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METASTATIC RENAL CELL CARCINOMA

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SUMMARY – Renal cell carcinoma is the third leading urologic cancer. Thirty percent of patients with renal cell carcinoma have metastatic disease at the time of diagnosis. The most frequent locations of metastases from renal cell carcinoma are the lungs, mediastinum, bone, liver, and brain. There are several treatment modifications for metastatic renal cell carcinoma, with varying results. Surgical therapy is contraindicated in patients with multiple metastases, due to poor survival. Relief of pain and other symptoms poses a serious problem in patients with metastases.

Key words: *Carcinoma, renal cell; Kidney neoplasms, pathology; Kidney neoplasms, drug therapy*

Introduction

Renal cell carcinoma (RCC) is the third leading urologic cancer causing approximately 7,000 deaths *per* year in the United States. It is three times more common in males than in females. Some 30% of RCC patients have metastases at the time of primary cancer diagnosis, and 95% on autopsy[1]. Although some of these patients may live relatively longer (about 10% of these patients will live for more than 3 years), the relative survival is only 6 to 9 months[2]. Secondary metastases, i.e. those that occur after nephrectomy, have better prognosis than those detected at the time of primary cancer diagnosis[3]. Metastases develop in relatively young patients at an avarege age of 56. These metastases are often associated with pain and other symptoms which need only palliative treatment. The distribution and localization of RCC metastases are shown in Tables 1 and 2 and Fig. 1.

Fig. 1. Metastatic involvement of the ileum and the mesentery

Table 1. Frequency and distribution of renal cell carcinoma metastases diagnosed on autopsy and at time of primary cancer diagnosis

Metastasis	At time of diagnosis (%)	On autopsy (%)
Multiple	97	
Solitary	3	
No. of organs involved		
Solitary organ	70	9
Multiple organs	30	81

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Table 2. Localization and frequency of renal cell carcinoma metastases

Localization (%)	At time of diagnosis (%)	On autopsy (%)
Lungs and mediastinum	50	67
Bone	49	39
Skin	11	13
Liver	8	39
Brain	3	6

Therapeutic Options

There are a number of therapeutic options for the treatment of metastatic RCC with a varying success. The main problems can be summarized in two questions: 1) should routine radical nephrectomy be performed if metastases are present?; and 2) what is the therapeutic approach to metastatic sites?

Radical Nephrectomy in Metastatic RCC

Palliative nephrectomy was for decades the procedure of choice for metastatic RCC because it was considered that: a) sponteneous regression of metastases would occur upon primary cancer removal; b) removal of a large symptomatic cancer may have a significant palliative effect; and c) palliative nephrectomy could improve survival. Our experience showed these presumptions to be too weak for routine nephrectomy in patients with metastatic RCC.

Spontaneous postnephrectomy regression of metastases occurs very rarely (in less than 0.5% of cases), and the regression is usually transient[4]. In addition, Freed et al.[5] recorded regression of cancer without surgical intervention in three cases. Therefore, surgery need not be associated with spontaneous regression. The more so, the mortality rate recorded after operative treatment based on the patient selection criteria amounts to 2% – 10%. Some reports suggesting the absence of metastases after angioinfarction and subsequent nephrectomy have yet to be proved before the procedure could be recommended as a standard.

Symptom Relief

Symptom relief is a major problem in patients with metastases. Primary cancer is rarely associated with frequent or significant symptoms, and patients with multiple metastases mostly (97%) have poor prognosis. Fifty percent of them will die within 6 months. In some cases, especially in high-risk patients, the indication for palliative nephrectomy (in symptomatic patients) can be replaced by selective angioinfarction (embolization).

There are little data showing that the survival of patients with distant metastases increased after 'additional' nephrectomy. DeKrenion and Lindner[6] and Chatelain[7] have demonstrated that the patients submitted to nephrectomy had the same survival rate as those with metastatic RCC.

However, some patients with metastatic RCC may benefit from nephrectomy: 1) patients with severe symptoms caused by primary cancer, e.g., pain or heavy bleeding, and patients who are likely to live for at least 5 months or longer; 2) patients with solitary metastases (3% of all cases). More than 60% of these patients will live for more than 2 years, therefore resection of the metastasis and nephrectomy will be a reasonable approach; and 3) the psychological effect on the patient should also be considered as well as the patient's desire to remove the desease. All other indications for nephrectomy are controversial.

Maladzyz and deKernion[8] studied survival in a large number of patients with RCC and identified some contributing factors: good general condition, cancer that can be removed completely, intrarenal cancer, and metastases confined to the lungs. A 3-year disease-free period after 'additional' nephrectomy is found in more than 30% of selected patients. The same result could be achieved without nephrectomy, however, implying a compromised quality of life.

Therapy for Metastases

1) Surgical excision of metastases
2) Radiotherapy
3) Systemic therapy
   – hormonal therapy
   – chemotherapy
4) Surgical excision of metastases

Local excision of metastasis as a successful therapeutic option is used in patients with solitary metastases (1% to 3% of all cases). Surgical approach is not indicated in

patients with multiple metastases, because their survival rate is low. The indications and technique of metastasis excision depend primarily on metastasis localization.

Lung metastases are most common and are usually removed within the healthy margin of pulmonary tissue, whereas lobectomy or pulmectomy are rarely performed. The best indication for surgical removal is a single metastasis, however, multiple metastases can also be removed if they are localized unilaterally.

The second most common metastases are those to the bone. Multiple metastases have a much worse prognosis. In some cases, the affected bone can be replaced, while in others orthopedic fixation can be performed, sometimes in combination with curettage of the lesion. This is mostly performed when the patient is expected to live for the next 4 to 5 months.

In some cases, metastasis to the brain is the first sign of the disease. Surgical operation is the first choice if the metastasis is solid. After the operation, patients are expected to live for more than 7 months, while those with untreated metastases have a 3-month survival at the most.

Metastases to the liver have poor prognosis, and are usually found on autopsy. Solid liver metastases can be treated by partial hepatectomy.

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Sažetak

METASTATSKI KARCINOM BUBREŽNOG PARENHIMA

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Karcinom bubrežnog parenhima je treći po učestalosti među urološkim karcinomima. U trećine bolesnika u trenutku otkrivanja primarnog tumora prisutna je diseminacija bolesti. Adenokarcinom bubrega najčešće metastazira u pluća i u medijastinum, zatim po učestalosti slijede koštane metastaze, metastaze jetre i mozga. U terapiji metastatskog adenokarcinoma upotrebljavaju se različiti pristupi s promjenjivim rezultatima. Kirurška terapija je kontraindicirana u bolesnika s višestrukim metastazama zbog slabog preživljavanja. Velik problem u bolesnika s metastazama predstavlja i ublažavaje simptoma.

Ključne riječi: *karcinom bubrežnog parenhima, metastaze, terapija*