

Metamorphopsia as the first clinical sign of renal cell carcinoma

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Dear Editor,

We would like to report visual disturbance due to choroidal metastasis as the first clinical sign of renal carcinoma.

Metastatic tumours are one of the most common type of intraocular malignancy in adults with the most common origins of metastasis being the lungs in men and breasts in women^[1-2]. Ocular choroidal metastases from renal cell carcinoma (RCC) are rare with 3.5% of ocular metastases originating from the kidneys^[3]. RCC predominantly occurs in individuals in their seventh and eighth decades of life and has been reported nearly twice as often in men as in women^[1,3].

Visual disturbance and metamorphopsia as the first clinical signs of renal cancer with multi-organ metastasis, according to our knowledge, has been described in only a few cases. Other

rare sites of RCC metastases include the pancreas, thyroid, skeletal muscle, skin or underlying soft tissues with these sites of metastasis rarely occurring simultaneously^[1]. This is the first documented case of coexistence of very rare sites of metastasis in patients with RCC namely choroid and the skin.

CASE REPORT

A 46-year-old male patient noticed left eye visual disturbances and metamorphopsia without any other systemic symptoms. Apart from posttraumatic stress disorder and painless hematuria reported six months prior to initial ophthalmological examination the patient had no previous history of illness and no current health issues.

Standard ophthalmologic examination revealed reduced visual acuity in the left eye measuring 0.3 (cc +1.00 dsph on Snellen chart) and normal right eye visual acuity. Intraocular pressure, ocular motility and biomicroscopy were normal. Dilated fundus examination of the left eye showed a creamy yellow, dome-shaped mass in the posterior pole on the superotemporal edge of the macula surrounded with serous retinal detachment (Figure 1A). In the early phase of fluorescein angiography (FA) small vessels within the tumour were revealed (Figure 1B) with dye leakage in the late phase (Figure 1C) confirming a choroidal tumour of metastatic origin and the site of the primary tumour being unknown.

During a general examination there were no clinical signs of anaemia, icterus or oedema. Complete blood cell count, bleeding time, urine analysis, serum electrolytes, routine blood hepatic and renal function tests were all within normal ranges. Hemogram and biochemical test results were also within normal limits.

Multiple detector computer tomography (MDCT) of the abdomen showed the right kidney entirely infiltrated by necrotic tumour mass with blurred anterolateral contour of the upper part spreading through the right renal sinus. There was no renal vein thrombosis, however a channel system of the upper and medium groups of calices and renal pelvis were infiltrated by tumour tissue. On the lower part of the left kidney a suspect tumorous infiltration was also found (Figure 2A, 2B).

MDCT of the thorax revealed multiple focal nodular changes of lung parenchyma diffusely distributed on both sides



Figure 1 Fundus and fluorescein angiography A: Left eye fundus examination showing a yellow lesion on the outer edge of the upper vascular arch of the posterior pole and serious retinal detachment; B: Fluorescein angiography of the left eye in the early phase demonstrating choroidal tumor small vessels; C: Dye leakage at sight of choroidal tumor in the late phase of fluorescein angiography.

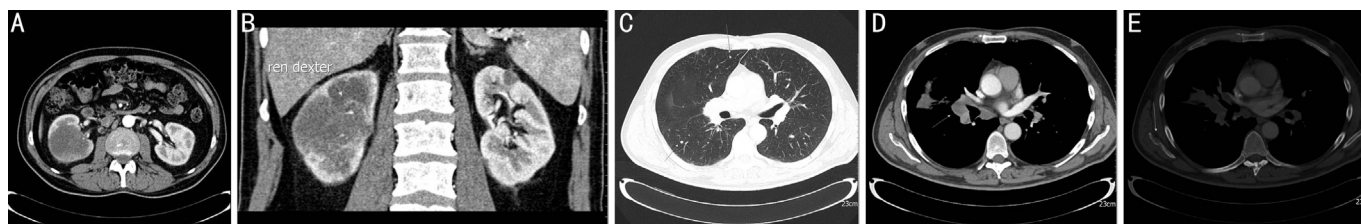


Figure 2 Thoraco-abdominal multiple detector computer tomography A: MDCT images showing tumor infiltration of the renal pelvis of the kidney transverse section; B: tumor infiltration of the renal pelvis of the right kidney longitudinal section; C: Thoraco-abdominal MDCT cross section of the lungs showing multiple focal nodular changes of lung parenchyma diffusely distributed on both sides; D: Thoraco-abdominal MDCT cross section of the lungs showing confluent necrotic extensive hilar lymphadenopathy on both sides; E: MDCT showing osteolytic lesions on the inferior margin of the right scapula as well as on the thoracic spine.

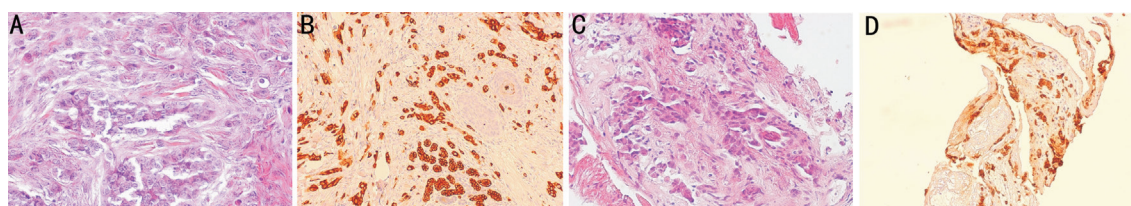


Figure 3 Histopathological skin analysis and immunohistological analysis of lung A: Skin biopsy with metastatic tumor tissue; atypical tumor cells forming small clusters and glandular formations, hematoxylin-eosin 200 \times ; B: Immunostaining pattern of CK7+ in the skin metastasis, counterstaining hematoxylin 100 \times ; C: Tumor tissue from a transbronchial lung biopsy, hematoxylin-eosin 200 \times ; D: Immunostaining pattern of CK7+ in lung metastasis, counterstaining hematoxylin 100 \times .

primarily corresponding to metastatic lesions (Figure 2C). Confluent necrotic extensive hilar lymphadenopathy on both sides and osteolytic lesions of margo inferior of the right scapula were also presented (Figure 2D, 2E).

Pathohistology of the skin tumour revealed adenocarcinoma composed of solid areas and abortive glandular structures (Figure 3A, 3B). A transbronchial lung biopsy was also performed showing both tumour samples having an identical immunohistochemical profile. Tumours were immunohistochemically positive for the CK7 marker (Figure 3C, 3D), and negative for the CK20, CK5/6, TTF-1, Napsin A, AMACR, CD10, CD117, and vimentin.

Pathological analysis of the tumour tissue due to CK7 positivity confirmed that it was an adenocarcinoma. CK7 is a keratin marker expressed in many adenocarcinomas, including adenocarcinoma of the lungs as well as several histological types of RCC^[4]. Primary carcinoma in the lungs was excluded due to TTF-1 and Napsin A negativity since double Napsin

A and TTF-1-positive immunostaining is highly specific for primary adenocarcinoma of the lungs^[5]. Radiological diagnostics, clinical data and immunohistochemical analysis implicated that the primary tumour site was the kidneys. However, the morphology of the tumour does not correspond to the classifications of recognized RCC histological subtypes. As the primary kidney tumour metastasized to the lungs, bones, skin and eye cisplatin-etopozid chemotherapy protocol was prescribed by an oncologist. However, general health status deteriorated and the patient died due to widespread metastatic disease two months after the diagnosis, receiving only one cycle of chemotherapy.

DISCUSSION

We presented an extremely rare case of a primary renal adenocarcinoma in which the initial symptoms were decreased visual acuity and metamorphopsia. The choroid is an uncommon site for RCC metastasis and this lesion can be difficult to differentiate from a primary choroid carcinoma.

Ocular metastases whilst rare may be the first symptom of RCC and thus a thorough medical history, ophthalmological and general physical examination should be performed in every questionable case. To our knowledge, this is the first documented case of simultaneous existence of very rare sites of metastasis in patients with RCC, namely choroid and the skin. The prognosis in this situation is generally poor with median survival being shorter than six months in the case of skin metastases and less than eight months in the case of choroidal metastases^[1,6]. This poor prognosis was also confirmed in our case since the patient unfortunately passed away only two months after being presented to the ophthalmology department. The localization of the metastasis on the skin in our patient facilitated taking a tissue sample for pathohistological evaluation. Pathological analysis of the tumour tissue confirmed that the tumour was an adenocarcinoma and according to radiological and clinical data, most likely of renal or lung origin. Immunostaining with TTF-1 and Napsin A excluded the lungs as the primary site of the tumour and led us to the conclusion that the primary tumour was of renal origin with metastasis to the lungs, bones, liver, adrenal glands, skin and the left eye. Immunohistochemical analysis for the traditional RCC markers namely AMACR, CD117, CD10 and vimentin standardly used in differentiating subtypes of RCC was negative making it difficult to determine the exact type of kidney tumour^[7]. It is known that even after immunohistochemical evaluation approximately 5% of tumours remain unclassified. Possible explanations are that the tumour is purely sarcomatoid, that the immune profile is not final or that there are unusual or overlapping morphological features^[8]. According to pathological and immunohistochemical analysis we concluded that in our case it was an unclassified RCC which represents 2%-6% of RCCs^[9-10]. An alternative explanation could be that the tumour may have lost characteristic morphological features and immune profile in the metastatic setting, making confirmation of the renal origin and tumour subtyping difficult^[8]. Ocular metastasis may be the first sign of systemic malignancies even in the absence of visible symptoms or signs of a primary tumour. In this paper, we highlighted the importance of considering the existence of metastatic disease when detecting

subretinal lesions of unknown aetiology during regular eye examinations due to reported visual disturbances. This fact suggests that ophthalmologists may have a key role in timely diagnosis and proper treatment of serious systemic illness.

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