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ENDOUROLOGY

Case Report

Undifferentiated metastatic renal cell carcinoma presenting as a cutaneous nodular lesion

Bir kütanöz nodüler lezyon olarak ortaya çıkan farklılaşmamış metastatik renal hücreli karsinom

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ABSTRACT

Cutaneous metastases may be the first sign of clinically silent visceral cancer. Approximately 30% of patients with primary renal cell carcinoma present with metastatic disease, and only 8% of them have skin metastases. We present the case of a 59-year-old male patient with a subcutaneous nodular on the upper chest extending to the jugular region. The lesion appeared skin colored and was not painful and 5 cm x 3.5 cm in diameter. The histological examination of the cutaneous biopsy showed an infiltration of undifferentiated epithelial cells positive to cytokeratins AE1/AE3, whereas they were negative to CK-20, CK5/6, cluster of differentiation 10, vimentin, thyroid transcription factor-1, S-100, human melanoma black-45, hepatocyte-specific antigen, carcinoembryonic antigen, and chromogranin A. A total-body computed tomography (CT) showed the presence of a tumoral lesion in the left kidney with multiple metastases in the lung, brain, and bones. According to the cutaneous biopsy and total-body CT, a final diagnosis of an undifferentiated renal carcinoma presenting as a subcutaneous metastasis was made. A chemotherapeutic treatment with gemcitabine and cisplatin resulted in the stabilization of the renal and metastatic lesions with an improvement in the quality of life of the patient. Considering that the prognosis of patients with cutaneous metastases is very poor, it is necessary to obtain an appropriate diagnosis in order to identify patients with treatable disease with the purpose of starting a therapeutic protocol.

Keywords: Cutaneous metastasis; immunohistochemistry; renal cell carcinoma; undifferentiated tumor.

ÖZET

Kütanöz metastazlar klinik olarak sessiz visseral kanserin ilk belirtisi olabilir. Primer renal hücreli karsinomu olan hastaların yaklaşık %30'u metastatik hastalık ile birlikte görülür ve bunların sadece %8'i cilt metastazına sahiptir. Biz göğüs üst kısmında juguler bölgeye uzanan subkütan nodülü olan 59 yaşında erkek hasta olgusunu sunmaktayız. Lezyon cilt renginde ortaya çıktı ve ağrısızdı ve 5 cm x 3,5 cm boyutlarındaydı. Kütanöz biyopsinin histopatolojik incelemesinde farklılaşmamış epitel hücrelerinin bir infiltrasyonu görüldü. Sitokeratin AE1/AE3 için pozitifti oysa CK-20, CK5/6, farklılaşma kümesi 10, vimentin, tiroid transkripsiyon faktörü-1, S-100, human melanoma black-45, hepatosit-spesifik antijen, karsinoembriyonik antijen ve kromogranin A için negatifti. Toplam vücut bilgisayarlı tomografisi (BT); akciğer, beyin ve kemiklerde çok sayıda metastaz ile birlikte sol böbrekte tümöral lezyonun varlığını gösterdi. Deri biyopsisi ve toplam vücut BT'sine göre son tanı, bir subkütanöz metastaz olarak ortaya çıkan farklılaşmamış renal karsinom olarak konuldu. Gemsitabin ve sisplatin ile kemoterapötik tedavi renal ve metastatik lezyonların stabilizasyonu ile birlikte hastanın yaşam kalitesinde iyileşme ile sonuçlandı. Cilt metastazı olan hastaların prognozunun çok kötü olduğu göz önüne alındığında, bir terapötik protokol başlamak amacıyla tedavi edilebilir hastalığı olan hastaları belirlemek için uygun bir tanı elde etmek gerekir.

Anahtar kelimeler: Kütanöz metastaz; immünohistokimya; renal hücreli karsinom; farklılaşmamış tümör.

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Introduction

Undifferentiated tumors are classified as a heterogeneous group of tumors with little or no evidence of differentiation.[1] Besides, an undifferentiated malignant tumor can represent either a metastasis of unknown origin or a primary neoplasia without differentiation.

Skin metastases occur in 0.6%–10.4% of all patients with cancer and may be the first sign of clinically silent visceral cancer in 37% of men and 6% of women.[2]

Taking into account that the average survival time after the appearance of a cutaneous metastasis is approximately 3–7.5 months,[2,3] it is neces-

sary to obtain an appropriate diagnosis in order to identify patients with a treatable disease and with a more favorable prognosis.

Here, we show the case of a rare metastatic undifferentiated renal carcinoma represented by a nodular sternal lesion with the occurrence of additional internal metastases.

Case presentation

A 59-year-old Caucasian man was admitted to our department with a 4-month history of a nodular and subcutaneous lesion on the upper chest extending to the jugular region. The lesion appeared skin colored and was not painful and 5 cm x 3.5 cm in diameter (Figure 1). At the clinical presentation in our department, the patient presented with heart failure for coronary artery disease (with an ejection fraction of 35%), sideropenic anemia (hemoglobin 9.2 g/dL), and several daily episodes of headache.

The personal medical history revealed that the patient was positive for psoriasis, hepatitis C virus (HCV) infection, and peptic ulcer; the patient also used to smoke 10 cigarettes a day. Conversely, the familial history was negative for malignancies and/or other diseases. The routine laboratory investigations were all within the normal range.

According to the rapid and voluminous growth of the thoracic lesions, a cutaneous biopsy was performed. Before the cutaneous biopsy, the surgical technique was explained to the patient, and his informed consent was obtained. Histological examination of the skin biopsy revealed the presence of a widely necrotic and hemorrhagic fibro-adipose tissue that was infiltrated by a population of undifferentiated epithelial cells with hyperchromatic nuclei and eosinophilic and granular cytoplasm (Figure 2a). Immunohistochemical analyses showed that tumor cells were positive to cytokeratins (CK)AE 1/AE 3 (CK-AE 1/AE 3), whereas they were negative to CK-20, CK5/6, cluster of differentiation 10 (CD10), vimentin, thyroid transcription factor-1, S-100, human melanoma black-45, hepatocyte-specific antigen, carcinoembryonic antigen, and chromogranin A (Figure 2b). Tumor markers were all within the normal range. Based on the histological features, which did not allow a final diagnosis, additional instrumental analyses were performed.

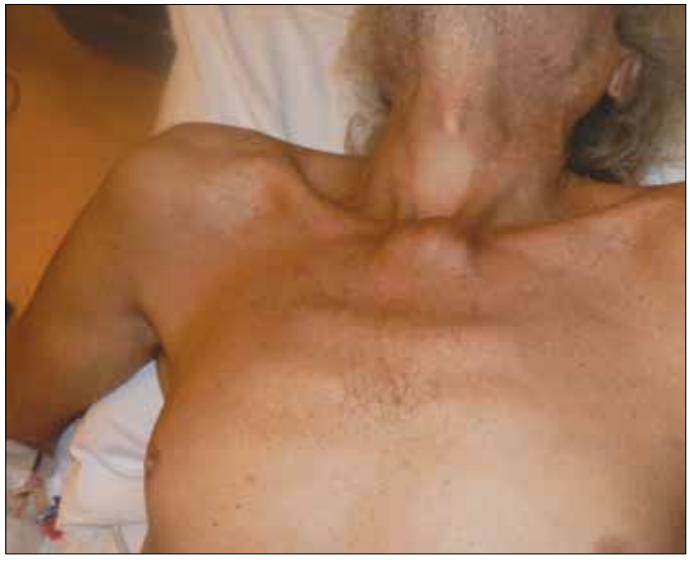

Figure 1. Nodular subcutaneous lesion

The total-body computed tomography (CT) showed the presence of a tumoral lesion in correspondence of the upper pole of the left kidney, 26.2 mm in diameter (Figure 3). In the pul-

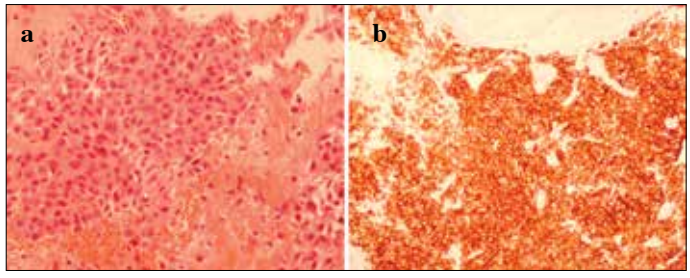

Figure 2. a, b. Widely hemorrhagic tissue infiltrated by a population of undifferentiated epithelial cells (Hematoxylin and eosin, 20x) (a). Undifferentiated epithelial cells positive to cytokeratin AE1/AE3 (Cytokeratin AE1/AE3, 20x) (b)

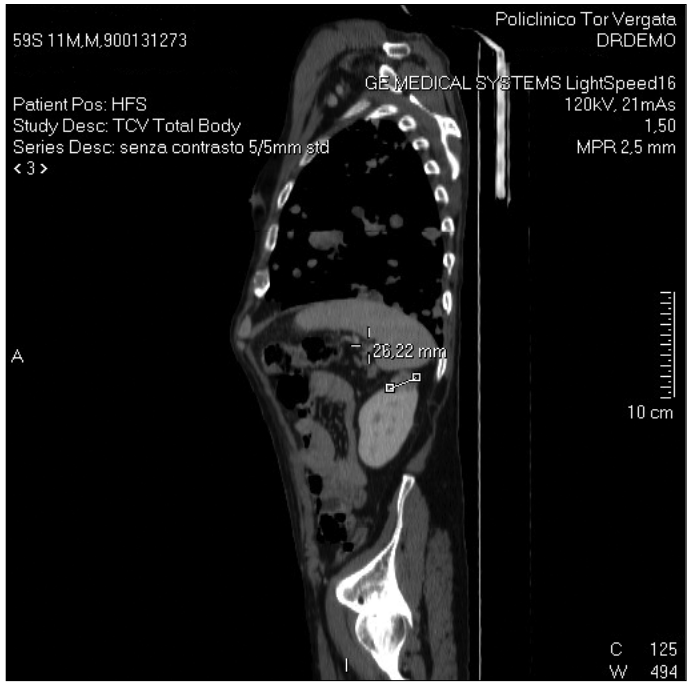

Figure 3. The total-body computed tomography (CT). Tumoral lesion in correspondence of the upper pole of the left kidney, 26.2 mm in diameter. The presence of multiple nodular metastatic lesions in the left lung.

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monary parenchyma, there were multiple and round metastatic lesions with a maximum diameter of 3 cm, with also a multiple involvement in the mediastinal and para-aortic and aortocaval lymph nodes. Besides, metastases were found also at the level of the liver (at the II, V, VI, and VIII hepatic segments). Finally, additional secondary lesions were detected at the level of the ribs and sternum, and one was detected in the brain parenchyma.

According to the cutaneous biopsy and total-body CT, a final diagnosis of an undifferentiated renal carcinoma presenting as a subcutaneous metastasis was made. The patient received a chemotherapy regimen consisting of gemcitabine 1250 mg/ mm^2 and cisplatin 75 mg/mm^2, associated with clinical and instrumental controls. The cycles of chemotherapy were performed every 3 weeks, until disease progression and/or unacceptable toxicity.

Currently, after a follow-up of 8 months, the patient showed stabilization of the subcutaneous and visceral lesions.

Discussion

Cutaneous metastases may be the first sign of clinically silent visceral cancer, and among them, those with an unknown primary account 4.4%, although the primary cancer is identifiable in approximately 20% of patients before death. Approximately 30% of patients with primary renal cell carcinoma present with a metastatic disease, and only 8% of them have skin metastases[2] with a significant decrease in the case of undifferentiated tumors.

In the absence of metastases, the surgical removal of the affected renal and lymph nodes provides a good probability of cure;[4] however, when renal carcinoma has already produced metastases, its prognosis remains poor. As in a previous report,[4] we performed the biopsy at only one metastatic site because the disease was in an advanced stage.

Histopathologically, most renal cell carcinomas (RCC) are clear cell RCC, and cutaneous metastases from RCC often show trabecular, papillary, tubulopapillary, or cystic patterns with a prominent vascular component and deposition of hemosiderin in the stroma.[2,5] The metastasis of our patient did not show a distinct pattern but instead showed an important extravasation of erythrocytes. Usually, neoplastic cells of RCC are positive for vimentin, epithelial membrane antigen, CD31 and less than 10% express CK7 or CK20, whereas CD10 is expressed in approximately 89%–100% of RCC. The analyzed metastasis was negative for all these markers, whereas it was positive for CK AE 1/AE 3, which are usually found in 80% of renal tumors with eosinophilic cytoplasm.[6] In this regard, in our case, immunohistochemical analyses of the cutaneous lesion failed to identify the origin of the tumor. The combination with the instrumental analysis allowed a refinement of the diagnosis.

In conclusion, surgeons, clinicians, and pathologists should always keep in mind that a tumor of the skin could arise from a visceral malignancy and that instrumental (as CT) analyses can provide precious additional advice about the origin of the tumor, thus allowing the start of a therapeutic regimen. All these considerations are even more important in the case of undifferentiated tumors.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

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References

1. Bahrami A, Truong LD, Ro JY. Undifferentiated tumor: true identity by immunohistochemistry. Arch Pathol Lab Med 2008;132:326-48.
2. Alcaraz I, Cerroni L, Rutten A, Kutzner H, Requena L. Cutaneous metastases from internal malignancies: a clinicopathologic and immunohistochemical review. Am J Dermatopathol 2012;34:347-93. [CrossRef]
3. Mahmoudi HR, Kamyab K, Daneshpazhooh M. Cutaneous metastasis of renal cell carcinoma: a case report. Dermatol Online J 2012;15:18:12.
4. de Paula TA, da Silva PS, Berriel LG. Renal cell carcinoma with cutaneous metastasis: case report. J Bras Nefrol 2010;32:213-5.
5. Hussein MR. Skin metastasis: a pathologist's perspective. J Cutan Pathol 2010;37:e1-20. [CrossRef]
6. Bonsib SM, Bhalodia A. Renal neoplasms: an update on immunohistochemical and histochemical features. Connection 2010:178-86.