Neurally Mediated Syncope Manifesting During Atrial Fibrillation

— A Case Report —

Takeshi Shirayama, MD; Keiji Inoue, MD; Takashi Sakamoto, MD; Midori Yamamura, MD; Hiroki Mani, MD; Akiko Yoshida, MD; Hiroti Imai, MD; Yayoi Matoba, MD; Masao Nakagawa, MD

A 64-year-old male was admitted to hospital because of repeated episodes of syncope and palpitation. Ambulatory monitoring revealed paroxysmal atrial fibrillation (AF) as the cause of palpitation; he did not have structural heart disease. The induction of AF by rapid pacing (50Hz for 1s) in an upright position provoked syncope with a vasodepressor response. Atropine sulfate blocked the induction of syncope. The possible etiology was neurally mediated syncope that manifested only during AF, which suggests that the abnormal vagal activity during AF in this case exaggerated the vasodepressor response while upright. (Circ J 2002; 66: 866–868)

Key Words: Atrial fibrillation; Head-up tilt; Neurally mediated syncope; Vagal nerve

Syncope is often encountered in an emergency room, but its etiology is not always clear. Neurally mediated syncope, which is characterized by abnormal vagal reflex, has been recently recognized as a major cause of syncopal episodes.1–3 and it can be provoked repeatedly by the head-up tilt test with fairly good sensitivity.2,4 A paroxysmal attack of atrial fibrillation (AF) is another pathological entity that can be concomitant with increased vagal tone,5 but because this arrhythmia hardly ever causes collapse while the patient has a structurally normal heart, syncope induced by the interaction of these 2 diseases has been neglected as a diagnosis.6–8

We describe a patient who suffered from syncope only in the presence of AF. The head-up tilt test was negative, but the induction of AF caused faintness or syncope in an upright position.

Case Report

A 64-year-old male was admitted to hospital because of repeated episodes of syncope during palpitation attacks for the past 7 months. He would lose consciousness abruptly, but recovered within 1 min without neurological symptoms. His history showed that he had had palpitation attacks for 20 years under the diagnosis of ‘arrhythmia’. He had general fatigue, and occasional sweating, with the palpitations, but had never had syncope or faintness until recently.

Physical examination showed mild hepatomegaly, possibly related to alcohol intake (800–900ml of Japanese sake daily for 40 years), but otherwise normal findings.

Laboratory tests revealed hyperlipidemia (triglyceride, 240mg/dl; total cholesterol, 208mg/dl) and hyperuricemia (8.6mg/dl). Liver enzymes (aspartate aminotransferase, alanine aminotransferase, γ-glutamyl transpeptidase) were normal. Blood pressure was 132/70mmHg, and heart rate was regular at 85beats/min. The ECG was normal, as was ultrasonic echocardiography. Ambulatory ECG monitoring revealed occasional episodes of AF concurrent with palpitation (Fig 1). Paroxysmal AF (heart rate ~150beats/min) was recorded during an episode of dizziness with collapse. Neither bradycardia nor long pause was recorded. The electroencephalogram was normal, which excluded epilepsy. Because no episode of syncope was detected during the hospital stay, a cardiac electrophysiological study was performed. Maximum sinus node recovery time was 1,240ms and corrected sinus node recovery time was 420ms. Sino-atrial conduction time was 114ms. Atrio-ventricular conduction was normal (effective refractory period: 240ms, functional refractory period: 390 ms, basic cycle length 500ms). No arrhythmia was induced by the extrastimulus method, but AF was easily induced by rapid
pacing (50 Hz, 1 s) at the right atrial appendage (the AF threshold was 3 mA)\textsuperscript{9,10} and sinus rhythm was restored spontaneously within 10 min. the patient’s hemodynamics were stable and no syncope was induced.

A head-up tilt test was performed to ascertain if there was an autonomic nerve etiology. Because palpitation always preceded his syncope, a temporary pacing electrode was inserted to induce the arrhythmia. Blood pressure was measured manually by a cuff-method at 1-min intervals and ECG (10-s strip) was recorded at the same time. When AF was induced, the ECG was continuously recorded until the arrhythmia was terminated (Fig 2). In the supine position, the induction of AF increased heart rate, but did not cause any change in blood pressure. At the head-up position of 80 degrees for 20 min, systolic blood pressure decreased slightly (152/68 mmHg to 120/70 mmHg) before stabilizing and no syncope was observed. After the induction of AF, blood pressure decreased to 66/30 mmHg with loss of consciousness. Blood pressure recovered when the AF terminated spontaneously.

The effects of autonomic drugs were examined during the head-up tilt test (Table 1). Isoproterenol infusion at a dose of 0.5 μg/min increased sinus heart rate by 20%, and facilitated the maintenance of AF, but it did not cause a vasodepressor response in the head-up position. Atropine sulfate (0.05 mg/kg body weight) blocked the vasodepressor response during AF, but not the induction of AF. After pharmacological denervation with propranolol (0.2 mg/kg) and atropine (0.05 mg/kg), neither sustained AF nor vasodepressor response was induced.

The patient had severe urinary retention after the oral disopyramide (300 mg/day) that was administered to block the abnormal vagal reflex and AF, so he was given oral pilsicainide (150 mg/day) to prevent the AF and has not had a syncopal episode for 1 year.

Table 1 Heart Rate and Blood Pressure During the Head-up Tilt Test and the Effects of Drugs

<table>
<thead>
<tr>
<th>Patient position</th>
<th>Atrial fibrillation</th>
<th>Sinus rhythm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>max HR</td>
<td>av HR</td>
</tr>
<tr>
<td>Supine Control</td>
<td>140</td>
<td>135</td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>168</td>
<td>154</td>
</tr>
<tr>
<td>Head-up Control</td>
<td>180</td>
<td>163</td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Atropine</td>
<td>180</td>
<td>170</td>
</tr>
<tr>
<td>Denervation</td>
<td>150</td>
<td>130</td>
</tr>
</tbody>
</table>

Doses of drugs: isoproterenol, 0.5 μg/ml; atropine, 0.05 mg/kg; propranolol, 0.2 mg/kg. denervation = atropine + propranolol. HR, heart rate; BP, blood pressure; AF, atrial fibrillation.

Discussion

Recurrent syncope is a common clinical problem, but its etiology is sometimes difficult to detect.\textsuperscript{1,3} When there are preceding palpitations, the syncope is usually caused by a tachyarrhythmia that disturbs the hemodynamics. The present case always had palpitations before he experienced syncope, but only AF was recorded during ambulatory monitoring, and his symptoms were reproducible during the arrhythmia, which usually does not cause syncope in patients whose cardiac function is normal. No ventricular arrhythmia was induced during the clinical electrophysiological test.

Neurally mediated syncope is a major cause of syncope\textsuperscript{1–3} and is characterized by a sudden onset of syncope that follows some early signs such as blurred vision, but without any neurological sequelae. Careful history taking often helps diagnose this syndrome. Recently, the head-up tilt test has been used to evaluate the syncope and an abnormal vagal response has been reported.\textsuperscript{5} However, in the present case, the head-up tilt test revealed a modest vasodepressor response, but could not induce his symptoms.

Taking into consideration that in most cases AF could occur under the strong influence of vagal tone,\textsuperscript{1} we suspected that the mechanism of this patient’s syncope was the concurrent emergence of AF and a vasodepressor reaction caused by an abnormal neural response. Indeed, an abnormal vasodepressor response during paroxysmal supraventricular tachycardia has been reported\textsuperscript{1} and another report observed that the arrhythmia occurred more often during the head-up tilt test in patients who suffered from tachycardia.\textsuperscript{12} Thus we tried to induce AF during the head-up tilt test to see if the syncope could be reproduced, with a positive result, but a somewhat complex mechanism. The test revealed that the maintenance of AF was facilitated by an adrenergic mechanism, because the arrhythmia was sustained for longer in the presence of isoproterenol or atropine, but was blocked by propranolol. On the other hand, the vasopressor response was induced under the influence of vagal tone, because atropine blocked the response.
The AF possibly influenced vagal tone afferently, which exaggerated the vasodepressor response. Atrial rapid pacing induced AF, but the patient did not have an abnormality in either sinus node or atrioventricular node function, so the bradycardia–tachycardia syndrome can be excluded.

It is possible that AF with a rapid ventricular response could decrease cardiac output, which would lead to a significant fall in blood pressure. However, AF in the supine position did not change blood pressure at all, despite a rapid heart rate, and was also the case after injection of atropine in the head-up position (Table 1). These observations suggest that the arrhythmia itself did not cause the deterioration in his hemodynamics, but exaggerated the abnormal vasodepressor response of the vagal nerve.

**Conclusion**

We report here a case of neurally mediated syncope that was exaggerated by AF, which is an unusual but very important mechanism of syncope. This case is instructive in recognizing the cause of syncope.

**References**