An unusual case of chronic coronary artery dissection: Did cisplatin play a role?

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Spontaneous coronary artery dissection is an unusual cause of acute myocardial ischemia. The natural history of spontaneous coronary artery dissection that persists on angiography after the acute event has not been well characterized. A case of a 36-year-old man who presented with monomorphic ventricular tachycardia 12 years following a myocardial infarction that occurred during his last course of bleomycin-etoposide-cisplatin therapy for testicular cancer is reported. On further investigation, coronary angiography revealed a long chronic dissection of the right coronary artery. The patient was successfully treated with medical management and insertion of an implantable cardioverter defibrillator. The case also highlights the increased cardiovascular morbidity in testicular cancer survivors and evokes the possibility of mechanisms of myocardial ischemia other than atherosclerotic disease in these young patients.

Key Words: Cisplatin; Coronary artery dissection; Myocardial infarction; Ventricular tachycardia

Spontaneous coronary artery dissection (SCAD) is an unusual cause of acute myocardial ischemia (1). It is more common in younger patients and in women, and has a propensity to affect patients without traditional cardiovascular risk factors (2). The tendency to affect women in high estrogenic states suggests that the hormonal and thrombogenic status of the patient may play etiological roles in SCAD. Similar factors have been implicated in increased cardiovascular event rates observed in young patients undergoing chemotherapy for testicular cancer (3). Despite this, no cases of SCAD occurring during cisplatin-based chemotherapy for testicular cancer have been reported.

The presentation, outcome and management of acute spontaneous coronary artery dissection have been described extensively (4-8). In all of these reports, there was either no angiographic follow-up of patients who survived the acute event or follow-up angiography demonstrated complete healing of the dissection. The long-term outcome of the dissection that persists is less well described (9,10).

We report a case of chronic coronary artery dissection that had its onset during a course of bleomycin-etoposide-cisplatin therapy for testicular cancer. The implications of testicular cancer and chemotherapy, and the significance of chronic coronary artery dissection persistent on angiography will be discussed.

CASE PRESENTATION

A 36-year-old man presented with a history of lightheadedness, shortness of breath and left-sided chest tightness after several minutes of playing hockey. Emergency medical services arrived at the scene and found the patient in monomorphic ventricular tachycardia at approximately 300 beats/min (Figure 1). The patient underwent electrical

Un cas inhabituel de dissection chronique de l'artère coronaire : La cisplatine est-elle en cause ?

La dissection spontanée de l'artère coronaire est une cause inhabituelle d'ischémie aiguë du myocarde. L'évolution naturelle de la dissection spontanée de l'artère coronaire qui persiste à l'angiographie après l'événement aigu n'est pas bien caractérisée. Est exposé le cas d'un homme de 36 ans qui a consulté à cause d'une tachycardie ventriculaire monomorphe 12 ans après un infarctus du myocarde étant survenu pendant la dernière série d'un traitement à la bléomycine-étoposide-cisplatine contre un cancer du testicule. À l'exploration, l'angiographie coronaire a révélé une longue dissection chronique de l'artère coronaire droite. Le patient a subi un traitement réussi par prise en charge médicale et insertion d'un défibrillateur à synchronisation automatique. Ce cas met également en lumière la morbidité cardiovasculaire accrue chez les survivants du cancer du testicule et évoque la possibilité d'autres mécanismes d'ischémie du myocarde que l'athérosclérose chez ces jeunes patients.

cardioversion, with almost immediate resolution of his symptoms. On admission to a local hospital, his troponin I peaked at 0.6 µg/L (10 times the upper limit of normal), and his electrocardiogram (ECG) showed significant Q waves in leads II, III and AVF, as well as ST depression in the inferolateral leads. The Q waves in the inferior leads were unchanged from previous ECGs recorded since July 1994. At the time of the current presentation, the patient was taking ramipril and Lipitor (Pfizer, Canada). He did not smoke and rarely used alcohol. He was started on acetylsalicylic acid, clopidogrel, enoxaparin and metoprolol by the referring centre, and was transferred to a tertiary care centre for further investigation.

His medical history was relevant. At the age of 24 years he developed testicular cancer, which was treated with four cycles of chemotherapy following orchiectomy. During his last course of bleomycin-etoposide-cisplatin chemotherapy, the patient developed left chest, neck and shoulder discomfort, and presented to the hospital 12 h later. Serial ECGs revealed the development of a Q wave inferior infarction and poor R wave progression across precordial leads on serial tracings. He did not receive thrombolysis, and cardiac catheterization was not performed. He was sent home on acetylsalicylic acid. During follow-up over the years, ramipril and statin therapy were added. He returned to an active lifestyle, which included recreational ice hockey.

On transfer to the tertiary care hospital, the patient was alert and oriented. His blood pressure was 108/78 mmHg, and his heart rate was 86 beats/min and regular. His respiratory rate was 20 breaths/min. A cardiac examination revealed normal jugular venous pressure and normal heart sounds. He had a midline abdominal scar corresponding to his previous staging laparotomy. Bilateral peripheral pulses were

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Figure 1) Electrocardiographic tracing of the ventricular tachycardia recorded during the initial patient assessment and post-shock

Figure 2) Right anterior oblique projection of the right coronary artery showing chronic right coronary artery dissection (between the two arrows)

present, and there was no ankle edema. The remainder of the physical examination was unremarkable.

A coronary angiogram revealed a radiolucent linear streak resembling a 'double lumen' appearance through the right coronary artery, characteristic of chronic coronary artery dissection (Figure 2). An exercise nuclear sestamibi test showed large inferior and lateral wall defects with minimal reversibility. The patient received an implantable cardioverter defibrillator for the secondary prevention of sudden cardiac death and was discharged home in stable condition. During the six-month follow-up, the patient had multiple recurrent episodes of ventricular tachycardia and was treated with antitachycardic pacing but without defibrillation.

DISCUSSION

The present patient was the first reported case of SCAD occurring in the context of chemotherapy for testicular cancer. It is interesting to speculate as to the mechanism of myocardial infarction (MI) in a 24-year-old man. Testicular cancer patients are at increased risk of myocardial ischemia and infarction, particularly in the context of chemotherapy (3). Cisplatin has been implicated in ischemic events occurring during or shortly after completion of bleomycin-etoposide-cisplatin therapy, even when other coronary risk factors are lacking (3). Mechanisms of cisplatin-related MI include diffuse coronary vasospasm, fibrous intimal proliferation and perturbations of the clotting system (3). A similar mechanism of SCAD has been reported with the use of the chemotherapeutic agent 5-fluorouracil (5-FU). Abbot et al (9) reported the case of a 39-year-old woman

who presented with an ST segment elevation MI while undergoing 5-FU treatment for cervical cancer. Angiography demonstrated the presence of an extensive coronary artery dissection, which, the authors postulated, was at least partially the result of 5-FU-precipitated vasospasm and hormonal changes related to pelvic radiation (9). Similarly, cisplatin-induced coronary spasm, thrombogenesis and the altered hormonal milieu after the orchiectomy might have precipitated SCAD and the consequent myocardial infarction in our case.

SCAD involves hemorrhagic separation of the media, resulting in a false lumen that may heal spontaneously or occlude the true lumen, resulting in distal ischemia (3). Some may occlude, some may thrombose the false lumen, and a few will re-endothelialize and become chronic, with two lumens. To our knowledge, only two other cases of angiographically persistent coronary artery dissection of similar duration (10 years or longer) have been reported in the literature to date. Kay and Williams (10) reported the case of a 48-year-old man who remained asymptomatic for 16 years after initially presenting with a long right coronary artery dissection and unstable angina. Successful angioplasty and stenting of the angiographically unchanged chronic coronary artery dissection was undertaken 16 years after the original event, when the patient presented once again with unstable angina and a positive exercise stress test (10). Osaki et al (11) described the case of a 58-year-old man originally presenting with MI and SCAD managed conservatively with medication. On 10-year follow-up, there was no recurrence of cardiac ischemia, and repeat angiography showed that the dissection had remained unchanged (11). The authors speculated that following the acute event, the residual dissection did not result in sufficient obstruction of flow to cause further ischemia. These two cases, along with the present case, demonstrate that extensive SCAD may become chronic and remain asymptomatic for a prolonged period.

Coronary dissection secondary to angioplasty involve the disruption of the coronary intima. In iatrogenic coronary artery dissection, the lesion may be propagated by subintimal injection of contrast and retrograde dispersion of contrast or blood. Limited dissections with a normal flow pattern following percutaneous intervention with balloon angioplasty (without stenting) generally tend to heal over time. However, as with SCAD, the outcome of extensive dissection is variable (12). Some may go on to acute closure and infarction, some may heal completely (13) and others may persist indefinitely, although, to our knowledge, published evidence for the latter is lacking. In the present era, acute vessel closure secondary to iatrogenic coronary artery dissection occurred in up to 11% of all elective percutaneous transcatheter coronary angioplasties (14). Given the uncertainty in predicting the behaviour of major dissection following angioplasty, stent deployment is the current standard of practice.

The monomorphic nature of the ventricular tachycardia episode makes it likely that the arrhythmogenic focus was myocardial scarring due to the original transmural MI. Therefore, the patient was medically managed and received an implantable cardioverter defibrillator as secondary prophylaxis. The finding of only minimal reversibility of myocardial perfusion defect in the inferior territory indicates that there was adequate flow through the two lumens of the chronic dissection and that the attending risks associated with percutaneous intervention of the dissection (for example, propagation of the

dissection, in-stent restenosis, etc) outweighed the likely minimal benefit gained from this intervention.

In conclusion, the present case demonstrates the potential for cisplatin-induced mechanisms underlying SCAD when patients with testicular cancer present with acute coronary syndromes. The case also illustrates that angiographically persistent coronary artery dissection may remain clinically silent for many years.

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