CASE REPORT

Successful treatment of bleeding large duodenal gastrointestinal stromal tumour in a patient under dual antiplatelet therapy after recent drug-eluting coronary stent implantation

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SUMMARY

We report a case of a 69-year-old man who started dual antiplatelet therapy (APT) with aspirin and clopidogrel after recent implantation of drug-eluting coronary stent and developed massive bleeding due to large duodenal gastrointestinal stromal tumour (GIST). Following endoscopic haemostasis and discontinuation of dual APT, neoadjuvant chemotherapy with imatinib was started under continuation of 'single' APT with aspirin. A good chemotherapeutic response was achieved without recurrence of bleeding, and subsequent less invasive surgical resection of the tumour was performed, while preoperative single APT was continued for prevention of stent thrombosis. The patient recovered well without any thromboembolic or bleeding events. Neoadjuvant imatinib therapy and subsequent less invasive surgery under continuation of APT is one of the preferred approaches for patients with duodenal GIST with severe thromboembolic comorbidities, as in the current case.

BACKGROUND

Patients with large duodenal gastrointestinal stromal tumours (GISTs) sometimes require a highly invasive procedure such as pancreaticoduodenectomy for complete resection.^{1 2} Currently, the optimal strategy for duodenal GIST remains to be undetermined, especially in the case of patients with critical cardiovascular comorbidities. We have to balance perioperative risks and oncological risk/benefit to make a therapeutic decision. We report a case of bleeding large duodenal GIST found after starting dual antiplatelet therapy (APT) for drug-eluting coronary stent (DES) implantation, which was successfully treated with neoadjuvant imatinib chemotherapy and subsequent less invasive surgical resection under continuation of single APT with aspirin.

CASE PRESENTATION

A 69-year-old Japanese man developed severe anaemia and tarry stool. He had been receiving dual APT with aspirin and clopidogrel for 3 months after implantation of biolimus-eluting stent into his left anterior descending coronary artery. His haemoglobin levels decreased to 5.8 g/dL and he received blood transfusions. Enhanced CT scan demonstrated a well-demarcated, heterogeneously enhanced tumour of the duodenum, measuring 5.3 cm in diameter (figure 1), without any evidence of distant

Figure 1 An enhanced CT scan demonstrating a well-demarcated, heterogeneously enhanced tumour of the duodenum, measuring 5.3 cm in diameter (white arrow head).

metastases. Gastrointestinal fiberoscopy showed a bleeding ulcerative submucosal lesion in the second portion of the duodenum (figure 2). Biopsy and endoscopic haemostasis was performed, and histological and immunohistochemical examinations revealed that the tumour was composed of spindle cells which were positively stained for CD117 (c-Kit), establishing the diagnosis of duodenal GIST (figure 3).

Figure 2 Gastrointestinal fiberoscopy showing a bleeding ulcerative submucosal lesion in the second portion of the duodenum (black arrow head).

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Figure 3 (A) Photomicrograph of the biopsy specimen from the duodenal lesion (H&E stain; original magnification $\times 10$). (B) Immunohistochemistry showing the tumour cells were positively stained for CD117 (c-Kit), establishing the diagnosis of duodenal gastrointestinal stromal tumour.

TREATMENT

Considering the size and location of the tumour, we thought the tumour requires pancreaticoduodenectomy for complete resection, while elective procedures for which there is significant risk of perioperative or postoperative bleeding should be deferred until 12 months after DES implantation for prevention of stent thrombosis.³ Surgeons and gastroenterologists discussed together with cardiologists how best to manage the current patient, and it was finally decided that discontinuation of dual APT to prevent recurrence of bleeding, neoadjuvant chemotherapy with imatinib and subsequent surgical resection under single APT with aspirin were scheduled. The patient was informed regarding risks, benefits and alternative therapeutic modalities, who agreed with the plan.

After the recovery from severe anaemia and hypovolaemia, single APT with aspirin was started instead of dual APT, and chemotherapy with imatinib (400 mg/body) was introduced and continued for 1 month. A follow-up CT showed dramatic decrease in the size of the tumour (figure 4), without recurrence of bleeding events. Considering a possible risk of tumour perforation, surgical tumour resection was scheduled at that point, under continuation of preoperative single aspirin APT.

Laparotomy revealed the collapsed tumour in the second portion of the duodenum which was firmly adhered to the

Figure 4 A follow-up CT after preoperative imatinib chemotherapy showing a decrease in the size of the tumour, with its wall being thinned (white arrow head).

Figure 5 Intraoperative photograph showed the collapsed duodenal tumour, measuring about 3 cm in size (white arrow head).

gallbladder (figure 5). Since downsizing of the tumour by neoadjuvant chemotherapy was achieved, tumour resection was possible only by cholecystectomy and wedge resection of the duodenal wall which was primary closed, and pancreaticoduodenectomy could be avoided. By meticulous dissection and pinpoint haemostasis, no severe intraoperative bleeding was encountered, and postoperative management was introduced in the intensive care unit, without any immediate critical complications.

A histopathological analysis confirmed GIST with a mitotic count < 1 mitosis/50 high power fields, measuring 4.5 cm in maximum diameter. The surgical margin was negative for malignancy. Although he was classed as low risk according to Fletcher's criteria⁴ at postoperative pathological assessment, the status before imatinib treatment could be classed as intermediate or high risk, because comparison of pre-imatinib-treatment and post-imatinib-treatment specimens showed changes in the mitotic count.⁵

OUTCOME AND FOLLOW-UP

The patient recovered soon postoperatively without any complications except for minor abdominal haemorrhage requiring 9-day postoperative discontinuation of APT, but no stent thrombosis occurred. He started adjuvant chemotherapy with imatinib postoperatively, and still remained well without any evidence of recurrence 12 months after his operation.

DISCUSSION

The current case involved a dilemma of how to manage two different critical conditions; treatment of the large duodenal GIST with bleeding tendency and prevention of stent thrombosis after recent DES implantation. In patients with DES implantation, elective surgery with a risk of perioperative or postoperative bleeding should be suspended until the patients have completed an appropriate course of APT (12 months after DES implantation if they are not at high risk of bleeding),³ for the purpose of prevention of stent thrombosis, a life-threatening complication.^{6,7} On the other hand, we have demonstrated the usefulness of our perioperative antiplatelet management protocol for patients with high risks of thromboembolic complications, which included preoperative continuation of single APT with aspirin instead of dual APT.⁸ Therefore, in the current case, continuation of not dual APT but 'single' APT with aspirin is thought to be acceptable during the therapeutic intervention for the bleeding duodenal GIST.

From the point of surgical treatment, pancreaticoduodenectomy, a highly invasive procedure, might be required for complete resection of a large duodenal GIST,^{1,2} which would

expose the APT-burdened patient to high perioperative risks of bleeding and thromboembolic complications. National Comprehensive Cancer Network (NCCN) guideline recommends preoperative imatinib, a synthetic selective tyrosine kinase inhibitor, as the primary treatment of resectable GIST in patients with a risk of significant morbidity.⁹ In the present case, considering the bleeding tendency of the tumour, neoadjuvant imatinib therapy and subsequent surgical resection were scheduled with continuation of 'single' APT. Preoperative treatment showed a dramatic decrease in size of the tumour, and the tumour was successfully resected by less invasive partial resection of the duodenum without any major bleeding or thromboembolic complications. Thus, this strategy is one of the promising approaches for compromised patients as in our case.

In the current case, preoperative imatinib therapy showed dramatic therapeutic effect but a possible tumour perforation was suggested. While good response in neoadjuvant imatinib therapy is expected,¹⁰ severe adverse effects such as perforation or agranulocytosis with sepsis after imatinib therapy is reported.¹¹ Tumour perforation can worsen prognosis probably due to peritoneal dissemination.¹² Therefore, not only follow-up CT with short interval, but also the decision of appropriate timing of surgical procedure is crucial in this situation.

Learning points

- ▶ An optimal strategy for duodenal gastrointestinal tumours (GISTs) remains to be undetermined, especially in case of patients with critical cardiovascular comorbidities.
- ▶ We have to balance perioperative risks and oncological risk/benefit to make a therapeutic decision in such a difficult situation.
- ▶ Combination of neoadjuvant imatinib therapy and subsequent less invasive surgery under continuation of single antiplatelet therapy is one of the preferred approaches for bleeding duodenal GIST patients with a high risk of stent thrombosis.

Contributors KF and TF operated on the patient. KF, TF and SK managed the patient perioperatively. KF prepared the manuscript and TF and AT reviewed it.

Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Beham A, Schaefer IM, Cameron S, *et al.* Duodenal GIST: a single center experience. *Int J Colorectal Dis* 2013;28:581–90.
- 2 Hoepfner J, Kulemann B, Marjanovic G, *et al.* Limited resection for duodenal gastrointestinal stromal tumors: surgical management and clinical outcome. *World J Gastrointest Surg* 2013;5:16–21.
- 3 Grines CL, Bonow RO, Casey JDE, *et al.* Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, With Representation From the American College of Physicians. *J Am Coll Cardiol* 2007;49:734–9.
- 4 Fletcher CDM, Berman JJ, Corless C, *et al.* Diagnosis of gastrointestinal stromal tumors: a consensus approach. *Human Pathol* 2002;33:459–65.
- 5 Bauer S, Hartmann JT, de Wit M, *et al.* Resection of residual disease in patients with metastatic gastrointestinal stromal tumors responding to treatment with imatinib. *Int J Cancer* 2005;117:316–25.
- 6 Iakovou I, Schmidt T, Bonizzi E, *et al.* Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. *JAMA* 2005;293:2126–30.
- 7 de la Torre-Hernandez JM, Alfonso F, Hernandez F, *et al.* Drug-eluting stent thrombosis: results from the multicenter Spanish registry ESTROFA (Estudio Español sobre TROMbosis de stents FArmacoactivos). *J Am Coll Cardiol* 2008;51:986–90.
- 8 Fujikawa T, Tanaka A, Abe T, *et al.* Does Antiplatelet therapy affect outcomes of patients receiving abdominal laparoscopic surgery? Lessons from more than 1,000 laparoscopic operations in a single tertiary referral hospital. *J Am Coll Surg* 2013;217:1044–53.
- 9 von Mehren M, Benjamin RS, Bui MM, *et al.* Soft tissue sarcoma, version 2.2012: featured updates to the NCCN guidelines. *J Natl Compr Can Netw* 2012;10:951–60.
- 10 Blesius A, Cassier PA, Bertucci F, *et al.* Neoadjuvant imatinib in patients with locally advanced non metastatic GIST in the prospective BFR14 trial. *BMC Cancer* 2011;11:72.
- 11 Åhlén J, Westerdaal J, Zedenius J, *et al.* Side-effects from imatinib treatment of advanced GIST—associated with a better outcome. *Journal of Cancer Therapeutics and Research* 2012;1. doi:http://dx.doi.org/10.7243/2049-7962-1-11
- 12 Wu TJ, Lee LY, Yeh CN, *et al.* Surgical treatment and prognostic analysis for gastrointestinal stromal tumors (GISTs) of the small intestine: before the era of imatinib mesylate. *BMC Gastroenterol* 2006;6:29.

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