CASE REPORT

Gastrointestinal stromal tumour in a recipient with kidney transplantation

Sertac Cimen,¹ Sanem Guler,¹ Romuald Panek,² Ian Alwayn¹¹Department of Surgery, Dalhousie University, Halifax, Canada²Department of Nephrology, Dalhousie University, Halifax, Canada

Correspondence to

Dr Ian Alwayn,
ian.alwayn@cdha.nshealth.ca

Accepted 7 May 2015

SUMMARY

Immunosuppression is associated with an increased risk of post-transplant malignancies. Gastrointestinal stromal tumours are the most common mesenchymal tumours of the gastrointestinal tract. However, they have seldom been reported recipient with transplantation. In this report, a 46-year-old woman, a recipient with kidney transplantation, who developed a gastric tumour is presented. Removal of this tumour required a partial gastrectomy. Histopathology and immunohistochemistry examinations revealed a high-risk gastric stromal tumour. Adjuvant imatinib mesylate treatment was initiated. There was no evidence of tumour recurrence at 12-month follow-up.

BACKGROUND

Efficient immunosuppression has reduced the incidence of graft failure in kidney transplant recipients.¹ Unfortunately, immunosuppression has been associated with an increased risk of post-transplant malignancies with skin cancer and lymphoproliferative disorders representing the most common de novo malignancies detected in renal transplant recipients.¹

Gastrointestinal stromal tumours (GIST) are the most common mesenchymal tumours of the gastrointestinal tract.² Despite this, GIST cases involving patients with transplantation have seldom been reported.^{3–4} In 2007, Agaimy *et al*³ reported the first two cases of GIST in renal transplant recipients. We present a third case of GIST in a recipient with kidney transplantation.

CASE PRESENTATION

A 46-year-old woman, a recipient with kidney transplantation, presented for a routine follow-up visit. She had end-stage renal failure due to hypertension and had received a cadaveric en bloc paediatric kidney transplant 18 years prior. Post-transplant maintenance immunosuppression therapy consisted of cyclosporine (CsA), azathioprine (AZA) and prednisone with which she had good graft function.

Physical examination revealed a hard, non-tender abdominal mass in the epigastrium.

INVESTIGATIONS

An abdominal ultrasound was obtained. A large vascular soft tissue mass was detected in the left upper quadrant (figure 1). Thoracoabdominopelvic CT scans with oral and intravenous contrast showed a 15 cm diameter abdominal tumour arising from the body of the stomach, located between the stomach and colon (figure 2). There was no evidence of

metastatic disease. A CT-guided biopsy demonstrated a spindle cell tumour consistent with GIST. Abdominal exploration confirmed the tumour as being connected to the greater curvature of the stomach; the tumour was removed in-toto requiring a partial gastrectomy. Final pathology revealed a fleshy, well-circumscribed GIST (figure 3A). The resection margin was free of tumour. There were 14 mitotic figures per 50 high power fields (hpf) (figure 3B). Immunohistochemistry (IHC) examination showed that tumour cells stained strongly positive for CD-117 (c-kit), CD-34 and vimentin; however, no staining was seen with s-100, desmin, actin and monokeratin (figure 3C).

Molecular genetic studies of exon 9, 11, 13 and 17 of the c-kit gene revealed mutation of exon 11 (c.1687_1722del) (p.11e563_Thr574del). Mutation analysis of the PDGFRA gene was inconclusive. Based on the tumour size (>10 cm) and the high mitotic activity (>10/hpf), this neoplasm was classified as high risk GIST.

DIFFERENTIAL DIAGNOSIS

- Leiomyoma
- Leiomyosarcoma
- Malignant fibrous histiocytoma
- Dedifferentiated liposarcoma

TREATMENT

Three-year adjuvant therapy with imatinib was recommended. Since imatinib is known to increase blood CsA levels, a reduced dose of 200 mg/day orally was initially started.

OUTCOME AND FOLLOW-UP

Trough CsA levels were followed closely in order to keep them in the range of 200–350 µg/L. Imatinib dose was increased to target (400 mg/day) 4 months after initiation of therapy. There was no evidence of tumour recurrence and the patient continued to have good graft function at 12-month follow-up. Her serum creatinine level was 124 µmol/L.

DISCUSSION

GIST is the most common mesenchymal tumour of the gastrointestinal tract, with an estimated incidence of 10 per million.⁵ It usually appears in patients above 50 years of age; whereas the highest incidence is observed in the fifth and the sixth decades of life.² Prevalence of GIST is similar in men and women.² Stomach and small bowel are predominant sites, but colon, rectum and oesophagus may also be involved.² It originates from the interstitial cells of Cajal and almost all GISTs have a

CrossMark

To cite: Cimen S, Guler S, Panek R, *et al*. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-207178

Figure 1 Ultrasound demonstrating a large vascular soft tissue mass in the left upper quadrant.

mutation in the tyrosine kinase receptor (KIT) or platelet derived growth factor receptor α (PDGFRA) genes.⁵ Approximately 95% of GISTs are positive for c-kit (CD-117) antigen, which is the specific defining immunohistochemical feature for this group of tumours.⁶ No risk factors or predisposing conditions have been identified.²⁻³ Gastrointestinal bleeding (50%) is the most common presentation, followed by abdominal pain (20–50%).⁴ Approximately a third is detected incidentally.⁴ Prognosis depends on the size of the tumour and number of mitoses per 50 high-power microscopic fields.² Approximately 25% of gastric and 50% of small intestinal GISTs are clinically malignant; the most common site of metastasis are the liver and lungs.⁶ According to the current clinical practice guidelines, surgery is the standard treatment option for low risk disease.⁷ Adjuvant treatment with tyrosine kinase inhibitor imatinib is proposed for patients with high risk GIST.²⁻⁷ Activating mutations of c-kit and PDGFRA are predictive of clinical response to imatinib.⁵⁻⁷

Although it is well-known that effective immunosuppression increases the incidence of post-transplant malignancies, it is uncommon to diagnose GIST in the organ transplant population.¹ Agaimy *et al*³ were the first to present two cases of GISTs in recipient with renal transplantation. They encountered two women, aged 59 and 58 years, who presented with non-specific abdominal pain, 40 and 96 months after kidney transplantation, respectively. Their first patient had a low-risk gastric GIST and remained disease-free 68 months postoperatively. However, they did not give any information regarding the fate of the renal graft. The second was more recent and had a high-risk small bowel GIST. Both tumours stained strongly for CD-117 (c-kit), however, genetic analysis was not performed. Although it has been suggested that viral infections do not appear to play a role

in the pathogenesis of GISTs, they examined Epstein-Barr virus (EBV) and human herpes virus 8 (HHV8) but could not find any evidence.⁸

Similarly, our patient was a middle-aged woman who had a tumour that stained strongly positive for c-kit. The pathological classification of this tumour was that of a high risk GIST. As such, we proceeded with genetic analysis and subsequent adjuvant imatinib treatment. Since viral infections have not been associated with GISTs, we did not test for EBV or HHV8.⁴

Tu *et al*⁹ presented a case of a rare extra-gastrointestinal stromal tumour (EGIST) located in the pelvic cavity of a patient with kidney transplantation. A 57-year-old woman was admitted due to non-specific abdominal pain 6 months after transplantation. Post-transplant IS consisted of CsA, mycophenolate mofetil and steroids. Final pathology revealed a low-risk EGIST that stained strongly for CD117 (c-kit). Sequence analysis of the c-kit and PDGFRA genes revealed a silent mutation of the PDGFRA gene. This neoplasm was classified as low risk and thus imatinib was not recommended. They also examined EBV and HHV8 but did not find any evidence. There was no evidence of tumour recurrence at 24-month follow-up. However, data regarding renal graft function were not given. In line with this case, our patient was also on CsA immunosuppression but presented significantly later post-transplant.

Saidi *et al*⁴ presented a case of GIST in a recipient with liver transplantation who was on tacrolimus and AZA for immunosuppression. A 54-year-old man underwent a routine colonoscopy 11 months after transplant, which revealed a 2.5 cm tumour located at the hepatic flexure. The patient underwent a right hemicolectomy. Final pathology revealed a well-circumscribed GIST, neoplastic cells of which stained strongly positive for c-kit. Based on the tumour size and mitotic activity,

Figure 2 Large, enhancing soft tissue mass (yellow arrows) inseparable from the stomach (black arrow).

Figure 3 (A) A 16 cm well-circumscribed serosalised tumour. There is a small-adhered wedge of gastric tissue at one end (indicated by an arrow). On cut section, the tumour has a variegated tan and lobulated appearance with soft texture (Bar =1 cm). (B) On microscopic examination, the tumour is seen to be composed of monomorphic spindle cells forming short fascicles. Its mitotic count is 7 per 5 mm² (H&E, ×200). A mitotic figure is indicated by an arrow. (C) IHC revealed neoplastic cells strongly and diffusely positive for c-kit (×200).

this neoplasm was classified as low-risk GIST. Therefore, genetic analysis was not performed and adjuvant imatinib treatment was

not recommended. There was no evidence of recurrent GIST during 18 months of follow-up. Consistent with our case, these authors did not search for EBV or HHV8. Their patient was also on AZA, as in our case, yet for a significantly shorter term before presentation with GIST.

Learning points

- ▶ Long-term follow-up with comprehensive physical examination is important in recipient with kidney transplantation for recognition of post-transplant malignancies.
- ▶ Although rare, gastrointestinal stromal tumours (GIST) should be included in the differential diagnosis whenever a mesenchymal tumour is encountered in a recipient with kidney transplantation.
- ▶ Immunohistochemical staining for c-kit (CD117) antigen is essential for diagnosis of GIST.
- ▶ Genetic analysis should be reserved for high-risk GIST cases.
- ▶ Surgery is the most effective treatment for GIST and long-term follow-up is necessary.

Acknowledgements The authors would like to thank Dr Weei-Yuan Huang and Dr Valerie Keough.

Contributors SC and SG participated in the sequence alignment and drafted the manuscript. RP and IA participated in its design and coordination. All authors read and approved the final manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Yildirim Y, Ozyilkan O, Emiroglu R, *et al*. Early diagnosis of cancer in renal transplant patients: a single center experience. *Asian Pac J Cancer Prev* 2006;7:336–9.
- 2 Cichoz-Lach H, Kasztelan-Szczerbinska B, Slomka M. Gastrointestinal stromal tumors: epidemiology, clinical picture, diagnosis, prognosis and treatment. *Pol Arch Med Wewn* 2008;118:216–21.
- 3 Agaimy A, Wunsch PH. Gastrointestinal stromal tumours (GIST) in kidney transplant recipients—a report of two cases. *Nephrol Dial Transplant* 2007;22:1489–90.
- 4 Saidi RF, Sepehr A, Cosimi AB, *et al*. Gastrointestinal stromal tumor in a liver transplant recipient. *Transplantation* 2008;85:1363.
- 5 Judson I. Gastrointestinal stromal tumours (GIST): biology and treatment. *Ann Oncol* 2002;13(Suppl 4):287–9.
- 6 Miettinen M, Lasota J. Gastrointestinal stromal tumors: review on morphology, molecular pathology, prognosis, and differential diagnosis. *Arch Pathol Lab Med* 2006;130:1466–78.
- 7 ESMO/European Sarcoma Network Working Group. Gastrointestinal stromal tumors: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2012;23(Suppl 7):vii49–55.
- 8 Su CC, Li CF, Liao YL, *et al*. Immunohistochemical and molecular assessment of human herpesvirus type 8 in gastrointestinal tumours. *J Clin Pathol* 2005;58:856–9.
- 9 Tu H, Li Q, Cai J, *et al*. Extragastrintestinal stromal tumor in a kidney transplant recipient. *Clin Exp Nephrol* 2012;16:350–3.

Copyright 2015 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