CASE REPORT

An atypical case of vasospastic angina: demonstrating the usefulness of Holter monitoring

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SUMMARY

Prinzmetal variant angina or vasospastic angina is a clinical syndrome characterised by episodic chest pain and transient reversible ST segment changes in ECG. The

aetiology and treatment of the condition are quite different compared to those of conventional coronary artery disease. The crux of the problem in variant angina patients remains the diagnosis, especially if coexisting

Figure 1 Twenty-four hour Holter monitoring (3 channel) showing sinus rhythm with episodes of significant ST elevation in channel 1 and 3 at 5 10:00.

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coronary artery disease is present. Timely diagnosis not only helps relieve symptoms, it also prevents complications such as ventricular tachycardia. Conventional provocative tests are used for diagnosis of such conditions; they have varied sensitivity and specificity, and are cumbersome to perform. We present a case of an elderly man who presented with recurrent episodes of breathlessness and chest pain, where Holter monitoring proved to be a better mode for diagnosing variant angina than more invasive provocative tests. In this report, we reemphasise the role of this simple non-invasive diagnostic mode for diagnosis of variant angina.

BACKGROUND

Prinzmetal *et al*¹ first described Prinzmetal variant angina (PVA) syndrome in 1959. This condition is characterised by episodic chest pain with transient ST segment elevation during the episodes. It is also known as 'coronary spastic angina' or 'vasospastic angina' because coronary spasm is believed to play an important role in patients with variant angina. The spasm is characterised by transient abnormal contraction of a segment of epicardial coronary artery. Exact pathophysiology of this entity is still not known. The angina usually occurs at rest, mostly between night and early morning, and is not generally precipitated by exercise.² Various arrhythmias can occur in patients with Prinzmetal angina, leading to significant cardiac mortality and morbidity. Holter monitoring, apart from provocative testing, can be useful in providing definitive diagnosis of this difficult to diagnose entity and also to rule out various forms of arrhythmias. We demonstrate the usefulness of Holter monitoring in diagnosis of vasospastic angina in a 75-year-old man with repeated episodes of atypical symptoms of breathlessness and orthopnoea at rest.

CASE PRESENTATION

A 75-year-old man presented with a history of recurrent episodes of breathlessness, chest pain and orthopnoea for the past 20 days. He also had a history of two episodes of syncope after experiencing chest pain. He was experiencing loss of sleep as his symptoms of breathlessness and orthopnoea were mostly present at night, with a frequency of one to two episodes/night. He also had a history of smoking.

INVESTIGATIONS

The patient's baseline ECG showed sinus bradycardia and no ST-T changes. Echocardiography was normal with normal left ventricular systolic function and no wall motion abnormality. His troponin T was also within normal limits. A contrast-enhanced CT was performed to rule out any mediastinal pathology as the cause of his symptoms; the CT was normal. In view of the syncope and sinus bradycardia, 24 h Holter monitoring was carried out, showing sinus rhythm with episodes of severe ST elevation (figure 1), corresponding with the patient's symptoms of episodic chest pain and orthopnoea, and suggesting a diagnosis of vasospastic or Prinzmetal angina.

Coronary angiography (CAG) was performed to rule out any flow limiting organic stenosis as the cause. CAG showed a 50% non-flow limiting plaque in the proximal left anterior descending artery, which was fractional flow reserve negative (figure 2).

DIFFERENTIAL DIAGNOSIS

Vasospastic angina

TREATMENT

The patient was started on a high dose of nitrates and calcium channel blockers. As he also had atherosclerotic coronary artery

Figure 2 Coronary angiogram of left system in right anterior oblique projection showing 50% non flow limiting plaque in proximal left anterior descending artery.

disease, clopidogrel instead of aspirin was also started, as aspirin can worsen coronary vasospasm in these patients.

OUTCOME AND FOLLOW-UP

The patient's symptoms of episodic chest pain improved and a repeat Holter was carried out, which showed no further episodes of ST elevations (figure 3). The patient was discharged after optimising his drugs; he was doing well on follow-up.

DISCUSSION

Coronary vasospastic angina, or Prinzmetal variant angina, was first reported by Prinzmetal *et al*¹ in a series of 30 cases presenting with chest discomfort at rest and associated transient ST elevation on ECG during periods of discomfort. As the symptoms and ECG changes are transient, it is not always possible to diagnose this syndrome. Its prevalence is greatest in Japan as compared to other parts of the world. Underlying coronary vasospasm is believed to be responsible for this syndrome. Often, the angina pain is severe and may be associated with syncope due to atrioventricular (AV) block, cardiac asystole and ventricular tachyarrhythmias.³ The episodes of angina usually occur between midnight and 8:00, and tend to occur in clusters of two to three episodes within 30–60 min.² Symptoms usually occur spontaneously at rest and during activities of daily living, but are not reproduced on exercise or on expression of emotion.

The exact pathophysiology is not entirely clear, but newly found mechanisms of coronary artery spasm are being considered.^{4–6} Risk factors for variant angina include smoking, being a young male, having lipid abnormalities and abnormal glucose metabolism, and certain genetic factors. Smoking is one of the major risk factors for coronary spasm and there are reports that a high percentage of patients of vasospastic angina in Japan are tobacco smokers.⁷ Two important pathophysiologic mechanisms include involvement of vascular endothelial cells and involvement of vascular smooth muscles. Endothelial cell dysfunction with reduced bioavailability of nitric oxide, a potent smooth muscle cell relaxant, is one of the major mechanisms of coronary

Figure 3 Twenty-four hour Holter monitoring (3 channel) showing sinus rhythm after the initiation of treatment (calcium channel blocker) showing normal sinus rhythm with no ST elevation.

spasm in patients with vasospastic angina and their vasospastic response to acetylcholine, which dilates the blood vessels if the vascular endothelium is normal, causes vasoconstriction in presence of endothelial injury or dysfunction.⁸ The second mechanism is excessive contraction of coronary vascular smooth muscle cells due to increased activity of myosin light chain kinase, which is under regulatory control of the molecular switch Rho-kinase.⁹

It is often difficult to diagnose PVA given the episodic nature of the syndrome, but our patient fitted into the diagnostic criteria given by the Japanese Circulation Society. We had particular difficulty in diagnosing the condition, as the patient had a predominant history of breathlessness and orthopnoea rather than angina. ECG may show ST elevation during episodes of chest pain, but, in many patients, episodes of coronary spasms

are asymptomatic, with chest pain occurring in only 20–30% of patients during episodes of ST change on Holter monitoring, suggesting its usefulness in suspected patients, as in our case.^{10 11} Besides diagnosis, Holter recording also helps to rule out various arrhythmias that may occur in these patients. Holter for extended periods of 24–48 h is given a class I recommendation in diagnosis of patients with PVA, in whom it is strongly suspected. Other methods for diagnosis include provocation testing with intracoronary ACh, which, again, is associated with potential complications. Since in our case the diagnosis was clear on Holter monitoring and as the patient improved once calcium channel blockers were initiated, provocative testing with ACh was not carried out. Other markers for vasospastic angina are C reactive protein and Rho-kinase activity in circulating

leucocytes.^{12 13} In a study by Kikuchi *et al*, elevated Rho-kinase activity in circulating leucocytes in a patient with variant angina, compared to a control group, was demonstrated. The authors also noted that Rho-kinase activity in the circulating leucocytes decreased significantly after treatment with calcium channel blockers, which correlated with decrease in symptoms.

CAG can either be normal or show organic stenosis in many patients. In 90% of patients, coronary spasm occurs at the site of organic stenosis, as reported by MacAlpin.¹⁴ Patients with vasospastic angina can have ventricular tachyarrhythmia's or AV block during episodes of angina, which can lead to syncope and sudden cardiac death.^{15 16} Therefore diagnosing this entity is important.

Most patients with PVA respond to medical management with nitrates and calcium channel blockers, with dramatic improvement in their symptoms. Our patient also improved with medical management and repeat Holter showed no further episodes of ischaemia. Patients with medically refractory symptoms and those who have organic stenosis on CAG can be treated with intracoronary stenting of the vasospastic segment, which is

reported to be the site of spasm in 90% of patients.¹⁷ However, results after stenting in patients with vasospastic angina are controversial, as many patients with PVA have multivessel coronary spasm.¹⁸

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Learning points

- Prinzmetal variant angina (PVA), or vasospastic angina, is due to transient coronary vasospasm and characterised by episodic chest discomfort and ST elevation on ECG during periods of chest discomfort.
- It is often difficult to diagnose, as only 20–30% of patients report chest discomfort during periods of coronary spasm and ischaemic ST elevation on ECG.
- Extended periods of Holter monitoring for 24–48 h is very useful in diagnosis of PVA in suspected patients and has a class I recommendation for this purpose.
- Most patients respond well to medical therapy with calcium channel blockers and nitrates.
- Elevated levels of Rho-kinase activity in circulating leucocytes are observed in patients with variant angina; these levels decrease with treatment, making it an attractive diagnostic and prognostic marker in patients with variant angina.
- Intracoronary stenting of the vasospastic segment can be performed in patients with medically refractory symptoms, the results of which are controversial.

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