CASE REPORT

Abdominal wall metastasis following open nephroureterectomy for upper tract urothelial carcinoma in a patient with Lynch syndrome

Michael John Stewart, Glen R Guerra, Tom R Sutherland, Sandra L Elmer

St Vincent's Hospital,
Melbourne, Fitzroy, Victoria,
Australia

Correspondence to
Dr Michael John Stewart,
stewart_mj@me.com

Accepted 2 March 2016

SUMMARY

A 74-year-old man developed the rare complication of an abdominal wall metastasis following open nephroureterectomy for upper tract urothelial carcinoma (UTUC). This occurred in the setting of synchronous contralateral ureteric and metachronous colorectal carcinomas. Immunohistochemistry demonstrated loss of the mutS homolog 6 (MSH6) mismatch repair (MMR) protein in the metastatic abdominal wall and colonic lesions, which in conjunction with meeting the Amsterdam II criteria, is strongly suggestive of Lynch syndrome (LS). Surgical resection of the recurrence was performed with clear margins and neither recurrence nor spread during short-term follow-up.

BACKGROUND

Wound recurrence following open surgery is an extremely uncommon but recognised event. To the best of our knowledge, this is only the second case of abdominal wall recurrence following open nephroureterectomy for upper tract urothelial carcinoma (UTUC) to be described in the literature.

CASE PRESENTATION

A 74-year-old man of Greek descent presented in December 2013, with 4 months of intermittent painless macroscopic haematuria. He reported no other concerning symptoms. His history included being an ex-smoker, and having hypercholesterolaemia, osteoarthritis and type 2 diabetes mellitus controlled with diet and oral hypoglycaemics. Notably, he had undergone a high anterior resection for a malignant rectal polyp in 2003. He had a significant family history of malignancy, with his father, two brothers and a paternal uncle dying in their late 50s from undefined malignancies. Additionally, his nephew was diagnosed with bowel cancer in his 40s. Physical examination was unremarkable, aside from a midline laparotomy scar.

Abdominal CT demonstrated a 20×50 mm mildly enhancing mass at the right pelviureteric junction (figure 1) and urine cytology was suggestive of urothelial malignancy. Ureteroscopy was performed with biopsies confirming high-grade urothelial carcinoma; assessment of invasion was limited due to fragmentation of the biopsy. Staging CT showed evidence of neither local nor distant metastatic disease.

In January 2014, the patient underwent an open transperitoneal nephroureterectomy (conversion from laparoscopy due to dense adhesions). A 12th

rib flank incision was utilised with difficult mobilisation of the kidney and ureter secondary to the adhesions. At the beginning of the case, the patient's distal ureter was circumscribed endoscopically and an endoloop was used to ligate the distal ureter. The kidney, ureter and bladder cuff were removed en bloc, with especial care to neither breach the urothelium nor spill urine. The patient was discharged home on day 5 postoperatively with a urethral catheter, following an uncomplicated recovery. On day 10, a cystogram confirmed no urinary leak, and he underwent a successful trial of void. Histopathological analysis revealed a 40×20×15 mm non-invasive high-grade papillary urothelial carcinoma at the right pelvi-ureteric junction with clear resection margins (figure 2).

Subsequent routine review of the case at the hospital multidisciplinary cancer meeting identified a previously unrecognised left mid-ureteric filling defect on CT. In March 2014, a left ureteroscopy and retrograde pyelogram confirmed the presence of a mid-ureteric filling defect. Biopsies demonstrated multifocal low-grade papillary urothelial neoplasia without evidence of invasion. The affected areas were treated with laser fulguration. Repeat ureteroscopy in May 2014 was clear, however, a small recurrence in August 2014 was managed endoscopically with repeat laser fulguration.

Surveillance abdominal and pelvic CT had, in April 2014, demonstrated an area of irregular mural thickening within the right colon.

Figure 1 Preoperative CT intravenous pyelogram. Portal venous phase image showing a delayed nephrogram in the right kidney, calyceal dilation and a soft tissue mass in the renal pelvis/proximal ureter (red arrow).

To cite: Stewart MJ, Guerra GR, Sutherland TR, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-214940

Figure 2 Representative sections of the pelvi-ureteric junction tumour. (A) Low magnification, demonstrating normal kidney on the top right and tumour on the bottom left. (B) High magnification, demonstrating high-grade papillary urothelial carcinoma.

Colonoscopy revealed a 20 mm broad-based polyp in the ascending colon, which was removed by hot snare polypectomy. Histopathology demonstrated a tubulovillous adenoma with low-grade dysplasia (LGD) and focal adenocarcinoma in situ (no invasion), 1 mm in maximum dimension and clear of resection margins. Immunohistochemistry revealed a lack of staining for the MSH6 protein, with preserved staining for mutS homolog 2 (MSH2), mutL homolog 1 (MLH1) and postmeiotic segregation increased 2 (PMS2). Follow-up colonoscopy in September 2014 identified a small sigmoid polyp (polypectomy—tubular adenoma with LGD) without evidence of recurrence in the ascending colon.

On routine follow-up in October 2014, the patient had developed a painful golf-ball sized mass deep in the right flank scar. Imaging demonstrated a circumscribed 45×35×22 mm hypodense mass with peripheral enhancement (figure 3). It was

Figure 3 Imaging of the abdominal wall metastasis. (A) Fused axial CT FDG PET image showing increased FDG avidity within the right anterior abdominal wall mass. (B) Post contrast axial T1-weighted image showing a peripherally enhancing soft tissue mass centred on the abdominal wall and displacing trans versus abdominus muscle. FDG PET, fluorodeoxyglucose positron emission tomography.

Figure 4 (A) Mass ex vivo, measuring 125×85×45 mm. (B) Intraoperative image, composite mesh utilised to close defect in abdominal wall.

situated within the abdominal wall musculature, 12 mm deep to the skin at the site of the previous scar. On review, this mass was not visible on prior imaging. Fused positron emission tomography and CT scanning demonstrated marked avidity of the mass without evidence of further metastatic disease. Image-guided percutaneous biopsy of the mass revealed poorly differentiated carcinoma. To assist operative planning, MRI was performed within a short time of the CT, revealing a significant increase in the size of the mass to 56×41×40 mm. It appeared heterogeneously hyperintense on T2-weighted images and was centred on the internal oblique with no invasion of the abdominal viscera and no bony surrounds (ribs/pelvis).

TREATMENT

Surgery was undertaken in December 2014, with collaboration between the Urology, Colorectal and Plastic Surgery Units. Radical en bloc resection of the abdominal wall mass was performed with entry into the peritoneal cavity to free the underlying adhesions. A wide surgical margin was taken with intraoperative frozen sections confirming them as clear of tumour. A local musculoaponeurotic transposition flap and composite mesh were utilised to repair the large defect (figure 4).

OUTCOME AND FOLLOW-UP

Histopathological review demonstrated a poorly differentiated carcinoma, measuring 125×85×45 mm, with clear resection margins and morphological features similar to the previous urothelial carcinoma (figure 5). Immunohistochemical analysis revealed an identical staining pattern to that seen on examination of the ascending colon lesion, with loss of staining for MSH6 and preserved staining for MLH1, PMS2 and MSH2.

The patient's postoperative recovery was unremarkable. Referral was made to a familial cancer service, but the patient and family declined further genetic testing and counselling.

Figure 5 Representative sections of abdominal wall tumour demonstrating poorly differentiated carcinoma (CK20+, CK7+, CD10 focally positive and P63 negative) with morphological features similar to previous urothelial malignancy. (A) Low magnification (×20); (B) High magnification (×100).

Three-month postoperative surveillance CT performed in March 2015 failed to identify evidence of local or distant recurrence. Clinical review indicated a satisfactory aesthetic and functional result with excellent wound healing without herniation.

DISCUSSION

This is a rare case of an abdominal wall metastasis secondary to an UTUC in a patient who had developed multiple malignancies at several known sites of predilection for Lynch syndrome (LS). The development of bilateral ureteric and metachronous colorectal malignancies, in the setting of a strong family history meeting Amsterdam II criteria, is highly suggestive of LS. Furthermore, both tumours demonstrated an identical immunohistochemical staining pattern, suggestive of a MSH6 germline mutation.

Retrospective studies show comparable oncological outcomes between open and laparoscopic nephroureterectomy for UTUC, with the latter increasingly favoured due to fewer postoperative complications and reduced length of hospital stay.¹ Incisional site tumour recurrence following surgery for urological malignancy is a very rare complication, with only a handful of case reports, mostly relating to port-site metastases following laparoscopic surgery.² Wound recurrence following open surgery is an extremely uncommon but recognised event, more frequent in certain gynaecological and general surgical malignancies.³ To the best of our knowledge, only one case of abdominal wall recurrence following open nephroureterectomy for UTUC has previously been described.⁴

The exact mechanism behind wound recurrence following open surgery has not been fully elucidated, however, traumatising of tissues, haematogenous seeding and direct spread of cancer cells have all been suggested as possible mechanisms.⁵ When considering port-site metastases following laparoscopic surgery, aerosolisation of tumour cells, peritoneal damage and specimen removal technique have additionally been proposed as contributing factors.⁶ It is increasingly recognised that many of the growth factors, chemokines and cytokines released in the wound healing process may promote carcinogenesis.⁷ These microenvironmental signals and homeostatic changes that orchestrate normal wound healing are not only implicated in local tumour growth, but have also been found to stimulate tumour growth at distant sites.

In the presented case, the patient's strong family history for malignancy meets the Amsterdam II criteria for LS.⁸ Furthermore, both the metastatic tumour deposit and the lesion in the ascending colon demonstrated lack of staining for the MSH6 mismatch repair (MMR) protein on immunohistochemistry. This suggests a high likelihood of the patient harbouring a MSH6 germline mutation. Although somatic mutations have been implicated in colorectal neoplasms demonstrating MMR defects and microsatellite instability (MSI)⁹ the probability of identical mutations in metachronous lesions at different locations would be infinitely low. Similarly, somatic mosaicism could explain the demonstrated immunohistochemical pattern but is considered extremely improbable.¹⁰ MSH6 germline mutations account for approximately 20% of all LS-associated mutations and commonly have a later age of diagnosis when compared to more frequently observed MLH1 and MSH2 mutations.¹¹ LS involves inherited defects in the DNA MMR system, resulting in MSI and predisposition to a number of malignancies. Classically, colorectal carcinoma is implicated but numerous extracolonic malignancies may occur at higher frequency in those with LS. UTUC is the third most common malignancy in these patients, after colon and endometrial cancer.¹²

In their recent review, Mork *et al*¹³ have suggested that urologists should consider the possibility of LS in any patient with de novo UTUC, and strongly recommend genetic testing and/or immunohistochemistry where patient's meet the Amsterdam II criteria or are diagnosed with UTUC under the age of 60 years. This is particularly important during the operative planning phase, where caution should be exercised when considering NU in patients with LS given the increased risk of recurrence in the contralateral kidney/ureter.¹⁴ Furthermore, the temporal lag between this patient's colorectal cancers demonstrates the need for ongoing surveillance in this cohort, preferably with guidance from a familial cancer clinic.

Learning points

- Wound recurrence following open surgery is an extremely uncommon but recognised event; this case highlights the need to pay particular attention to the wound area on follow-up examination and imaging.
- The development of multiple malignancies in a patient with strong family history of cancer should raise the suspicion of a familial cancer syndrome such as Lynch syndrome.
- Urologists should consider the possibility of Lynch syndrome in any patient with de novo upper tract urothelial carcinoma.

Acknowledgements Elements of this case report were presented at the 35th Congress of the Société Internationale d'Urologie (SIU), held in Melbourne in 2015. The authors would like to acknowledge the contributions of the Pathology Department at St Vincent's Hospital, in particular Dr Cesar Salinas-La Rosa and Professor Ken Opekin.

Contributors MJS, GRG and SLE were directly involved in treating the patient. MJS was involved in reviewing the literature and drafting the manuscript. GRG, TRS and SLE were involved in contributing to and reviewing the manuscript in their given field of expertise. All the authors reviewed and approved the final version of the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Rai BP, Shelley M, Coles B, *et al*. Surgical management for upper urinary tract transitional cell carcinoma (UUT-TCC): a systematic review. *BJU Int* 2012;110:1426–35.
- 2 Kadi N, Isherwood M, Al-Akara M, *et al*. Port-site metastasis after laparoscopic surgery for urological malignancy: forgotten or missed. *Adv Urol* 2012;2012:609531.
- 3 Iavazzo C, Madhuri K, Tailor A, *et al*. Incisional site metastasis in a patient with cervical carcinoma: a case report and review of the literature. *Case Rep Obstet Gynecol* 2012;2012:593732.
- 4 Saredi G, Di Pietro C, Spasciani R, *et al*. Tumor seeding after open nephroureterectomy for ureteral transitional cell carcinoma. *Tumori* 2008;94:600–1.
- 5 Pahlman L. The problem of port-site metastases after laparoscopic cancer surgery. *Ann Med* 1997;29:477–81.
- 6 Tsivian A, Sidi AA. Port site metastases in urological laparoscopic surgery. *J Urol* 2003;169:1213–18.
- 7 Ceelen W, Pattyn P, Mareel M. Surgery, wound healing, and metastasis: recent insights and clinical implications. *Crit Rev Oncol Hematol* 2014;89:16–26.
- 8 Vasen HF, Watson P, Mecklin JP, *et al*. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative group on HNPCC. *Gastroenterology* 1999;116:1453–6.
- 9 Kastrinos F, Syngal S. Screening patients with colorectal cancer for Lynch syndrome: what are we waiting for? *J Clin Oncol* 2012;30:1024–7.
- 10 Haraldsdottir S, Hampel H, Tomsic J, *et al*. Colon and endometrial cancers with mismatch repair deficiency can arise from somatic, rather than germline, mutations. *Gastroenterology* 2014;147:1308–16.e1.

- 11 Peltomäki P. Epigenetic mechanisms in the pathogenesis of Lynch syndrome. *Clin Genet* 2014;85:403–12.
- 12 Lynch HT, Lynch PM, Lanspa SJ, *et al.* Review of the Lynch syndrome: history, molecular genetics, screening, differential diagnosis, and medicolegal ramifications. *Clin Genet* 2009;76:1–18.
- 13 Mork M, Hubosky SG, Rouprêt M, *et al.* Lynch syndrome: a primer for urologists and panel recommendations. *J Urol* 2015.
- 14 Crockett DG, Wagner DG, Holmång S, *et al.* Upper urinary tract carcinoma in Lynch syndrome cases. *J Urol* 2011;185:1627–30.

Copyright 2016 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow