CASE REPORT

Acute coronary artery thrombosis and vasospasm following capecitabine in conjunction with oxaliplatin treatment for cancer

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SUMMARY

Oral capecitabine is a prodrug of 5-fluorouracil that has been used into the management of multiple cancers because of the convenience of administration and efficacy at least comparable with 5-fluorouracil. While cardiac complications associated with the use of 5-fluorouracil are well-documented, capecitabine-induced acute coronary syndrome has rarely been reported and often attributed to coronary vasospasm. We report a patient presented with acute coronary syndrome secondary to thrombotic coronary occlusion following treatment with oral capecitabine and intravenous oxaliplatin after resection of non-metastatic, node positive colon carcinoma. Capecitabine may induce acute coronary thrombotic occlusion in addition to coronary vasospasm.

BACKGROUND

This case demonstrates the importance of primary percutaneous coronary intervention (PPCI) in the setting of capecitabine-induced acute coronary syndrome, suggesting that not all the myocardial infarctions associated with capecitabine are caused by vasospasm and that acute thrombotic occlusion in these cases with no known risk factors for coronary artery disease could potentially be catastrophic.

CASE PRESENTATION

A 35-year-old woman, with no history of cardiovascular disease and no predisposing factors for coronary artery disease was admitted as a PPCI call with a left anterior descending coronary artery (LAD) ST-elevation myocardial infarction (STEMI). The pain was severe and started 60 min prior to admission. Six weeks earlier, she was admitted as an emergency with an intussusception associated with a pT1 N1b colonic carcinoma and underwent laparoscopic left hemicolectomy. Postoperatively, she was initiated on standard chemotherapy with an initial infusion of oxaliplatin (130 mg/m²) followed by a 14-day long course of oral capecitabine (1000 mg/m²/twice daily), standard dose so called 'CAPOX' or 'XELOX' regimen. Three days after the initiation of capecitabine however, she had 3–4 transient episodes of chest pain of 2–10 min duration, which resolved spontaneously. Four days later, while she was still taking capecitabine, she presented in A&E with STEMI. On admission, she

was haemodynamically stable, normotensive and had a normal cardiovascular examination.

INVESTIGATIONS

Electrocardiogram showed sinus rhythm with ST-segment elevation in leads II and III and hyperacute T wave changes in leads aVF and V3 to V6 (figure 1A). Her admission troponin was elevated at 57 ng/mL. She received 600 mg clopidogrel, 4000 units heparin, 160 mg aspirin and nitrates prior to coronary intervention. Coronary angiography showed total thrombotic occlusion of the distal LAD with grade 0 thrombolysis in myocardial infarction (TIMI) flow (figure 2A, B and E) and a proximal vasospasm (figure 2D), which relieved by giving nitrates prior to crossing the thrombotic lesion. The right coronary artery was normal (figure 2C).

TREATMENT

Immediate thrombus aspiration was performed with no stent deployed. TIMI three flow restored (figure 2F), note distal tip of LAD was still occluded. After PPCI the ST segment normalised and T wave changes resolved (figure 1B, C).

OUTCOME AND FOLLOW-UP

Echocardiography following intervention showed normal left ventricular volumes, localised apical dyskinesia with an ejection fraction of 82%, normal valves and no pericardial effusion. Capecitabine, a drug with known cardiotoxic properties, was considered as a triggering factor for STEMI and after consultation with her oncologist, the drug was discontinued.

DISCUSSION

Capecitabine (Xeloda) is an orally administered prodrug of 5-FU. Capecitabine is an established treatment for several cancer types as a single agent or in combination with a number of other agents and has replaced intravenous 5-FU to some extent in patients with early and metastatic colorectal cancer.¹ The toxic effect of intravenous 5-FU on the coronary endothelium and myocardium is rare but can lead to death following MI, ventricular arrhythmias.² The incidence of cardiotoxicity following capecitabine was comparable to that of 5-FU in a retrospective analysis of studies performed in patients treated for metastatic breast and colon cancer.³ A number of case reports of cardio-

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Figure 1 The ECG on admission. (A) showing ST-segment elevation in leads II and III and hyperacute T wave changes in leads aVF and V3–V6, consistent with transmural myocardial ischaemia in the territory of a dominant left coronary artery. Subsequent ECG's showing resolution of ST-segment elevation and T-waves changes directly, (B) and 24 h (C) after primary percutaneous coronary intervention (25 mm/s, 10 mm/mV).

toxicity using oral 5-FU analogue capecitabine have been published^{14–19} but the pathophysiology of cardiac injury remains unclear. All suggested, however the possibility of vasospasm and all had normal coronary angiography. Like ours, just one other case report presented a patient with acute coronary thrombosis, presumably attributed to capecitabine,²⁰ but a causal link may not be conclusive. Cardiac effects are dose dependent and can occur early within 24 h after taking the drug. From animal models, a direct toxic effect on the coronary endothelium, or toxic myocarditis with vasospasm, have been proposed as possible mechanisms. Treatment with nitroglycerin or calcium channel blockers, have not proved to be consistently effective for relieving angina in affected patients suggesting that other mechanisms other than coronary vasospasm be responsible.^{2 21 22}

Learning points

- In conclusion, capecitabine is extensively used for the treatment of multiple cancer types. The possibility of inducing acute coronary thrombotic occlusion and vasospasm has been highlighted.
- We consider that patients under capecitabine treatment should be referred for primary percutaneous coronary intervention if they experience acute coronary events, as coronary vasospasm is not always the only underlying mechanism and dismissing the possibility of thrombotic occlusion in these cases could be catastrophic for patient.

Figure 2 Selective left coronary angiogram and right coronary angiogram taken before (A–E) and during (F) angioplasty. A thrombotic occlusion was present at distal left anterior descending coronary artery (LAD; white arrows A, B and E), and right coronary artery was normal (C). Thrombolysis in myocardial infarction three flow restored after primary percutaneous coronary intervention (F), note distal tip of LAD was still occluded. Note coronary vasospasm relieved by giving nitrates prior to crossing the thrombotic lesion (black arrow D).

Contributors ODaD was involved in writing the case report. SC advised on chemotherapy aspects. PN conceived and instigated the case report.

Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Scheithauer W, McKendrick J, Begbie S, *et al.* Oral capecitabine as an alternative to i.v. 5-fluorouracil-based adjuvant therapy for colon cancer: safety results of a randomized, phase III trial. *Ann Oncol* 2003;14:1735–43.
- 2 Kosmas C, Kallistratos MS, Kopterides P, *et al.* Cardiotoxicity of fluoropyrimidines in different schedules of administration: a prospective study. *J Cancer Res Clin Oncol* 2008;134:75–82.
- 3 Van Cutsem E, Hoff PM, Blum JL, *et al.* Incidence of cardiotoxicity with the oral fluoropyrimidine capecitabine is typical of that reported with 5-fluorouracil. *Ann Oncol* 2002;13:484–5.
- 4 Scott PA, Ferchow L, Hobson A, *et al.* Coronary spasm induced by capecitabine mimicks ST elevation myocardial infarction. *Emerg Med J* 2008;25:699–700.
- 5 Goldsmith YB, Roistacher N, Baum MS. Capecitabine-induced coronary vasospasm. *J Clin Oncol* 2008;26:3802–4.
- 6 Papadopoulos CA, Wilson H. Capecitabine-associated coronary vasospasm: a case report. *Emerg Med J* 2008;25:307–9.
- 7 Arbea L, Coma-Canella I, Martinez-Monge R, *et al.* A case of capecitabine-induced coronary microspasm in a patient with rectal cancer. *World J Gastroenterol* 2007;13:2135–7.
- 8 van Halteren HK, Liem AH, Planting AS. [Myocardial ischaemia as a result of treatment with capecitabine]. *Ned Tijdschr Geneesk* 2007;151:1469–73.
- 9 Wijesinghe N, Thompson PI, McAlister H. Acute coronary syndrome induced by capecitabine therapy. *Heart Lung Circ* 2006;15:337–9.
- 10 Sestito A, Sgueglia GA, Pozzo C, *et al.* Coronary artery spasm induced by capecitabine. *J Cardiovasc Med* 2006;7:136–8.
- 11 Rizvi AA, Schauer P, Owlia D, *et al.* Capecitabine-induced coronary vasospasm—a case report. *Angiology* 2004;55:93–7.
- 12 Frickhofen N, Beck FJ, Jung B, *et al.* Capecitabine can induce acute coronary syndrome similar to 5-fluorouracil. *Ann Oncol* 2002;13:797–801.
- 13 Gorgulu S, Celik S, Tezel T. A case of coronary spasm induced by 5-fluorouracil. *Acta Cardiol* 2002;57:381–3.
- 14 Schnetzler B, Popova N, Collao Lamb C, *et al.* Coronary spasm induced by capecitabine. *Ann Oncol* 2001;12:723–4.
- 15 Ang C, Kornbluth M, Thirlwell MP, *et al.* Capecitabine-induced cardiotoxicity: case report and review of the literature. *Curr Oncol* 2010;17:59–63.
- 16 Camaro C, Danse PW, Bosker HA. Acute chest pain in a patient treated with capecitabine. *Neth Heart J* 2009;17:288–91.

- 17 Cardinale D, Colombo A, Colombo N. Acute coronary syndrome induced by oral capecitabine. *Can J Cardiol* 2006;22:251–3.
- 18 Golias C, Dimitriadis G, Dimitriadis D, *et al.* Acute presentation of vasospastic angina induced by oral capecitabine: a case report. *J Med Case Rep* 2014;8:18.
- 19 Marti V, Monell J, Seixo F, *et al.* [Acute coronary syndrome during oral capecitabine monotherapy]. *Rev Esp Cardiol* 2008;61:548–9.
- 20 Guvenç TS, Celiker E, Özcan KS, *et al.* Acute myocardial infarction after capecitabine treatment: not always vasospasm is responsible. *Chin Med J (Engl)* 2012;125:3349–51.
- 21 Robben NC, Pippas AW, Moore JO. The syndrome of 5-fluorouracil cardiotoxicity. An elusive cardiopathy. *Cancer* 1993;71:493–509.
- 22 Eskilsson J, Albertsson M. Failure of preventing 5-fluorouracil cardiotoxicity by prophylactic treatment with verapamil. *Acta Oncol* 1990;29:1001–3.

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