

Caso clínico raro de metastização bilateral síncrona das glândulas supra-renais. Há indicação para supra-renalectomia laparoscópica no carcinoma de células renais?

Uncommon case of isolated bilateral synchronous adrenal gland metastases. Is there a place for laparoscopic adrenalectomy in renal cell carcinoma?

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Resumo

Introdução: O objectivo deste artigo é apresentar um caso clínico raro de carcinoma de células renais com metastização bilateral síncrona das glândulas supra-renais. Os pontos de discussão são as opções terapêuticas e a possibilidade de cirurgia laparoscópica para a metastasectomia nas glândulas supra-renais.

Caso Clínico: Apresenta-se o caso clínico de uma doente do sexo feminino com 80 anos que recorre ao Serviço de Urgência por dispneia e edema dos membros inferiores. As análises sanguíneas revelaram insuficiência renal severa e a ecografia renal revelou uma massa no rim direito. Realiza hemodiálise desde então. A etiologia da insuficiência renal não foi determinada. A tomografia computadorizada (TC) abdominal e pélvica revelou um tumor renal extenso à direita e glândulas supra-renais com dimensões significativamente aumentadas, sem outras suspeitas de metastização.

A massa da glândula supra-renal pode ser adenoma ou carcinoma das glândulas supra-renais ou metástases do tumor renal. A doente foi submetida a nefrectomia radical e adrenalectomia à direita. O exame histológico revelou carcinoma de células renais (padrão convencional) e metástases na glândula supra-renal homolateral. Três semanas após a cirurgia a doente manteve anúria e de acordo com a opinião do Serviço de Nefrologia de perda irreversível

da função renal, a doente foi submetida a supra-renalectomia e a nefrectomia radical à esquerda. Iniciou terapêutica de substituição com adrenocorticóides no pós-operatório. O exame histológico revelou carcinoma de células renais com metastização bilateral síncrona das glândulas supra-renais.

Discussão: Muitos doentes podem beneficiar da ressecção cirúrgica de metástases isoladas de carcinoma de células renais com uma cirurgia segura. A nefrectomia pode ser curativa se for realizada a excisão completa das metástases. A supra-renalectomia laparoscópica para metástases nas glândulas supra-renais continua a ser uma opção em discussão. Apesar do carcinoma das células renais ser a causa de morte mais frequente nestes doentes, a metastasectomia pode prolongar significativamente a sobrevida em alguns.

Palavras-chave: carcinoma de células renais; metastização bilateral das glândulas supra-renais; metastasectomia.

Abstract

Introduction: The purpose of this article is to present a very rare clinical case of a renal cell carcinoma with isolated bilateral synchronous adrenal gland metastases. The points of discussion are the therapeutic options and laparoscopic surgery for adrenal gland metastases.

Case Report: An 80-yr-old female presented at the Emergency Room with lower limbs oedema and dyspnoea. Blood tests revealed severe renal failure and the kidney ultrasound showed a renal mass on the right side.

The patient has required haemodialysis since then. Aetiology of the renal failure was not determined. Computed tomography (CT) revealed an extensive renal tumour on the right side and considerable bilateral enlargement of the adrenal glands. There were no other metastatic suspicious sites. The adrenal gland mass could be adenoma or carcinoma of the adrenal glands or metastasis from the renal cell carcinoma. The patient underwent radical nephrectomy and adrenalectomy on the right side. Histologic examination revealed renal cell carcinoma (conventional pattern) and metastasis in the ipsilateral adrenal gland. Three weeks later as the patient maintained anuria and according to the nephrology department's opinion of irreversible loss of renal function the patient was submitted to adrenalectomy and radical nephrectomy on the left side. Postoperative adrenal steroid replacement therapy was instituted. Surgical pathology demonstrated synchronous bilateral adrenal metastasis from renal cell carcinoma (RCC).

Discussion: Many patients may benefit from surgical resection of limited metastasis from RCC with a safe surgery. Tumour nephrectomy can be curative if surgery can excise all tumour deposits. Laparoscopic adrenalectomy for adrenal gland metastasis remains debated. Although most patients ultimately die from RCC, metastasectomy can significantly prolong survival in some.

Key-words: renal cell carcinoma; bilateral adrenal gland metastases; metastasectomy.

Introduction

Renal epithelial neoplasms represents 2-3% of all cancers worldwide¹, having an incidence of approximately 10 cases per 100,000 people².

Despite advances in diagnosis around 20-30% of patients still have metastatic RCC at the time of diagnosis³ and approximately 30-40% of patients with malignant renal cortical tumours will either present with or later develop metastatic disease⁴.

RCC can metastasize to practically all organs, following routes of spread and patterns that are not yet fully understood^{5,6,7}.

The most common metastatic sites are the lungs, liver, lymph nodes, ipsilateral adrenal gland, bones and brain. Whereas metastases of RCC to different sites are not uncommon, contralateral adrenal metastasis is found clinically in only 0,51% of patients

and synchronous bilateral adrenal metastasis is rare^{5,6}.

Contra-lateral adrenal metastasis of RCC is thought to occur via the haematogenous route as is the case for other organ metastasis⁶.

Case report

An 80-yr-old Caucasian female with a good performance status (score of 90% in the Karnofsky performance status scale) presented at the emergency room due to dyspnoea, reduced urine output in previous days and lower limbs oedema. Medical history revealed a previous known history of renal failure (creatinine: 2,5mg/dL) and pacemaker placement, without any acute cause for renal function deterioration. Blood tests revealed severe renal dysfunction with urea: 236mg/dL; creatinine: 8,1mg/dL. Ultrasound showed a mass on the right kidney.

The patient was started on renal replacement therapy. Aetiology of the renal failure was not determined.

Abdominal and pelvic computed tomography (CT) (figure 1) revealed: renal tumour at the right side measuring 9cmx8cm; permeable inferior vena cava; considerable bilateral enlargement of the adrenal glands measuring 5,4cm on the right side and 7,7cm on the left, both of them with focal central necrosis; abdominal organs and lymphatic system with no morphologic evidence of disease dissemination.

Blood tests proved normal adrenal gland function and urinary tests revealed mildly elevated levels of metanephrines. This excluded the possible diagnosis of pheochromocytoma and the mildly elevated urinary levels of metanephrines were considered as a consequence of focal central necrosis on the adrenal glands.

Thoracic CT and bone scan demonstrated no metastasis.

The adrenal gland masses aetiology could be adenoma or carcinoma of the adrenal glands or metastasis of renal cell carcinoma (RCC). The patient underwent right side nephrectomy and adrenalectomy. During surgery, we found the right renal vein and the inferior vena cava tumour free. Histologic examination revealed renal cell carcinoma (RCC, conventional pattern, grade 2 according to Furman's classification) (figure 2) with invasion of the perinephric adipose tissue and metastasis in the ipsilateral adrenal gland, with free surgical margins (pT3aNxM1 according to the 2009 TNM staging classification system).

Probability of metastasis on the contralateral adrenal gland was very high.

We proposed left side adrenalectomy and radical nephrectomy (figure 3). A point of discussion is our

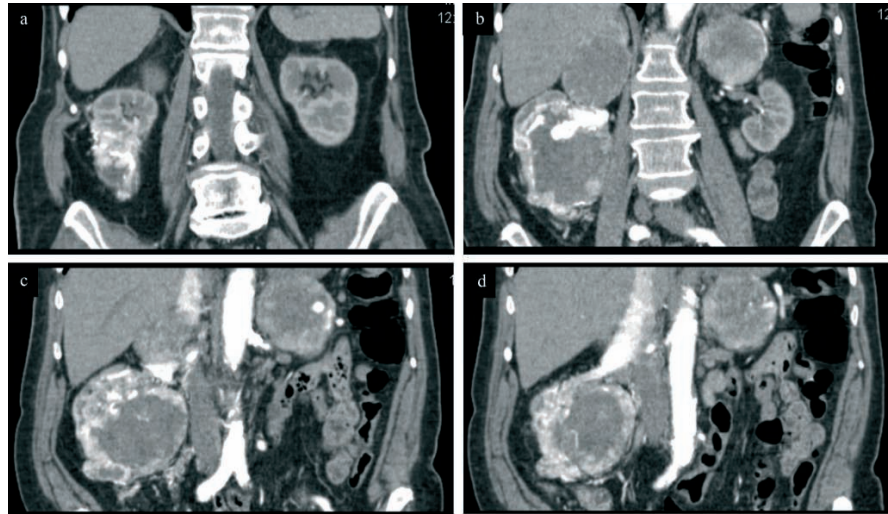


Figure 1 CT coronal images of a 50-yr-old woman with good performance status demonstrating a renal tumour at the right side, and huge bilateral adrenal glands mass, both of them with focal central necrosis; (d) inferior vena cava without suspicious images of tumour thrombus.

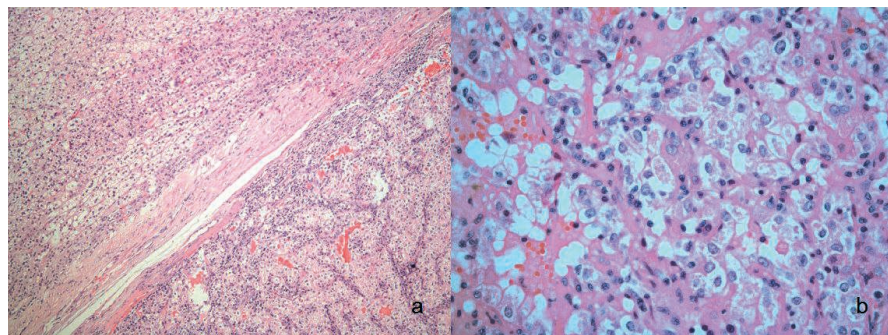


Figure 2 Histologic examination with Hematoxylin-Eosin (HE) stain. (a) Clear cell RCC on the right of the image (x100); (b) Amplified image of the clear cell RCC (x400).

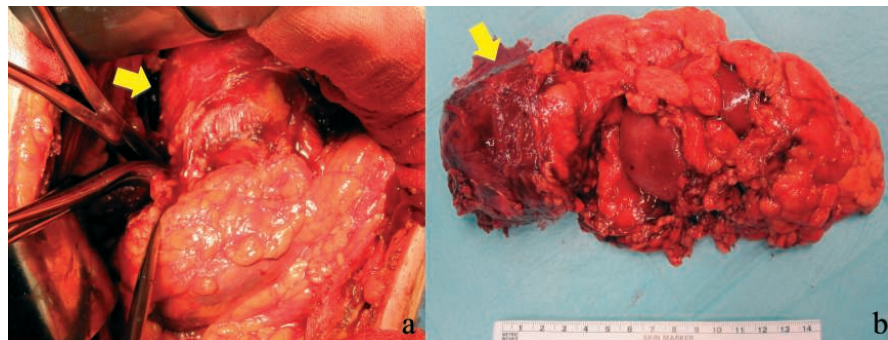


Figure 3 (a) Intraoperative photograph demonstrating a big left adrenal gland (arrow) manipulated after the vascular cross-clamping of the renal artery and vein to avoid tumour dissemination and to prevent haemodynamic changes due to the excessive release of catecholamines. (b) Left nephrectomy and adrenalectomy specimen showing a huge left adrenal gland. Histopathological examination revealed metastasis on the adrenal gland (pathologically identical to the right renal tumour).

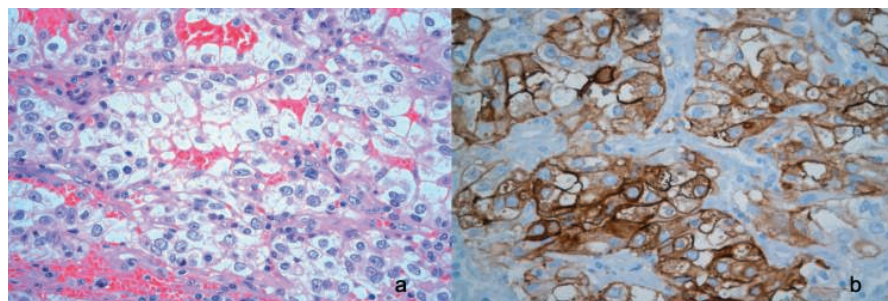


Figure 4 (a) Histologic examination of the left adrenal gland, with a tumour identical to the renal tumour and the right adrenal gland metastasis; this image is not conclusive for adrenal gland or metastatic tumour (HE, x400); (b) As in the right adrenal gland, after immunohistochemical study, the tumour cells stained with CD10 marker, compatible with RCC metastasis from the contra-lateral renal tumour (CD10, x400).

option to perform nephrectomy on the left side. The reasons for this decision were: the patient maintained anuria during three weeks after the first surgery without any known cause of renal dysfunction, the thin renal parenchyma and the nephrology department's opinion of irreversible loss of renal function.

Histopathological examination revealed metastasis on the adrenal gland (pathologically identical to the right renal tumour) (figure 4) and kidney free of tumour with associated acute tubular necrosis and free surgical margins.

The woman was placed on adrenal steroid replacement therapy after the surgery.

Postoperative course was uneventful.

Discussion

In autopsy series of patients with RCC, the incidence of adrenal gland metastasis from RCC is 6-29%. The involvement of the ipsilateral adrenal gland is 19% in the autopsy and 5.5% in the surgical series, whereas the contralateral adrenal is involved in up to 11% of the autopsy series but there are only a few cases published in the literature^{7,8}.

Radiologic studies cannot determine with certainty whether an adrenal tumour in a patient with RCC is a primary adrenal neoplasm (the most common type), an adrenal cortical adenoma, or metastatic disease⁵. Any suspicious ipsilateral or contralateral adrenal mass should be explored because there is a high probability of removing a metastasis⁷.

The distinction often comes only from the surgical removal of the adrenal gland and, in some cases, the application of immunohistochemical markers to the adrenal tumour⁵.

Memorial Sloan Kettering Cancer Center (MSKCC) investigators reported prognostic factors associated with enhanced survival in 278 patients who underwent surgical metastasectomy. Favourable features for survival were a disease-free interval greater than 12 months from the time of nephrectomy (55 vs. 9% 5-year overall survival), solitary versus multiple sites of metastases (54 vs. 29% 5 year overall survival) and age younger than 60 years (49 vs. 35% 5 year overall survival)⁹.

The survival of patients with untreated widely metastatic RCC is poor, and may differ from that of patients with solitary or limited metastasis, in many of whom removal of the RCC metastasis is associated with prolonged survival^{1,5,7,10}.

In patients with synchronous metastatic spread, metastasectomy should be performed when it is feasible and the patient has a good performance status. Clinical prognosis is worse in patients who have surgery for metachronous metastases¹.

One point of discussion is the laparoscopic surgery

for adrenal gland metastasis. In a series of 32 patients with different primary tumours, 34 adrenalectomies were performed for suspected metastasis in the adrenal glands. In two patients (9,1%) the margins were positive. The mean tumour size was 4,3cm¹⁰. The size of the adrenal gland metastasis can be considered a limiting factor for laparoscopic approach. Metastatic adrenal masses greater than 5cm have a high likelihood of open conversion (60% of the cases), or at the very least, a long and difficult dissection¹¹. And we don't know if the laparoscopic approach raise the probability of tumour spillage or has the same oncologic outcome in metastatic adrenal gland masses. Especially the masses extremely large in size.

In more recent series, it is suggested that laparoscopic adrenalectomy for metastases is feasible and oncologically safe in properly selected patients¹²⁻¹⁴. Eligibility requirements are not clear and indication for laparoscopic adrenalectomy for adrenal gland metastasis remains debated¹⁰.

RCC is relatively resistant to nonsurgical modalities and therefore is primarily managed by surgery^{10,15}. Until the past 4 years, systemic treatments in patients with metastatic RCC were largely ineffective³.

Cytotoxic chemotherapy and hormonal therapies alone or in combinations are ineffective in treating patients with RCC metastasis. Cytokine therapy, including interleukin-2 and interferon alpha, have been used widely over the last 20 years in several clinical trials and oncological practice and albeit they have some activity overall response rates are low (10-15%) and only rarely associated with durable complete remission⁴.

A number of other agents targeting angiogenesis are under investigation as well as combinations of agents with each other or with cytokines. The role of the new drugs is still to be defined. Until now there is no data indicating that the new agents have a curative effect; on the other hand they appear to stabilise metastasized RCC¹.

Five years survival rate for patients undergoing RCC metastasis resection ranges from 35 to 60%^{3,4}. Selection criteria are not well defined and there is no age limit⁹. Carefully selected patients with good performance status undergoing nephrectomy and subsequent metastasectomy may experience prolonged survival in the range of 30 months, which could be attributed to a combination of patient selection factors and the surgical resections, in many cases for more than 5 years after metastasectomy^{4,5}.

Therefore, aggressive treatment of such lesions is indicated with complete surgical excision of the adrenal gland currently offering the patient's best possibility for cure^{1,5}. Immunotherapy, where there

has been complete resection of metastatic lesions or isolated local recurrences, does not contribute to an improvement in clinical prognosis¹.

Many patients may benefit from surgical resection of limited metastasis from RCC with a safe surgery. Although most patients ultimately die from RCC, metastasectomy can significantly prolong survival in some^{1,5,6,9}.

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