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Cutaneous metastasis of renal cell carcinoma: A case report and review of the literature

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Abstract

Introduction: *Renal cell carcinoma (RCC) accounts for 2-3% of adult solid malignancies. About 25-30% develop metastasis at the time of diagnosis and 60% corresponds to clear cell type.* **Case Presentation:** *A 66-year-old man, with a personal history of left radical nephrectomy, presents with an asymptomatic skin tumor he noticed one month earlier. Histopathologic study reported metastatic cutaneous infiltration of clear cell carcinoma, suggestive of a primary renal carcinoma.* **Discussion:** *Cutaneous metastasis of RCC represents 6.0-6.8% of all cutaneous metastases. These patients have poor prognosis and, therefore, their treatment is palliative. It is essential to perform a complete periodic dermatologic examination for proper restaging and treatment.* (Gac Med Mex. 2015;151:497-501)

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KEY WORDS: *Renal cell carcinoma. Clear cell carcinoma. Cutaneous metastasis.*

Introduction

Renal cell carcinoma (RCC) accounts for 2-3% of solid malignancies in adults, it is more common in males than in females (2:1) and mean age of presentation is 66 years[1]. Main etiologic factors are: smoking, renal cystic disease, tuberose sclerosis and Von Hippel-Landau syndrome[2,3]. From 25 to 30% of patients have metastasis at diagnosis[4]. RCC is a much vascularized tumor and, therefore, dissemination is predominantly by the hematogenous route. It is the primary tumor in 6-6.8% of all skin metastases[1,5,6]. The most common RCC type is clear cell carcinoma, which accounts for up to 60% of cases[1,2,7,8].

Cutaneous metastases represent a sign of bad prognosis, and opportune detection is essential in patients with previously-diagnosed malignant tumors, as it may help to restage the disease and, consequently, to have a more accurate prognosis.

Clinical case presentation

This is the case of a 66-year-old Caucasian male patient who presented with dermatosis located at the anterior side of the neck on the midline (Fig. 1), characterized by a 3-cm-diameter subcutaneous neoformation, hard in consistency, mobile, not adhered to deep planes, with well-defined margins and a red-violet coloration and some telangiectasias observed on its surface (Fig. 2).

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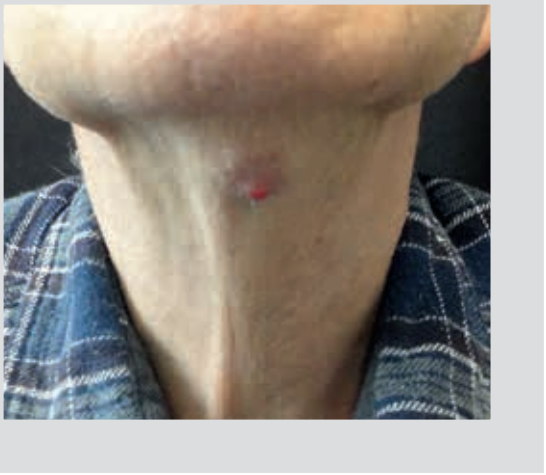

Figure 1. *Caucasian patient with single dermatosis located at the anterior side of the neck on the midline.*

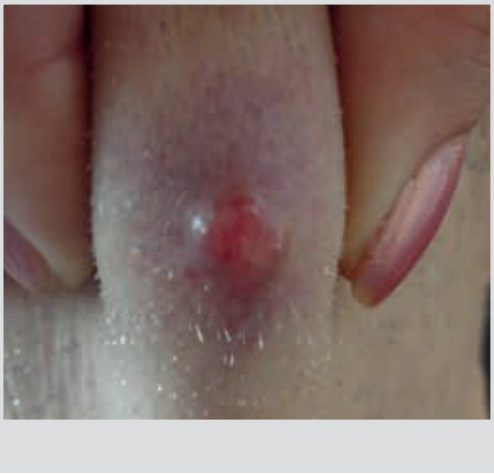

Figure 2. *Subcutaneous neoformation with erythematous-violet coloration, hard consistency, non-adhered to deep plains, of approximatedly 3 cm in diameter, well-defined margins and central thinning of epidermis, through which some blood vessels are observed.*

The patient referred he had noticed the lesion one month before though it was smaller in size. Initially, the lesion had an accelerated growth and subsequently the patient tried to squeeze it without obtaining any material.

Two months prior to his evaluation by the Dermatology Department, he had undergone a left radical nephrectomy due to low back pain, palpable mass in left flank and hematuria. Histopathological analysis of the kidney confirmed a clear-cell renal carcinoma. Due to this previous condition, and in view of the clinical characteristics of the lesion, a wedge excision biopsy was performed with diagnostic suspicion of cutaneous metastasis versus pyogenic granuloma.

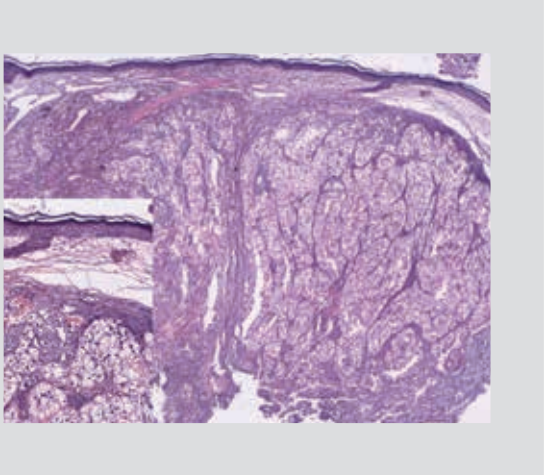

Figure 3. *Proliferation of atypical cuboidal epithelial cells grouped in lobes, with other forming glandular structures, is observed from the papillary dermis to the deep reticular layer. The neoplastic cells have abundant clear cytoplasm and a pleomorphic and hyperchromatic nucleus with occasional mitosis features, and numerous dilated and congestive capillary blood vessels intertwined. The described findings are observed in detail in the image (H&E 4x, panel 20x).*

On microscopic examination, proliferation of atypical cuboidal epithelial cells clustered in lobes or forming gland structures from the papillary dermis to the deep reticular dermis layer were observed. The neoplastic cells showed abundant clear cytoplasm and pleomorphic and hyperchromatic central nucleus with occasional mitosis figures. There were smaller and hyperchromic neoplastic cells in the deep dermis, intertwined between collagen bundles. There were numerous dilated and congestive capillary blood vessels intertwined between the neoplastic cells and an inflammatory infiltrate composed of lymphocytes, some neutrophils, histiocytes, nuclear dust and red blood cell extravasation (Fig. 3). With immunostaining, infiltrating neoplastic cells were positive with membranous and cytoplasmic pattern for CD10 (Fig. 4) and positive for renal cell carcinoma marker (RCC-Ma) in the cytoplasm (Fig. 5). With morphology and the immunohistochemical analysis, a clear cell carcinoma cutaneous metastatic infiltration of a renal primary was confirmed.

The patient continued his oncologic follow up at the National Institute of Cancerology and later he presented with a volume increase of stony consistency in the

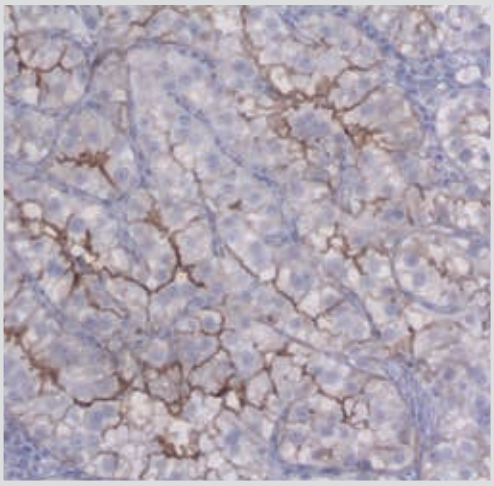

Figure 4. *Neoplastic cells cytoplasm and cell membrane CD10-positive immunostaining, which confirms the presence of clear cell carcinoma metastatic infiltration of a primary renal neoplasm (60x).*

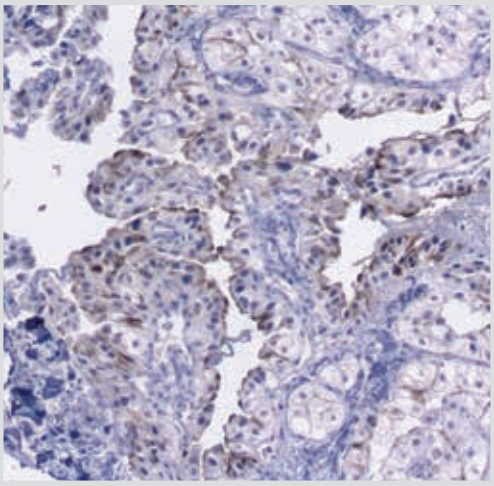

Figure 5. *Positive immunostaining for RCC-Ma in the cytoplasm of neoplastic cells, which confirms the clear cell carcinoma metastatic infiltration of a primary renal neoplasm (40x).*

left scrotal area, which prompted a testicular ultrasonography that showed a tumor in the right testicle. Bilateral pulmonary metastases were identified in the thoracoabdominal computed tomography. A radical left orchiectomy was performed with histopathologic report of clear cell RCC metastasis in the left testicle. The patient only received surgical treatment.

Two months after the cutaneous biopsy was performed, during the follow-up by Medical Oncology, the pacient had a nasogastric feeding tube placed, as he presented a very poor general condition. His evolution is unknown, since he never returned to the dermatology outpatient clinic.

Discussion

According to Lambert and Schwartz, in the context of dermatology, a metastasis is defined as any neoplastic lesion originating from other lesion, with which it is not contiguously or proximally located within the same tissue[10].

Cutaneous metastases of internal neoplasms are uncommon: they occur in 0.7-9% of patients with internal malignant tumors. Tumor invasion can take place through different routes: hematogenous, lymphatic, by contiguity and iatrogenic implantation[11]. This concept may vary according to the authors, since for some, the iatrogenic and contiguous routes are not considered to be metastasis.

The metastasis patterns proposed by Brodland and Zitelli are the following: tumor mechanical stasis (which accounts for 50-60% of metastases and depends on lymphatic drainage and anatomical proximity), organ-specific adhesion molecules (by selectivity of tumor cells for certain organs, e.g., prostate-bone, melanoma-brain) and non-specific pattern (in multiple organs, it is characteristic of aggressive tumors where metastatic cells secrete autocrine growth factors)[12,13].

In general, cutaneous metastasis most frequent topography is the trunk[5,12]. If location of the primary tumor is taken into account, the thorax is also the most frequent location in the case of breast and lung cancer, whereas in colorectal carcinoma, it is the abdominal wall and the perineal region[12]. There are other sites with special characteristics that make them frequent target of metastasis, as for example the scalp in the case of cutaneous metastasis from renal cell carcinoma (CMRCC), since it is a highly vascularized tissue[5]; this last location is the second in frequency in our hospital[6].

The morphology of cutaneous metastases is considerably variable. The most frequently observed corresponds to one or multiple skin-colored or erythematous neoformations, firm or elastic in consistency, painless and asymptomatic[5,12]. Presence of neoplastic alopecia has been occasionally observed in the case of breast cancer metastasis to the scalp[12].

In the Hospital General Dr. Manuel Gea González, a review was made of all 32,607 cutaneous biopsies

obtained in 35 years (from January 1977 to January 2012) and a total of 44 patients with cutaneous metastases was found, which accounted for 0.13% of all biopsies. The most common primary tumor was that of the breast (36.6%), which affected more the female sex (68%) and the 31 to 40 years age-group. Presentation time with regard to the primary tumor was late (43.1%), most were single lesions (54%) located in the trunk (34%) and the histologic type most commonly found was adenocarcinoma (68%). There were a total of 3 (6.8%) RCC, out of which two were in men, and 100% of the lesions were single, with histopathologic report of clear cell adenocarcinoma[6].

In the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ), López-Tintos, et al. conducted a review of cutaneous biopsies obtained between the years 1979 and 2006, and found a total of 40 patients with cutaneous metastases with no difference between sexes; mean age of presentation was 57 ± 17 years, most common primary tumor was also that of the breast (17.5%) and most were lesions with nodular morphology (78.4%), located in the trunk (27.5%) and with a survival average of 5.43 months. They reported that the primary tumor was renal in 7.5% of cases, a similar percentage to that reported in our hospital. In this study, cutaneous biopsy was the diagnostic method to detect the primary tumor in 45% of the cases, which evidences the tendency to seek medical care in a late manner in our country[14].

RCC, also known as renal adenocarcinoma or hypernephroma, accounts for 2-3% of solid malignancies in adults, it is the third neoplasm most common of the genitourinary tract and represents 90-95% of renal tumors[7]. It occurs more frequently in the male sex (2:1)[1]. Its incidence peak is between 50 and 70 years, with a mean age of 66 years[1]. The main etiologic factors are: smoking, obesity, hypertension, renal cystic disease, tuberous sclerosis and von Hippel-Landau syndrome[2,3]. The most common type of RCC is clear cell carcinoma, which accounts for up to 60% of cases[1,2].

The diagnosis is made as an incidentaloma in up to 50% of cases[3]. Thanks to the increased use of imaging diagnostic methods in the past few years, it has become easier to diagnose at early stages; therefore, the incidence has increased by 2.5% per year[8]. When symptomatic, RCC is usually diagnosed with a single symptom of the classic triad: hematuria (60%), low back/flank pain (40%) and palpable abdominal mass (30-40%)[2,3,7]. The classic triad occurs only in 10% of the cases[2,9], which in most occasions correspond to advanced stages and therefore it can predict a bad prognosis[2], as in the case we report. Other RCC symptoms are: weight loss, fatigue, anemia, fever, varicocele and some paraneoplastic syndromes, present in 5% of cases, including erythrocytosis, hypercalcemia, liver failure and amyloidosis[1,3,8].

From 25 to 30% of the patients have metastasis present at diagnosis[4]. Dorairajan, et al. report that up to 10% of cutaneous metastases were the first manifestation of the disease, while up to 50% of patients had metastases after the renal tumor diagnosis[15]. In the INCMNSZ, in up to 45% of cutaneous metastases, skin biopsy was reported to be the diagnostic method for an occult tumor; unfortunately, this figure is not exclusive of CMRCC[14]. RCC is a highly vascularized tumor, and for this reason, dissemination by the hematogenous route is predominant[2]. The most common sites of metastasis are, in order of frequency, are: lung (50%), bone (33%), regional lymph nodes and skin (6-11%), liver (8%), adrenal gland and brain (3%)[1,2]. Metastases occur on the scalp in up to 50% of cases[2,15], although in the described case this didn't happen. RCC corresponds to a primary tumor in 6-6.8% of all cutaneous metastases[1,5,6].

Porter NA, et al. report that in a study conducted in 1943 by Hale NG, where 6,577 autopsies were performed, the skin was the seventh place of metastases in the 54 cases of RCC[1]. In Japan, a study of 75 cases of RCC conducted in the year 2000 reported that 24% had cutaneous metastases at diagnosis, and the most common topography was the trunk (40%), the scalp (25%) and the face (8%)[16], as in the case of pur patient. In other study carried out in India in 1999, where 306 RCC cases were followed for 12 years, 90% of the patients were found to have distant metastases at diagnosis and during the follow-up only 3.3% had cutaneous metastases[15]. In Greece, six CMRCC cases were reviewed in 1995 and three of them had isolated lesions, whereas the remaining three had multiple lesions, all of them in the scalp, the thorax and the abdominal wall[17].

CMRCC sometimes can be the first sign of the disease[14,15]. Their development has place at between 6 months to 5 years of the primary tumor diagnosis[8]. Typical morphology of a CMRCC is an intra- or subcutaneous vascular neoformation, rounded or oval, well circumscribed, firm or elastic in consistency, erythematous-violet, which can even be dark-brown or black colored, located mainly on the scalp or face and that tends to bleed. Its presentation has also been reported as cutaneous horn. Differential diagnosis should be made with pyogenous granuloma, hemangioma, basal

cell carcinoma and Kaposi's sarcoma[4,7,8,12]. Dermoscopy of CMRCC demonstrates more similarities than differences with pyogenous granuloma and more studies are required in order to establish dermoscopic criteria for CMRCC[18].

Histology usually shows a neoformation covered by atrophic or ulcerated epidermis, formed by vacuolar-appearing tumor cells, clear cytoplasm, with mild lymphocytic infiltrate, numerous neoformation capillary vessels and some trabecular areas. It involves predominantly the dermis, leaving a superficial Grenz zone that demarcates the lesion (Fig. 3). With immunochemistry studies, 60% of CMRCC tumor cells are posive for vimentin, EMA, CEA, CD10, RCC-Ma and keratins (Fig. 4 and 5). These immunomarkers are considered indicators of high probability for RCC[2,8,18]. In our patient's biopsy, tumor cells were positive to CD10 and RCC, which, together with the previous RCC diagnosis, supports the diagnosis of cutaneous metastasis of a renal primary lesion.

Prognosis for patients with CMRCC is poor, and most die within six months after diagnosis[9]. Treatment of metastatic RCC is, therefore, limited and palliative; it can comprise a combination of radical nephrectomy with multi-kinase/angiogenesis inhibitors (sunitinib or sorafenib), surgical resection of the cutaneous lesion with or without radiotherapy and intralesional interferon[2,8,9,12]. We are unaware of the patient's evolution, who only received surgical treatment, but we think that he probably passed out, since in his last visit to the clinic he was in very bad general condition and subsequently he didn't return.

Conclusions

The presence of CNRCC and in general of any other cutaneous metastasis represents a sign of bad prognosis[9] and, therefore, in patients with previously diagnosed malignant tumors, early detection of cutaneous lesions is essential. RCC is a highly metastatic tumor, with an incidence of cutaneous metastases of 4-6%. In patients with previous history of malignancy it is essential for a complete dermatologic examination to be periodically performed, which should include the scalp, as well as a biopsy of any recently-appearing cutaneous lesion, since this ca help both to detect recurrences opportunely and to restage the disease and, this way, to have a more accurate diagnosis.

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