CASE REPORT

Xp11 translocation renal cell carcinoma paraneoplastic syndrome presenting as cutaneous vasculitis: first reported case of yet another mask

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SUMMARY

Renal cell carcinoma is historically known as the 'great masquerader' with 40% of patients experiencing a paraneoplastic syndrome. Translocation carcinoma represents one-third of renal cancer in paediatric patients but less than 3% of renal cancers in patients aged 18–45 years where the clinical course is often rapidly terminal. There are less than 10 reported cases of leucoclastic vasculitis associated with clear cell carcinoma reported in the literature and 10 case reports of translocation carcinoma in adults. To our knowledge, we present the first reported case of Xp11 translocation carcinoma presenting as cutaneous vasculitis, as part of a paraneoplastic syndrome, in an adult patient. Our case highlights that renal cell cancers are truly the 'great masquerader' and a rash can be the first sign of renal malignancy.

BACKGROUND

Paraneoplastic syndrome refers to a constellation of signs and symptoms that are secondary to the presence of a malignancy, not related to mass effect. Renal cell carcinoma (RCC) is often called the 'great masquerader' of tumours. Although the classical clinical triad of 'flank pain, haematuria and a palpable abdominal mass' is experienced by up to 15% of patients with RCC, up to 40% of patients experience paraneoplastic syndrome variants.¹ A less frequently reported condition is that of cutaneous vasculitis as part of the paraneoplastic syndrome secondary to clear cell RCC.

Translocation carcinoma represents one-third of renal cancers in paediatric patients, but less than 3% of all renal cancers in patients aged 18–45 years,²

followed by a clinical course that is often rapidly terminal.³ Current literature is mostly limited to case reports or small case series relating to either translocation carcinoma in adults or cutaneous vasculitis as part of a paraneoplastic syndrome as separate entities. We contribute to the finite body of literature with, to our knowledge, the first reported case of Xp11 translocation carcinoma presenting with cutaneous vasculitis as part of a paraneoplastic syndrome in an adult patient. We also provide an updated review of the current evidence surrounding this unusual pathological entity.

CASE PRESENTATION

A 45-year-old man was referred to the emergency department by his local medical officer with a 1-week history of a progressive rash on his right lower limb, initially managed as cellulitis. This was preceded by 3 months of right leg swelling and hip pain. On presentation to the emergency department, it was noted that the petechial, non-blanching rash had spread to his left leg, bilateral forearms and back (figure 1). The patient reported 5 kg loss of weight over the preceding 5 months but was otherwise well with no other constitutional 'B symptoms', such as fevers or night sweats.

INVESTIGATIONS

Basic serum testing revealed progressive impairment of renal function with creatinine increasing from 126 to 146 $\mu\text{mol/L}$ over the preceding 4 months. Ultrasound scans performed to investigate the presence of deep vein thrombosis were negative. Referral was made to dermatology and nephrology, and a full vasculitic screen was performed for the

Figure 1 Photograph of rash on the patient's right leg, thigh and abdomen.

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Figure 2 CT of the patient with arrow pointing to inferior vena cava thrombus.

differential diagnosis of vasculitis of unknown type with possible renal involvement. Punch biopsies of the sites were performed with histopathology revealing perivascular inflammation, eosinophil migration into the interstitium and dermal oedema consistent with an urticarial vasculitic reaction. Serum screening for vasculitis yielded no positive results. A chest X-ray revealed hilar lymphadenopathy that was further characterised by CT scanning of the chest, abdomen and pelvis. This revealed an extensive right-sided renal mass extending into the inferior vena cava with lung, liver and mediastinal metastases (figure 2).

TREATMENT

The patient was referred to a urologist and underwent right radical nephrectomy and adrenalectomy, retroperitoneal lymph node dissection, repair of inferior vena cava and extraction of renal vein thrombus, 1 month after initial presentation to emergency. Following surgery, the patient went on to have adjuvant systemic treatment with sequential tyrosine kinase inhibitors and radiation therapy to sites of metastasis.

OUTCOME AND FOLLOW-UP

Histopathological analysis revealed grade T3bN1 RCC (figure 3A) with inferior vena cava thrombus. Transcription Factor E3 (TFE3) staining displayed Xp11 translocation variant of RCC (figure 3B). Renal parenchyma had almost been entirely replaced by tumour in the right kidney with extensive renal vein invasion. There was extensive involvement of the renal sinus fat with ulceration of the renal pelvis (figure 3C). In the postoperative weeks, prior to commencement of tyrosine kinase inhibitors, the cutaneous manifestations completely regressed and had not recurred at 18 months' postoperative review. The patient remains in the community with intermittent admissions for palliative radiation, physiotherapy and pain management.

Figure 3 3A Microscopic image of kidney specimen. 3B Microscopic image of kidney specimen with positive TFE3 staining. 3C Cut section of histopathological right kidney specimen, showing tumour replacing virtually the entirety of kidney.

DISCUSSION

The term vasculitis encompasses a group of disorders characterised by inflamed blood vessels and can be broken down into three broad categories: small, medium and large vessel disease. Cutaneous or leucoclastic vasculitis can be classified as small or medium vessel

disease and is commonly associated with drug reactions, infection, allergy, autoimmune disorders or malignancy. The prevalence of malignancies in patients who have vasculitis is between 3% and 8% with the majority of these cases being secondary to haematological malignancy rather than those of solid organ origin.^{4,5} Malignancy associated vasculitis classically presents with palpable purpura, preferentially located in dependant areas.^{5,6}

The term paraneoplastic syndrome refers to a constellation of systemic signs and symptoms that are secondary to the presence of a malignancy and not attributable to direct tumour extension or metastasis.¹ Hypercalcaemia is the most common of the paraneoplastic syndromes in patients with RCC and in 75% of cases, represents underlying high-stage lesions.¹

We performed a review of the literature in an attempt to identify cases of cutaneous vasculitis associated with RCC as part of a paraneoplastic syndrome, as well as underpin the proposed mechanisms of this unusual pathological entity. We identified 10 cases of cutaneous/leucoclastic vasculitis associated with RCC. The histopathology revealed clear cell carcinoma in all cases. There were no reported cases of leucoclastic vasculitis associated with translocation carcinoma, exemplifying the rarity of this tumour type in adult patients.

Learning points

- We describe, to our knowledge, the first case of Xp11 translocation renal cell carcinoma (RCC) presenting with a cutaneous paraneoplastic syndrome.
- We highlight that not all rashes are cured with steroids or antibiotics and remind readers that solid malignancy such as RCC may initially present with cutaneous signs as part of a paraneoplastic syndrome.
- We highlight that RCCs are truly the 'great masquerader', and a rash may be the first sign of renal malignancy.
- We suggest that in the presence of a vasculitic rash that fails to respond to conventional therapy the possibility of a paraneoplastic syndrome and RCC could be considered.

It has been suggested that the likely mechanism that underpins most leucocytoclastic paraneoplastic vasculitis is the formation of immune complexes of tumour associated antigens/antibodies⁵ or cytokine production by malignant cells. Both of these mechanisms have been reported for RCC,⁷ however the exact aetiology remains largely unknown. All 10 cases identified reported similar temporal relationships between nephrectomy and resolution of the cutaneous manifestations. Interestingly, Sarma describes a case where the rash recurred 20 months postnephrectomy in association with RCC recurrence.⁸ In our case, resolution of vasculitis following effective treatment of the putatively linked Xp11 translocation carcinoma provides strong evidence for this episode of vasculitis being a true paraneoplastic syndrome.

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