



Autonomic dysfunction in postoperative primitive neuroectodermal tumor of heart

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Received: July 8, 2021

Revised: September 2, 2021

Accepted: September 3, 2021

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pISSN 2508-691X

eISSN 2508-6960

We present a patient with a primitive neuroectodermal tumor arising from the right atrium who experienced multiple syncope episodes daily, which had first appeared 1 month after surgery. The symptoms continued to worsen over the course of chemotherapy, and the autonomic function test (AFT) was performed after the 14th chemotherapy cycle. The AFT revealed orthostatic hypotension and reduced baroreflex-dependent sympathetic reactivity. Physical counterpressure techniques were applied with a visual biofeedback intervention, and were found to be effective in reducing the syncope episodes.

Key words: Autonomic nervous system disease; Neuroectodermal tumors; Primitive; Peripheral; Orthostatic hypotension

Primitive neuroectodermal tumors (PNETs) are aggressive malignant tumors caused by a balanced reciprocal translocation t(11; 22) involving the EWSR1 and FL1-1 genes in pluripotent neural crest cells.¹ Primary tumors arising from the right atrium are extremely rare.² Surgical resection of a PNET with adjuvant chemotherapy generally produces a good prognosis.³ We present a patient who was referred for evaluation of syncope due to experiencing frequent episodes of loss of consciousness. The autonomic function test (AFT) was performed to assess the parasympathetic and sympathetic reactivity. Physical counterpressure techniques were applied in the form of biofeedback for the management of syncope.⁴

CASE

A 23-year-old female presented with a 6-week history of palpitation and breathlessness.

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Contrast computed tomography angiography (Fig. 1) revealed an anterior mediastinal large soft-tissue mass (10.2 × 8.2 × 8.2 cm) arising from the junction of the right atrium and superior vena cava (SVC). The right atrium and ventricle were small, and the inferior vena cava appeared dilated due to compression by the mass. Functionally the heart appeared normal on echocardiography, and the metastatic workup was negative. The histopathological evaluation was suggestive of PNET expressing CD99 and FL1-1. The tumor was positive for EWSR1 translocation, confirming a diagnosis of PNET. Median sternotomy, anterior pericardiectomy, and dissection of the aorta and pulmonary artery were performed, and an intrapericardial mass was dissected from the right atrium-SVC junction. A bovine pericardial patch was placed to close the defect. Episodes of syncope appeared at 1 month after surgery, before chemotherapy was started. Fourteen cycles of the standard regimen of doxorubicin, vincristine, cyclophosphamide, and dactinomycin alternating with courses of ifosfamide and etoposide were given over a period of 1 year.

At the end of the 14th cycle of chemotherapy, the syncope episodes gradually increased to 15-20 per day. Usually one episode of syncope lasted 1-2 minutes and was associated with prodromal symptoms of lightheadedness and headache. The syncope was triggered by a change in posture from supine to sitting or standing. It was not associ-

ated with emotional states, urination, defecation, or abrupt neck movement. There was no evidence of metastasis on positron-emission tomography. A postsurgery cardiac evaluation by electrocardiography (ECG) produced no abnormal findings. Normal findings for the nerve conduction velocity ruled out the possibility of vincristine-induced neuropathy. The possibility of functional disorder was ruled out by a psychiatric evaluation.

Since the symptoms of the patient continued to aggravate, she was referred to the AFT laboratory for autonomic evaluation and the first recordings were made on the same day. ECG, stethography, grip force, and beat-to-beat blood pressure were recorded digitally using Powerlab and Finapres devices (ADInstruments), respectively. Follow-up recordings were made after 2 months and 4 months. In all three recordings, p-waves were predominantly inverted with different PR intervals on lead II. In the head-up tilt (HUT) test, a decrease in systolic blood pressure (SBP) of > 20 mmHg was recorded within 3 minutes after reaching 70°, which was suggestive of orthostatic hypotension and loss of baroreflex-dependent sympathetic reactivity. However, in a cold pressor test (CPT), when the patient's hand was dipped in 10°C water, the diastolic blood pressure increased by > 15 mmHg in all recordings, suggesting normal baroreflex-independent sympathetic reactivity. Parasympathetic reactivity could not be evaluated

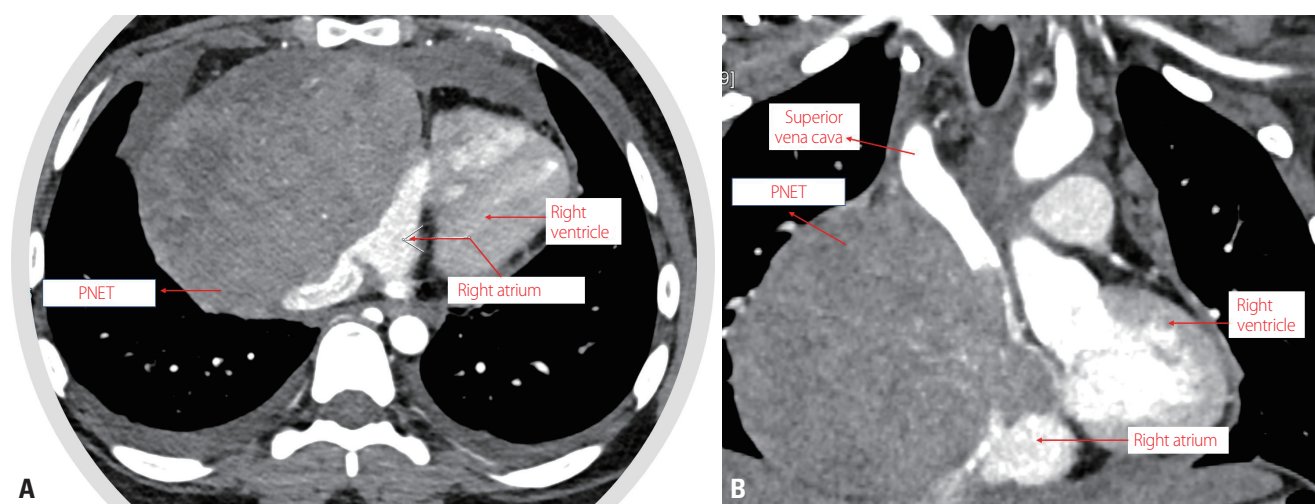


Fig. 1. Computed tomography coronary angiography: (A) axial view and (B) coronal view. A large well-defined heterogeneously enhanced soft-tissue mass is seen on the right side of the anterior mediastinum with loss of fat planes and compression of the right atrium and ventricle. The lesion is compressing the inferior vena cava and the lower part of the superior vena cava, with invasion into the right atrium. PNET, primitive neuroectodermal tumor.

due to the presence of ectopic beats. These findings were consistent with the presence of neurogenic orthostatic hypotension. In view of symptomatic autonomic neuropathy, the subsequent chemotherapy was completed without vincristine. Due to the worsening renal function and frequent urinary tract infection, we were advised to manage syncope using nonpharmacological methods, such as increasing salt and water intakes, physical counterpressure techniques, compression stockings, and abdominal binders.

To demonstrate the effect of applying counterpressure techniques to the patient, the HUT test was performed after instructing the patient to press against the footrest at the time of symptom onset and sustain this pressure when the symptoms aggravated (Fig. 2). She was instructed to

perform physical counterpressure techniques such as muscle tensing, ball compression, and leg crossing,⁴ and the HUT test was repeated. Changes in SBP were displayed on a computer monitor to provide visual biofeedback to the patient, and she was instructed to practice the techniques at home whenever she experienced presyncopal symptoms. These syncope simulation sessions were repeated multiple times. After 2 months, the frequency of syncope episodes reduced to 5-10 per day.

DISCUSSION

This was a rare case of PNET arising from the right atrium,

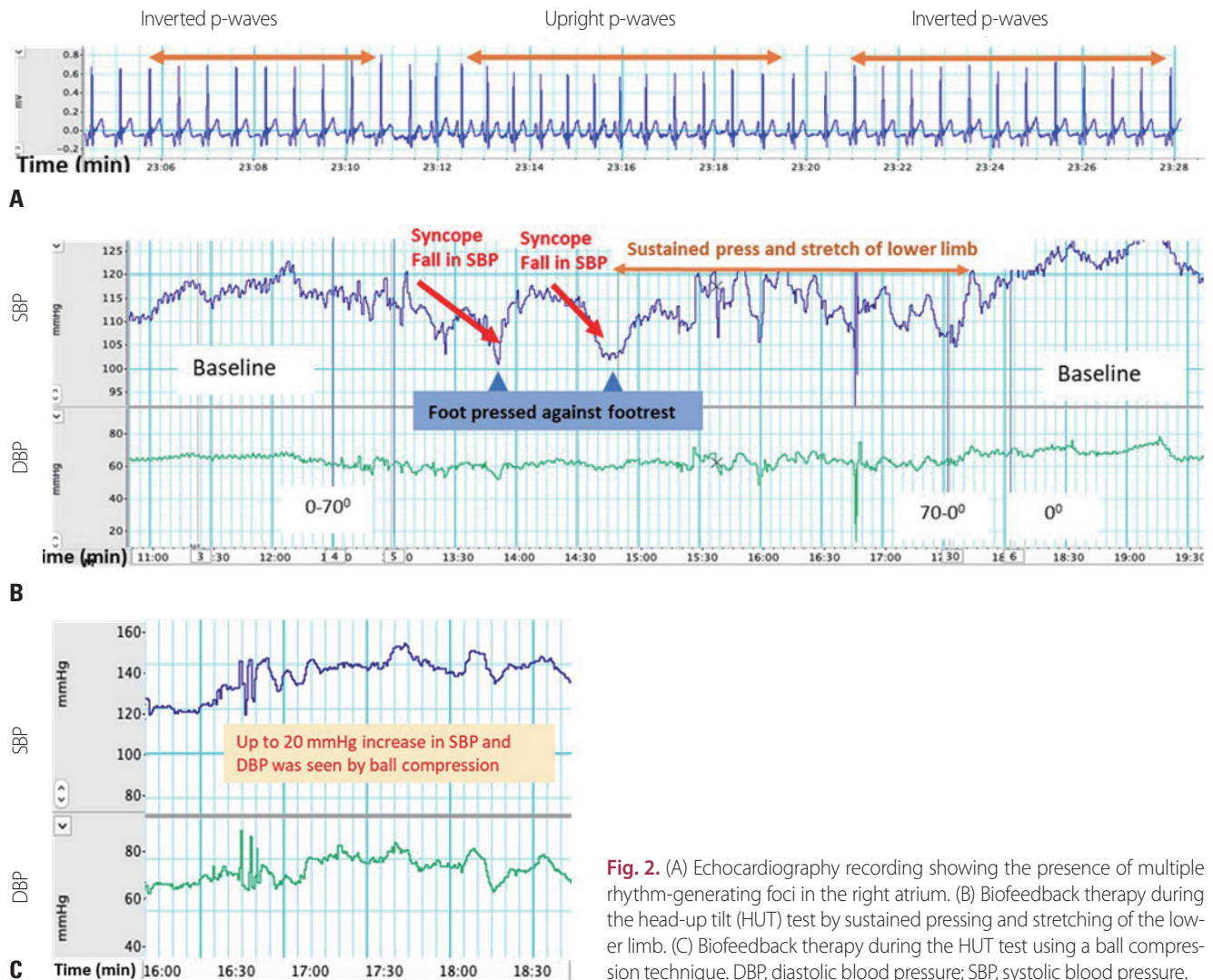


Fig. 2. (A) Echocardiography recording showing the presence of multiple rhythm-generating foci in the right atrium. (B) Biofeedback therapy during the head-up tilt (HUT) test by sustained pressing and stretching of the lower limb. (C) Biofeedback therapy during the HUT test using a ball compression technique. DBP, diastolic blood pressure; SBP, systolic blood pressure.

for which there are few published reports.^{2,5,6} This is also the only report mentioning syncope after surgery and its management by visual biofeedback. ECG showed normal rate and rhythm with normal morphology before surgery. After surgical resection of the tumor and chemotherapy, arrhythmia and abnormal p-wave morphology were noted. This could be attributed to damage to the pacemaker cells in the right atrium during surgical resection of the tumor, but ECG showed normal cardiac hemodynamic functionality. The standard regimen of chemotherapy was used, for which there are no reports on the occurrence of arrhythmias or autonomic dysfunction in the literature.^{2,7,8} Among the sympathetic reactivity tests, dysfunction was noted in the HUT test whereas the CPT findings were normal. Orthostatic hypotension and loss of baroreflex-dependent sympathetic reactivity were noted on all three recordings. This indicates that the baroreflex-dependent sympathetic reactivity was affected while the baroreflex-independent pathways were unaffected.⁹ Damage to baroreceptors located on the aorta, right atrium, and other vessels during the surgery and several months of bed rest during the course of treatment might have reduced the baroreflex sensitivity. During increased demand or stress, a ventilation perfusion mismatch could lead to reduced oxygenation of the brain, possibly leading to syncope. The patient was instructed to perform physical counterpressure techniques such as leg crossing, isometric handgrip, and arm tensing recommended by American Heart Association and American Red Cross,¹⁰ with the aid of a visual biofeedback intervention. These techniques rely on baroreflex-independent pathways to increase the blood pressure. We found that an increase of up to 20 mmHg could be expected with this technique. The biofeedback therapy helped our patient to understand the techniques, improved her compliance, and reduced the frequency of syncope episodes.

Conflicts of Interest

The authors have no conflicts to disclose.

Funding

Study was done using department resources.

Acknowledgements

The study was done in Autonomic Function Testing Lab, Department of Physiology, AIIMS.

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