PARANEOPLASTIC SYNDROMES IN RENAL TUMOURS

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Abstract: *Renal malignant tumours have an increasing incidence and affect lower age groups, with an average age of diagnosis of 65 years, with twice the incidence of the male gender versus females. The paraneoplastic syndromes (PS) that accompany them are the result of complex pathophysiological mechanisms, some of which are still insufficiently known. The multitude and variety of these syndromes is the subject of this paper, based on a retrospective study of renal tumours hospitalized and treated in Sibiu Urology Clinic during 2012-2017. The analysis of the cases in terms of PS frequency, their evolution as a result of surgical treatment and their influence on the prognosis of the disease are the main objectives aimed at in this paper.*

INTRODUCTION

Renal malignant kidney tumours represent 3% of the adults' neoplasms and the second cause of death in industrialized countries.(1) In recent years, malignant kidney tumours have become more frequent, affecting groups of lower age, the mean age of diagnosis being 65 years old.(2)

Risk factors thought to play a part in the incidence of renal tumours with an important role in pathogenesis are smoking, hypertension, obesity, estrogen therapy, occupational exposure to certain noxious substances and hereditary tumour syndromes: von Hippel-Lindau (VHL) disease, Birt-Hogg-Dube syndrome, renal cancer syndrome and hereditary leiomyomatosis (HLRCC). In neoplastic processes, the literature shows a higher incidence in males (7%) than in females (4%).(3)

The classification of adult malignant kidney tumours from an anatomo-pathological point of view includes: conventional carcinoma (with clear cells - Grawitz tumour) - represents 70% of renal carcinomas, papillary renal carcinoma (with chromophilic cells) represents 7-14%, renal carcinoma with chromophobe cells represents 6-11% with a better prognosis, Bellini's duct carcinoma (BDC) represents 1%, very aggressive medullary renal carcinoma with a survival rate of 3.5 ± 2.4 months after diagnosis, mucinous tubular and spindle cell carcinoma.(2)

Renal tumour is the condition that may have polymorphic clinical symptoms, associating a multitude of symptoms and signs. Classically, the most common manifestations are urological, such as lumbar pain, haematuria, palpable renal tumour, although they can be grouped into the classical triad that is increasingly rare and most often, it represents the manifestation of tumours in an advanced stage.

Renal cancer can be manifested by various signs and symptoms, many of which are unrelated to the urinary system and are grouped into paraneoplastic syndromes with an incidence of approximately 30%.

Paraneoplastic syndromes are represented by: endocrine syndrome, haematological syndrome, febrile syndrome, Stauffer syndrome (reversible liver syndrome), cardiovascular syndrome, others (myopathy, IgM paraprotein).(4)

PURPOSE

There have been analysed the forms and the frequency with which paraneoplastic syndromes are present in the symptomatic picture of renal cancer; the correlation between the presence of PS and the tumour stage; influence on prognosis of the disease; the way surgical treatment altered the evolution of PS.

MATERIALS AND METHODS

A retrospective study was performed on a group of 127 patients diagnosed with renal neoplasm and admitted to the Urology Clinic of the Sibiu County Clinical Hospital during January 2012 - February 2017, using the hospitalization records, observation sheets and operating protocol as the source of information.

The diagnostic investigation protocol consisted of the clinical examination: anamnesis; objective examination. Paraclinical investigations for positive diagnosis: abdominal ultrasound, intravenous urography, computed tomography, histopathological examination.

Paraclinical investigations for staging: pulmonary radiography, abdominal ultrasound, bone scintigraphy, computed tomography. The pre- and postoperative laboratory examinations included: renal function tests, liver function tests, blood counts, inflammatory markers, serum ionogram, coagulogram, urinalysis, uroculture.

Cases have been analyzed for diagnosis, treatment, and postoperative development.

RESULTS AND DISCUSSIONS

Distribution of patients by gender

It is noticed that the incidence of renal tumours is approximately two times higher in males than in females (female: male ratio = 1: 1.7), which corresponds to literature data, without being able to find a pathogenetic explanation for this.(5)

Distribution of patients by age group

Age varied between 26 and 83 years with an average of 63 years for females and 59 years for the male gender. The increase in incidence of renal neoplasm is directly proportional

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to aging, the maximum frequency occurring between the 5th and 6th decades of life.

Incidence of PS in adults' malignant tumours

Based on clinical examination and paraclinical investigations, the presence of PS was found in 26% of patients diagnosed with malignant renal tumours. Thus, the most common highlighted changes are cardiovascular and inflammatory (table no. 1.).

Table no. 1. Incidence of PS in adults' malignant tumours

Diagnosis	No. of patients	Percentage
Malignant renal tumour	127	100 %
Malignant tumour with paraneoplastic syndrome	33	26%
- endocrine	2	1,57%
- hematological	2	1,57%
- Stauffer	0	0%
- febrile	17	13,4 %
- cardiovascular	12	9,46%
- myopathy	0	0%

Correlation between tumour stage and PS. There is an increase in the incidence of PS in advanced tumour stages (III, IV), unlike the early tumour stages where the frequency of paraneoplastic changes is reduced (table no. 2).

Table no. 2. Correlation between tumour stage and PS

Diagnosis		No. of patients		Percentage	
TNM I	- PS	33	29	26.0%	87.8%
	+ PS		4		12.2%
TNM II	- PS	44	35	34.6%	79.55%
	+ PS		9		20.45%
TNM III	- PS	31	19	24,4%	61.29%
	+ PS		12		38,71%
TNM IV	- PS	19	6	14,9%	31.58%
	+ PS		13		68,42%

Mortality in patients with renal tumours and PS. The annual study of deaths in these patients reveals a moderate increase in deaths in the group of patients with PS accompanying the renal tumour. Overall, there were 29 deaths, resulting in a mortality rate of 22.83%. It can also be seen that among patients with PS, death occurs more frequently (70%) than in non-PS patients (30%).

Post-operative evolution of PS. Of the 127 patients, 19 showed malignant renal tumours in stage IV without indication of surgical treatment.

Perifascial radical nephrectomy, applied to 108 patients, consisted of "en-block" extirpation of the kidney along with the cellulose and the fatty tissue of Gerota's fascia, partial ureterectomy, homolateral suprarenalectomy and regional lymphodissection.(6,7)

The postoperative follow-up protocol was based on clinical examination, ultrasound, CT scan and laboratory investigations performed at 3 months, 6 months, and then yearly. Paraneoplastic syndrome resolved in 87.83% of cases. Four patients (12.12%), in the metastatic stage, continued to experience paraneoplastic changes following surgery.

Renal cancer is often incidentally detected during routine medical check-ups and the importance of ultrasound examination of the kidney should be emphasized even in the absence of a specific symptomatology of renal impairment. Although it is an extremely aggressive tumour with increased resistance to chemo and radiotherapy, kidney cancer diagnosed early and treated correctly has a favourable development, being even curable.(8)

A feature of malignant renal tumours is the highly polymorphic clinical manifestation, comprising a plurality of signs and symptoms, most of them being urological: hematuria, palpable tumour formation in the lumbar region, localized pain. Often, renal neoplasm injury also has an impact on other organs and systems, leading to clinical manifestations apparently without any connection to the urinary system. These can be grouped into paraneoplastic syndromes occurring - according to specialized data - in about 30% of patients.(1,2,9)

CONCLUSIONS

According to our study, paraneoplastic syndromes were found with a frequency of 26% regarding the manifestations of malignant kidney tumours. Antibiotic-resistant fever and cardiovascular forms are the most common paraneoplastic changes: 13.4% and 9.46%, respectively.

There is a correlation between the tumour stage and the presence of paraneoplastic syndromes: in tumour stage III, PS was present in 38.71% of patients and in tumour stage IV in 66.42% of them.

The mortality rate is higher for PS patients (70%) than for other patients (30%), indicating a negative influence of paraneoplastic changes on the progression and prognosis of the disease.

Total nephrectomy in patients in operable stages resulted in a 87.83% remission of PN manifestations.

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