Vertebrobasilar Insufficiency Revealed by Xenon-133 Inhalation SPECT

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A study of cerebral and cerebellar blood flow reactivity to acetazolamide by xenon-133-inhalation single photon emission computed tomography (133Xe SPECT) was carried out in a patient with bouts of transient basilar ischemia, whose neurological examination, computed tomographic scan, and auditory evoked potentials were normal. Though the patient was symptom-free at the time of the study, 133Xe SPECT demonstrated vertebrobasilar insufficiency by showing an impaired vasodilatory response in both the occipital lobes and the right cerebellar hemisphere. Three weeks later, the patient suffered an extensive stroke in these same areas. We therefore suggest that this method could be of great value in the assessment of vertebrobasilar insufficiency. (Stroke 1989;20:952-956)

Vertebrobasilar insufficiency (VBI) is a difficult clinical diagnosis because of the variety and nonspecificity of its signs and symptoms. Yet early diagnosis and consequent therapy can help prevent the transition from transient ischemia to extensive occipital stroke or lethal brainstem infarction. Unfortunately, ancillary tests such as electroencephalography (EEG), computed tomography (CT scan), Doppler ultrasonography, auditory evoked potentials (AEPs), and magnetic resonance imaging can do little to confirm this clinical diagnosis since their results remain normal until infarction develops. Only selective four-vessel angiography can help the clinician in VBI by giving an anatomic evaluation of the posterior circulation. But this invasive procedure has significant morbidity and is preferably avoided in the elderly or atheromatous patient and can give no functional data on blood flow adequacy.

Since various cerebellar imaging techniques seemed unhelpful in diagnosing VBI, we decided to focus on cerebellar vascular function as evaluated by its reactivity to acetazolamide and determined by xenon-133-inhalation single photon emission computed tomography (133Xe SPECT). We report the first case in which 133Xe SPECT and the acetazolamide test successfully demonstrated VBI by revealing hypoperfusion and impaired vasoreactivity in both the occipital lobes and the right cerebellar hemisphere of a patient who later suffered an extensive stroke in these same anatomic regions.

Case Report

A 60-year-old chronically hypertensive man was admitted for blood pressure stabilization. He reported a 2-month history of weekly attacks of vertigo, nausea, blurred vision, bifacial numbness, and lingual paresthesias of a few seconds' duration. These attacks were unrelated to postural changes, extreme head movement, or modifications in drug therapy. Blood pressure on admission was 180/90 mm Hg; the general physical and neurologic examination was otherwise normal, including the optic fundi and the visual fields. The electrocardiogram (EKG) was normal, while bidimensional cardiac echography showed only a slight left ventricular hypertrophy. EEG, electronystagmography, and brainstem AEPs were normal, as was cerebral CT scan. SPECT imaging of cerebral blood flow (CBF) distribution by means of the diffusible technetium-99m-labeled tracer hexa-methyl propylethanol amine oxime (HMPAO) was normal. Digitized angiography showed a large, mildly atheromatous left vertebral artery; the right vertebral artery was not clearly seen (Figure 1). Digitized angiography also incidentally revealed a small asymptomatic aneurysm of the anterior communicating artery, later confirmed by conventional carotid angiography.

A dynamic cerebral and cerebellar perfusion study was performed on admission by the xenon-133-inhalation method and a dedicated single photon emission computed tomograph (Tomomatic 564 SPECT, Medimatic, Copenhagen, Denmark) described in detail elsewhere. In brief, this tomo-
The graph consists of four arrays of 64 scintillation detector crystals rotating every 10 seconds around the patient’s head. A complete CBF study required only 10 minutes, during which 120 mCi of xenon-133 in 4 l air and oxygen were inhaled in a closed circuit. Five transaxial slices of brain tissue were studied simultaneously, each by a sequence of four tomographic images of the cerebral radioactive distribution. Arterial cerebral input was estimated by a lung curve obtained by placing a narrowly collimated detector over the apex of the right lung. A standard algorithm, based on a combination of sequential tomography, early picture methods, and the time-activity lung curve, was carried out after correction for tissue attenuation and background. Thus, we obtained average flow maps, where mean regional CBF and its standard deviation were calculated for all pixels. A semiautomatic fitting procedure delineated standardized, paired regions of interest corresponding to the two cerebellar hemispheres on the lowermost slice (Slice 1 at OM+1 cm), and to the three main intracranial arteries’ distribution on Slices 3 (OM+5 cm) and 4 (OM+7 cm). To test cerebral and cerebellar vasoreactivity, we performed a second CBF measurement in the same way, 20 minutes after an intravenous injection of 1 g acetazolamide, a powerful cerebral vasodilator, and then compared the two consecutive examinations. This method has been validated and standardized on the same equipment. In a population of 12 healthy subjects, the mean±SD resulting CBF increase was found to be almost constant at 15.7±5.1 ml/100 g/min, independent of age or basal flow values. Our own normative data were in accordance with this observation.

The test was carried out in a quiet, dark room with the patient’s eyes closed, but his ears unoccluded. End-tidal Pco₂ was monitored by an infrared capnograph. Between the two examinations, the patient remained recumbent in the same position. Reference marks placed on his face in alignment with a positioning laser assured identical head placement. At no time during this procedure did the patient report any transient neurologic incident.

While mean resting hemispheric cerebral CBF was normal at 63 (normal range 47–74) ml/100 g/min, mean resting cerebellar flows were abnormally asymmetrical, with an 11% decrease on the right (Figure 2). The administration of 1 g acetazolamide (Figure 3) induced 1) a paradoxical decrease in the right cerebellar hemisphere flow value of 6 ml/100 g/min, 2) a nonsignificant flow increase of 1 ml/100 g/min in the parieto-occipital regions (a markedly impaired vasodilatory response), and 3) a normal flow increase in the frontotemporal regions of 11 ml/100 g/min.

The incidental discovery of an unruptured cerebral aneurysm in an otherwise healthy patient is widely considered as an operative indication, and surgery was recommended. Eighteen days after the Xe SPECT study, having remained asymptomatic, the patient underwent right frontal craniotomy and aneurysmal clipping. The operation was uneventful, with systemic blood pressure maintained at >120/60 mm Hg; no signs of previous bleeding or ischemia were seen. Three days after surgery, the

FIGURE 1. Digitized angiography on admission. The left vertebral artery is wide but atheromatous, but the right vertebral artery is not clearly seen. There is no significant carotid stenosis.
FIGURE 2. $^{133}$Xe SPECT on admission: resting CBF distribution. On the lowermost slice (OM+1 cm), cerebellar perfusion is abnormal, with relative hypoperfusion in the right cerebellar hemisphere. The cerebral flow distributions 5 and 7 cm above the orbitomeatal line are normal. There is an artificial anterior flow "defect" on the lowermost slice, which is due to the elimination of the high activity pixels due to airway contamination. The same artifact is seen on Figure 3.

patient gradually developed right oculomotor paralysis, dysphagia, intense drowsiness, right hemiparesis, and cortical blindness. Brainstem AEPs showed a pathologic lengthening of the I-V interval on right-sided stimulation. A CT scan revealed sharply delineated areas of hypodensity in both occipital lobes and in the right cerebellar hemisphere (Figure 4), the same areas first described as pathological by $^{133}$Xe SPECT 3 weeks earlier. Static CBF imaging by HMPAO SPECT showed only a relative occipital hypoperfusion.

Discussion

This case represents the first successful use of $^{133}$Xe SPECT and the acetazolamide test in the diagnosis of VBI, a difficult clinical syndrome unidentified by any quantitative ancillary test to date.

Though regional CBF measurements by xenon-$^{133}$ administration and multiple detectors has been available for many years, the bidimensional measure of resting cerebral or cerebellar flows have often been of limited practical value, in particular, a study of VBI in which there was a great overlap between patients and controls. The three-dimensional study of CBF has been made possible by the use of CT techniques. Three such modalities are now in use: positron emission tomography, CT scan coupled with the administration of high doses of stable xenon, and SPECT, in which a rotating gamma camera detects single photon-emitting radionuclides and reconstructs the acquired data in three dimensions. Since 1983, the use of SPECT in the evaluation of cerebral vascular disease has been growing rapidly, particularly CBF imaging by such diffusible tracers as $^{[123]}$I-isopropyl-$p$-iodoamphetamine and the technetium-99m-labeled complex of HMPAO, whose high cerebral uptake and prolonged cerebral retention allow sufficient data acquisition for tomographic reconstruction by a single conventional rotating gamma camera. The CBF images thus obtained are of excellent quality. However, there are some major limitations to static SPECT CBF imaging. Because of the nonlinear relation between blood flow and HMPAO uptake due mainly to flow-dependent back-diffusion of this tracer from the brain to the bloodstream, no absolute quantification of CBF is routinely possible. Evaluation is either by visual inspection or relative count ratios, and closely repeated examinations for dynamic studies are difficult because of the tracers' long biologic half-lives.

$^{133}$Xe SPECT does not suffer the same limitations; though it demands a dedicated system with a rapidly rotating tomograph (such as the Tomomatic 564) and the use of xenon-$^{133}$, the lower energy photons of which generate more scattered radiation and a lower resolution, the very rapid washout of xenon-$^{133}$ allows quantitative CBF studies, not just imaging. The short biologic half-life of xenon-$^{133}$ permits retesting after 25 minutes, allowing different types of dynamic CBF study: by sensory activation, by vertebral artery compression (VAC), by induced vasodilation by 7% CO$_2$ inhalation, or by the intravenous administration of 1 g acetazolamide. Dynamic CBF testing has as yet been little applied to cerebellar pathology. The only
FIGURE 3. \(^{133}\)Xe SPECT on admission: CBF distribution, 20 minutes after injection of acetazolamide. There is a paradoxical flow decrease in the right cerebellar hemisphere and absent vasodilatory response in the posterior circulation. The response in the anterior circulation is normal.

FIGURE 4. Computed tomographic scan performed one month after admission. Three days after the acute onset of stroke, CT scan demonstrated a) large bilateral hypodensities in both occipital lobes and b) a large hypodensity in the right cerebellar hemisphere, visible despite the artifacts due to the aneurysmal clip.
published study on VBI with dynamic CBF evaluation used VAC as the vascular challenge in 10 patients suspected of postural VBI to no avail. Cerebellar vasoreactivity testing by acetazolamide seems more opportune, having shown particular promise in the work-up of carotid transient ischemic attacks and in carotid stenosis. A harmless but powerful cerebral vasodilator, acetazolamide provides a more intense vascular challenge than VAC and is easier to administer than 7% CO2 inhalation, which can provoke nausea, tachycardia, and increased blood pressure. The vasodilation thus induced is not only powerful but dose-dependent and reproducible, with no relation to age or to the resting blood flow. How acetazolamide produces this vasodilation is still in doubt. Three concurrent actions have been proposed: induced cerebral acidosis by carbonic anhydrase inhibition in the erythrocytes, direct action on the carbonic anhydrase within the media of cerebral arteries, and a direct action on the vascular smooth muscle cell, independent of carbonic anhydrase inhibition. With such a sensitive drug challenge, any regional impairment of vasoreactivity preventing maximum vasodilation could be revealed and quantified by 133Xe SPECT. In studies on cerebral ischemic disease, this kind of induced regional hyperperfusion has indeed been demonstrated since acetazolamide enhanced regional side-to-side CBF asymmetry in both thomboembolic and essentially postural carotid disease. The same can be expected of the posterior cerebral circulation. The multifactorial nature of VBI should make a vasodilatory challenge with acetazolamide an extremely sensitive test, as we saw in our patient. That altered vasoreactivity in the posterior cerebral circulation could be demonstrated even when the patient was asymptomatic and recumbent suggests that 133Xe SPECT and the acetazolamide test should be explored as a means of early detection and perhaps diagnosis in VBI. A prospective study to evaluate these propositions is now under way.

References

Key Words • acetazolamide • tomography, emission computed • cerebral blood flow • vertebrobasilar circulation
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Stroke. 1989;20:952-956
doi: 10.1161/01.STR.20.7.952

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1989 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/20/7/952

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