

Oncology

Paraneoplastic bullous pemphigoid – A sign of clear cell renal carcinoma



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A B S T R A C T

Paraneoplastic bullous pemphigoid is a rare paraneoplastic syndrome. Rash is pruritic, with erythematous eruption of large subepidermal bullae over skin and often mucosal surfaces. We present an 84y woman with a three week history of erythematous rash, and 48hrs of bullae. A left clear cell renal cell carcinoma was identified on CT imaging during the presentation. Subsequent removal of the tumour resulted in resolution of bullous pemphigoid symptoms. This first-of-kind case and successful result strengthens the association between renal cell carcinoma and paraneoplastic bullous pemphigoid, arguing for a high degree of clinical suspicion in unexplained presentations of bullous pemphigoid.

Introduction

The vast majority of renal cell carcinoma (RCC) are incidentally identified on imaging. However, when symptomatic, 35–40% of RCC are associated with a paraneoplastic syndrome (PNS). PNS are a collection of symptoms and signs which arise secondary to non-metastatic systemic effects of malignancy. PNS associated with RCC are varied, including both endocrine and non-endocrine types.¹

Bullous pemphigoid has a neoplastic association in 11% of cases, most commonly associated with lymphoproliferative disorders including B-cell lymphoma, chronic lymphocytic leukaemia, Waldenström macroglobulinemia, thymoma and spindle cell neoplasms.² Comparatively, paraneoplastic bullous pemphigoid (PNBP) is a rare and controversial PNS of renal malignancies, documented only a few times in the literature.

We present a dermatologically naive patient with PNBP as a herald for subsequent investigation, and diagnosis of clear cell RCC.

Case presentation

An 84-year-old female presented to emergency with 3 weeks duration of pruritic, erythematous rash; and wide spread eruption of large bullae over the preceding 48 hours on torso, upper limbs, face and oral mucosa (Fig. 1). Comorbidities included type 2 diabetes mellitus (HbA1c 9%), hypertension, obesity, and atrial fibrillation. There were no systemic symptoms otherwise, specifically no pyrexia, cachexia, nor fatigue. Routine bloods were within normal ranges.

Skin biopsy suggested bullous pemphigoid, showing features of subepidermal blisters with eosinophils on histology (Fig. 2). Immunofluorescence confirmed bullous pemphigoid, demonstrating linear deposits of immunoglobulin G and C3 at the dermo-epidermal junction. The presence of mucosal lesions with bullous pemphigoid, combined with a lack of other clear cause, prompted radiological investigation with computed tomography of chest, abdomen and pelvis. This occurred 5 days after presentation, and demonstrated a 5 × 5.5 × 4.5cm lesion of the left lower renal pole, highly suspicious of RCC (Fig. 3). No other pathology was identified on imaging. No associated abdominal mass could be palpated on clinical examination, nor was haematuria present on urinalysis.

Staged treatment was planned for semi-elective nephrectomy. This was undertaken to allow medical optimisation of comorbidities, without compromising oncological outcomes of the planned nephrectomy. The bullous pemphigoid was initially managed with an oral tetracycline, high dose oral steroids, and topical steroid creams. This regimen underwent accelerated weaning over the next 3 weeks prior to surgery. Wet dressings were applied daily during this time.

Laparoscopic left nephrectomy was undertaken 31 days after initial presentation. Recovery was uneventful, with both a noticeable healing of old and a reduction of new lesions noted within 2 days of operation. The patient was discharged in good health, 9 days post-surgery, with a marked reduction in bullae. On subsequent review at day 40 post surgery, skin lesions were resolved. Anatomical pathology revealed a pT3a pN0 pMX grade 2 clear cell, renal cell carcinoma (ISUP/WHO nucleolar grade 2–3).

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Fig. 1. Initial clinical presentation of paraneoplastic bullous pemphigoid to emergency department. Lesions demonstrated similarly across torso, upper limbs, face and oral mucosa.

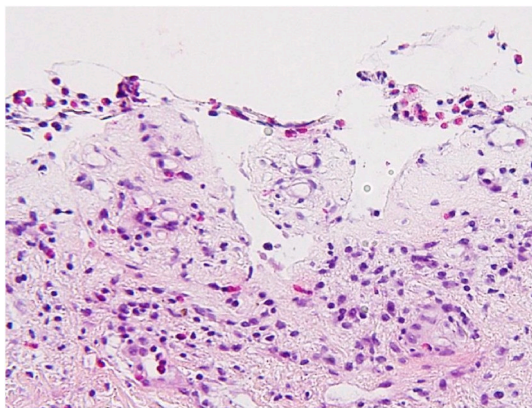


Fig. 2. Skin biopsy shows complete sloughing and loss of epidermis due to subepidermal blister. Eosinophils are present in the residual blister and there is chronic inflammation with eosinophils in the superficial dermis (H&E stain, $\times 200$ magnification).



Fig. 3. Initial computer tomography, demonstrating $5 \times 5 \times 4.5$ cm lesion of the left lower renal pole, highly suspicious of renal cell carcinoma.

Discussion

Bullous pemphigoid is a rare blistering disorder with an estimated incidence of 2–14 new cases per million people. It is most associated with the elderly, specifically those with neurological disorders, psychiatric disorders, bedridden condition, and chronic use of multiple drugs.^{2,3}

PNBP is most commonly associated with non-solid organ malignancy. It is however rarely associated with solid organ malignancy, with several case reports demonstrating association with tumours of the lung, breast or squamous cell carcinoma.⁴

In our review of the literature only 6 cases have been demonstrated with renal cell carcinoma, 2 of which occurred synchronously with other solid organ malignancies.^{1,4,5} Of note, this case presentation appears to be the first reported case of PNBP associated with clear cell carcinoma alone. Significantly, this occurred with mucosal surface bullae, a characteristic which is suggested to be more commonly associated with PNBP.⁴

The causative relationship of renal carcinoma and PNBP remains controversial in the literature.⁴ A neoplastic link is suggested by both remission of symptoms after solid tumour resection, and reappearance of lesions with cancer recurrence. The prior has been demonstrated in our case.

Previously, temporal delay from PNBP diagnosis until cancer diagnosis has raised suggestion that immunosuppressive treatment of non-paraneoplastic bullous pemphigoid may be a major contributing factor for subsequent malignant disease.^{4,5} The near synchronous nature of our case's presentation, immunosuppressive treatment and tumour diagnosis is contrary to this view. The only long term immunosuppressive characteristic of note was our patient's poorly controlled type 2 diabetes.

Conclusion

A high degree of clinical suspicion should be maintained in cases of bullous pemphigoid. This case demonstrates a first report of non-synchronous clear cell renal cell carcinoma with PNBP in the literature. Crucially, malignancy was found during the same presentation as skin eruptions, and with corresponding mucosal lesions which are suggestive of a paraneoplastic presentation. Our case supports a broad investigative approach for patients presenting with bullous pemphigoid, especially in the elderly.

Credit author statement

Stuart R Jackson – Conceptualization; Writing – original draft, review and editing.

Jakob Koestenbauer – Writing – original draft.

Adam Carol – Data curation.

Than-Htike Oo – Data curation; formal analysis of renal cell carcinoma pathology.

Shaun Chou – Data curation; formal analysis of pemphigoid skin biopsy pathology.

Balasubramaniam Indrajit – Supervision; Writing – review and editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.eucr.2020.101119>.

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