Unusual presentation of more common disease/injury

Haematuria as an uncommon initial presenting symptom of metastatic squamous cell carcinoma (SCC) to kidney

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Summary

A 47-year-old female presented with a 2-week history of painless haematuria. Urine dipstick showed moderate leucocytes. Blood and urine cultures were negative and cytology was negative for malignant cells. Flexible cystoscopy was negative for any bladder pathology. An ultrasonogram of the abdomen showed a mass in the left kidney. CT showed a mass-like lesion within the left kidney suspicious for renal carcinoma, and cavitary lesions in both lungs. Biopsy of the lung showed clusters of atypical cells suspicious for squamous cell carcinoma (SCC), and left kidney lesion showed malignant cells derived from SCC. A whole body positron emission tomography/CT showed lesions in the lungs, left kidney and skeleton. Complete clinical examination, laboratory and imaging studies did not reveal any site of primary tumour in any part of the body. Haematuria is a very unusual initial presentation of metastatic tumour to kidney.

BACKGROUND

Haematuria can be microscopic or macroscopic (gross), ranging from trivial to lethal, and causes can be myriad, including urinary tract infections, stones, benign prostatic hypertrophy, malignancies etc. Gross haematuria in adults is considered a sign of malignancy until proven otherwise.¹ Any patient presenting with haematuria should undergo a thorough history, physical examination and laboratory and radiographic investigation.² Associated risk factors, symptoms and medical problems may also provide diagnostic clues. Initial laboratory investigations should include a urinalysis and urine culture. Urinary cytology, urinary tract imaging and cystoscopy is warranted in selected cases. Absence of common causes of haematuria should raise the suspicion of rare pathologies and appropriate diagnostic investigation should be done. Renal malignancies should be included in the differential diagnoses and absence of typical risk factors for malignancy should not eliminate the appropriate diagnostic evaluation.

Here, we present a report on a 47-year-old female, non-smoker, who initially presented with painless haematuria and was found to have metastatic renal and pulmonary squamous cell carcinoma (SCC) with cancer of unknown primary.

CASE PRESENTATION

A 47-year-old white female came to our hospital with haematuria for 2 weeks. She denied frequency, burning sensation, nocturia, fever, chills, night sweats, back/pelvic or abdominal pain. She did not have any recent history of trauma or similar episode in the past. She drinks approximately 1 gallon of water a day. Her last menstrual period was 8 days ago and lasts for 5–7 days occurring at every 21–22 days. She is sexually active with one male partner for last 1 year and does not use any barrier contraceptive. She is a lifelong non-smoker and did not have any history of occupational exposure to noxious substances. Her vitals

were stable, skin colour, texture and turgor was normal. Heart and lungs examination was unremarkable, abdomen was soft, non-tender; bowel sound was present in all quadrants. No masses or abdominal organomegaly was appreciated. There was no tenderness on palpation over spine or costovertebral angles. Complete blood count was significant for platelet of $463 \times 10^9/l$, and complete metabolic profile was within normal limit. Urine analysis showed 1+ haemoglobin/blood, trace amount of protein, 3+ leucocyte esterase, 2–5 white blood cell/high power field (hpf), 6–10 red blood cell/hpf, 1–3 casts/hpf and few squamous epithelial cells/hpf. Urine culture was negative and cytology showed atypical uroepithelial cells. Blood cultures were negative. Blood IgE level was 56.4 kU/l. IgG, IgA and IgM levels were 1230, 358 and 159 mg/ml respectively. Purified protein derivative test was negative. C reactive protein was elevated to 4.3 mg/dl. An abdominal ultrasonogram showed a $3.5 \times 3.4 \times 2.5$ cm heterogenous mass with large cystic component in superior medial aspect of left kidney. Flexible cystoscopy was negative for any bladder pathology. CT scan of the abdomen and pelvis with and without contrast showed mass-like lesion within upper left kidney suspicious for renal carcinoma (figure 1, asterisk). A CT chest showed multiple cavitary lesions scattered within both lungs, largest lesion in mid right lung adjacent to right hilum measuring 3.3×2.6 cm. The cavitary lesions had thick walls with nodularity. There were ill-defined nodular densities within posterior left lung base with the largest measuring 2.1×1.4 cm and adjacent minimal ground glass attenuation. Two non-calcified nodules were noted within mid right lung with the largest measuring 1.3×1.0 cm. The lung findings were suspicious for aspergillosis or tuberculosis and differential diagnoses included metastatic diseases and SCC of lungs (primary or secondary). Tests for aspergillus, blastomyces, histoplasma and coccidioides were negative. Indirect immunofluorescence and enzyme immunoassay for classical antineutrophil cytoplasmic

Figure 1 A CT scan of the abdomen and pelvis showing mass-like lesion (asterisk) within upper left kidney suspicious for renal carcinoma.

antibodies (ANCA) and protoplasmic ANCA were negative. Antinuclear antibody and rheumatoid factor were also negative. Transbronchial biopsy of lung showed clusters of atypical cells suspicious for SCC. Gram stain of bronchoalveolar lavage was negative for any bacteria and also negative for *Pneumocystis jirovecii*, nocardia, legionella, acid-fast bacillus, herpes simplex, cytomegalovirus and fungi. A CT-guided fine needle aspiration biopsy of left kidney cystic lesion showed malignant cells derived from SCC. Fluid aspirated from cystic lesion of the kidney was negative for acid-fast bacillus, bacteria or fungal growth. A whole body positron emission tomography (PET)/CT scan showed numerous hypermetabolic cavitary and nodular lesions in the lungs, intensely hypermetabolic lesion in the upper pole of the left kidney and hypermetabolic skeletal lesions (figure 2). Treatment was started with carboplatin, gemcitabine and pegfilgrastim. Zolendronic acid was added because of bone metastases. She was tolerating the treatment well. Follow-up PET scan showed metastases to her distal left femur. To search for the primary source of her SCC of kidney and lungs, molecular testing of the cancer cells from kidney and lungs indicated 65% likelihood that the primary site is in the head neck area. Complete clinical examination including head and neck examination by an otolaryngologist, laboratory and imaging studies did not reveal any site of primary tumour in any part of the body.

DISCUSSION

An estimated 58 240 new cases and 13 040 deaths from kidney cancer were expected to be diagnosed in 2010.³ Kidney cancer includes renal cell carcinoma (92%), renal

pelvis carcinoma (7%) and Wilms tumour (1%). Smoking is a strong risk factor for kidney cancer. Other risk factors include obesity, hypertension and rare hereditary conditions. Metastatic kidney tumours are more than twice as common as primary ones,⁴ and the incidence of renal metastases at autopsy are between 2% and 20%.^{5 6} Metastatic kidney tumours are usually asymptomatic in early stage, but as the disease progresses patient may present with haematuria, pain and/or lump in lower back or abdomen, weight loss, fatigue or leg swelling. These patients usually become symptomatic after primary lesion has been recognised and/or treated.⁴ Mean interval of 1.9–2.2 years between initial diagnosis of the primary malignancy and the discovery of renal metastases has been reported.^{7 8} Excluding spread from lymphoma and chronic leukaemia, the common primary sites of the tumours are lung, stomach, colon, malignant melanoma and breast.^{4 9 10} Other rare primary tumour sites include head and neck cancer,¹¹ uterine sarcoma and seminoma.⁷ Solitary metastatic renal tumours are infrequently encountered clinically; typically both kidneys are involved.⁹ Renal metastases of squamous differentiation are not common, but reported cases are usually from bronchial carcinoma, and rarely from other sites, such as anus,¹² penis, oesophagus,¹³ larynx,¹⁴ oropharynx¹⁵ and hypopharynx.¹¹ In patients who have tumours in both lung and kidney, usually the lung is the site of primary tumour.⁴ A renal tumour in a patient with an already known primary malignant tumour not necessarily is always a metastasis, but may represent a different and independent primary malignancy of the kidney.¹⁰ Symptoms related to secondary renal tumours are present only in 20% patients, and include haematuria and

Figure 2 A PET/CT scan showed numerous hypermetabolic cavitary and nodular lesions in the lungs, intensely hypermetabolic lesion in the upper pole of the left kidney and hypermetabolic skeletal lesions.

proteinuria,⁹ and a cytological examination infrequently shows malignant cells in the urine.⁷ A complete diagnostic investigation including laboratory studies, imaging studies and histopathology is required to localise the primary tumour site, yet in 2–4% of all cancer patients, a primary tumour site is never found.³ Since solitary metastatic renal

tumours are not commonly diagnosed before death, the best approach to treat metastatic renal tumour has not been established. In one case series, nephrectomy did not improve the prognosis,¹⁶ and nephrectomy may not be recommended in metastatic renal lesions even if no metastases can be detected in other organs.

This report exemplifies a rare case of SCC of unknown primary with multi-organ metastases initially presenting with haematuria, and clear treatment recommendations in this situation are lacking.

Learning points

- ▶ Metastatic kidney tumours are twice more common than the primary tumours.
- ▶ Metastatic kidney tumours are usually asymptomatic in early stage but may present with haematuria as the disease progresses.
- ▶ Mean interval of initial diagnosis of the primary malignancy and the discovery of renal metastases has been reported to be 1.9–2.2 years.
- ▶ Renal metastases of squamous differentiation are not common, but metastases from larynx, lungs, oesophagus, penis and anus have been reported.

Competing interests None.

Patient consent Obtained.

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