Clinical Case Report

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Syncope and hypotension associated with carotid sinus hypersensitivity in a patient with nasopharyngeal carcinoma

A case report

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Abstract

Rationale: Carotid sinus hypersensitivity (CSH) is traditionally classified into 3 subgroups: cardioinhibitory, vasodepressor, and mixed subtypes. However, the underlying mechanism of CSH in head and neck cancer is controversial. Several pathological mechanisms of CSH have been proposed: atherosclerotic noncompliance, sternocleidomastoid proprioceptive denervation, and generalized autonomic dysfunction.

Patient concerns: We reported a 75-year-old man who had recurrent syncope attacks secondary to hypotension and reduced plasma norepinephrine (NE) levels. CSH was suspected when carotid massage induced syncope-like symptom.

Diagnoses: Nasopharynx carcinoma with regional lymph node involvement and CSH.

Interventions: On admission, dopamine was administered to maintain the blood pressure. When NE deficiency was confirmed, intravenous NE combined with oral midodrine replaced the dopamine treatment.

Outcomes: The syncopal episodes completely resolved with periodic occurrence of hypertension.

Lessons: Our case suggests a potential role of carotid sinus in regulating the release of NE in adrenal gland and that the monitoring of catecholamine level is recommended in the CSH cases either from head and neck tumors or other mechanical manipulation of carotid sinus.

Abbreviations: ACTH = adrenocorticotropic hormone, CSH = carotid sinus hypersensitivity, ECG = electrocardiograph, NE = norepinephrine, PET = positron emission tomography.

Keywords: carotid sinus hypersensitivity, hypotension, nasopharyngeal carcinoma, syncope

1. Introduction

Carotid sinus hypersensitivity (CSH) is one common cause of syncope in elderly, which accounts for 26% to 60% of elderly patients with unexplained syncope.[1,2] Although rare, it has been reported that tumor from head and neck was responsible for some cases of syncope secondary to CSH since 1933,[3] which is secondary to mechanical compression of the carotid sinus. CSH is traditionally classified into 3 subgroups: cardioinhibitory (defined as asystole for >3 seconds without a fall in arterial pressure), vasodepressor (isolated decline in systolic blood pressure of >50 mmHg) and mixed (asystole for >3 seconds and decline in systolic blood pressure of >50 mmHg) subtypes.[3,4] The physiology of normal carotid sinus reflex is well established, however, the pathophysiology of CSH remains unclear. Here we reported a patient who presented with syncope secondary to hypotension and remarkably reduced plasma norepinephrine (NE) levels. He was then diagnosed as nasopharyngeal carcinoma, indicating a potential effect of carotid sinus on the release of NE in adrenal medulla.

The ethics committee of West China Hospital approved this study as a case report for retrospective analysis. The informed consent was obtained from the patient. We anonymized all information before analysis.

2. Case report

A 75-year-old man presented with a history of frequent and recurrent syncope for the last 2 months. The syncopal episodes lasted about 40 seconds. Pre-syncopal symptoms included palpitation and dizziness. The frequency of the syncope was

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SZ and CW contributed equally to this work.

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up to 3 to 4 times per day. Seizures were not observed during these attacks. Electrocardiograph (ECG) revealed sinus arrest and complete right bundle branch block, which met the diagnostic criteria of sick sinus syndrome. The patient accepted the treatment of pacemaker in his local hospital. One month after pacemaker implantation, he had syncopal attacks again with an increased frequency. Meanwhile, he developed slurring of speech. The physical and neurological examination proved to be unremarkable except for hoarseness and dysphonia. Blood pressure was 104/54 mmHg when he was conscious. ECG displayed normal sinus rhythm of 72 bpm with the implantable cardiac pacemakers (Fig. 1).

On admission to our hospital, the patient still had syncopal attacks from 2 to 3 times per day despite continuous pumping of dopamine. Specifically, he suffered an episode of palpitation and dizziness, followed by loss of consciousness with blood pressure of 59/39 mmHg. ECG detected the launch of the pacemaker with sinus rhythm of 60 beats/min. CSH was suspected since carotid massage induce pre-syncopal symptoms like dizziness and palpitation. In addition to the basal dosage of dopamine, extra shot was necessary to raise his pressure to 100/60 mmHg during the attack of syncope. The level of adrenocorticotropic hormone (ACTH) and catecholamine in plasma was measured at specific time points on 3 days continuously. The level of ACTH, epinephrine and dopamine was normal but NE was decreased to 13, 13, and 107 ng/L on the 3 consecutive days (normal values from 272 to 559 ng/L). The 24-hour catecholamine in urine was also measured. The 24-hour dopamine increased to 3845.91ug/24 hour (normal values from 107.2 to 246.6 ug/24 h); the 24-hour NE decreased to 10.31ug/24 h (normal values from 16.3 to 41.5 ug/24 h) and the 24-hour epinephrine decreased to 2.81ug/24 hour (normal values from 7.5 to 21.9 ug/24 h). The cortisol level was normal.

The color sonography cardiac ultrasound result was normal for a 75-year-old man. The contrast-enhanced cervical CT scan revealed slightly thickening of the wall of the right nasopharynx and a narrowing of the bilateral pharyngeal recess without enhancement. Multiple small lymph nodes were detected in the bilateral cervical regions. Positron emission tomography (PET) scan revealed an increased accumulation of FDG (2-deoxy-2-[^{18}F] fluoro-D-glucose) in the thickening posterior pharyngeal wall, the left retropharyngeal lymph nodes and right carotid lymph nodes (Fig. 2), suggesting a diagnosis of nasopharyngeal carcinoma with regional lymph node involvement. A strategy of intravenous NE combined with oral midodrine was applied to replace the dopamine treatment. The syncopal episodes completely resolved with periodic occurrence of hypertension, suggesting that NE deficiency was accounting for syncopal attacks of the patient. One week later, the patient was transferred to oncology department for radical chemoradiation therapy.

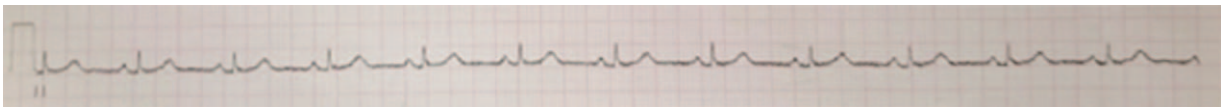

Figure 1. Demonstration of the pacemaker heart rate at 72 bmp.

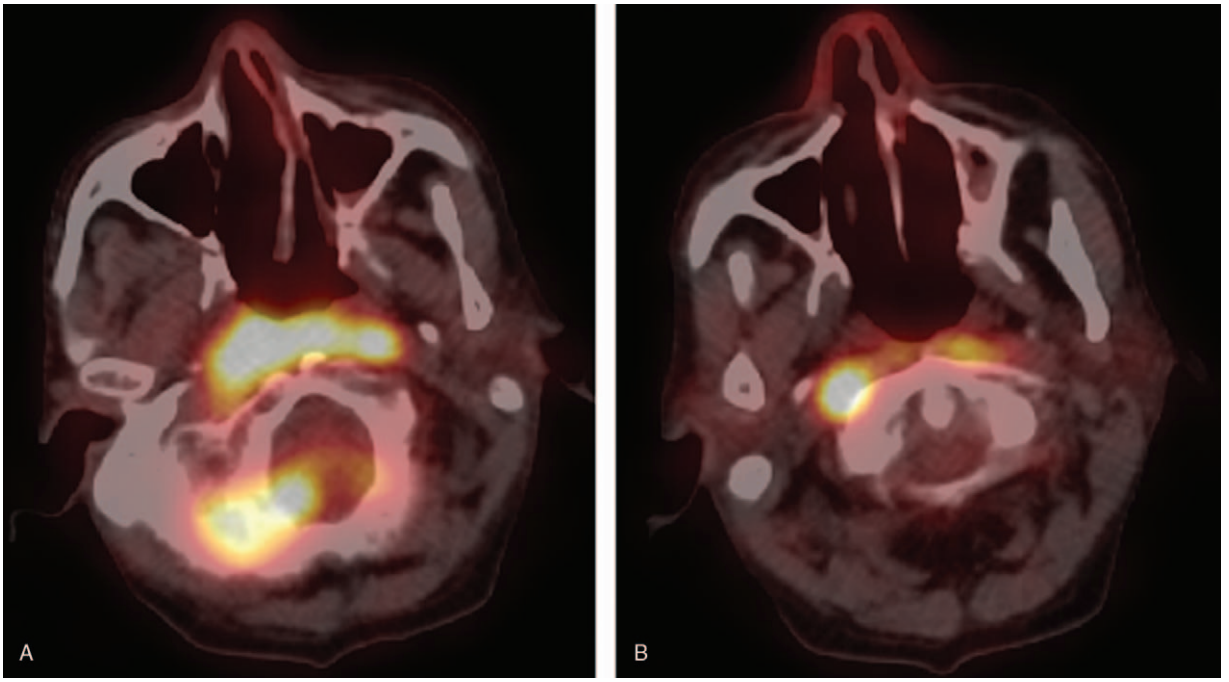

Figure 2. Positron emission tomography (PET) scan demonstrated an increased accumulation of FDG (2-deoxy-2-[^{18}F] fluoro-D-glucose) in the thickening posterior pharyngeal wall (A) and an increased accumulation of FDG in the retropharyngeal lymph node (B).

3. Discussion

Although rare, syncope was reported as an early symptom in a few cases of nasopharyngeal carcinoma.[5] In the context of head and neck cancer, the underlying pathophysiological mechanisms of syncope include stimulation of carotid sinus or glossopharyngeal nerve, both of which are afferent to the medullary vasodepressor region leading to increased vagal tone (bradycardia) and decreased sympathetic tone (vasodilation).[6] Here we reported a patient with newly diagnosed nasopharyngeal carcinoma, whose initial presentation was syncope and the slurring of speech for 2 months. The PET scan suggested a diagnosis of nasopharyngeal carcinoma with involvement in cervical lymph nodes, anatomically supporting the possibility of tumor-associated CSH. The patient accepted the implantation of pacemaker in local hospital, while ruled out the cardioinhibitory effect of CSH. We propose that, in this case, the vasopressor mechanism (hypotension) responsible for the syncope was due to tumor-associated CSH that is cardioinhibitory effect-independent.

Here we reported a patient with carotid-sinus syncope of vasodepressor subtype of CSH. For the classical vasodepressor subtype of CSH, the fall in arterial pressure is mediated by stimulation of medullary vasodepressor region and following decreased sympathetic tone (vasodilation). Several pathological mechanisms of CSH have been proposed: atherosclerotic noncompliance, sternocleidomastoid proprioceptive denervation, and generalized autonomic dysfunction,[7] however, there is no consensus on the exact mechanism. Here, we propose the effect of CSH on downregulation of NE secretion. The release of NE from the adrenal medulla is tightly regulated by multiple central and peripheral mechanisms, one of which is the direct regulation by sympathetic nerves (sympathetic tone) in adrenal medulla.[8] Animal studies indicated that reduction in the activity of carotid sinus results in preferential secretion of NE, suggesting that carotid sinus reflex (baroreceptor reflex) might regulate the adrenal medulla activity to influence the plasma levels of NE.[9,10] The development of implantable electric carotid baroreflex stimulation device provided insight into the mechanisms underlying the blood pressure-lowering effects of baroreflex activation.[11] It was found that manipulations around carotid sinus field such as carotid endarterectomy significantly affected the release of NE [12] and electric field stimulation of carotid sinus baroreflex afferents acutely decreased sympathetic vasomotor tone and blood pressure in patients with hypertension, concomitant with reduction of plasma NE concentration.[11,13,14] In our case, the syncopal episodes were accompanied with the decreased secretion of NE, both in the plasma and urine, supporting the possibility that the decline of blood pressure in CSH might be mediated by the releasing of NE in adrenal gland directly or indirectly. Our report and other studies suggest that serum NE level should be considered as one of the first-line investigations in CSH in future clinical practice.

Nevertheless, there are limitations of the case study. First, this is a single case report of CSH in the setting of nasopharyngeal carcinoma. Although we performed a number of measurements of adrenal function and found that plasma NE levels were reduced, these observations in a single patient cannot be regarded as definitive. Second, the reduced NE could be result of other pathological mechanism of adrenal gland like microadenoma, which was difficult to detect in the early stage.

In summary, we reported a case of nasopharyngeal carcinoma with recurrent syncope as initial symptom. To our knowledge, this is the first case report carotid-sinus syncope accompanied with NE secretion deficiency, suggesting that NE secretion deficiency might play a role in CSH-induced vasodilation. The monitoring of catecholamine level is recommended in the CSH cases either from head and neck tumors or other mechanical manipulation of carotid sinus. Future experimental animal study is needed to further investigate the relationship between CSH and secretion deficiency in adrenal medulla.

Author contributions

Conceptualization: Sen He, Yong He.
Data curation: Shuting Zhang, Sen He, Yong He.
Investigation: Shuting Zhang, Chenchen Wei.
Methodology: Chenchen Wei, Minggang Su.
Supervision: Sen He, Yong He.
Writing – original draft: Shuting Zhang.
Writing – review & editing: Chenchen Wei, Mingming Zhang.

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