Acute myocardial infarction is usually caused by rupture of an atheromatous plaque in the coronary arteries. For patients without risk factors of atherosclerosis, other causes should be considered. We report on a 47-year-old woman with acute myocardial infarction but no cardiovascular risk factors, which was followed by deep vein thrombosis one week after recovery from acute myocardial infarction. Although deep vein thrombosis may be medically addressed by prolonged bed rest or heart failure in patients with acute myocardial infarction, the clustering of these two diseases in patients without risk factors of atherosclerosis or venous thrombosis is unusual. In situ coronary thrombosis secondary to hypercoagulable state was presumed to be the cause for her myocardial infarction. Further investigation revealed hidden advanced ovarian cancer in the patient. This case should remind cardiologists that, for patients without clinical evidence of atherosclerosis, unusual underlying causes of acute myocardial infarction should be comprehensively investigated, such as malignancy-related hypercoagulable state.

Key Words: Deep vein thrombosis • Hypercoagulability • Myocardial infarction • Ovarian cancer • Trousseau’s syndrome.

INTRODUCTION

Acute myocardial infarction (AMI) is usually due to rupture of atherosclerotic plaques. Nonetheless, mechanisms other than atherosclerosis, such as coronary spasm, embolism, and in situ thrombosis may cause myocardial infarction, especially in patients with no clinical manifestation of atherosclerosis. 1 In recent issues of the journal, cases with different etiologies of acute myocardial infarction had been discussed. 2-4 Herein, we reported a 47-year-old woman with an unusual presentation of acute myocardial infarction. Further investigation disclosed a hidden ovarian cancer responsible for the unexplained hypercoagulable state. Although the relationship between neoplasm and hypercoagulability had been recognized by Armand Trousseau as early as 1865, presentation with AMI was rare and association with ovarian cancer has not been reported in the literature. 5,6 This case highlights the importance of suspecting malignancy-related hypercoagulability as an etiology of AMI, especially in patients without clinical evidence of atherosclerosis.

CASE REPORT

A 47-year-old woman presented to our emergency department (ED) due to progressive anterior chest pain for twelve hours. The patient was a non-smoker, without any history of hypertension, hyperlipidemia, diabetes mellitus, coronary artery disease, use of illicit drugs or any other significant illness. The physical examination revealed a female patient with mild cardio-
pulmonary distress secondary to chest pain, which was afebrile and had stable vital signs. There were regular heart beats with clear first and second heart sounds, without any murmur, gallop or rub. The initial patient electrocardiogram revealed sinus rhythm with borderline ST segment elevation and significant T wave inversion in the precordial leads (Figure 1). Because the time from onset of symptoms to presentation to ED was more than 12 hours, she was admitted to the intensive care unit after aspirin, unfractionated heparin, nitroglycerin, and propranolol were given. The presence of AMI was further confirmed by the elevation of cardiac enzymes (serum creatine kinase peaked at 630 U/L and troponin I peaked at 14.1 ng/ml) and severe hypokinesis at the mid-apical septum and apex of the left ventricle, demonstrated by transthoracic echocardiogram. After medical treatment, the patient became free of chest pain and remained hemodynamic stable; her cardiac enzymes were highest at the ED, and then gradually declined. Coronary angiography four days later revealed a filling defect in the distal segment of the left anterior descending artery without any other luminal irregularity or stenosis (Figure 1). The filling defect did not reverse after intra-coronary administration of nitroglycerin. The transthoracic echocardiogram examination was repeated five days later and revealed no evidence of intra-cardiac thrombus, valvular vegetation or septal defect, but only mild hypokinesis at the apex of the left ventricle. Serum antiphospholipid antibodies and lupus anticoagulant were absent. Serum anti-thrombin III, protein C, and protein S were drawn during unfractionated heparin infusion and all were within normal limits. The patient was discharged on the sixth day with a recommended drug regimen of aspirin.

Unfortunately, one week after discharge, the patient visited our ED again because painful swelling of her left calf had suddenly developed. Duplex ultrasonography revealed thrombus in the left superficial femoral vein and popliteal vein. After therapy with unfractionated heparin and warfarin, the swelling of the left calf resolved smoothly. Further history revealed that the patient was fully ambulatory after discharge and she denied use of contraceptive or estrogen therapy. There was no personal or family history of thromboembolic disease, nor any other significant illness. Because of clustering of arterial and venous thrombosis in a short period without identifiable causes, an extensive survey for occult malignancy was undertaken. Her chest film, abdominal ultrasonography, colonoscopy, gastroscopy, and mammography revealed no abnormal findings. No mass or lymphadenopathy was found upon physical examination. Her alpha-fetoprotein and carcinoembryonic

Figure 1. Left: Serial electrocardiography and cardiac enzyme changes from emergency department (ED) to one month after discharge; Right: Right anterior oblique-cranial view of the left coronary arteries, showing the filling defect at the distal segment of left anterior descending artery (white arrow) without any other luminal irregularity or stenosis.
antigen were within normal limits, but cancer antigen-125 and cancer antigen-199 levels were up to 3235 U/mL and 1690 U/mL, respectively. Contrast-enhanced computed tomography of the abdomen and pelvis was performed and disclosed a mass in the left adnexa of the uterus with inhomogeneous contrast enhancement, accompanied by multiple masses in the spleen (Figure 2). Exploratory laparotomy disclosed the mass to be a mucin-secreting adenocarcinoma of the ovarian area with splenic metastasis, confirmed by surgical pathology. After that, the patient received debulking surgery and chemotherapy for the ovarian cancer and was anticoagulated with warfarin. However, recurrent deep vein thrombosis and pulmonary embolism developed, despite prophylactic anticoagulation therapy was given with satisfactory effect.

DISCUSSION

AMI is usually caused by rupture of an atheromatous plaque in the coronary arteries. Myocardial infarction without clinical and angiographic evidence of atherosclerosis is uncommon, and possible causes include coronary artery spasm, embolism, and in situ thrombosis. Coronary angiograms of the patient revealed an abrupt filling defect only at the occluded site, without any other lumen irregularity or stenosis. In addition, there were no traditional risk factors for atherosclerosis, such as age, male gender, smoking, hyperglycemia, hyperlipidemia, or family history of premature cardiovascular diseases. Coronary embolism is usually due to valvular vegetations, intra-cardiac thrombus, and rarely, venous thrombosis in patients with septal defect. While these embolic complications cannot be fully excluded in our patients, the findings of echocardiograms, as well as the absence of atrial fibrillation or other peripheral embolic phenomena, weight against these scenarios. The negative study for autoimmune tests, antiphospholipid antibodies, and the absence of joint or skin lesions precludes the possibilities of coronary vasculitis in this patient. Given the above reasons, the etiology of AMI may be best attributed to hypercoagulable state with in-situ coronary thrombosis.

In addition to causing venous thrombosis, hypercoagulability is one of the risk factor for arterial thrombosis, both for atherosclerotic and non-atherosclerotic diseases. Inherited coagulation disorders, contraceptives or estrogen replacement therapy, cigarette smoking, as well as excess of lipoprotein (a) and type-1 plasminogen activator inhibitor may all lead to coronary thrombosis without a localized factor. The development of deep vein thrombosis without risk factors further supports the presence of a hypercoagulable state in our patient. Deep vein thrombosis in patients with AMI typically manifests symptoms such as bed rest or heart failure. The patient was fully ambulatory after recovery from AMI, and the venous thrombosis lagged one week after discharge. There were no identifiable risk factors of deep vein thrombosis, such as trauma, surgery, or immobilization. Accordingly, inherited or acquired hypercoagulable state may again be the most probable cause. Although comprehensive genetic study for hypercoagulable state was not performed in this case, it is less likely in the absence of personal or family history of thromboembolic diseases. In addition, common causes of acquired hypercoagulable state, such as smoking, pregnancy, estrogen or contraceptive use, nephrotic syndrome and anti-phospholipid syndrome were all absent in this patient. In such a circumstance, malignancy is likely the most possible cause and extensive investigation for occult malignancy should be seriously considered.
There were several possible mechanisms which trigger AMI in a patient with malignancy. A variety of medications used for malignancy will cause coronary thrombosis (such as taxotere and hormone therapy) or vasospasm (such as 5-fluorouracil). For this case, this possibility could be easily excluded by the absence of offending medications. Non-bacterial thrombotic endocarditis (NBTE) is a subclinical complication of malignancy that could lead to coronary embolism. While NBTE could not be fully excluded, the echocardiographic findings and the absence of other embolic phenomenon did not support this mechanism. Hypercoagulable state is the most common cause of malignancy-related thrombosis and this phenomenon had been first described by Armand Trousseau as early as 1865. There are several mechanisms explaining the increased risk of arterial and venous thrombosis by tumors: first, mucin secreted into the bloodstream can interact with P- and L-selectins, inducing the formation of platelet-rich micro-thrombi; second, exposure of tissue factor-rich tumor surfaces and cysteine proteinase secreted into the bloodstream can directly activate factor X to generate thrombin; third, hypoxic conditions within the tumors may enhance the production of pro-coagulant factors and inflammatory cytokines, which may activate endothelial and platelet adhesion molecules.

The prevalence of Trousseau’s syndrome ranged around 1 to 11%, and thromboembolic events often precede the initial manifestation of underlying malignancy. The use of Trousseau’s syndrome is usually restricted to unexplained thrombotic events which precede the diagnosis of an occult malignancy or appear concomitantly with the tumor. A hallmark of Trousseau’s syndrome is that breakthrough thromboembolic events may still have occurred despite of satisfactory level of anticoagulation. Screening of coagulation parameters is not helpful as it neither predicts the thromboembolic events nor identifies patients who may benefit from prophylaxis. Trousseau’s syndrome was more common in patients with pancreatic, breast, lung or colon cancers and was previously considered uncommon in patients with ovarian cancer. After the first reported case in 1952, series of cases with ovarian cancers have been reported and it was now accepted that thromboembolic events may be more common in ovarian malignancy than previously thought. Broad spectrum of thromboembolism phenomenon has been described in Trousseau’s syndrome but presentation with AMI is rarely reported. In our extensive review of the literature, there was no case reported on the association of AMI with ovarian cancer.

For the acute myocardial infarction in our case, there were still some possible causes that had to be addressed. First, we could not exclude the possibility that paradoxical coronary embolism originated from deep vein thrombosis, because transesophageal echocardiogram was not done to exclude patent foramen ovale. Second, negative intracoronary nitroglycerin response cannot exclude the possibility of prolonged coronary vasospasm with subsequent thrombosis. A provocation test with acetylcholine chloride may be needed but is seldom performed as it entails the risk of coronary occlusion and malignant arrhythmia.

**CONCLUSION**

In conclusion, we herein reported an unusual case of Trousseau’s syndrome presented with AMI in association with ovarian cancer. For a patient with AMI lacking clinical evidence of atherosclerosis, hypercoagulable state with in-situ coronary thrombosis should be kept in mind. The importance of comprehensive investigation for occult malignancy cannot be over-emphasized, especially for patients without identifiable causes.

**REFERENCES**


