

CASE REPORT

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Synchronous carcinomas of primary origin: Squamous cell carcinoma of the skin and clear cell renal cell carcinoma

Carolina Cortes, Jhon Bermúdez, Andrés Toscano, Héctor Pérez

ABSTRACT

Introduction: Synchronous carcinomas are defined multiple primary neoplasms occurring in different locations belonging to different morphologic or histologic origin occur at the same time in a patient. This is the first report of a cutaneous squamous cell carcinoma presenting synchronically with a clear renal cell carcinoma, confirming is not a metastatic process. **Case Report:** A 53-year-old man had a clinical course of eight months of evolution, of a continuously growing mass in the left gluteus and thigh with inguinal adenopathies, in the same place of a previously burn area, for which complementary imaging studies were indicated to establish the extent of the lesion, with an incidental finding of a tumor in left kidney. Biopsies of the gluteal and left kidney lesions were performed, showing a verrucous variant squamous cell carcinoma in gluteal region and a clear cell differentiation concordant with clear cell renal cell carcinoma in left kidney. **Conclusion:** Synchronous carcinoma implies a complex interactions between genetic and environmental factors for its development. Clinical manifestations usually presents in advance stages of both carcinomas, but can be detected with extension studies as in this case.

Keywords: Carcinoma, Kidney, Multiple, Skin, Synchronous

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Received: 22 September 2018

Accepted: 08 January 2019

Published: 18 March 2019

How to cite this article

Cortes C, Bermúdez J, Toscano A, Pérez H. Synchronous carcinomas of primary origin: Squamous cell carcinoma of the skin and clear cell renal cell carcinoma. Int J Case Rep Images 2019;10:101013Z01CC2019.

Article ID: 101013Z01CC2019

doi: 10.5348/101013Z01CC2019CR

INTRODUCTION

Cancer is one of the main causes of morbidity and the second leading cause of death in the world according to WHO, reaching 8.8 million deaths in 2015 [1]. In recent years, the detection of neoplasms in early stages has increased due to the efforts made in screening programs and the improvement of diagnostic methods. This has led to the detection of multiple primary tumors in some individuals. Multiple primary neoplasms are defined as the presence of more than one malignant neoplasm (synchronous) in the same individual in different locations belonging to different morphological and/or histological groups [2].

The frequency of multiple primary neoplasms worldwide is between 2.4% and 17% [3]. They have multiple risk factors including genetic and hormonal factors of the individual, as well as previous diagnosis of cancer with exposure to antineoplastic treatments; lifestyle factors such as smoking and alcohol consumption and environmental elements. However, there have been established factors in the population that confer high risk of presenting a second primary neoplasm, among those are: male sex, diagnosis of a primary neoplasm in early stage and low grade and patients with hereditary neoplastic syndromes [3].

Available reports in the current literature have focused on four groups of neoplasms that are at higher risk of presenting with a second primary malignant tumor, these are: Breast cancer, prostate, Hodgkin's lymphoma and lung cancer. However, there are other locations where the presence of second primaries has been documented and which are currently of clinical interest such as bladder cancer, pancreatic cancer and multiple endocrine neoplasms (MEN). In the skin, the occurrence of primary seconds after the melanoma diagnosis is quite documented and valuations are described of up to 12% [4]. On the other hand, as for renal carcinoma and specifically the clear cell variant, which is the most common among renal neoplasms, there is data on metastatic manifestations to liver, lymph nodes, lung and in a lesser proportion to soft tissues [5].

The search of the literature was done, including databases MEDLINE, PUBMED, BIREME and EMBASE, and there were reports in Colombia that described the coexistence of squamous carcinoma and clear cell renal carcinoma as a manifestation of multiple primary neoplasms in an individual.

Next, we present the case of a patient who presented a clinical history of two primary carcinomas of different origin: squamous carcinoma of skin and clear cell renal cell carcinoma.

CASE REPORT

A 53-year-old, farmer, without pathological antecedents or relatives of oncological disease arrived at the emergency department with clinical history of eight months of evolution, consisting of extensive mass of fetid smell that compromised left gluteus and thigh associated to paresthesia and with decrease of the force in lower limb ipsilateral. The patient did not show weight loss, gastrointestinal or urinary disturbances and relates the lesion with antecedent of burn in that region years ago. On physical examination, the patient presents verrucous round ulcer with multiple focuses of keratosis, involving left gluteus and thigh of approximately 20x15 cms, of elevated, irregular, poorly defined edges, foul smelling, serous sanguinolent exudate (Figure 1), and at inguinal level inguinal, bilateral adenomegalies were found. Blood chemistry tests on admission showed no alterations in the white or red line, blood urea nitrogen at normal limits (BUN 9.06 mg/dl, creatinine 0.73 mg/dl), high C-reactive protein (72.41 mg/dl), electrolytes at normal limits.

Considering the occupational and demographic background of the patient, the possibility of a tropical verrucous syndrome was raised within differential diagnoses, and within this a chromoblastomycosis versus a squamous cell carcinoma in the burned area, probably advanced because of the adenomegaly findings at the time of physical examination; however, based on these diagnostic possibilities, more extension studies were performed.

Among the studies, tissue cultures were performed which reported the presence of *Enterobacter cloacae*, However, this microorganism was not considered as part of an infectious process because the patient did not present signs of systemic inflammatory response. The computed tomography (CT) scan of the abdomen showed a neoplastic lesion involving the left kidney, which due to its characteristics most probably corresponded to renal cell carcinoma (Figure 2).

On the other hand, to determine the involvement of deep soft tissues in the gluteal region, a magnetic resonance was performed which evidenced a neoplastic inflammatory process involving the subcutaneous fat plane of the left gluteal region and thigh with extension to the gluteus maximus muscle with a maximum depth of 28 mm, and enlarged lymph node, predominantly on the left side, the largest being 12 mm in diameter on its short axis (Figure 3). During the hospital stay the patient presents urinary retention and macroscopic hematuria of acute instauration.



Figure 1: Verrucous ulcer with multiple focuses of keratosis, involving left gluteus.

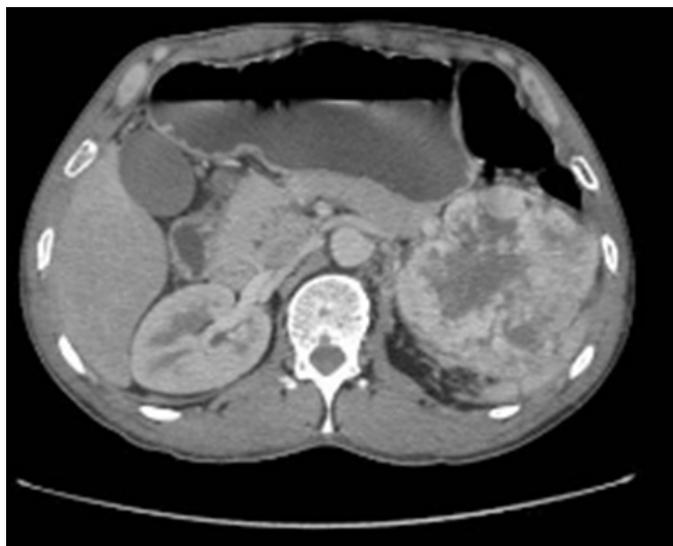


Figure 2: Contrast abdominal Computed tomography image showing neoplastic lesion involving the left kidney.

Two biopsy samples were taken from the gluteal and thigh region, lesion was reported as well differentiated verrucous variant squamous cell carcinoma, and well differentiated conventional large keratinizing cell infiltrating squamous cell carcinoma (Figure 4). Subsequently, left renal biopsy was performed confirming diagnosis of WHO/ISUP grade/group 1 clear cell renal cell carcinoma, without evidence of vasculoneural invasion (Figure 5). Additionally, the results of immunohistochemistry studies showed reactivity in the neoplastic cell population for CD10 and vimentine with a proliferation rate measured with KI67 of 10%. Finally, after diagnosis, management with cisplatin and 5-fluoracyl chemotherapy was initiated, and outpatient follow-up was ordered to evaluate resection of squamous cell carcinoma by oncological soft tissue surgery.

DISCUSSION

The importance of multiple primary neoplasms has increased in recent years, not only by the increase in reports about this entity but by the difficulties involved in the treatment of two different neoplasms in the same individual.

Renal carcinoma is the most frequent solid lesion in the kidney constituting up to 90% of all malignant renal

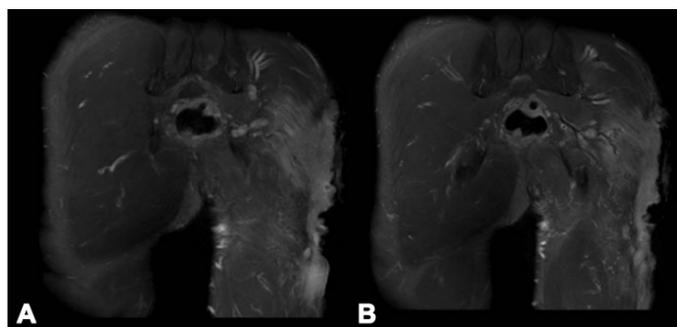


Figure 3: (A) MRI of the pelvis and hip showing neoplastic inflammatory process with extension to the subcutaneous fatty plane of the gluteal region and left thigh (B) with extension to the gluteus major.

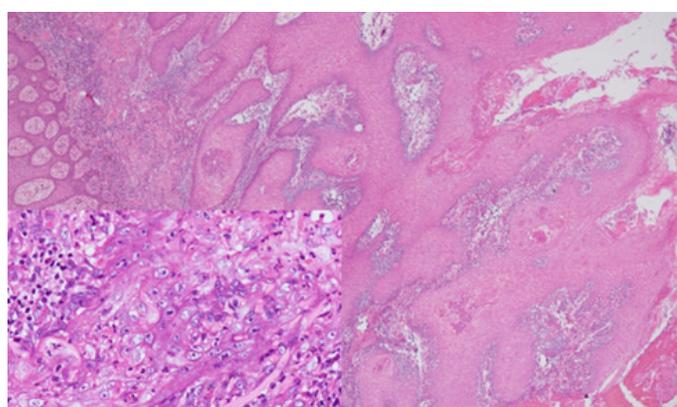


Figure 4: Histological appearance of fragments of a malignant squamous tumor lesion, 40x in lower image, and 10x in the large image.

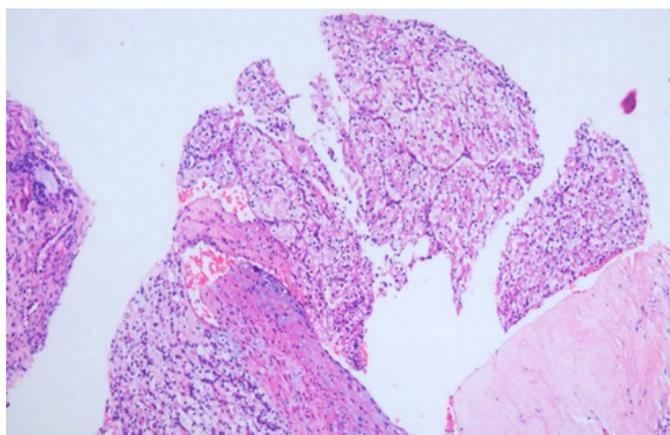


Figure 5: Microscopic view shows renal tissue cylinder where a tumor lesion is recognized, formed by solid aggregates of polygonal cells with defined contours and broad clear cytoplasm with a nuclear atypia variable. The lesions are accompanied by a delicate capillary vascular weft, 20x.

tumors. Etiological factors include smoking, obesity, first-degree familial obesity, kidney cancer, and high blood pressure. In 2014 in the United States, renal carcinoma ranked ninth with an incidence of 16.2 per 100,000 inhabitants [6], and moved up to eighth place in 2017 with 63,990 new cases, 14,400 of which are attributed to it [7].

The tumors most associated with kidney metastases are lymphoma, lung, breast, melanoma and stomach. On the other hand, there are data suggesting that renal cell carcinoma confers a risk of developing a second primary neoplasm (0.6%) including prostate, breast, bladder, colon, melanoma, and lymphoma neoplasms [8].

Post mortem studies revealed that the frequency of metastases from primary tumors to kidney was between 7–20%, however, contemporary data from antemortem studies published by Pate et al showed that the frequency is low reaching 0.9% [9].

It is important to differentiate between the two phenomena (metastasis and primary tumor) because the prognosis and treatment are different. Diagnostic imaging studies such as computed tomography (CT) or positron emission tomography (PET) should be performed to characterize the kidney lesion and identify morphological and topographic features that help differentiate between metastasis and a primary tumor. In addition, biopsy is a fundamental element in the diagnostic approach of a renal mass and, consequently, in order to differentiate between a metastasis and a primary renal tumor. For this it is necessary to carry out an immunohistochemistry study that in the case of renal carcinoma shows expression of CD10 and vimentin [9], as we saw in the biopsy of our patient.

In our country, during 2003, the incidence of squamous cell carcinoma (SCC) was determined to be between 5 and 250 per 100,000 inhabitants, reaching an annual age standard rate of 6.3 per 100,000 men and 3.8 per 100,000 women, according to data published between

2007 and 2011 by the Epidemiological Surveillance group of the National Cancer Institute. The cases diagnosed with SCC occupied second place during the year 2011 corresponding to 15.8% of skin cancer, surpassed only by basal cell carcinoma (56.9%) [10].

The frequency of malignant skin tumors, especially melanoma, that are associated with renal cell carcinoma as a second primary in the same individual is 0.5% [11]. This association has been well established in the current literature, in which plausible links between both neoplasms are described, such as exposure to common carcinogens, alteration in cellular immunity and shared genetic susceptibility reflected in mutations of the CDKN2A gene [4, 11].

Although exposure to ultraviolet radiation is the most important environmental cause of skin cancer, it has also been documented that 2% of cases of squamous cell carcinoma may develop in areas of chronic scar tissue ulcerated by lesions associated with burns, which generates an ulcer known as Marjolin's ulcer which could be included as part of our patient's differential diagnoses, since the risk of such a lesion developing a cancerous transformation is 76.5% when associated with burns [12]. Although the mechanism is not completely clear, it is believed that there is prolonged proliferation due to chronic inflammation and tissue irritation that is exposed to toxins and co-carcinogens after injury, associated with poor vascularization of scar tissue resulting in altered immune defense, related to mutations in the p53 and Fas genes [12–14].

In most cases, alteration of two systems by a malignant neoplastic disease is more common when its due to the development of a metastatic form. However, there are few reported cases in which the involvement is the product of two neoplastic diseases of different cellular origin such as verrucous variant squamous cell carcinoma and clear cell renal cell carcinoma, which have managed to develop synchronously.

CONCLUSION

Thus, the clinical case of this patient as previously described is rare, not only in our environment, but also worldwide, and the relationship that exists in developing multiple synchronic malignancies involve genetic and environmental factors synergistically exposed, as evidenced in this picture. Clinical manifestations usually comes from an extensive involvement of the affected organ or system, but in this case, the urinary symptoms were infrequent and the diagnosis methods were once again of great help.

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Author Contributions

Carolina Cortes – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Jhon Bermúdez – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Andrés Toscano – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Héctor Pérez – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None.

Consent Statement

Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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