CASE REPORT

A rare complication of transitional cell carcinoma of the renal pelvis: parathyroid hormone-related peptide-induced hypercalcaemia

Eoin O Sullivan,¹ William Plant²

¹Department of Medicine, Cork University Hospital, Cork, Munster, Ireland
²Cork University Hospital, Cork, Munster, Ireland

Correspondence to
 Dr Eoin O Sullivan,
 eoindosullivan@gmail.com

Accepted 6 June 2014

SUMMARY

We describe a rare occurrence of parathyroid hormone-related peptide (PTHrp) associated hypercalcaemia with a recurrence of transitional cell carcinoma of the renal pelvis. Our patient presented with serum calcium of 3.9 mmol/L, PTH of 5 ng/L and a PTHrp of 9.8 pmol/L (<2 pmol/L). He had no evidence of metastatic disease. His hypercalcaemia responded to bisphosphonate therapy. He chose to be treated conservatively and died 5 weeks after presentation. This is the seventh such case described in the literature. PTHrp-induced hypercalcaemia is associated with a grave prognosis, with a mean survival of 65 days from presentation.

BACKGROUND

Transitional cell carcinoma (TCC) accounts for 7% of all renal tumours and current epidemiological trends suggest it is increasing in incidence.¹ In contrast to other solid organ tumours, hypercalcaemia is an uncommon complication of TCC.^{2–3} We describe a case of a patient with a rare mechanism of hypercalcaemia in the setting of transitional cell carcinoma. Only six cases of parathyroid hormone-related peptide (PTHrp) associated with TCC have been reported in the literature to date. It appears that the occurrence of PTHrp-related hypercalcaemia has some prognostic significance. Mean survival following occurrence of PTHrp-induced hypercalcaemia in the setting of TCC is 65 days (range 13–210). Our patient responded to conventional therapies for hypercalcaemia. In previous cases patients have required cytoreduction therapy to control serum calcium.

CASE PRESENTATION

A 59-year-old male was referred by his general practitioner to the emergency department with a 1-week history of lethargy, generalised weakness, confusion and abdominal pain.

He was 5 months post a right nephroureterectomy for T3 M0 N0 TCC of the renal pelvis. Serum calcium prior to surgery was normal.

He was a non-smoker, non-drinker, and had a background of hypertension, hypertriglyceridemia and type 2 diabetes.

His medications were:

- ▶ Aspirin 75 mg orally once daily,
- ▶ Ezetimibe 10 mg orally once daily
- ▶ Glimepiride 30 mg orally once daily
- ▶ Sitagliptin/metformin 50/850 mg orally once daily
- ▶ Olmesartan 20 mg orally once daily.

INVESTIGATIONS

His laboratory tests on arrival are listed below and in [table 1](#):

- ▶ Corrected calcium was 3.91 mmol/L (2.2–2.5)
- ▶ PTH was 5 ng/L (16–65 ng/L)
- ▶ PTHrp was 9.8 pmol/L (<2 pmol/L).

Urinary protein creatinine ratio was 5.2 (<0.2) indicating nephrotic range proteinuria. This may have indicated membranous nephropathy associated with the underlying malignancy, or a more gross disruption renal architecture with leakage of blood into the urinary tract.

Immunoglobulin/myeloma screen was negative.

CT thorax/abdomen/pelvis showed recurrence of disease in the right renal bed with local invasion into surrounding structures. There was no distant or metastatic disease. A nuclear medicine bone scan was negative for distant disease.

TREATMENT

Initial treatment was fluid resuscitation of 1 L of normal saline at 100 mL/h. This was followed by 2 L of Hartmann's over the subsequent 12 h. When his calcium failed to normalise with fluid therapy, 4 mg intravenous zoledronic acid was administered.

Within 72 h of bisphosphonate therapy his calcium had returned to normal.

OUTCOME AND FOLLOW-UP

Our patient's clinical status continued to deteriorate despite normalisation of his serum calcium. Although his symptoms of confusion and abdominal pain resolved, his mood worsened and he became bedbound. He became anorexic, nauseated, reported of generalised weakness and became cachectic. He declined chemotherapy and opted instead to return home with his family. He was attended to by community palliative services and was provided psychiatric support, antiemetic therapy and analgesia. He passed away 5 weeks after his initial presentation.

DISCUSSION

It is interesting to note our patient's normal serum calcium prior to surgery. This would suggest that the tumour cells only initiated their production of PTHrp when the tumour reoccurred. Of the six previous published cases, three describe PTHrp secretion in conjunction with other paraneoplastic-associated hormones, namely ectopic PTH secretion⁴ and granulocyte colony-stimulating factor.^{5–6} The remaining three cases describe isolated PTHrp

CrossMark

To cite: O Sullivan E, Plant W. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-202796

Table 1 The results of the patient's relevant blood tests

Na	138 mmol/L (137–145)	Alb	33 µmol/L (35–48)
K	4.9 mmol/L (3.6–5)	ALT	16 µ/L (7–56)
CL	106 mmol/L (98–105)	Alk phos	238 µ/L (53–128)
Ur	16 mmol/L (3–7)	Phos	0.6 mmol/L (0.8–1.5)
CR	160 µmol/L (68–90) (baseline 100)		

secretion.^{7–9} Therapies varied from cytoreduction to surgery, but were invariably associated with poor survival.

Learning points

- ▶ Parathyroid hormone-related peptide (PTHrp) in the setting of transitional cell carcinoma (TCC) is an extremely rare occurrence.
- ▶ Despite the novel mechanism, the hypercalcaemia can respond well to standard therapies.
- ▶ PTHrp in TCC has carried a universally grave prognosis thus far.
- ▶ Mean survival following occurrence of PTHrp-induced hypercalcaemia in TCC is 65 days.

Contributors EOS suggested the case report, performed background research and literature review, and wrote the script. WVP was the supervising physician involved in inpatient care and diagnosis of the patient. He reviewed the script and offered alterations and suggestions which were incorporated.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Jemal A, Siegel R, Ward E, *et al.* Cancer statistics. *CA Cancer J Clin* 2009;59:225–49.
- 2 Grubb RL, Collyer WC, Kibel AS. Transitional cell carcinoma of the renal pelvis associated with hypercalcemia in a patient with autosomal dominant polycystic kidney disease. *Urology* 2004;63:778–80.
- 3 Patel AB, Wilson L, Blick C, *et al.* Paraneoplastic hypercalcaemia associated with TCC of bladder. *ScientificWorldJournal* 2004;4:1069–70.
- 4 Eid W, Wheeler TM, Sharma MD. Recurrent hypercalcemia due to ectopic production of parathyroid hormone-related protein and intact parathyroid hormone in a single patient with multiple malignancies. *Endocrine Pract* 2004;10:125–8.
- 5 Hirasawa K, Kitamura T, Oka T, *et al.* Bladder tumor producing granulocyte colony-stimulating factor and parathyroid hormone related protein. *J Urol* 2002;167:2130.
- 6 Tsuchiya F, Ikeda I, Kanda F, *et al.* A case of bladder tumor producing granulocyte-colony stimulation factor and parathyroid hormone-related protein. *Hinyokika Kyo* 2001;47:873–6.
- 7 Matsuoka S, Miura Y, Kachi T, *et al.* Humoral hypercalcemia of malignancy associated with parathyroid hormone-related protein producing transitional cell carcinoma of the ureter. *Intern Med* 1994;33:107–9.
- 8 Maeda Y, Nakazawa H, Yoshimura N, *et al.* Bladder carcinoma presenting with hypercalcemia: a case report. *Hinyokika Kyo* 1997;43:137–40.
- 9 Chaudhary UB, Milling DL, Bissada NK. Transitional cell carcinoma of the bladder producing parathyroid hormone-related protein (PTHrP). *Can J Urol* 2004;11:2136–8.

Copyright 2014 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