Cerebral Hypoperfusion in Orthostatic Hypotension with Globally Denervated Myocardium

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A 57-yr-old woman had frequent syncope when rising from a seated position. Her blood pressure fell from 140/80 mmHg to 60–70/40 mmHg while changing positions. Iodine-123-metaiodobenzylguanidine ([^{123}I]MIBG) did not accumulate in the heart, whereas ^{201}Tl-Cl (^{201}Tl) did. Raise-up ^{99m}Tc-hexamethyl-propyleneamine oxime (^{99m}Tc-HMPAO) brain SPECT revealed decreased activity in the bilateral frontal areas, and subsequent supine ^{99m}Tc-HMPAO brain SPECT revealed filling in these areas, indicating that the cerebral blood flow (CBF) was transiently decreased in the frontal areas more than others in a standing position. The plasma norepinephrine (NE) level of this patient was normal during supine rest, but when she stood up, failure to increase the plasma level of NE uncovered a sympathetic nervous dysfunction. The CBF abnormality in patients with orthostatic hypotension may be due to a "functional" hemodynamic mechanism that induces orthostatic stress. This patient had transient hypoperfusion in the frontal areas when standing, without organic cerebral arterial stenosis. Only CBF in the frontal areas revealed relative hypoperfusion. These regions might be highly susceptible to a change in blood flow. The causes of orthostatic hypotension of this patient were autonomic failure with a disturbance of the sympathetic nerve endings, which was revealed by ^{99m}Tc-HMPAO brain SPECT and cardiac [^{123}I]MIBG imaging.

Key Words: iodine-123-MIBG; thallium-201; technetium-99m-HMPAO; postural cerebral hypoperfusion; orthostatic hypotension-

J Nucl Med 1996; 37:1824–1826

Iodine-123-metaiodobenzylguanidine ([^{123}I]MIBG) is an analog of norepinephrine (NE) which concentrates in adrenergic neurons (*1*) in regions such as the heart. Cardiac imaging with mismatched uptake between [^{123}I]MIBG and ^{201}Tl-Cl (^{201}Tl) suggests globally denervated but viable myocardium, which are attributed to transplanted heart (*2*) or sympathetic nervous dysfunction, such as in diabetes mellitus (*3*). The ability to maintain adequate blood pressure in an upright position depends on the successful integration of the cardiovascular, neural and endocrine systems. Dysfunction of an individual component, or of the integration of these systems, results in impaired blood pressure control (*4*). Orthostatic hypotension is defined as systolic blood pressure drops more than 20 mmHg when the patient rises from a supine position (*5*). Technetium-99m-hexamethyl-propyleneamine oxime (^{99m}Tc-HMPAO) brain SPECT, used to visualize conditioned cerebral blood flow (CBF), revealed postural cerebral hypoperfusion (*6*) in patients with orthostatic hypotension.

We describe a patient with globally denervated but viable myocardium who had orthostatic hypotension. The nuclear images of the heart and brain revealed useful findings.

Received Oct. 3, 1995; revision accepted Feb. 9, 1996.

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CASE REPORT

A 57-yr-old woman was referred to our hospital with frequent syncope when rising from a seated position. Her symptoms gradually deteriorated into feeling faint and frequently lost consciousness. On physical examination at admission, her blood pressure fell from 140/80 mmHg to 60–70/40 mmHg when changing position for a repeat study and her resting heart rate was 92 bpm.

She had constipation and decreased sweating but no bruits in the neck or significant neurological findings. Biochemical analysis showed an elevated erythrocyte sedimentation rate (32 mm in 1 hr), but fasting blood glucose was 99 mg/dl. The plasma and urine noradrenaline and adrenaline levels were normal. After a 14-g NE injection, the patients' blood pressure increased from 126/70 to 203/100 mmHg. A rest electrocardiogram revealed no arrhythmic changes. A cervical ultrasonic Doppler test showed no significant stenosis and normal flow. Brain x-ray CT also showed no abnormalities.

Myocardial Thallium-201 and Iodine-123-MIBG Imaging

After administration of 111 MBq ^{201}Tl at rest, an anterior view was obtained for 5 min at 15 min postinjection (p.i.) and thereafter with the patient in a supine position. On administration of 111 MBq [^{123}I]MIBG, anterior views were obtained for 5 min at 15 min p.i. and at 4 hr thereafter. Iodine-123-MIBG images were taken 9 days after ^{201}Tl imaging. The heart-to-mediastinum (H/M) activity ratio was calculated to quantify cardiac [^{123}I]MIBG uptake. Thallium-201 and [^{123}I]MIBG myocardial images were obtained using a single-head gamma camera equipped with a low-energy, general all-purpose collimator. Energy discrimination was provided by a 20% window centered on 81 keV for ^{201}Tl and 160 keV for [^{123}I]MIBG.

Raise-Up Test with Technetium-99m-HMPAO Brain SPECT

After inserting a plastic flexible needle into the antecubital vein, the patient lay on a couch in a quiet, dim room with her legs elevated. After being recumbent for 30 min, the patient was instructed to stand up within about 3 sec. As soon as the patient was upright, she was injected with 370 MBq ^{99m}Tc-HMPAO in a bolus flushed with 20 ml saline and then moved to the imaging room to initiate the first SPECT scan (*7*). Afterwards, another 480 MBq ^{99m}Tc-HMPAO were administered while the patient remained in the SPECT bed. Her blood pressure was measured using a sphygmomanometer at 1-min intervals.

Technetium-99m-HMPAO brain SPECT was performed using a ring-type gamma camera with 8-mm FWHM. During the SPECT acquisitions, the patient was firmly positioned within the headrest by a restraint and the head position was monitored by alignment with reference points to facilitate comparisons for an attenuation of 0.11 cm^{-1}. The tomographic data were reconstructed using a filtered backprojection algorithm. Transaxial slices of 5 mm in thickness were obtained. For semiquantitation, four regions of

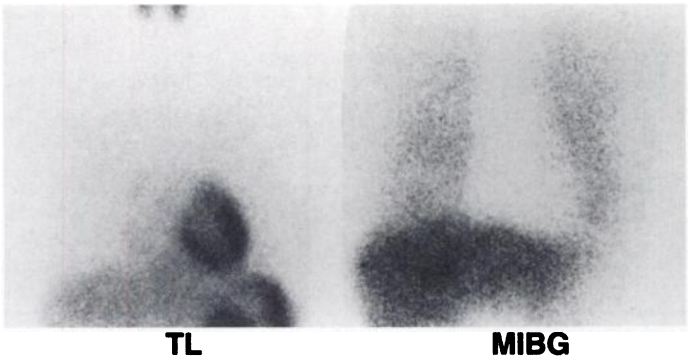

FIGURE 1. Thallium-201 scintigram (anterior view) shows normal distribution, but [^{123}I]MIBG scintigraphy (anterior view) shows none.

interest (ROIs) were drawn in the frontal and cerebellar areas on a transverse slice, and the mean counting rate per voxel was estimated in each ROI with reference to an anatomical map. The count ratio of the frontal to the cerebellar areas was calculated.

RESULTS

The heart was not visualized with [^{123}I]MIBG but not with ^{201}Tl (Fig. 1). The [^{123}I]MIBG H/M activity ratio was 1.71 in the delayed image.

Her blood pressure fell from a seated value of 118/88 mmHg to 78/50 mmHg when she stood. Raise-up ^{99m}Tc-HMPAO brain SPECT revealed decreased activity in the bilateral frontal areas, and subsequent supine ^{99m}Tc-HMPAO brain SPECT revealed filling in these areas (Fig. 2). Semiquantitation showed that the frontal-to-cerebellar ratio between the standing and supine positions changed significantly from 0.84 to 0.92 and from 0.88 to 0.94 in the right and left areas, respectively. There was, however, no relative decrease in CBF in any other areas between the standing and supine positions, indicating that the amount of CBF was transiently decreased in the frontal areas more than in others by standing up.

Blood noradrenaline and adrenaline levels were 358 and 58 pg/ml, respectively, while seated, 375 and 76 pg/ml while standing and 478 and 53 pg/ml while supine.

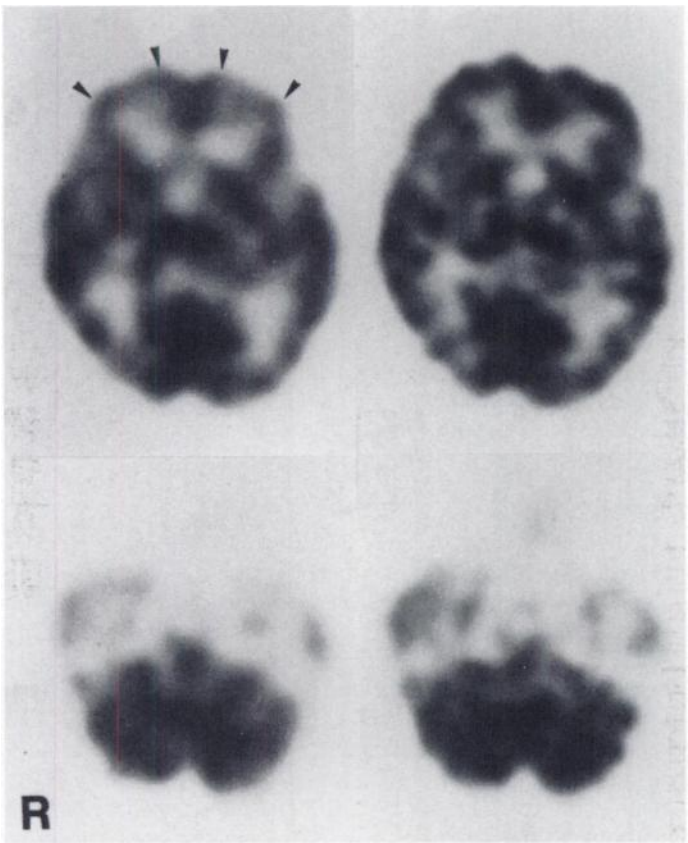

FIGURE 2. Technetium-99m-HMPAO shows hypoperfusion in the frontal areas (arrows) upon standing but normal distribution while supine.

DISCUSSION

This patient showed globally denervated but viable myocardium and postural cerebral hypoperfusion in the frontal areas, which was diagnosed by ^{201}Tl, [^{123}I]MIBG myocardial imaging and ^{99m}Tc-HMPAO brain SPECT scans. Semiquantitative ratios confirmed these findings (*4*). They indicated a relationship between orthostatic hypotension and denervated myocardium in patients with autonomic dysfunction.

Globally denervated myocardium is considered to be drug-induced, or caused by sympathetic nervous dysfunction, an implanted heart or severe left ventricular dysfunction such as dilated cardiomyopathy. This patient had not received reserpine, tricyclic antidepressants or other drugs interfering with [^{123}I]MIBG uptake. No organic heart disease was revealed by physical examination or electrocardiogram. The results indicated noncardiac disease associated with a neurogenic sympathetic fiber abnormality innervating the heart. We excluded multiple neuritis with autonomic failure because there were normal neurological findings in this patient. Since glucose tolerance was normal, we excluded the possibility of diabetes mellitus.

The plasma NE level in this patient, derived mainly from sympathetic nerve endings, was normal during supine rest. When she stood up, however, the plasma NE levels failed to increase, indicating a sympathetic nervous dysfunction. After NE injection, her blood pressure immediately increased. Autonomic insufficiency is characterized by a loss of sympathetic nerve endings (*9*) and low basal plasma NE levels while supine, little or no increase in the NE level when the patient stands up and a low threshold of the pressor response to infused NE (*9,10*). These findings are consistent with the depletion of NE from sympathetic nerve endings, with resultant postsynaptic denervation supersensitivity.

The abnormality in CBF in patients with orthostatic hypotension may be due to a "functional" hemodynamic mechanism that induces orthostatic stress, because this patient had transiently relative hypoperfusion in the frontal areas at standing and there was no evidence of organic cerebral arterial stenosis. Postural cerebral relative hypoperfusion was evident only in the frontal areas. This region might be highly susceptible to a change in blood flow (*11*). The functions of the frontal areas of the brain are not well established. We considered that the cause of the disturbed blood flow increase was an autonomic insufficiency that caused globally denervated, but viable myocardium.

ACKNOWLEDGMENT

This work was supported by special coordination funds for promoting science and technology (Encouragement system of COE) from the Science and Technology Agency of Japan.

REFERENCES

1. Sisson JC, Wiewland DM, Sherman P. Metaiodobenzylguanidine as an index of the adrenergic nervous system integrity and function. *J Nucl Med* 1987;28:1620–1624.
2. Dae MW, Marco TD, Botvinick EH, et al. Scintigraphic assessment of MIBG uptake in globally denervated human and canine hearts-Implications for clinical studies. *J Nucl Med* 1992;33:1444–1450.

3. Mantysaari M, Kuikka J, Mustonen J. Noninvasive detection of cardiac sympathetic nervous dysfunction in diabetic patients using ^{123}I-metaiodobenzylguanidine. *Diabetes* 1992;41:1069–1075.
4. Mader SL. Aging and postural hypotension. *J Am Geri Soc* 1989;37:129–137.
5. Rodstein M, Zeman FD. Postural blood pressure changes in the elderly. *J Chronic Dis* 1957;6:581–582.
6. Hayashida K, Nishimura T, Hirose Y, et al. Visualization of posture-dependent cerebral blood flow in a patient with Takayasu's disease by means of ^{99m}Tc-HMPAO brain single-photon emission tomography. *Eur J Nucl Med* 1992;19:987–989.
7. Hayashida K, Hirose Y, Kaminagata T, et al. Detection of postural cerebral hypoperfusion with technetium-99m-HMPAO brain SPECT in patients with cerebrovascular disease. *J Nucl Med* 1993;34:1931–1935.
8. Tsuchimochi ST, Tamaki N, Tadamura E, et al. Age and gender difference in normal myocardial adrenergic neuronal function evaluated by iodine-123-MIBG imaging. *J Nucl Med* 1995;36:969–974.
9. Ziegler MG. Postural hypotension. *Ann Rev Med* 1980;31:239–245.
10. Polinsky RJ, Kopin IJ, Ebert MH, Weise V. Pharmacologic distinction of different orthostatic hypotension syndromes. *Neurology* 1981;31:1–7.
11. Hayashida K, Nishiooeda Y, Hirose Y, et al. Maladaptation of vascular response in the frontal area in patients with orthostatic hypotension. *J Nucl Med* 1996;37:1–4.

Lung Scan Detection of SVC Clot with Collateral Flow to Liver

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We present a case of visualization of a clot in the superior vena cava with collateral flow to the liver during a lung perfusion scan. A digital venogram performed after injection through the right central venous line confirmed the presence of a clot in the superior vena cava with retrograde flow into the azygous venous system.

Key Words: technetium-99m-macroaggregated albumin; lung scintigraphy; SVC clot

J Nucl Med 1996; 37:1826–1827

The visualization of organs, other than the lungs, during a lung perfusion study using ^{99m}Tc-macroaggregated albumin was studied. The causes of visualization include: poor radiopharmaceutical tagging, degradation to submicron particle size of injected material, right-to-left cardiac shunts or shunting of material away from the heart after injection (*1,2*). We report on a lung perfusion scan in a patient with a superior vena cava (SVC) obstruction, which showed both hepatic visualization and uptake within the obstructing SVC clot, secondary to a central line placement.

CASE REPORT

An 89-yr-old woman was admitted to the hospital with increasing shortness of breath over a 2-wk period. Significant past medical history included severe cardiovascular disease. Physical examination revealed tachypnea with diffuse ronchi. Bilateral calf tenderness was present.

Arterial blood gases revealed a pH = 7.44, pCO_2 = 37, pO_2 = 112, HCO_3 = 25, O_2 saturation = 96% (the patient was on 3 liters of O_2 via nasal canula). An EKG showed atrial fibrillation. A chest radiograph showed clear lungs and a right central venous line in the superior vena cava (Fig. 1). Doppler ultrasound of the lower extremities revealed a thrombus in the left popliteal vein.

A perfusion scan was performed to rule out pulmonary emboli (Fig. 2); 4 mCi ^{99m}Tc-MAA (98% tagging efficiency) were injected in the right central venous line (there was no other venous access). A ventilation scan was not performed because the patient could not fully cooperate. There was decreased perfusion in the left lung with a large irregular defect in the left mid-lung field. In addition, there was a vertical focus of activity at the tip of the central venous catheter despite several saline flushes, as well as uptake within the quadrate lobe of the liver. A digital venogram performed immediately after the lung scan confirmed the presence of a large SVC clot with collateral flow into the azygous vein (Fig. 3).

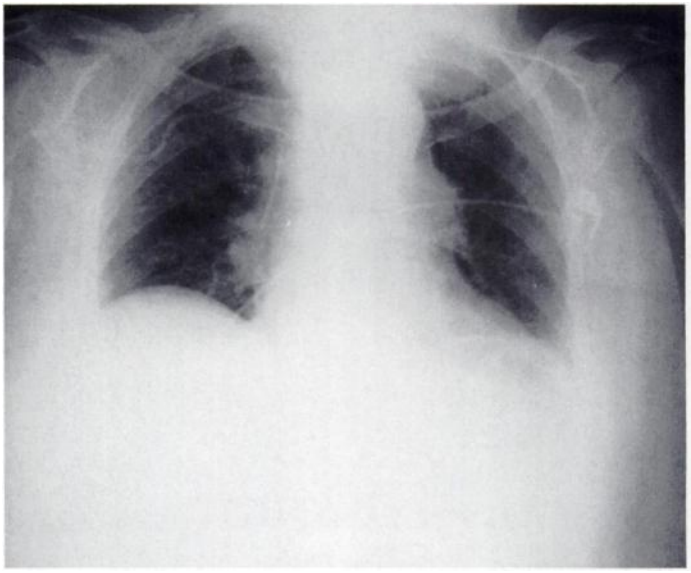

FIGURE 1. Portable chest radiograph showing underaeration, prominent hila and a right central line in the superior vena cava.

DISCUSSION

Occlusion of the SVC may be an acute thrombotic event or may occur gradually. Although malignancy is the underlying cause in 85%-90% (*3*) of superior vena caval occlusions, benign causes include a growing incidence caused by indwelling catheters and fibrosing mediastinitis (*4*). Patients typically present with a violaceous hue and venous distension and edema of the head, neck and upper extremities. Patients may also experience respiratory embarassament, headache and neurological dysfunction (*3*).

Collateral pathways for venous blood return in superior vena caval obstruction include: azygous and hemi-azygous, superior and inferior intercostal, internal mammary, lateral thoracic, epigastric and vertebral veins (*5,6*). A common collateral pathway involves retrograde flow from the innominate veins to the internal mammary veins and the paraumbilical plexus and then thorugh a recanalized umbilical vein into the left branch of

Received Jan. 1, 1996; accepted Mar. 27, 1996.
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