CASE REPORT

Chest pain caused by pulmonary vein thrombi could be curable by dabigatran

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SUMMARY

Chest pain is a common clinical event that overwhelms many patients and is often a sign of coronary ischaemia. The comprehensive influence of pulmonary vein thrombosis (PVT) on coronary artery ischaemia is underappreciated. A 64-slice multidetector CT (64-MDCT) scan can detect pulmonary vein thrombi. A 68-year-old man was referred for the assessment of recent chest pain. A 64-MDCT scan was performed to assess his coronary artery. Although the scan did not show a coronary artery plaque, it did show a thrombus in the right lower pulmonary vein. After 3 months of dabigatran therapy, some parts of the thrombus had dissolved, and the image of the thrombus was more vague. The darkness of the thrombus was lost, indicating that the thrombus had loosened in structure and that the contrast enhancements were able to penetrate into the thrombus. PVT was identified as the likely aetiology for the cause of the chest pain.

BACKGROUND

Approximately 70% of patients with an acute myocardial infarction (AMI) have coronary artery stenosis of less than 50%.¹ Rupture of a coronary artery plaque resulting in occlusion is believed to be an important precipitating step of an AMI.

Pulmonary vein thrombosis (PVT) symptoms can be subtle prior to the occurrence of a systemic thrombosis, which may present as an AMI or a cerebral infarction; therefore, the disease often goes undiagnosed, and the influence of PVT on AMI is almost certainly underestimated. Some AMIs may be caused by large PVT types. Acute coronary syndromes are considered to result from the rupture of vulnerable plaques, which frequently are only moderately stenosed and are not visible by conventional angiography. Some acute coronary syndromes may be caused by large PVT tips. To investigate the aetiology of chest pain, clarifying the existence of PVT may be important. As the symptoms of PVT frequently are subtle and go undiagnosed, the comprehensive influence of PVT on coronary artery ischaemia is almost certainly underestimated.

The main causes of PVT are thought to be lung surgeries, such as lung lobectomies and bilobectomies, radiofrequency catheter ablation and certain lung tumours. Although PVT is a life-threatening condition, it is thought to be rare and is not recognised as a cause of AMI or stroke. Since 2012, we have reported six cases of pulmonary vein thrombi in patients with chest pain using 64-slice multidetector CT (64-MDCT). A 64-MDCT scan is a non-

Figure 1 The axial images reveal a thrombus in the right lower pulmonary vein as a defect of contrast enhancement (arrow). DAo, descending aorta; LA, left atrium; RLPV, right lower pulmonary vein.

invasive option used to evaluate coronary artery plaques, but it can more easily and completely assess left atrial appendage (LAA) thrombi and pulmonary vein thrombi.² No association between PVT and coronary artery ischaemia has yet been recognised. We discuss a case of a pulmonary vein thrombosis in a patient with chest pain using a non-invasive 64-MDCT scan.

CASE PRESENTATION

The patient was a 68-year-old man with hypertension, dyslipidaemia and a historical cerebral infarction. The patient had right hemiparesis but could walk with a cane. The patient was referred for the

Figure 2 The coronal images reveal a thrombus in the right lower pulmonary vein as a defect of contrast enhancement (arrows). There are no thrombi in the LAA. LA, left atrium; LAA, left atrial appendage; LV, left ventricle; RLPV, right lower pulmonary vein.

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Figure 3 The sagittal images reveal a thrombus in the lower branch of the right lower pulmonary vein (RLPV) (arrow) merging with the upper branch of the RLPV without a thrombus.

assessment of his coronary artery because of chest pain. The ECG revealed a complete right bundle-branch block with no significant ST-T changes. The patient's D-dimer concentration was less than 0.5 µg/mL (normal <1 µg/mL), his protein S activity was 0.66 (normal 0.60–1.50), and his protein C activity was 1.55 (normal 0.64–1.46). He was not treated with anticoagulants. A roentgenogram of the chest did not reveal lung cancer. The patient did not present with cough or any symptoms of cancer. The volume of the left atrium was 68.2 mL. A 64-MDCT scan was performed and merely indicated calcification of the coronary artery rather than a coronary artery plaque. A thrombus in the right lower pulmonary vein was evident in the axial (figure 1), coronal (figure 2) and sagittal planes (figures 3 and 4). After 3 months of dabigatran therapy, some parts of the thrombus were dissolved (figures 5–8). During the dabigatran therapy, the patient had no chest pain.

DISCUSSION

In this case, a PVT was found in a patient with chest pain.

Figure 4 A thrombus in the sagittal images is illustrated in the lower right-hand corner of the right lower pulmonary vein as a defect of contrast enhancement (arrow). RLPV, right lower pulmonary vein.

Figure 5 The axial images reveal a thrombus in the right lower pulmonary vein that was partly dissolved as demonstrated by the disappearance of the dark imagings, as viewed as a defect of contrast enhancement (arrow). The clear identification of a thrombus in the right lower pulmonary vein is difficult. DAo, descending aorta; LA, left atrium; RLPV, right lower pulmonary vein.

In our previous case studies since 2012, we have reported a small round thrombus in the right upper pulmonary vein of a patient with a cerebral infarction and a thin thrombus in the left upper pulmonary vein. In 2013, we reported a case of a completely occluded PVT and a case of a pulmonary vein thrombus connected to a thrombus in the left atrium detected using a 64-MDCT scan, which was confirmed by transthoracic echocardiography. We have also reported some possible effects of thrombi in the left pulmonary vein, which activates some transcription factors, such as hypoxia inducible factors (HIFs), nuclear respiratory factor-1 (NRF-1) and metal-response transcription factor-1, and may affect the pulmonary vein myocardium.² When PVT develops, NRF-1 and HIFs must cooperate to function efficiently.

At present, dabigatran is one useful option for dissolving pulmonary vein thrombi.³ Dabigatran has been demonstrated to dissolve a floating thrombus in the pulmonary vein,² which suggests that dabigatran can prevent the progression of atrial fibrillation (AF). In this case, dabigatran dissolved some parts of the thrombus in the pulmonary vein. Although dabigatran-rich

Figure 6 The coronal images may reveal a thrombus in the right lower pulmonary vein as a vague defect of contrast enhancement (arrows). LA, left atrium; RLPV, right lower pulmonary vein.

Figure 7 The sagittal images reveal a thrombus in the lower branch of right lower pulmonary vein (RLPV) (arrow), which has become rather vague and bright.

blood can flow around a floating thrombus, blood cannot flow past the side of a thrombus that is in contact with a pulmonary vein wall. Dissolving such contacting thrombi may be difficult.

Microclots released during PVT are important because they can occlude small arteries of all organs.

Cerebral microvascular occlusion is known to be a common phenomenon but may be an under-recognised mechanism of brain pathology. If prompt recanalisation fails, then microvessels may experience hypoxia and undernourishment, leading to significant functional deficits.

Recanalisation of occluded cerebral capillaries and terminal arterioles, which mitigates hypoxia and undernourishment, occurs by a mostly unknown mechanism of microvascular plasticity. Recanalisation occurs by a mechanism involving the rapid envelopment of emboli by endothelial membrane projections which leads to the extravasation of the embolus and subsequent formation of a new vessel wall.⁴

Approximately 10–20% of patients with typical chest pain, such as angina pectoris, have normal coronary arteries, and

Figure 8 A thrombus in the sagittal images is vaguely illustrated in the centre of the right lower pulmonary vein (RLPV) as a defect of contrast enhancement (arrow). The contacting surface of the thrombus has disappeared.

most of these patients exhibit signs of syndrome X. However, syndrome X is a heterogeneous disease that includes slow coronary flow (SCF). SCF is an angiographic finding characterised by the late opacification of the epicardial coronary arteries without identified occlusive coronary disease. Although the aetiopathogenesis of SCF is not yet fully understood, the occlusive disease of the small coronary arteries has been suggested to be a cause.⁵ Microclots released during PVT may cause cerebral microvascular occlusion and SCF by occluding microarteries.

The LAA in patients with AF promotes thromboembolism through a variety of mechanisms, most significantly through the mechanical dysfunction of the atria, which leads to impaired blood flow and stasis. Additional factors, including endothelial dysfunction, inflammation, platelet activation and a hypercoagulable state, have also been implicated in the formation of LAA thrombi. However, the mechanisms underlying the formation of PVT remain unknown. We believe that impaired blood flow and stasis, which are caused by decreased bodily activity in elderly patients, may play important roles in the formation of PVT. Daily exercise such as jogging, walking or swimming could prevent the formation of PVT.

Learning points

- ▶ A 64-slice multidetector CT scan can assess the quality of a pulmonary vein thrombus. The fibrin structure of the thrombus can be loosened via the thrombin inhibitor dabigatran, after which the thrombus may be observed more clearly.
- ▶ Microclots thrown from pulmonary vein thrombi may cause chest pain via the occlusion of small branches of the coronary artery, although this outcome cannot be demonstrated by coronary angiography.
- ▶ Dissolving a thrombus of the pulmonary vein using dabigatran can recanalise the occluded branch of the coronary artery by inhibiting the release of microclots, which suggests that dabigatran can cure one type of angina pectoris.
- ▶ Microclots extravasation has occurred in mouse cerebral microvascular occlusion. If the mechanism for the extravasation of occluded small branches of the coronary artery fails, then the patients may have slow coronary flow.
- ▶ Decreases in bodily activity in elderly populations may cause pulmonary vein thrombosis. To prevent this condition, daily exercise may be useful.

Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Fuster V, Fayad ZA, Badimon JJ. Acute coronary syndromes: biology. *Lancet* 1999;353(Suppl 2):S115–9.
- 2 Takeuchi H. Floating thrombus in the left upper pulmonary vein dissolved by dabigatran. *BMJ Case Rep*. Published Online: 9 Oct 2013 doi:10.1136/bcr-2013-200836
- 3 Rasmussen LH, Larsen TB, Graungaard T, et al. Primary and secondary prevention with new oral anticoagulant drugs for stroke prevention in atrial fibrillation: indirect comparison analysis. *BMJ* 2012;345:e7097.
- 4 Lam CK, Yoo T, Hiner B, et al. Embolus extravasation is an alternative mechanism for cerebral microvascular recanalization. *Nature* 2010;465:478–82.
- 5 Mosseri M, Yarom R, Gotsman MS, et al. Histologic evidence for small-vessel coronary artery disease in patients with angina pectoris and patent large coronary arteries. *Circulation* 1986;74:964–72.

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