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Case presentations

# Multisystemic paraneoplastic autoimmune syndrome associated with renal adenocarcinoma

Case report

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**ABSTRACT**

**Introduction:**Preneoplastic multisystem autoimmune syndrome is a rare entity in which systemic autoimmune disorders present as preneoplastic manifestations of malignant tumors.

**Objective:**To report a case of paraneoplastic multisystem autoimmune syndrome associated with renal adenocarcinoma.

**Methods:**We report the case of a 62-year-old male with skin lesions and urinary tract alterations of several years of evolution, who was diagnosed with left renal adenocarcinoma. Initially, he received symptomatic treatment without significant improvement. Given the persistence of symptoms and the appearance of systemic signs, a comprehensive evaluation was performed including skin biopsies, immunological studies, and imaging tests. The results led to the finding of a renal adenocarcinoma as the probable origin of the clinical picture.

**Results:**The patient underwent radical nephrectomy, after which a 90% remission of skin lesions and significant improvement in urinary symptoms were observed, suggesting a preneoplastic mechanism in the genesis of the multisystem autoimmune syndrome. Subsequent follow-up

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confirmed the absence of tumor recurrence and sustained recovery of autoimmune manifestations.

**Conclusions:**Preneoplastic multisystem autoimmune syndrome is a rare entity that may sometimes go unnoticed due to limited clinical suspicion. Treatment includes topical and systemic treatment of skin lesions, as well as left radical nephrectomy for resolution of renal adenocarcinoma and consequently resolution of skin lesions. This case highlights the importance of considering preneoplastic autoimmune manifestations in the evaluation of patients with dermatological and systemic symptoms without an apparent cause.

**Keywords:**Paraneoplastic multisystem autoimmune syndrome; Renal adenocarcinoma; Preneoplastic pemphigus.

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## Introduction

Renal cancer is one of the most common urological tumors in adults, accounting for approximately 100,000 deaths annually worldwide. About 20% of patients with renal cancer present with preneoplastic manifestations. (1) The term “preneoplastic” refers to the presence of a cancer that produces distant effects not attributable to either its direct invasive or metastatic properties. This is the case with preneoplastic autoimmune multisystem syndrome, a rare condition characterized by the appearance of autoimmune skin manifestations associated with a malignant tumor. Formerly known as preneoplastic pemphigus (PP), this rare entity was first described in 2001 by Dr. Marcelo Rivitti and Dr. Thomas P. Lynch and their research team.

Preneoplastic autoimmune multisystem syndrome is a skin and mucous membrane disease associated with a neoplasm, usually of lymphoid origin, characterized by involvement of several

organs in addition to the skin. The pathophysiological mechanisms involved in mucosal, cutaneous, and internal organ lesions (2) cause this phenomenon to occur when the patient's immune response, directed against the neoplasm, also attacks healthy tissues, generating a variety of clinical manifestations. (3)

Among the organs frequently affected are the skin, urinary tract, and nervous system. Clinically, it presents heterogeneously in the skin, with mucocutaneous lesions resembling pemphigus, but which in other areas can mimic pemphigoid, erythema multiforme, bullous lichen planus, or even a graft-versus-host reaction. Painful erosions are prominent, not only in the mouth but also in the upper aerodigestive tract, eyes, nose, and genitals. Diagnosis is challenging due to the overlap of symptoms with primary autoimmune diseases and other inflammatory pathologies. (4) This article presents a clinical case of paraneoplastic autoimmune multisystem syndrome associated with renal adenocarcinoma, in which the patient's favorable evolution after tumor resection was evident.

## Case presentation

This is a 62-year-old male patient with a history of hypertension and ischemic heart disease, for which he was receiving regular treatment. He reports that approximately one month ago he began to develop dermatological lesions on his scalp, for which he was seen by his family physician without improvement. He reports that the lesions subsequently spread to his trunk and arms, presenting with redness and small blisters, expanding daily and including some lesions on the oral mucosa. He was admitted for further evaluation and treatment.

**Clinical findings**

Physical examination of the skin

Disseminated lesions, predominantly on the trunk, upper limbs, and scalp, characterized by erythematous, vesicular, and bullous lesions that coalesced to form large plaques with well-

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defined, irregular borders. Pinkish erythema, numerous vesicles and bullae of varying sizes, with clear contents, some covered by adherent, dry, medium-thickness brown crusts. Isolated opalescent areas were present on the oral mucosa.

Subjective symptom: mild itching

Based on the patient's dermatological clinical presentation (Figure 1), associated with urinary symptoms and supported by the results of complementary examinations, histological examination, and computed tomography scan, it was confirmed that the patient had an adenocarcinoma in the left kidney and, consequently, a preneoplastic autoimmune multisystem syndrome. Although most of these cases have a poor prognosis, with a mortality rate of 90%, this patient had a favorable prognosis with resolution of more than 90% of the skin lesions after the nephrectomy, and to this day the patient has not shown any relapses and his skin is in excellent condition (Figure 2).

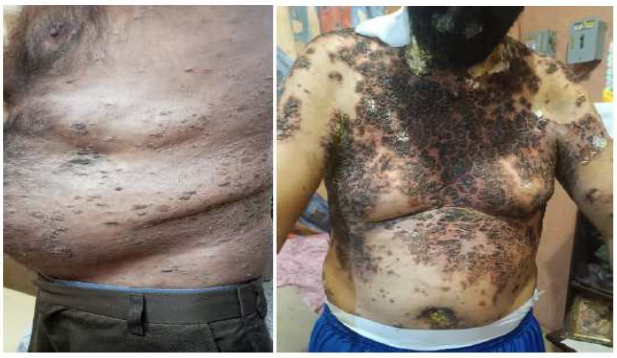

**Fig. 1**Preneoplastic autoimmune multisystem syndrome: disseminated erythematous-vesicobullous lesions in plaques and adherent crusts of medium thickness.

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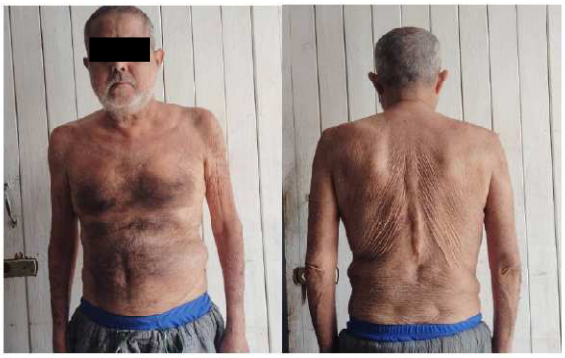

**Fig. 2**Images after surgical and dermatological treatment

**Diagnostic evaluation**

Additional tests

Leukocytes 9.0x109 /L Poly 0.60 Lymphocytes 0.25

Hemoglobin 131.1 g/L Creatinine 142 mmol/L Urea 10.5 mmol/L

Ca 2.28 mmol/LK 3.51 mmol/L Phosphorus 0.29 mmol/L

Na 153.3 mmol/L Cl 134.6 mmol/L Cholesterol 2.5 mmol/L

Erythrocyte sedimentation rate: 98mm/hour.

Histological study: in the fragment corresponding to skin examined microscopically, morphological characteristics corresponding to bullous disease of pemphigus vulgaris are observed.

Tomography

In computed tomography (CTP)) sThe liver appeared homogeneous, of normal size and density. The gallbladder appeared normal, without radiopaque stones or demonstrable tumors. The biliary tract was not dilated. The pancreas was visualized in its entirety, with normal density, appearance, and diameter. No solid nodules or pancreatic calcifications were identified within the gland. The spleen was homogeneous, of normal size and density, without solid nodules or cysts. The peritoneum appeared normal. The aorta, abdominal artery, and iliac arteries were

normal, and no lymphadenopathy was observed. Both kidneys were of normal shape, size, and position, and the density and thickness of their parenchyma were adequate.

At the upper pole of the right kidney, images of varying densities with irregular, partially defined borders are observed. The soft tissue attenuation coefficient, after intravenous contrast administration, measured at more than 24 HU in an axial slice (40x35 mm), appears to correspond to a space-occupying lesion (SOL) at this level. No other abnormalities are noted at this level.

Conclusions: Right renal lesion.

**Therapeutic intervention**

Topical treatment

Use of antiseptic compresses and baths with potassium permenganate (1 x 20000). Compresses three times a day for one hour.

Baths twice a day

Systemic treatment

Prednisolone (20 mg tablets) at a dose of 80 mg daily

Diphenhydramine (25 mg tablets) one tablet every eight hours.

Surgical treatment

Left radical nephrectomy.

Ethical considerations: the patient's informed consent was obtained for the taking of images.

## Discussion

Paraneoplastic autoimmune multiorgan syndrome is part of the group of autoimmune blistering diseases secondary to neoplasms, affecting both the skin and internal organs; it is also known as paraneoplastic pemphigus. (5) This syndrome can be accompanied by involvement of other organs, including the skin, as occurred in the present case, in which the improvement of the dermatological lesions was seen after the surgical procedure. In these cases, the definitive

treatment was the management of the underlying neoplasm, although the combination of steroids and immunosuppressants can also be indicated as other therapy options. (6)

In this clinical report, the presence of persistent skin lesions along with urinary abnormalities led to the identification of a renal adenocarcinoma as a possible trigger of the syndrome. (7) The patient's clinical course, with resolution of more than 90% of the skin lesions after radical nephrectomy, supports what has been described in the literature regarding the paraneoplastic nature of these symptoms. The rapid improvement after tumor removal reinforces the hypothesis that these disorders are mediated by immunological mechanisms triggered by the neoplasm, rather than by direct effects of the cancer.

Although renal cell carcinoma is not highlighted in the literature as one of the main entities causing preneoplastic autoimmune multisystem syndrome, this case emphasizes the importance of considering renal etiologies as paraneoplastic manifestations in patients with autoimmune manifestations refractory to conventional treatments. (8)

When compared with recent reports in the literature, significant similarities and differences are identified. For example, Ortúzar Menesia and other authors described a case of paraneoplastic pemphigus as the initial manifestation of an occult renal tumor, in which painful mucosal lesions (oral, conjunctival, and nasal) also predominated, although with a less extensive cutaneous presentation than in the case presented here. In both cases, treatment of the neoplasm proved essential for the resolution of the autoimmune condition, although in the case reported by Ortúzar, remission was partial after embolization and treatment with oral corticosteroids. (9)

In this case, as in the one reported by Lu et al. in a 2024 study, in which squamous cell carcinoma of the tonsil was associated with paraneoplastic pemphigus, surgery played a fundamental role. In both cases, tumor resection led to almost complete remission of the mucocutaneous lesions, which reaffirms the paraneoplastic and immunologically mediated nature of these manifestations.Carey RMet al. also implemented adjuvant treatment with topical corticosteroids and antifungals and achieved complete healing without recurrence. From a clinicopathological standpoint, most cases share histological findings of epidermal acantholysis,

keratinocyte necrosis, and lichenoid patterns, with positive direct immunofluorescence for IgG and C3 at intercellular junctions, as also occurred in the case reported in this article. Furthermore, anti-envoplaquin and anti-desmoglein 3 autoantibodies have been reported with high frequency and specificity in paraneoplastic pemphigus, which contributes to the definitive diagnosis. (10)

The prognosis for paraneoplastic pemphigus depends largely on the type and management of the underlying neoplasm. Although the literature reports a high mortality rate, up to 90% in some cases, patients who receive curative surgical treatment of the neoplasm have a more favorable outcome, as evidenced in this case and in the recent reports reviewed.

## Conclusions

In conclusion, this clinical case, along with others from recent literature, reinforces the need to consider paraneoplastic pemphigus as the initial manifestation of an occult neoplasm, even in solid tumors such as renal cell carcinoma. Early identification of the tumor and its surgical treatment can lead to significant or complete resolution of the syndrome.

autoimmune, which highlights the importance of a comprehensive and multidisciplinary approach.

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## Conflict of interest

The authors declare no conflicts of interest.

## Authorship contribution

Yaniet Jiménez Montero: conceptualization, supervision, rwriting – original draft, writing the initial draft,data curation, research.

Martha Delfina Mengana Medina:data curation, research.

Rosaida Fonseca Gómez: research, visualization.