

# Synchronous oligometastatic lung acinar adenocarcinoma and clear cell renal cell carcinoma: a case report

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## ABSTRACT

Synchronous tumours are complex cases, being challenging to distinguish between primary neoplasms and metastatic disease, as well as to accurately determine the origin of metastasis. Although synchronous tumours are relatively rare, its incidence has increased over the years. The authors report on a patient with localized clear cell renal carcinoma and synchronous adenocarcinoma of the lung with solitary brain metastasis, highlighting the uncertainties of the therapeutic approach and the implications to the final outcomes.

**Key-words:** Synchronous; Adenocarcinoma of the lung; Renal Cell Carcinoma.

## INTRODUCTION

The simultaneous growth of malignancies at more than one location is a rare situation called multiple primary cancers (MPC). MPC can be classified as synchronous cancers if diagnosed at the same time or within six months, or, as metachronous cancer, if diagnosed after six months.<sup>1</sup> Three diagnostic criteria have been proposed for MPC: 1) each tumour must present definite features of malignancy; 2) each tumour must be distinct; and 3) the possibility of one tumour being a metastasis of the other must be excluded.<sup>2</sup>

In situations with radiographic evidence of pulmonary and renal tumours, differentiating primary neoplasms and metastatic disease could be challenging. Indeed, at the time of diagnosis, non-small cell lung cancer (NSCLC) and renal cell carcinoma (RCC) present with metastatic disease in approximately 56% and 30% of cases, respectively.<sup>3</sup> It is estimated that 16-23% of NSCLC metastasizes to the kidney, and 45% of RCC metastasizes to the lungs.<sup>4,5</sup>

## CLINICAL CASE

A 74-year-old man was admitted at the Emergency Department (ED) of Centro Hospitalar of Baixo Vouga (CHBV) due to a sudden onset of dizziness and left eye blurred vision, with one hour evolution. At ED, the patient started with numbness and weakness of left side, remaining unable to walk without support. His past medical history was significant for cardiovascular risk factors such as arterial hypertension, dyslipidemia, and smoking (60 packs/year).

On physical examination, the following neurological signs were present: left homonymous hemianopsia, left-sided paresis grade 4 and left-sided neglect.

On computed tomography (CT), performed at admission, a 2cm right cortical and subcortical parietal expansile lesion, surrounded by edema was observed, suggestive of a metastatic lesion or high-grade glioma. Without clinical or analytical markers of infection, serologic test excluded HIV infection and chest-radiography abnormalities of parenchyma.

On brain magnetic resonance imaging (MRI) performed one day later, a 22x23mm nodular structure was detected, which was hypointense on T1-weight and hyperintense on T2/FLAIR images, surrounded by vasogenic edema, and causing a slight mass effect on lateral ventricle, suggestive of metastatic nature. The patient started treatment with 4mg of oral dexamethasone bid and, considering potential epilepsy, with 1000mg of oral levetiracetam bid. After neurosurgery evaluation, the patient was admitted in the internal medicine ward for etiological study.

With a complete resolution of neurological complaints within the first 48 hours, during hospital admission, the patient remained asymptomatic and was submitted to a thorough study to identify a primary tumour.

On thoracic-abdominal-pelvic CT, two different suspicious lesions were observed: a spiculate right inferior lobe opacity measuring 28x30mm (Figure 1) and an 70x68mm oval-shaped formation at the posterior side of the left upper kidney (Figure 2).

After pneumology evaluation, a bronchofibroscopy was performed, which revealed a left main bronchus bulge by extrinsic compression; a bronchial lavage cytology excluded the presence of malignant cells. In order to clarify the diagnose, a transthoracic lung biopsy was conducted, which revealed the presence of primary acinar adenocarcinoma of the lung. Measurement of tumour markers such as neuron-specific enolase was negative (12.5µg/L) and there was a slight increased for CYFRA 21-1 (3.73µg/L). Skeletal metastases were excluded by a whole-body bone scan.

Concomitantly to the pulmonary investigation, the patient was also evaluated by urology, that based on the radiological findings, proposed to perform a radical nephrectomy. The patient refused the procedure of radical nephrectomy without histologic confirmation of neoplasia. Considering the accessibility to the left renal mass, a CT-guided percutaneous biopsy was performed, confirming the diagnose of clear cell renal cell carcinoma (CCRCC).

Considering that the patient had two primary tumours (acinar adenocarcinoma of lung and CCRCC) and a single cerebral metastasis, which in theory could originate from any of these tumours, the patient was forwarded to radiosurgery. The patient was subjected to radiosurgery with a total dose of radiation of

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Figure 1. A spiculate right inferior lobe opacity on thoracic-CT

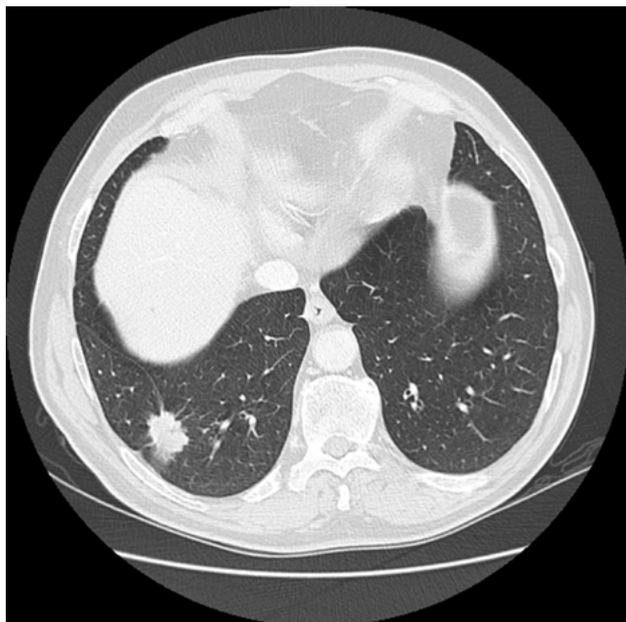


Figure 2. An oval-shaped formation at the posterior side of the left upper kidney on abdominal CT



21Gy/Fr; one month later, on reevaluation brain MRI, a reduction of the size of the right parietal metastasis was confirmed and the presence of new cerebral lesions was excluded.

Considering the prevalence of brain metastasis on lung cancer, and the positive response to radiosurgery, it was clinically assumed that cerebral metastasis most likely originated from lung adenocarcinoma, and the clinical state was designed as T1N2M1b. Since there was no expression of programmed death-ligand 1 (PD-L1), the patient started chemotherapy with carboplatin and pemetrexed. After five cycles of chemotherapy without significant intercurrents, the patient presented a reduction of the size of the pulmonary lesion.

Regarding CCRCC, the patient was submitted to left radical nephrectomy without complications.

Presently, the patient is under treatment with pemetrexed in a maintenance dose, remaining asymptomatic and without unusual neurological symptoms.

## DISCUSSION

Synchronous primary malignancies are complex cases that present with diagnostic, prognostic and therapeutic uncertainties, mainly if metastatic spread from one or both primary sites has already occurred. We report a case of solitary brain metastasis that presented synchronously with adenocarcinoma of the lung and a primary CCRCC. The challenges surrounding this case stem from the propensity of lung cancer to metastasize to the kidneys and brain, and likewise, the ability for kidney cancers to metastasize to the lungs and brain. In the literature, MPC cases are mostly seen in lung, genitourinary, hepatobiliary and gastrointestinal tract, and the coexistence of lung cancers with primary renal tumours is less common than other uroepithelial tumours.<sup>6</sup> Virtually, any tumour can metastasize to the brain, being lung cancer, breast cancer, melanoma and gastrointestinal cancers the most common.<sup>7</sup>

In this case, knowing that lung cancer is the most common cause of brain metastasis and RCC is relatively radio-resistant, it was clinically assumed that the brain metastasis originated from the lung neoplasia.

Distinguishing between a renal metastasis of lung origin and a primary RCC, or vice versa, is challenging. Although the kidney is a rare site of metastatic disease<sup>8</sup>, and renal metastases are typically bilateral and multi-focal, they can also present as extensive, solitary metastases in the breast, lungs and colorectal patients.<sup>9</sup> Without symptoms of renal disease, in the case reported here, the detection of the left renal mass was a radiological finding, which by its characteristics undoubtedly suggested a malignant nature. The indications to perform a biopsy for a renal mass in patients with a nonrenal malignancy should be based on the prognosis and the importance of differentiating the presence of an additional metastatic organ site from another primary malignancy. The patients with a nonrenal primary tumour with a long-life expectancy and a single small renal mass are more likely to benefit from surgical

extirpation over a biopsy.<sup>8</sup> In this case, urology had proposed radical nephrectomy, which the patient did not accept at first. Knowing that surgery is the gold standard treatment for primary renal neoplasm<sup>10</sup>, we may consider that this decision delayed the treatment; however, nephrectomy was eventually performed upon histological confirmation of the malignancy and this delay had no implications in the final outcome.

About treatment regiment, considering immunotherapy as the first line, the patient was evaluated for the expression of PD-L1. Since this expression was approximately 20%, this treatment was discarded. It has been described that cisplatin-based adjuvant chemotherapy provides a significant advantage in the overall survival of patients with stage II and III NSCLC and pemetrexed plus carboplatin has better chemotherapy compliance and efficiency in advanced NSCLC<sup>11</sup>; this findings were taken into account and guided our choice.

For the treatment of limited brain metastases, radiosurgery has become the standard of treatment and could defer as late as possible whole brain radiotherapy to avoid neurocognitive dysfunction.<sup>12</sup>

The rate of synchronous or metachronous cancers has been increasing over the last few decades. This is related to genetic factors of the host, environmental factors connected to exposure to risk factors, and the interplay of all these factors.<sup>13</sup> In this case, we believe that smoking had an important role, since it is a risk factor for both tumours. This further highlights that control of smoking, as a preventable cause of cancer, remains a priority in the prevention of lung cancer and other malignancies.

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