Objective: To evaluate the frequencies of symptoms and signs in patients with posterior circulation ischemia in a large case series of prospectively collected patients.

Design: Case series.

Setting: Outpatient and inpatient setting at the New England Medical Center, a tertiary care referral center in Boston, Massachusetts.

Patients: Consecutive sample of 407 adult patients who had stroke and/or transient ischemic attacks in the posterior circulation within 6 months of study inclusion. All patients were examined by senior stroke neurologists. All patients had either computed tomography or magnetic resonance imaging of the brain as well as vascular imaging of the head and neck. The study included 256 men (63%) and 151 women (37%).

Main Outcome Measures: Frequencies of posterior circulation ischemic symptoms and signs. These outcome measures were planned before data collection began. Correlations between symptoms and signs with separate vascular territories of the posterior circulation were then analyzed.

Results: The most frequent posterior circulation symptoms were dizziness (47%), unilateral limb weakness (41%), dysarthria (31%), headache (28%), and nausea or vomiting (27%). The most frequent signs were unilateral limb weakness (38%), gait ataxia (31%), unilateral limb ataxia (30%), dysarthria (28%), and nystagmus (24%). Logistic regression analysis reveals that the clinical features dysphagia ($P=0.004$; 95% CI, 1.8-24.4), nausea or vomiting ($P=0.002$; 95% CI, 1.6-8.2), dizziness ($P=0.047$; 95% CI, 1.0-5.4), and Horner syndrome ($P=0.001$; 95% CI, 2.4-26.6) were positively correlated with the proximal vascular territory. Unilateral limb weakness ($P=0.001$; 95% CI, 1.7-8.7) and cranial nerve VII deficits ($P=0.02$; 95% CI, 1.1-5.3) were positively correlated with the middle territory. Limb sensory deficit ($P=0.001$; 95% CI, 1.8-7.8), lethargy ($P=0.001$; 95% CI, 2.3-12.4), and visual field loss ($P=0.001$; 95% CI, 5.3-23.9) were positively correlated with the distal territory.

Conclusions: We report the most frequent symptoms and signs in the largest published registry, the New England Medical Center Posterior Circulation Registry, of patients with posterior circulation ischemia who had complete neurological examinations and extensive cerebrovascular imaging. Knowledge of the vascular territory involved aids in the diagnosis of the causative vascular lesion and stroke mechanism.


SYMPTOMS AND SIGNS TAKE center stage during the clinical encounter. They provide the basis for clinical diagnosis. Separation of transient and persistent brain ischemia from other neurological causes as well as localization of the findings to the anterior or posterior circulation are based on symptoms and signs and are important to effectively plan brain and vascular imaging and other investigations. Past estimates of the frequency, sensitivity, and specificity of various clinical findings in patients suspected of having vertebrobasilar occlusive disease were not based on documentation of posterior circulation infarction. In some early series, the diagnosis of vertebrobasilar disease was not confirmed by angiography or other vascular imaging. In other series, symptoms and signs were reported in patients with specific subtypes of posterior circulation ischemic disease (eg, basilar artery occlusion, lateral medullary infarction, cerebellar infarction). More recently, a prospective study of 116 patients with posterior circulation ischemia from Qatar was published.

We analyzed the symptoms and signs in a prospectively collected large database of patients with posterior circulation transient ischemic attacks (TIAs) and strokes. From 1988 to 1996 at the New England Medical Center, Boston, Massachusetts, we extensively evaluated 407 patients with posterior circulation ischemia.
using brain imaging, vascular imaging (initially digital subtraction dye angiography and later magnetic resonance angiography), and relevant cardiac and hematological studies. Patient data were entered into the New England Medical Center Posterior Circulation Registry (NEMC-PCR). Previous reports from this registry analyzed risk factors, distribution of infarcts, mechanisms of ischemia, location of occlusive vascular lesions, and outcomes.2-4,6-17

METHODS

The NEMC-PCR, which consisted of patients collected from 1988 to 1996, had 3 major inclusion criteria. First, all patients were examined by 3 senior stroke neurologists. Second, all patients must have had strokes or TIAs in the posterior circulation within the prior 6 months. Strokes must have been documented by computed tomography or magnetic resonance imaging (MRI) of the brain (>80% had MRI of the brain). The TIAs were in the vertebrobasilar territory with vascular imaging demonstrating vertebrobasilar occlusive lesions. Third, all investigations needed to be adequate.

The NEMC-PCR data included demographic characteristics and risk factors as described in a prior article.4 The following data were also recorded: stroke localization, vascular lesions, stroke mechanisms, cause of vascular, cardiac, and hematological conditions, and outcome data. All patients had head and neck vascular imaging (80% had conventional angiograms). Extracranial ultrasonography was used extensively, and more than 80% of patients had transcranial Doppler ultrasonography performed. Cardiac studies included electrocardiography, transthoracic echocardiography, transesophageal echocardiography, and/or 24-hour rhythm monitoring. Each case was reviewed at least twice to ensure accurate data entry as well as correct and complete diagnoses. The criteria for stroke mechanisms were described in a previous article.4

The location of ischemic events was determined clinically and by brain imaging. In the NEMC-PCR, brain lesions were categorized as involving proximal, middle, and distal intracranial posterior circulation territories. The proximal territory included regions supplied by the intracranial vertebral artery—the medulla oblongata and the posterior inferior cerebellar artery–supplied region of the cerebellum. The middle territory included brain regions supplied by the basilar artery up to its superior cerebellar artery branches—the pons and anterior inferior cerebellar artery–supplied region of the cerebellum. The distal territory included regions supplied by the rostral basilar artery, superior cerebellar artery, posterior cerebral artery, and their penetrating artery branches—midbrain, thalamus, superior cerebellar artery–supplied cerebellum, and posterior cerebral artery territories. The distribution of territories is shown in Figure 1.2

We analyzed the frequency of various symptoms and signs that occurred at or soon after presentation in patients with posterior circulation ischemia. We also analyzed the frequencies of symptoms and signs of infarcts in each of the 3 vascular territories of the posterior circulation. Logistic regression analysis was conducted to establish correlations between infarct symptoms and signs with vascular territories. In the logistic regression analysis, symptoms and signs that were similar were considered as 1 variable; these included dysarthria, unilateral limb weakness, bilateral limb weakness, hiccups, nausea or vomiting, hearing loss, cranial nerve V deficits, limb sensory deficits, loss of consciousness, and lethargy. Others were considered as either symptoms or signs.

RESULTS

The NEMC-PCR included 256 men (63%) and 151 women (37%). The average age was 60.5 years. At presentation, 100 subjects were outpatients and 307 were inpatients. Strokes without TIA occurred in 240 patients (59%). Ninety-eight patients (24%) had a TIA before stroke, and 4 patients (1%) had a TIA after stroke. Sixty-five patients (16%) had only a TIA.

Three hundred thirty-nine patients (83%) had territorial infarcts on brain imaging. Another 8 patients had signs localizing to 1 intracranial territory. The most frequent location of single-territory infarcts was the distal intracranial territory (143 patients). Fifty-six patients had infarcts localized to the middle intracranial territory, and 62 patients had infarcts localized to the proximal intracranial territory. Eighty-three patients had infarcts in multiple territories. The percentages of infarcts in the proximal, middle, distal, and multiple territories were 18%, 16%, 41%, and 25%, respectively.

In the entire posterior circulation, the most frequent symptoms are shown in Figure 2 and the most frequent signs are shown in Figure 3. In the proximal territory, the most frequent symptoms are shown in Figure 4 and the most frequent signs are shown in Figure 5. In the middle territory, the most frequent symptoms are shown in Figure 6 and the most frequent signs are shown in Figure 7. In the distal territory, the most
Logistic regression analysis reveals that the clinical features dysphagia \( (P = .004; 95\% \text{ CI}, 1.8-24.4) \), nausea or vomiting \( (P = .002; 95\% \text{ CI}, 1.6-8.2) \), dizziness \( (P = .047; 95\% \text{ CI}, 1.0-5.4) \), and Horner syndrome \( (P = .001; 95\% \text{ CI}, 2.4-26.6) \) were positively correlated with the proximal territory.

Logistic regression analysis shows that unilateral limb weakness \( (P = .001; 95\% \text{ CI}, 1.7-8.7) \) and cranial nerve VII deficits \( (P = .02, 95\% \text{ CI}, 1.1-5.3) \) were positively correlated with the middle territory.

Logistic regression analysis reveals that the variables limb sensory deficit \( (P = .001; 95\% \text{ CI}, 1.8-7.8) \), lethargy \( (P = .001; 95\% \text{ CI}, 1.9-8.1) \), and dysarthria \( (P = .001; 95\% \text{ CI}, 1.3-7.0) \) were positively correlated with the distal territory.
95% CI, 2.3-12.4), and visual field loss (P = .001; 95% CI, 5.3-23.9) were positively correlated with the distal territory.

**COMMENT**

Prior estimates of symptom and sign frequencies in vertebrobasilar ischemia were based on knowledge of brain structures and assumptions as well as small case series. These early case series had many limitations. Patients who had strokes and TIs were often not differentiated. Data were obtained primarily via necropsy. If conventional angiography was done at all, it was typically for the most ill patients. Modern brain imaging (eg, computed tomography and MRI of the brain) was not available. Details of vascular stenoses and occlusions were sometimes scanty and not quantitative.

The classic 1946 article by Kubik and Adams[^1^] detailed the clinical features of vertebrobasilar ischemia due to basilar artery occlusion in 18 patients who were studied post mortem. Early ischemic features included sudden alterations of consciousness ranging from mild confusion to coma. Decreased level of consciousness sometimes improved temporarily. Headache and dizziness (usually without vertigo) also occurred early. All the patients had weakness—many were hemiplegic, but some were quadriplegic. Four patients had ipsilateral cranial nerve signs and contralateral limb signs. Prominent features included pupillary defects, oculomotor palsies, facial palsy, bilateral extensor plantar reflexes, and dysarthria. Some patients had pathological laughing and crying.

According to Bradley et al[^2^], salient features of brainstem ischemia included the combination of long tract signs and cranial nerve deficits. The presence of a crossed sign (an ipsilateral cranial nerve deficit and a contralateral long tract sign) helped localize a lesion to the brainstem. Fre-
quent features of posterior circulation ischemia included coma, ataxia, nystagmus, and vertigo. Signs that are seen only in vertebrobasilar ischemia include internuclear ophthalmoplegia, unreactive pupils, and skew deviation. Bilateral pyramidal tract lesions in the pons may cause locked-in syndrome. Patients with locked-in syndrome are quadriplegic with preserved consciousness but are unable to speak. They can communicate only by blinking and vertical eye movements. Vertebrobasilar ischemia may produce “top of the basilar” syndrome with infarcts in the midbrain, thalamus, medial temporal lobe, and occipital lobe. Patients may have somnolence, delirium, memory loss, and peduncular hallucinations. The syndrome may present with oculomotor deficits including impaired upgaze or downgaze, convergence deficit, eyelid retraction, and skew deviation. Other findings may involve hemianopia, cortical blindness, and Balint syndrome.

More recent investigations of the posterior circulation have used modern brain imaging to identify ischemic lesions and their corresponding clinical features. Striking variability was apparent between the frequency of clinical features in the NEMC-PCR and a prospective collection of 116 patients from Qatar with posterior circulation ischemic strokes studied between 2005 and 2008. All of the patients from Qatar were imaged with computed tomography and/or MRI of the brain as well as either with magnetic resonance angiography or computed tomographic angiography of the brain and neck or with conventional angiography. The frequencies of symptoms were as follows: dizziness, 75%; unsteadiness, 65%; dysarthria, 64%; nausea or vomiting, 60%; limb weakness, 49%; and altered mental status, 18%. The NEMC-PCR and Qatar studies had a similar symptom frequency of altered mental functions but had widely different frequencies of dizziness, dysarthria, and nausea or vomiting. The symptom limb weakness was slightly more frequent in the Qatar study than in the NEMC-PCR study (49% vs 44%, respectively). The sign frequencies in the Qatar study were as follows: limb weakness, 61%; ataxia, 65%; facial palsy, 65%; and nystagmus, 48%. The NEMC-PCR and Qatar studies had sharply divergent frequencies of the signs limb weakness, ataxia, facial palsy, and nystagmus. Multiple symptoms and signs were not reported by the Qatar study.

Why were the frequencies so different in Boston and Qatar? Differences in the severity of vertebrobasilar ischemia between the 2 patient populations in the NEMC-PCR and Qatar studies may have influenced results. Referral bias may have resulted in one center having more critically ill patients. Based on mortality rates, the patients from Qatar seemed more ill. Whereas the mortality rate in the NEMC-PCR study was 4% at 30 days, in the Qatar study it was 10% at hospital discharge and 11% at 90 days.5,6 Disability rates in the 2 studies were comparable. In the NEMC-PCR study, 28% of patients had no disability and 51% had minor disability at 30 days (based on the Modified Rankin Scale score).4 In the Qatar study, 68% of patients had a Modified Rankin Scale score of 2 or lower at 33 days. If one study had a higher percentage of very ill patients, this may have skewed the percentage of particular clinical features, perhaps increasing the frequency of hemiparesis, for instance.

The MRI technology was less advanced during the NEMC-PCR study than during the Qatar study, especially with regard to diffusion-weighted imaging, which was just becoming available. This may have limited detection of anterior or posterior circulation infarcts. Also, events classified as TIAs in the NEMC-PCR may actually have been strokes.

In the NEMC-PCR, logistic regression analyses demonstrated correlations between clinical features and particular vascular territories. However, the presence of these clinical features in a patient does not prove localization to a vascular territory. Instead, these correlations raise awareness that these localizations should be considered.

The logistic regression analysis reveals that dysphagia, nausea or vomiting, dizziness, and Horner syndrome are important features of proximal territory infarcts. While these features can occur throughout the posterior circulation, it may be the frequency of lateral medullary infarcts (30%) in the proximal territory that accounts for these findings. Two studies that each examined 33 patients with lateral medullary infarcts found high frequencies of the features dizziness (52%-91%), nausea (48%-73%), and dysphagia (52%-61%).

The middle territory was positively correlated with facial weakness and unilateral limb weakness. Quadriparalysis has long been thought to be the hallmark of bilateral pontine base infarction, but in our study hemiparesis was more common than quadriparesis. Occlusions of penetrating pontine arteries (resulting in anteromedial or anterolateral pontine infarcts) or occlusions of the basilar artery account for most middle territory infarcts. Prior studies, weakness occurred in 83% to 99% of anteromedial pontine infarcts and 77% to 100% of anterolateral pontine infarcts. Patients with basilar artery occlusions in the NEMC-PCR had weakness 56% of the time. However, facial and/or limb weakness is not specific to the pons or middle territory given that it can localize to several other areas, including the internal capsule, basal ganglia, subcortex, and motor cortex. Facial and limb paralyses point to a pontine location and most often penetrating artery or basilar artery occlusion.

The distal posterior circulation territory is most often involved. Infarcts in this region were positively correlated with limb sensory deficits, lethargy, and visual field loss. Limb sensory deficits may be correlated with the distal territory because this may occur as a result of lateral thalamic infarcts as well as spinthalamic and medial lemniscus tract infarcts. Lethargy and somnolence are common in patients with rostral midbrain and thalamic infarction. Visual field loss is specific for the distal territory because the visual cortex, part of the optic radiations, and the lateral geniculate nucleus are included within the posterior cerebral artery territory. Similar results were found by 3 posterior cerebral artery stroke registries, which described high frequencies of sensory deficits (15%-46%), confusion (17%-29%), and visual disturbances (57%-94%).

Prognosis, stroke mechanisms, and vascular lesions vary according to localization to proximal, middle, or distal posterior circulation territory. Proximal territory infarcts are associated with a better prognosis than middle or distal territory infarcts. The relative risk of proximal ter-
ritory infarcts for a poor outcome (severe disability or death measured as Modified Rankin Scale scores of 4 or 5) was 0.81 (95% CI, 0.5-1.3; P = .37). Proximal territory infarcts are most often due to occlusive disease of the intracranial vertebral artery or embolism from the vertebral artery or heart. The relative risk of middle territory infarcts for a poor outcome was 1.88 (95% CI, 1.28-2.79, P = .002), and the relative risk of distal territory infarcts was 3.12 (95% CI, 1.92-5.07; P = .001). Middle territory infarcts are most often due to basilar artery occlusion or penetrating artery disease. Distal territory infarcts are predominantly cardio-embolic or intra-arterial embolic. Patients with distal territory infarcts accounted for 42% of cases with mortality or major disability after 30 days, while involvement of proximal and middle territories accounted for 4% and 13%, respectively. The most probable reason for higher risk with distal territory infarcts was the greater proportion of embolic causes. Middle territory infarcts likely have higher morbidity and mortality due to basilar artery occlusions.4 In summary, in the NEMC-PCR, every patient had a thorough neurological examination, complete brain and vascular imaging, and detailed reporting of symptoms and signs. Posterior circulation brain ischemia is complex, and patients present with a multitude of symptoms and signs. Certain clinical features are correlated with particular vascular territories. Localization of an infarct to a particular vascular territory has important implications for diagnosis, prognosis, and treatment.

Accepted for Publication: September 21, 2011. Published Online: November 14, 2011. doi:10.1001/archneurol.2011.2083

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Financial Disclosure: None reported.

REFERENCES