Two depressed young patients with angina pectoris induced by microvascular dysfunction detected by stress perfusion cardiac magnetic resonance

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Introduction
Up to 70% of angina patients who received Invasive Coronary Angiography (ICA) were found to have no obstructive coronary artery stenosis (stenosis degree ≥ 50%) [1], and among them, 26%-54% were with microvascular angina [2].

Clinically, microvascular angina is common, and it is often misdiagnosed as non-cardiac symptoms, leading to inadequate treatments. Especially, microvascular angina patients combined with depression are often neglected and given only psychiatric medication, which may cause them repeatedly seeking medical attention for chest pain symptoms.

Depression is a highly prevalent disease that affects approximately 10% of the population [3]. The prevalence of depression in patients with coronary heart disease is 15-30% [4]. And studies have shown that depression is closely related to peripheral and cerebral microvascular dysfunction [5]. Therefore, it is not surprising that depression is comorbid with microvascular angina. Microvascular angina is closely related to heart failure and myocardial infarction [6]. Moreover, microvascular angina could increase the risk of future cardiovascular events and repeated hospitalizations, reduce the quality of life, and increase medical expenses.

This report describes two depressive patients with angina. Obstructive coronary heart disease was ruled out by Computed Tomography Coronary Angiography (CTA) or Invasive Coronary Angiography (ICA).

They underwent a stress perfusion cardiac MRI, using Adenosine Triphosphate (ATP) as the first-pass vasodilator. We visually compared patients’ stress and rest myocardial perfusion images to determine myocardial ischemia. Circle CVI42 (Circle Cardiovascular Imaging Inc. Canada) was used to evaluate the Myocardial Perfusion Reserve Index (MPRI).

Case series

Case 1

A 32-year-old woman presented to the cardiology clinic due to chest tightness and feeling breathless for 2 months. It mainly occurred during anger and quarrels. Each lasted for 20-30 minutes and was alleviated spontaneously after rest. She couldn’t go to work because of her symptoms. She has been diagnosed with depression for more than two years and has received drugs for depression, including lorazepam, agomelatine and buspirone tablets. She had no history of smoking or drinking. She was not married, having no children. She had menstruation of about 30 days, without, dysmenorrhea.

Her imaging findings were shown in Figure 1 and Table 1. 24-hour Holter showed that there were occasional atrial premature contractions, 642 times every 24 hours, and the dyadic rhythm (64 arrays) was seen; abnormal changes in ST-T (flat T wave in I and V3-V6) were seen in some periods. Echocardiography found she had normal cardiac structure and function, and then her CTA showed normal coronary artery. She was diagnosed with non-obstructive coronary ischemia.

Table 1: Patients characteristics.

<table>
<thead>
<tr>
<th>Age/Gender</th>
<th>Patient 1</th>
<th>Patient 2</th>
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</thead>
<tbody>
<tr>
<td>ECG</td>
<td>Flat T wave in I and V3-V6</td>
<td>ST-T depression in II and V1-V4</td>
</tr>
<tr>
<td>CTA/ICA</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>MPRI</td>
<td>1.51</td>
<td>1.93</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>GAD-7</td>
<td>21</td>
<td>9</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Microvascular angina, depression, occasional atrial premature contractions</td>
<td>Microvascular angina, depression</td>
</tr>
<tr>
<td>Management</td>
<td>Shexiang Tongxin dripping pills, Lorazepam, Agomelatine, Buspirone</td>
<td>Exercising, Enough sleep</td>
</tr>
<tr>
<td>Follow-up</td>
<td>6 months</td>
<td>12 months</td>
</tr>
<tr>
<td>Symptom</td>
<td>Her symptoms had improved significantly, her seizure frequency was reduced. The patient had not experienced chest discomfort for 1 month.</td>
<td>The patient had occasional chest discomfort symptoms, 1-2 times a month, mostly when he stayed up late and had high work pressure.</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>GAD-7</td>
<td>5</td>
<td>9</td>
</tr>
</tbody>
</table>

The myocardial perfusion of adenosine triphosphate in cardiac MRI suggested that there was a ring-shaped area of decreased perfusion under the endocardium of the left ventricle, and the MPRI was abnormal (1.51, normal >2.0). These findings were consistent with the diagnosis of microvascular angina. The cardiologist gave nicorandil (5 mg TID) for treatment. The patient developed headache symptoms after taking nicorandil for 3 days and switched to Shexiang Tongxin dripping pills (2 capsules TID). At 1 month, her symptoms had improved significantly; her symptom frequency was reduced, and she was able to work normally. At 6 months follow-up, the patient had not experienced any chest discomfort for the past 1 month.

Case 2

A 36-year-old man presented to the doctor with a 1-month history of chest pain and chest tightness, mainly in the early morning every day (1-3 times a week), each lasting 3-5 minutes. The symptoms were not related to activities, and most of which occurred during rest. This symptom appeared after the birth of his second child. There was no history of smoking or drinking. He suffered from insomnia because of the great pressure. He was diagnosed with depression for more than 5 years and received medications for depression including fluoxetine and Lorazepam. Two years ago, he stopped medication after the symptoms improved. He had suffered from psoriasis for 12 years and received intermittent medical treatment.

His imaging findings were shown in Figure 2 and Table 1. The Electrocardiogram (ECG) showed abnormal changes of ST-T (ST-T depression in leads II and V1-V4). The echocardiogram was
Figure 2: patient 2 (A) electrocardiogram (ECG); (B) computed to-mography coronary angiography (CTA); Stress perfusion CMR: (C) Rest and stress imaging contouring; (D) Polar map demonstrates; (E) Rest and stress SI curve.

considered normal, and CTCA also showed normal coronary arteries. His attending cardiologist diagnosed non-obstructive coronary ischemia.

The myocardial perfusion of adenosine triphosphate stress in cardiac MRI suggested that there was a circular area of decreased perfusion under the left ventricular endocardium, and MPRI was abnormal (1.93, normal >2.0). These findings were consistent with the diagnosis of microvascular angina pectoris. Cardiologists treated him with Shexiang Tongxin Dropping Pills (2 capsules TID). At one month, his symptoms had improved significantly, while the frequency of attacks decreased (2 times a month). All drugs were stopped by himself, and his heart symptoms were improved by practicing a healthy lifestyle, including 8 hours of sleep and more than 40 minutes of jogging every day. At 12 months, the patient had occasional chest discomfort symptoms, 1-2 times a month, mostly when he stayed up late and had high work pressure. The frequency of chest pain decreased significantly.

Discussion

Most patients with angina have no obstructive coronary stenosis, notably in women [7,8]. Among these patients, microvascular angina pectoris accounts for a large proportion [9]. Although studies revealed that traditional risk factors (smoking, age, diabetes, hypertension, dyslipidemia, obesity and some proinflammatory indicators) were associated with coronary microcirculatory disturbance [10], the above risk factors could only explain less than 20% of the variation of coronary microvascular dysfunction [11], indicating some other factors contribute to coronary microvascular dysfunction especially among those who are young and without obstructive coronary disease.

We found that some young patients with microvascular angina while without any traditional risk factors often have symptoms of anxiety and depression. Is there a potential link between depression and microvascular angina?

Previous studies have shown that depression is related to brain and peripheral microvascular dysfunction, which may originate from endothelial dysfunction [5]. Moreover, systemic microvascular dysfunction may also lead to the development of depression, and the two promote each other [5].

The underlying mechanism between depression and microvascular angina is not fully understood. Some researchers have suggested that depression leads to unhealthy lifestyles, such as sleep disorders, irregular eating, lack of physical exercise, and smoking [12,13], which are the risk factors for microvascular angina pectoris. In addition, depression increases the risk of diabetes [14], which can cause microvascular angina [15]. Moreover, increased proinflammatory activity and potential immune system disorder may play a role in the link between microvascular angina pectoris and depressive symptoms [16,17].

Recognizing depression symptoms and providing relevant treatment may be a vital and promising strategy to improve the prognosis of young patients with microvascular angina. And it should be practiced in further research and clinical work.

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication: A written informed consent form disclosing clinical details and images was obtained from the patient. A copy of the consent form is available for review by the editors of this journal.

Availability of data and material: All relevant data are included in the manuscript.

Competing interests: The authors declare that they have no competing interests.

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