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Letter to Editor

Renal cell carcinoma and cutaneous paraneoplastic syndromes

Vitorino Modesto dos Santos[1], Taciana Arruda Modesto Sugai[2], Lister Arruda Modesto dos Santos[3]

[1]Department of Medicine, Catholic University, Brasilia-DF, [2]Department of Dermatology and Neurophysiology, American Society of Neurophysiology, [3]Oncosurgery, Department of Surgery, State Workers Hospital, São Paulo, Brasília, Brazi.

Dear Editor,

We read the very recent article of this Journal by Mondal, reporting a 61-year-old man who had a papulosquamous eruption with generalized, erythematous, scaly, plaques and papules after utilizing pembrolizumab in the treatment of renal cell carcinoma (RCC).[1] The patient refused the skin biopsy, and the final conclusion was based on Naranjo's score.[1] Additional conundrum in the diagnostic evaluation might include challenges inherent to the RCC, a malignancy very frequently diagnosed by incidental imaging findings, and in up to 40% of the symptomatic cases may evolve with some paraneoplastic syndrome (PNS), which justifies eponyms such as "the great imitator" or "the great dilemma."[2-8] The RCC accounts for 3% of all adult cancers and 85% of all kidney tumors.[5] Therefore, the objective of this contribution is to briefly comment on new data from the literature about the skin changes developed in patients, even before the diagnosis of RCC.

An 84-year-old woman was reported with a recent pruritic erythematous rash and disseminated large bullae involving the torso, upper limbs, face, and oral mucosa.[2] Laboratory investigations were unremarkable, and skin biopsy evaluation was consistent with bullous pemphigoid; the abdominal imaging studies disclosed advanced, clear cell RCC in the left kidney lower pole with invasion of fat and vessels.[2] This was the first report of non-synchronous clear cell RCC with paraneoplastic bullous pemphigoid presenting with skin eruptions and mucosal lesions.[2] A 67-year-old male patient presented with multiple keratotic spicules on the palmar surfaces of the hands diagnosed as spiny keratoderma, and a computed tomography study showed a nodule in the left kidney with the histological pattern of a clear cell RCC.[3] The authors emphasized that the spiny keratoderma has been rarely described in association with malignancies such as esophageal and laryngeal carcinomas, lung adenocarcinoma, and melanoma, more often preceding the development of the tumor.[3] A 63-year-old woman with lower back pain, concomitant hypertension, and pulmonary sarcoidosis presented with a lumbar spinal syndrome and a lesion at the T7 vertebra, besides a left kidney mass and multiple right pulmonary nodules and bone lesions.[4] Although 20% of patients present with PNS, in this specific case, the diagnosis was established while investigating the symptomatic presentation.[4] After the left radical nephrectomy and the diagnosis of a disseminated clear cell RCC, she underwent immunotherapy with avelumab and axitinib, maintaining a good outcome.[4] An Indian retrospective study on RCC, from April 2016 to February 2020, included 142 patients with 58 years of median age at presentation, 67% symptomatic, and 33% incidental diagnoses.[5] More than 50% of the total patients presented with PNS: Elevated erythrocyte sedimentation rate (62.5%), hypertension (25%), anemia (17%), Stauffer's syndrome (16%), thrombocytosis (12%), polycythemia (4%), or hypercalcemia (3%).[5] The age of presentation was earlier, and the patients had a higher tumor stage; almost 69% were clear cell RCC, followed by papillary (20%) and chromophobe (8%) carcinomas.[5] The authors stressed the elevated number of cases with early age of presentation presenting with PNS, may be attributed to biological differences either in tumor genetic or environmental factors.[5] A 75-year-old man who had a rapidly progressive scleroderma even after treatment with methotrexate and prednisone was diagnosed with a right renal mass; the specimen of the partial nephrectomy revealed a papillary RCC with a negative surgical margin.[6] However, he evolved to develop scleroderma renal crisis and end-stage renal disease despite the institution of captopril, mycophenolate mofetil, plasmapheresis, and immunoglobulin; contrary to the reports where scleroderma improved after nephrectomy; and the authors emphasized the hypothesis of the scleroderma being a risk factor for RCC.[6] A 37-year-old man presented with chronic papules and pruritus on the hands and erosive arthritis in hands, hips, and knees; the biopsy samples revealed dermal

***Corresponding author:** Vitorino Modesto dos Santos, Department of Medicine, Catholic University, Brasilia-DF, Brazil. vitorinomodesto@gmail.com

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infiltrates of histiocytoid cells besides multinucleated cells resembling Touton-type giant cells.[7] Considering these findings consistent with the final diagnosis of multicentric reticulohistiocytosis, the patient underwent treatment with infliximab, methotrexate, and folate.[7] After several years of treatment, he was diagnosed with a grade II right clear cell RCC; a partial right nephrectomy was performed, and methotrexate and infliximab were restarted.[7] Subsequently, the patient had no digital skin lesions, and he showed improvement in the arthritis. A 47-year-old woman with systemic sclerosis (SSc) diagnosed in March 2020 also presented with a high nuclear-grade RCC with a predominant tubuloalveolar growth pattern and papillary features confirmed by left nephrectomy.[8] She was initiated on mycophenolate mofetil in February 2021, and the clinical improvement of sclerodactyly and cutaneous sclerosis was confirmed 5 months later. The authors highlighted the rapidly progressive course of the disease, the short time from the onset of SSc till the RCC diagnosis, and the prompt clinical improvement after the treatment of the neoplasia, all supporting the hypothesis that the SSc was paraneoplastic.[8] In conclusion, we highlight the need to have a high index of suspicion to enable the early diagnosis of RCC.

Authors' contributions

All authors contributed to the conception and design of the study, acquisition of data, analysis and interpretation of data, drafting of the article, and revising it critically for important intellectual content and final approval of the submitted version.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

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Conflicts of interest

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Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Mondal A. Pembrolizumab-induced resolving papulosquamous eruption: An enigmatic presentation in a patient with renal cell carcinoma. Indian J Skin Allergy. doi: 10.25259/IJSA_3_2024.
2. Jackson SR, Koestenbauer J, Carroll AP, Oo TH, Chou S, Indrajit B. Paraneoplastic bullous pemphigoid-a sign of clear cell renal carcinoma. Urol Case Rep 2020;30:101119.
3. Linares-Gonzalez L, Ródenas-Herranz T, Ruiz-Villaverde R. Spiny keratoderma as a paraneoplastic condition in clear cell renal cell carcinoma. Actas Dermosifiliogr 2022;113:514-5.
4. Maestroni U, Gasparro D, Ziglioli F, Guarino G, Campobasso D. Metastatic clear cell renal cell carcinoma: The great pretender and the great dilemma. World J Oncol 2021;12:178-82.
5. Pallagani L, Choudhary GR, Himanshu P, Madduri VK, Singh M, Gupta P, *et al*. Epidemiology and clinicopathological profile of renal cell carcinoma: A review from tertiary care referral centre. J Kidney Cancer VHL 2021;8:1-6.
6. Patel HS, Aggarwal V, Thapa R. Scleroderma associated with renal cell carcinoma: A case report and literature review. J Scleroderma Relat Disord 2021;6:316-9.
7. Patel S, Alhajj M, Brimhall C. A novel case of multicentric reticulohistiocytosis associated with renal cell carcinoma successfully treated with infliximab and methotrexate. Case Rep Dermatol 2023;15:10-6.
8. Ruffilli F, Padovan M, Ciancio G, Venturelli V, Maranini B, Govoni M. Scleroderma as paraneoplastic disease: A new case of a rare association with renal cell carcinoma. J Scleroderma Relat Disord 2021;6:330-1.

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