arranged in solid mantles or nests separated by an abundant proliferation of vasculature. Nuclei are round to irregular.

DISCUSSION

Clinically, patients with renal cell carcinoma are reported asymptomatic or nonspecific symptoms such as fatigue, weight loss and vague symptoms (Table 3), with the possibility of presenting in advanced stages the classic triad of hematuria (80%), flank pain (20- 45%) and a palpable abdominal mass (10-48%) as well as paraneoplastic syndromes, the most frequent hypercalcemia, polycythemia, hypertension, Stauffer syndrom (nonmetastatic hepatic dysfunction), cachexia, pyrexia, neuromyopathy, amyloidosis, elevated syndrome the erythrocyte sedimentation rate, anemia, among others. The spread is usually by local extension, tending to spread along the route of the renal vein, reaching submitted an invasion of the renal vessel in 16%, 8% in the inferior vena cava and 6% in the cardiac cavities, why which at diagnosis in up to 30% of patients documented metastasis being the lung tissue, lymph nodes and liver the most affected.[7]

Table 3: Diagnostic methods: sensitivity and specificity.

Diagnostic methods		Percentage of patients with signs or symptoms	
Clinical	Hematuria	56%	
	Flank pain	38%	
	Abdominal mass	45%	
	Diagnosis triad Hematuria + flank pain + abdominal mass	9%	
	Weightloss	27%	
	Hematuria + flank pain + weightloss	6-10%	
	Anemia	21%	
	Fever	7%	
	Paraneoplastic syndrome (cachexia, weight loss, hyperpyrexia, neuromyopathy, hypertension, varicocele, edema, bone pain, amyloidosis, elevated ESR, polycythemia, anemia, abnormal liver function and hypercalcemia)	30%	
Medical imaging		**Sensitivity**	**Specificity**
	Computed tomography (CT) abdominopelvic with or without contrast	>94%	>87%
	CT with iodinated contrast medium for the identification of tumor thrombus	78-95%	96%
	Magnetic resonance (MR)	100%	94%
	Contrast-enhanced ultrasound (CEUS)	88%	80%
	FDG PET-CT for lymph nodes	85%	100%
	Intravenous urography	21% for lesions smaller than 2 cm 52% for lesions between 2-3cm 85% for lesions larger than 3cm	100%
	Computed tomography dual energy to distinguish clear cell renal carcinoma versus papillary carcinoma.	95.3%	98.2%
Histopathologic	Carbonic anhydrase IX (CaIX)	86.2%	85.96%
	miR-378 and miR-451(37)	81%	83%

Up to 30% of patients present manifestations related to lung, bone and brain metastases at diagnosis. The locations and frequency of invasion are: lung (67- 76%), lymph nodes (40-66%), bone (42%), liver (41%), contralateral kidney (23%), adrenal gland ipsilateral (17%), contralateral adrenal gland (11%), brain (11%).[15] The urological manifestations are highly related with this carcinoma, due the localization of the tumor. The triad of Guyon (hematuria, renal pain and palpation of the tumor) is associated with disseminated disease and has been reported in only 6-10% of the patients so it is not one of the most common manifestations. Like hematuria, pain is a late sign, the first by pyelocalyceal invasion, while the pain is secondary to capsular distension by the mass effect of the tumor. It has been reported at low frequencies presenting a sharp left varicocele, which has been correlated with tumor invasion of the left renal vein or secondary to obstruction of venous drainage of the spermatic vein into the left renal vein (given its anatomical location) by retroperitoneal lymphadenopathy.

Survival rate is approximately 45% at 5 years of renal cell carcinoma, which is remarkably improved to be absence of metastasis, as it has become established in 70% the median survival rate. Cases with renal vein or perinephric fat impaired, the median survival rate drops to 15-20%.[15]

Until a few years ago the "open" radical nephrectomy described by Robson in the decade of the most discussed 60'era to treat clinically localized renal carcinoma way, but now with the advent of minimally invasive techniques to laparoscopy is positioned as a new type of surgery and offers clear advantages in postoperative morbidity.[31] The complete tumor excision is the treatment of choice for renal malignancies, therefore radical nephrectomy is considered the gold standard for the management of renal tumors. The initial description of the radical nephrectomy was in the early clamping of the renal hilum, dissection around Gerota fascia, ipsilateral adrenalectomy and retroperitoneal lymphadenectomy, which consists in lymph node dissection from the diaphragmatic pillars to the bifurcation of the aorta. However, this surgery has been modified according to morbidity and therefore currently the adrenal gland or lymph node is not included but in selected cases.[32]

Radical nephrectomy must meet the following criteria: choice of the most suitable approach path, ligation of the renal artery without opening the perirenal space, lymphadenectomy, complete excision of the tumor and venous thrombus and metastasis if any.

Surgical technique: (1) The unilateral extraperitoneal technique is similar to the simple nephrectomy, although the pedicle must be dissected first; (2) the transperitoneal technique differs depending on the affected side and is independent of the path like.[33]

Radical nephrectomy is curative only when all tumor remnants are found during the study patient or surgery are removed, while in patients with metastases, only has a palliative role, requiring a systemic treatment at the same time. The radical nephrectomy combined with administration of IFN-alpha may increase the survival and functional status in metastatic renal cell carcinoma.

In the medical literature there are various opinions regarding the conduct of the procedure with radical or partial technique, demonstrating that the 10-year follow-up oncologic results are equivalent in both procedures. Currently it is considered poor prognosis if you have a tumor larger than 4 cm, but the type of nephrectomy (partial versus radical) would not impact on cancer-specific survival in patients with T1 greater than 4 cm. Considering the most significant study on the oncological outcome of the procedures in tumors smaller than 5 cm, an overall 10-year survival was found of 75.2% in patients with partial nephrectomy compared with 79.4% in patients with radical nephrectomy, so it was found that there is no significant difference, besides the absence of a greater tendency death risk of cancer specific in one of the two procedures.[34] Comparing this with the study by Badalato et al where tumor masses of dimensions between 4 and 7 cm were observed, data showed similar results without changes in survival of patients with surgical procedures partial nephrectomy compared with nephrectomy radical. The results of overall survival at five years with radical nephrectomy was 85% compared with 82.5% with partial nephrectomy.[35] Today, we are aware of the immense need to understand better the mechanisms of the disease and the risk of subsequent renal disease nephrectomy staging risk, providing survival and optimize patient management. A comprehensive, interdisciplinary and personalized attention is needed to choose treatment options based on understanding the disease.

CONCLUSION

Early identification by means of clinical and diagnostic aids is vital in the management of patients with renal cell carcinoma, representing prognosis due to act before the tumor dissemination in which vascular structures involved are as vein renal or perirenal fat. Radical nephrectomy has proven to be the best option for treating patients with this condition because the benefits in terms of recurrences and complications are concerned, although a partial nephrectomy will preserve renal function in unaffected parts and it must be established by studies with a larger population the existence of tangible and reliable representative for implementation in medical practice benefits.

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