Case Report

Pemphigus in Sarcomatoid Renal Cell Carcinoma: A Rare Paraneoplastic Manifestation

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Abstract

Renal cell carcinoma with sarcomatoid features is a rare presentation with a 5% incidence. Sarcomatoid renal cell carcinoma is usually associated with poor prognosis. It commonly metastasizes to the lungs, bones, and liver. Dermatological manifestation with paraneoplastic syndrome is extremely rare. Pathogenesis of PNP in renal cell carcinoma is not cleat; till date, however, few literature suggest antibodies against a group plakin family which plays a key role in intermediate filament attachment in RCC. We present PNP in a 64-year-old female associated with renal cell carcinoma.

Keywords: *Paraneoplastic, pemphigus, sarcomatoid*

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Introduction

Dermatological manifestations of paraneoplastic syndromes in patients with renal cell carcinoma are very rare. Paraneoplastic pemphigus (PNP) is an autoimmune blistering and erosive mucocutaneous syndrome associated with underlying neoplasm. It is primarily associated with lymphoproliferative disorders and uncommonly with malignancies of epithelial origin. It is characterized by painful mucosal erosions, ulcerations, and polymorphous skin lesions that progress to blistering eruptions on the trunk and extremities.

We present PNP associated with a rare variant of renal cell carcinoma.

Case Report

A 64-year-old female presented to a surgical clinic with a chief complaint of right upper abdominal dull-aching pain for 2 years and painful oral ulcer for 6 months. There was no history of fever, vomiting, gross hematuria, jaundice, altered bowel habits, or menstrual irregularities. Oral cavity examination revealed multiple erythematous ulcer with crusting of lip, for which she was advised for application of topical steroid in view of recurrent painful mouth ulcer. Head-and-neck examination revealed a firm, fixed, nontender, 2 cm × 2 cm-sized mass in the left supraclavicular area with no other evident lymphadenopathy. Abdominal examination revealed a 20 cm × 15 cm lump palpable in the right hypochondrium and the lumbar, epigastric, umbilical, and right hypogastrium region. There was no free fluid in the abdomen, and digital rectal and vaginal examinations were unremarkable. Her routine blood investigations were normal including renal function test and liver function test, except increased total leukocytes count. Urine analysis revealed 4–5 pus cells/high power field rest normal. Chest X-ray was normal. Ultrasound of the abdomen revealed a right polycystic kidney with thinned out renal parenchyma. Right kidney was grossly hydronephrotic kidney with hetero echoic lesion. Left kidney, urinary bladder, and bilateral ovaries were normal. Contrast-enhanced computed tomography of the thorax, abdomen, and pelvis reported multiloculated polycystic

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right kidney with irregular boarder extending into the pelvis with variable consistency. Renal vessels were grossly dilated [Figure 1]. Fine-needle aspiration cytology of the left supraclavicular lymph node was done which showed moderate cellularity comprising predominantly dispersed cells and cells arranged in loose clusters with nuclear pleomorphism, prominent nucleoli, and abundant vacuolated cytoplasm, suggestive of metastatic renal cell carcinoma [Figure 2]. The patient was considered for radical nephrectomy. Intraoperatively, liver, omentum, and mesentery were normal, and a right polycystic kidney measuring 20 cm × 20 cm was seen. It was densely adherent to mesocolon and inferior surface to liver. Cysts varied in consistency. Pelvicalyceal system was grossly dilated. There was no thrombus in renal vein nor any retroperitoneal lymphadenopathy was present.

Postoperative period was unremarkable. Histopathological examination of the resected specimen (measuring 15.5 cm × 10 × cm 10 cm) showed bosselated surface with calcified cyst. Tumor was extending into perinephric fat and pelvicalyceal system with necrosis and lymphovascular invasion consistent with clear renal cell carcinoma with sarcomatoid features [Figure 3]. She also had a complaint of flaccid blisters and exfoliated skin involving extremities with crusted erosions involving buccal mucosa and tongue. Skin biopsy was done and showed suprabasal acantholysis with bullous cleft formation which was compatible with PNP [Figure 4a and b]. She was advised for bolus dose of corticosteroid at frequent interval, and the lesions responded well except buccal mucosa. The patient was then referred for tyrosine kinase inhibitor therapy.

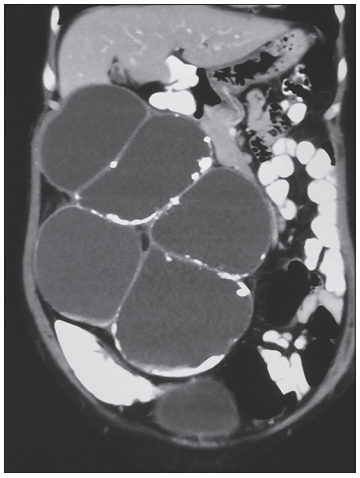

Figure 1: Coronal section of contrast-enhanced computed tomography abdomen showing multiloculated polycystic right kidney with irregular boarder extended into pelvis variable density in the contents of the cyst locules

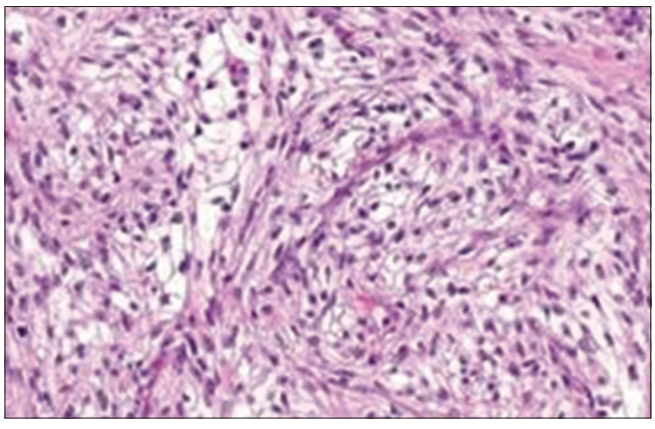

Figure 3: Showing sheets of pleomorphic cells, irregular nuclei, moderate pale cytoplasm with spindle cells (H and E, ×400)

Discussion

Renal cell carcinoma is also associated with paraneoplastic syndrome in 10%–40% of patients. In renal cell carcinoma, paraneoplastic syndrome comprises metabolically and biochemically varieties such as hypercalcemia (20%),[1] hypertension (20%), polycythemia (1%–8%), Stauffer syndrome (3%), and dermatological manifestations which are very rare.[2] In 1990, Anhalt *et al*.[3] described PNP, a mucocutaneous disease associated with malignancy. Subsequently,

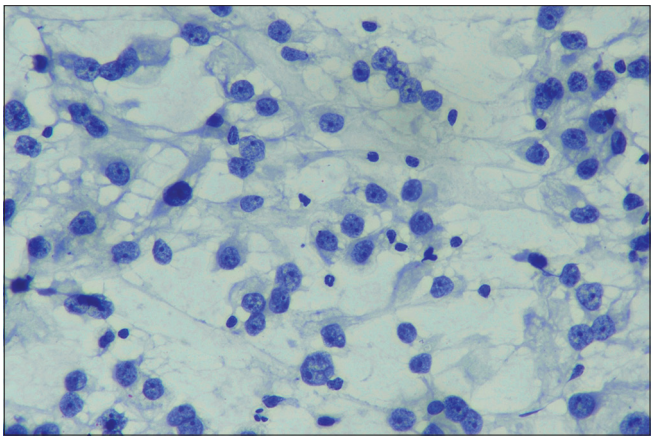

Figure 2: Fine-needle aspiration cytology from left supraclavicular lymph node showing discohesive clusters of cells, prominent nucleoli suggestive of metastasis from renal, ×400

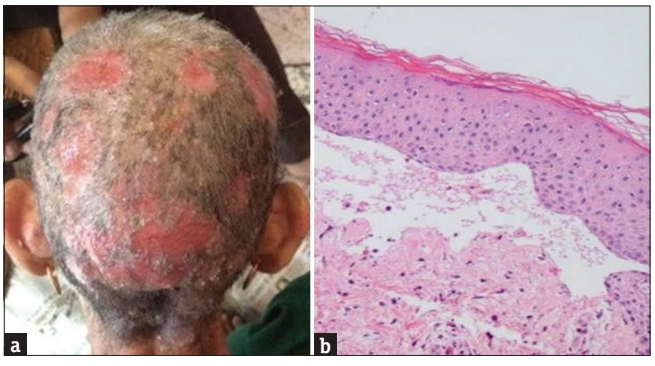

Figure 4: (a and b) Multiple small ruptured bullae with erythematous base on scalp and tense bulla on flexural areas of skin

>150 cases have been reported, usually in association with a previously diagnosed lymphoreticular malignancy. It is rarely associated with epithelial malignancy. Till date, only 13 cases among 163 PNP cases have been reported secondary to epithelial carcinomas. Diagnosis of PNP is based on clinical features, histology, direct and indirect immunofluorescence (DIF and IIF), and immunoprecipitation tests. Revised diagnostic criteria reported by Camisa and Helm[4] include major signs of polymorphic mucocutaneous eruption, concurrent internal neoplasia, and serum antibodies with a specific immunoprecipitation pattern and minor signs of histologic evidence of acantholysis, DIF showing intracellular and basement membrane staining, and IIF staining with rat bladder epithelium. Three major or two major and two minor signs are needed for diagnosis.

Pathogenesis of PNP in renal cell carcinoma is not cleat; till date, however, few literature suggest antibodies against a group plakin family which plays a key role in intermediate filament attachment. Various other target antigens (in decreasing order of incidence) include desmoglein 3 and 1, envoplakin, periplakin, desmoplakin I and II, bullous pemphigoid antigen I, and alpha 2-macroglobulin-like-1 have also been found.[5]

Tumor cells have been demonstrated to produce autoantibodies to epidermal proteins. Dysregulated cytokine interleukin-6 may be a triggering factor for autoimmune reactions.[6] PNP responds poor to treatment, especially mucosal lesions. Initial therapy is to prevent superinfection by applying warm compresses, nonadherent wound dressings, and topical antibiotic. In Immunosuppressive agents first line therapy is corticosteroids followed by non-steroid agents such as azathioprine, cyclosporine, and mycophenolate mofetil.[7] In general, mucosal pemphigous lesions respond poorly to immunosuppressive agents like our patient. A recent study suggested the role of rituximab and alemtuzumab in paraneoplastic bullous pemphigoid.

PNP is associated with poor prognosis. Ninety percent of patients in a series of study died due to this associated dermatological manifestation.[8] This grave prognosis is due either to the presence of underlying malignancy and accompaniments of targeted therapy to treat disease or to PNP itself in cases in which the respiratory mucosa is involved. Treatment of the underlying malignancy diminishes the PNP lesions.

Through this study, we wish to communicate that if any other systemic manifestations are seen in the patient apart from primary malignancy, paraneoplastic process should always be kept in mind because it will not respond to any treatment except management of primary tumor or malignancy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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