

## CASE REPORT

## A rare cause of chest pain in a cancer patient

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It is well known that cancer and hypercoagulability go hand in hand. Most thromboembolism is venous in nature although arterial thrombosis can occur. Arterial thrombosis secondary to malignancy is usually seen in the lower extremities; however, it can also be seen elsewhere. This is a case of bronchogenic carcinoma with no history of typical atherosclerotic risk factors including smoking, diabetes mellitus, hypertension, or hyperlipidemia presented with chest pain and was found to have an acute ST segment elevation myocardial infarction. Coronary angiography showed a large thrombus in the left anterior descending artery in the absence of any atherosclerotic lesions. Malignancy is considered to be the major contributing factor for this myocardial infarction in the absence of both atherosclerotic risk factors and atherosclerotic lesions in the coronary angiography. We will focus on the relationship between cancer and thrombosis with special emphasis on arterial thromboembolism with subsequent development of myocardial infarction.

Keywords: *cancer; arterial thrombosis; coronary artery disease*

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Received: 3 January 2016; Revised: 20 February 2016; Accepted: 26 February 2016; Published: 25 April 2016

Cancer is a multisystem disease, and one of the most often affected systems is the hemostatic system; in turn, the most common hemostatic manifestation is a thrombotic event (1). The relationship between cancer and thrombosis has been extensively studied over the past century (2), but most research has been directed toward venous rather than arterial thromboembolism (3). Henceforth, we discuss a case of coronary artery thrombosis in a patient with bronchogenic carcinoma presenting with an acute myocardial infarction, with emphasis on arterial thromboembolism in cancer patients.

### Case presentation

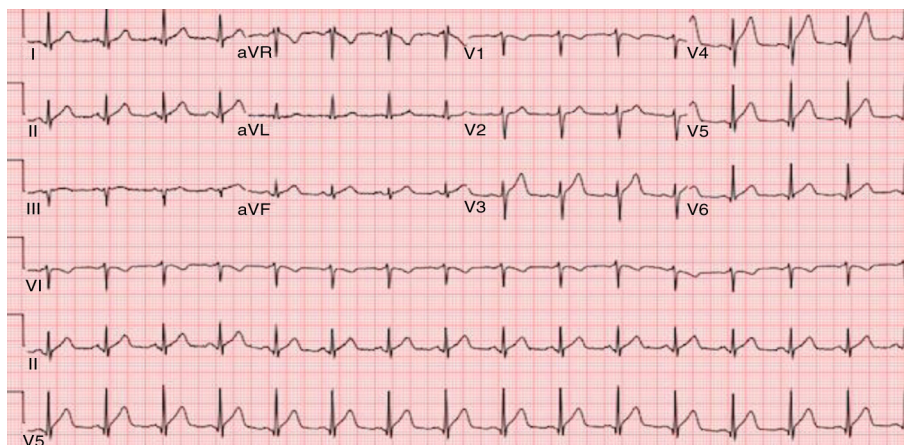
A 42-year-old Caucasian man on chemotherapy with carboplatin and paclitaxel for bronchogenic carcinoma, metastatic to the bone, presented to the Emergency Department complaining of sudden onset of chest pain for 1 h. The patient described the pain as constant, pressure like, located mainly to the retrosternal region, radiating to the neck, and not relieved by over the counter analgesics. He denied experiencing any similar episodes in the past. Past medical history was otherwise unremarkable; the only additional medication he was taking was ondansetron on an as-needed basis for chemotherapy-induced nausea and vomiting. Family history was negative for premature coronary artery disease, blood dyscrasia, and/or throm-

boembolic events. The patient denied smoking cigarettes, drinking alcohol, or using any recreational drugs.

Initial vital signs were normal except for mildly elevated blood pressure (blood pressure 145/85 mmHg, temperature 97.3°F, heart rate 68 bpm, respiratory rate 18, 98% arterial oxygen saturation on room air). Complete physical examination was unremarkable. Blood work included complete blood count, basal metabolic panel, lipid panel as well as one set of troponin T, and all were within normal limits.

Electrocardiogram showed ST segment elevation in leads V3 and V4 (Fig. 1); the patient was loaded with aspirin and clopidogrel and rushed to the cardiac catheterization laboratory. Coronary angiography showed a proximal thrombus in the left anterior descending artery with 80% occlusion and embolization with occlusion of the distal portion of the vessel (Fig. 2). Thrombectomy of the proximal thrombus was achieved with no evidence of residual lesions (Fig. 3). Surprisingly, there were no atherosclerotic changes in the coronary arteries, and hence, balloon angioplasty and/or stent placement was not performed. The patient reported sudden relief of pain once the thrombus was removed.

It was challenging to decide which medications to treat this patient with given the lack of atherosclerotic disease or vasospasm. A transthoracic echocardiogram was



*Fig. 1.* Electrocardiogram showing ST segment elevation in leads V3 and V4.

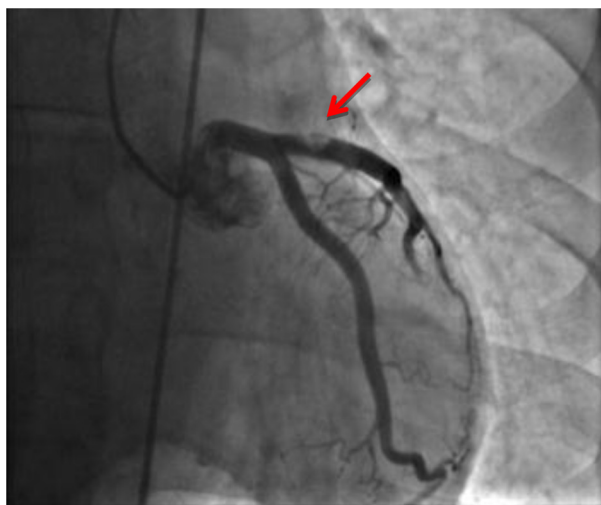
performed and no structural abnormalities were found including septal defects. Empirical continuous infusion of eptifibatide, a glycoprotein IIb/IIIa inhibitor, was administered for a period of 48 h and low-dose aspirin and clopidogrel were continued. He was not started on beta-blockers or statins as there was no clear indication for their use. The patient was discharged on aspirin and clopidogrel to be followed as outpatient. At his 6-month follow-up, he denied any bleeding and/or thrombotic events as well as any recurrent episodes of chest pain.

### Discussion

Although the coronary angiography did not show any atherosclerotic lesions, this does not necessarily rule out atherosclerotic coronary artery disease, as we did not perform endovascular ultrasonography, which would be required to rule out early lesions within the vessel wall (4). Furthermore, coronary microvascular dysfunction, which affects the intramural vessels rather than the epicardial

vessels, is another possible cause of coronary artery disease in a patient with a normal coronary angiography (5, 6). The absence of well-known risk factors for atherosclerotic disease including hypertension, diabetes mellitus, dyslipidemia, positive family history, and smoking makes these possibilities less likely and malignancy comes into play as a possible major contributor for this patient's myocardial infarction. Active malignancy is a definite risk factor for hypercoagulability with subsequent thrombosis. To our knowledge, acute myocardial infarction secondary to hypercoagulability caused by malignancy is a rare event. In our discussion, we will focus on the relationship between cancer and thrombosis with special emphasis on arterial thromboembolism with subsequent development of myocardial infarction.

The French physician Armand Trousseau is credited for being the first to relate cancer and thrombosis in his textbook 'Clinique Medicale de l'Hotel-Dieu de Paris' published in 1865 (7). Since then extensive research has been done to further understand this unique relationship.



*Fig. 2.* Coronary angiography showing a large thrombus in the left anterior descending artery.



*Fig. 3.* Coronary angiography status post-thrombectomy with no residual lesions in the left anterior descending artery.

It is estimated that cancer is responsible for 18% of all venous thromboembolism, while cancer patients have a sevenfold increase in risk of developing thromboembolism (2).

The incidence of thromboembolism in cancer patients differs according to the site of the primary tumor. In a large case control study including 3,220 patients, those with hematological malignancies had the highest incidence of thromboembolic events (28-fold) followed by lung cancer and gastrointestinal malignancies; on the other hand, patients with head and neck malignancies had the lowest incidence. Interestingly enough, further data analysis showed higher incidence of thromboembolic events in the first 3 months from the time of cancer diagnosis, with rapid decline in incidence thereafter (8). In this case, the patient had been diagnosed with lung cancer 3 months before the event.

Multiple factors are thought to contribute to hypercoagulability in malignancy including platelet activation by tumor cells, procoagulant generation by tumor cells (e.g., tissue factor) (9, 10), procoagulant generation by inflammatory cells (monocytes and macrophages), increased fibrinogen and platelet catabolism, and decreased production of coagulation inhibitors (9–11). Cancer treatment itself is known to increase the risk for venous thromboembolism; chemotherapy, antiangiogenic therapy, and hormonal therapy have all been implicated (2). Chemotherapy agents can potentiate thrombosis by decreasing fibrinolytic activity as well as plasma levels of antithrombin III (12–14); they are also cytotoxic to endothelial cells and can lead to a release of von Willebrand factor, which at least *in vitro* enhances platelet adhesion (15). This patient was on carboplatin and paclitaxel, and he was not on any antiangiogenic or hormonal agents.

The incidence of cancer-induced thrombosis in the venous side is much higher than the arterial side. It is estimated that more than 80% of thromboembolic events in cancer patients are venous in nature. No clear data exist on arterial thromboembolism secondary to cancer given that the low number of patients affected (3, 16).

Cardiovascular disease is considered to be the most common cause of arterial thromboembolism, while occult malignancies have been found in 5–10% of cases (11). Arterial thromboembolism in small arteries can be attributed to several factors including tumor invasion in the sympathetic chain resulting in vessel spasm, precipitation of cryoglobulins as well as a hypercoagulable state overall. Medium vessel disease usually results from direct invasion of the vessel by the tumor in the presence of a hypercoagulable state with possible underlying cardiovascular disease (17).

Most arterial thromboses in cancer patients are located in the lower extremities, more precisely the femoral arterial bed. Coronary arteries are not a common site of thrombosis in cancer patients, and there is very little data

addressing the relationship between cancer and ischemic heart disease (18, 19). In a retrospective study by Kopelson et al, the incidence of first coronary events, the incidence of all coronary events, and the coronary event burden in 366 cancer patients were calculated and compared to 100 patients with benign prostatic hypertrophy; there was a significant increase in coronary events in the 2-year period before the diagnosis of cancer in comparison with the control subjects. In this report, the effect of chemotherapy was excluded, as these patients were not previously diagnosed with cancer, and hence, no antineoplastic treatment had been initiated (19). An additional risk factor for coronary artery disease in cancer patients can be a history of thoracic irradiation. It has been found that patients who received thoracic irradiation at some point during their lives have a higher chance of having a coronary artery bypass graft (3.2-fold) or percutaneous coronary intervention (1.6-fold) (20). The patient discussed in this case did not have a history of chest irradiation.

Unlike the treatment of venous thromboembolism, which is well established in the literature, treating cancer-induced arterial thromboembolism remains challenging (21, 22). Most reported cases of cancer-induced arterial thrombosis were treated with modalities similar to the conventional modalities including thrombolytic therapy (23). Interestingly enough, some reports showed that chemotherapy can enhance the anticoagulation treatment by eliminating prothrombotic tumor factors. In one case report where a patient with metastatic ovarian cancer was diagnosed with subclavian artery thrombosis, there was subjective as well as objective improvement in the perfusion of her upper extremity with chemotherapy cycles (11).

## Conclusions

Cancer-induced arterial thromboembolism is an uncommon, yet serious event. There are no established guidelines for managing cancer patients, who are actively receiving chemotherapy and develop an embolic acute myocardial infarction. These patients have a high thrombotic burden and yet anticoagulants and/or antiplatelet agents should be used cautiously as their bleeding risk is likewise high. The decision as to whether to anticoagulate or not should be based on a risk-benefit assessment of bleeding versus a recurrent thromboembolic event.

## Acknowledgements

We thank Dr. Sapna Kuehl, Program Director of the Internal Medicine Residency Program at Saint Agnes Hospital for reviewing the manuscript and providing valuable comments.

## Conflict of interests and funding

The authors declare that they have no conflicts of interest concerning this case report.

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