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Ultrasound Diagnosis of Spontaneous Carotid Dissection With Isolated Horner Syndrome

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Background and Purpose—Isolated Horner syndrome without associated cranial nerve palsies or ischemic symptoms is an important presentation of spontaneous internal carotid artery dissection (sICAD). Ultrasound is often used as a screening method in these patients because cervical MRI is not always available on an emergency basis. Current knowledge on ultrasound findings in patients with sICAD presenting with isolated Horner syndrome is limited.

Methods—Patients were recruited from prospective cervical artery dissection databases of 3 tertiary care centers. Diagnosis of sICAD was confirmed by cervical MRI and MR angiography or digital subtraction angiography in all patients. Data on Doppler sonography and color duplex sonography examinations performed within 30 days of symptom onset were analyzed.

Results—we identified 88 patients with Horner syndrome as the only sign of sICAD. Initial ultrasound examination was performed in 72 patients after a mean time interval from symptom onset to examination of 11 (SD 8) days. The overall frequency of false-negative ultrasound findings was 31% (22 of 72 patients). It showed stenosis ≥80% or occlusion in 34 (47%) patients, and stenosis ≤80% in 16 (22%). It visualized mural hematoma in 7 patients and intimal flap in one. Patients with normal ultrasound were less frequently smokers (9% versus 28%, P = 0.034), and had less frequently migraine without aura (9% versus 43%, P = 0.012) or neck pain (18% versus 62%, P = 0.003) than those with pathological ultrasound findings.

Conclusions—Nearly one third of patients with Horner syndrome as the only sign of sICAD presented with normal ultrasound findings. These results indicate that ultrasound is not a reliable method to diagnose sICAD in patients with isolated Horner syndrome.

Key Words: carotid artery ■ diagnostic methods ■ ultrasound

Most patients with spontaneous dissection of the internal carotid artery (sICAD) come to clinical attention after stroke and other ischemic events. However, about 20% of patients with sICAD experience only local symptoms (head or neck pain, pulsatile tinnitus), local signs (Horner syndrome, cranial nerve palsy), or both. Horner syndrome, mostly accompanied by headache or neck pain, without associated cranial nerve palsy and without ischemic symptoms (isolated Horner syndrome) is the most common presenting local sign and occurs in 10% to 13% of patients with sICAD. This group of sICAD patients is of particular interest, because ischemic stroke may potentially be prevented. Nowadays, the diagnosis of sICAD is mainly based on cervical MRI and MR angiography (MRA). In contrast to ultrasound, cervical MRI and MRA are not always available on an emergency basis. Therefore, ultrasound is still widely used to screen patients with suspected sICAD. We have recently shown that ultrasound is a reliable screening tool for evaluating the presence of sICAD in patients presenting with carotid territory ischemia. However, few data exist about the diagnostic accuracy of ultrasound in patients with sICAD causing isolated Horner syndrome.

The aim of this study was to describe ultrasound findings and determine the sensitivity of this method to diagnose sICAD in patients presenting with acute isolated Horner syndrome.

Methods

Patient Selection
We analyzed prospectively collected data of consecutive patients presenting with sICAD at 3 tertiary care centers from December 1996 through January 2006. ICAD were categorized as spontaneous. The aim of this study was to describe ultrasound findings and determine the sensitivity of this method to diagnose sICAD in patients presenting with acute isolated Horner syndrome.
Patients were included if they had (1) isolated Horner syndrome (with or without headache or neck pain) without associated cranial nerve palsies and without ischemic symptoms caused by sICAD, (2) ultrasound studies performed within 30 days of symptom onset (to avoid inclusion of many patients with early recanalization),22–24 and (3) MRI/MRA or digital subtraction angiography (DSA) signs of sICAD.  

Symptom onset was defined as follows: (1) new headache or neck pain on the side of Horner syndrome, or (2) unusual bilateral headache or neck pain, or (3) acute ipsilateral Horner syndrome reported by the patient or diagnosed on clinical examination, or (4) a combination of these symptoms and signs. The definite diagnosis of sICAD was based on cervical MRI and MRA or DSA, or both using the criteria mentioned below. Clinical or ultrasound findings of some patients have been reported previously.1,14,15

Baseline Investigations  
All patients underwent neurological examinations, routine blood examinations, ECG, cervical MRI with fat suppression technique and MRA or DSA, or both. The following risk factors were assessed: current smoking,16 hypercholesterolemia,4 and hypertension defined as a history of antihypertensive treatment or a history of hypertension (systolic blood pressure >160 mm Hg or diastolic blood pressure >90 mm Hg, or both until September 2000. The new WHO criteria for diagnosis of hypertension (systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg, or both) were used since October 2000.17 Diabetes mellitus was defined as reported previously.1 A history of migraine was defined according to the criteria of the International Classification of Headache Disorders.18 Family history of spontaneous cervical artery dissection was based on affected first-degree relatives.

Ultrasound Studies  
Ultrasound studies of the cerebral arteries were performed within 24 hours of admission by certified neurologists using color duplex sonography (Acuson XP 10 or Sequoia) and Doppler sonography (EME or Multi-Dop X4; DWL; or Angiodyne DMS). For extracranial insonation of the ICA origin, the common carotid artery and the cervical ICA, transorbital, transtemporal and transforaminal studies, external carotid, the vertebral artery and subclavian artery, 4- to 6-MHz linear probes were used. For extracranial insonation of the cervical ICA, transorbital, transtemporal and transforaminal studies, 2- to 3.5-MHz color duplex sonography sector probes or 2-MHz Doppler probes were used. Transorbital insonation was used to investigate the ophthalmic arteries and the carotid siphon. The temporal window was used to insonate the terminal (C1) segment of the ICA, the middle, anterior, and posterior cerebral arteries, and the anterior communicating artery.19,20 Transforaminal insonation was used to assess the intracranial vertebral artery and basilar arteries.  

SICAD was suspected in patients presenting with stenosis or occlusion of the cervical ICA in color duplex sonography in the absence of significant atherosclerotic disease of the extracranial carotid arteries (carotid plaques with at best ≤30% stenosis) or vasculitis.9 Stenoses of the cervical ICA were quantified as reported before.1,9 A ≤50% stenosis was diagnosed, when intrastenotic peak systolic velocity was >90 cm/s in women and >80 cm/s in men, and the peak systolic velocity ratio intrastenotic ICA/contralateral cervical ICA was >1.12. A 51% to 80% stenosis was diagnosed when intrastenotic peak systolic velocity was >120 cm/s and the peak systolic velocity ratio intrastenotic ICA/contralateral cervical ICA was >1.5. Intrastenotic velocities are frequently decreased in ICAD causing high-grade stenosis.21 Therefore, an 81% to 99% stenosis was diagnosed using prestenotic and poststenotic hemodynamic criteria.22–24 ICA occlusion was assessed as reported before.25 Using DSA as standard of reference, we have shown that ultrasound may misdiagnose subtotal stenosis as occlusion in acute sICAD.23 Therefore, sICAD causing 81% to 99% stenosis and occlusion were grouped together. Intracranial arteries were investigated according to previously published criteria.26,27 The degree of stenosis and the following ultrasound findings assumed to be typical for sICAD were entered in the database: hypoechoegenic wall hematoma, false lumen, hypererechoegenic flap, and pseudoeuryeurysem.28–30 All except 2 patients with insufficient temporal bone window had complete ultrasound evaluation. None of the patients with normal US findings had insufficient temporal bone window.

Cervical MRI and Angiographic Studies  
MRI and MRA were performed with 1.5 Tesla magnet equipment. Wall hematoma was diagnosed with T1-weighted MRI with fat suppression technique. The following MRA techniques were used for assessing the degree of stenosis and dissecting aneurysm: first-pass gadolinium enhanced 3-dimensional MRA, 2-dimensional time of flight MRA, or 3-dimensional time-of-flight MRA. Stenoses were classified using the local degree of stenosis. Cervical MRI diagnosis of sICAD was based on the detection of a wall hematoma. Angiographic diagnosis of sICAD was based on detection of a flame-shaped occlusion, a string sign, a segmental stenosis distal to the carotid bulb, a dissecting aneurysm, double lumen or intimal flap. Flame-shaped carotid occlusions were assumed to result from sICAD when cervical MRI delineated a wall hematoma.6,31

All ultrasound and radiological findings including confirmation of sICAD diagnosis were reviewed by an experienced neurologist in each center (M.A. and C.S. in Paris, M.A. in Berne, and R.W.B. in Zurich). In patients with multiple cervical artery dissections only the carotid artery causing Horner syndrome was analyzed.

Statistical Analysis  
Statistical analysis was performed with the SPSS 10.0 for Macintosh program. The overall frequency of patients with normal initial ultrasound finding was calculated, and subgroup analyses were performed according to (1) the date of initial ultrasound examination (first versus second half of the observation period) and (2) by center dataset. Differences between patients with normal- and those with abnormal-presenting ultrasound findings were analyzed. For differences in categorical variables χ² test was performed. Continuous variables were compared with Mann–Whitney test. The variables included were sex, age, family history of dissection, headache, neck pain, current smoking, diabetes, hypertension, hypercholesterolemia, history of migraine with aura, history of migraine without aura, history of minor trauma, presence of multiple dissections, and time from symptom onset to ultrasound examination. Then logistic regression analysis with a forward stepwise method was performed to determine the independent association of normal ultrasound findings with other variables. The cutoff in the univariate analyses as requirement for inclusion in the multivariate analyses was P<0.25.

Results  
Demographic Data and Presenting Characteristics  
Among 415 consecutive patients with sICAD, we identified 88 patients (21%) with isolated Horner syndrome. Patients were recruited in the University Hospitals of Paris Lariboisière (n = 51, 58%), Zurich (n = 19, 22%) and Bern (n = 18, 20%). Sixteen patients were not included, because the ultrasound examination was performed >30 days after symptom onset. Thus, 72 patients were included. The mean time interval from symptom onset to ultrasound examination was 11 ± 8 days (median, 11 days; range, 4 hours to 30 days). The mean age of the patients was 45 ± 15 years. Forty-seven (65%) patients were men. Thirty-two (44%) patients presented with single left, 32 (44%) with single right, and 4 (6%) with bilateral sICAD. In 4 patients with unilateral sICAD (6%), additional spontaneous vertebral artery dissections were detected, unilateral in 3 and bilateral in 1 of them.
interval from symptom onset to MRI was 11/1006. Cervical MRI was performed in all 72 patients. The mean MRI Findings cervical MRI, angiographic, and cerebral ultrasound findings in the dissected ICA including a 51% to 80% stenosis syndrome. The remaining 50 patients had pathological ultrasound findings in the dissected ICA resulting in a sensitivity of 69% for detecting sICAD causing Horner syndrome in 16 (22%) patients and a stenosis of the ICA distal to the carotid bulb on MRA and DSA. Sixty-eight patients underwent MRA, one DSA, and 3 both MRA and DSA. The mean interval from symptom onset to MRA was 11 ± 8 days, and from symptom onset to DSA 11 ± 2 days. MRA or DSA showed on the side of the Horner syndrome in the cervical ICA normal findings in 4 patients, a stenosis >80% or occlusion in 33 patients, a 51% to 80% stenosis in 13 and a stenosis <50% in 22 patients. Five patients with a stenosis of the cervical ICA showed also an aneurysm distal to the stenosis. In all patients the site of the dissection was typical and started distal to the carotid bulb. Brain MRI was normal in all patients.

### Ultrasound Findings

Twenty-two (31%) of 72 patients showed falsely normal ultrasound findings in the dissected ICA resulting in a sensitivity of 69% for detecting sICAD causing Horner syndrome. The remaining 50 patients had pathological ultrasound in the dissected ICA including a 51% to 80% stenosis in 16 (22%) patients and a >80% stenosis or occlusion in 34 (47%) cases. A mural hematoma was visualized in 7 (10%) patients and an intimal flap in one (1%). The overall frequency of patients with normal initial ultrasound findings did not differ between the 3 centers (Lariboisière Paris, 17 [35%] of 48 patients; Zurich 3 [21%] of 14 patients; and Bern 2 [20%] of 10 patients; \( P = 0.447 \)). There was no difference according to the date of initial ultrasound examination in the first (December 1996 to December 2001) and the second half (January 2002 to January 2006) of the observation period. In the first period 9 (25%) of 36 patients had normal initial ultrasound findings and in the second period 13 (36%) of 36 patients; \( P = 0.31 \).

Compared with patients with pathological ultrasound findings, those with normal ultrasound findings tended to have a longer mean interval from symptom onset to examination (14 ± 10 versus 10 ± 7 days, \( P = 0.644 \)), were less often current smokers (9% versus 28%, \( P = 0.034 \)), and had less frequently a history of migraine without aura (9% versus 43%, \( P = 0.012 \)) or neck pain caused by the dissection (18% versus 62%, \( P = 0.003 \)).

### Cervical MRI, Angiographic and Cerebral MRI Findings

Cervical MRI was performed in all 72 patients. The mean interval from symptom onset to MRI was 11 ± 8 days. MRI showed a mural hematoma in 71 patients. The patient without mural hematoma on MRI had an aneurysm and a stenosis of the ICA distal to the carotid bulb on MRA and DSA. Sixty-eight patients underwent MRA, one DSA, and 3 both MRA and DSA. The mean interval from symptom onset to MRA was 11 ± 8 days, and from symptom onset to DSA 11 ± 2 days. MRA or DSA showed on the side of the Horner syndrome in the cervical ICA normal findings in 4 patients, a stenosis >80% or occlusion in 33 patients, a 51% to 80% stenosis in 13 and a stenosis <50% in 22 patients. Five patients with a stenosis of the cervical ICA showed also an aneurysm distal to the stenosis. In all patients the site of the dissection was typical and started distal to the carotid bulb. Brain MRI was normal in all patients.

### Discussion

We found that the sensitivity of ultrasound for detecting patients with sICAD causing isolated Horner syndrome without associated ischemic symptoms or cranial nerve palsies was only 69%. This means that nearly a third of patients showed normal ultrasound findings.

Different studies have reported conflicting results with respect to ultrasound findings in patients with acute sICAD. The results of the present study are in contrast to those of previous studies evaluating the accuracy of ultrasound to diagnose sICAD causing exclusively or mainly carotid territory ischemia. The largest study reported a sensitivity of 96% for color duplex ultrasound to diagnose an acute sICAD defined by MRI/MRA or DSA in 177 patients with first carotid territory ischemia. Another investigation found a sensitivity of 84% with subsequently proven ICAD. Nine of 55 patients had normal initial neurovascular ultrasound findings despite comprehensive examination. A third survey reported a sensitivity of 95% for combined extracranial
duplex/Doppler sonography and transcranial Doppler sonography performed to diagnose sICAD in 43 patients with clinical suspicion of this disease.\textsuperscript{25} Another study including 23 patients with sICAD with or without ischemic symptoms and signs reported a sensitivity of 73.9\% on admission and a sensitivity of 91.3\% on repeated examinations after an average of 4.5 weeks.\textsuperscript{33} In a previous study we have shown that patients with sICAD causing ischemic events had a higher prevalence of >80\% stenoses and occlusions of the ICA than those causing no ischemic events.\textsuperscript{1} These observations and the results of the current study suggest that normal initial ultrasound findings are mainly observed in patients with ICAD causing only local signs such as Horner syndrome. These differences may be explained by the fact that mural hematomas in patients with sICAD with isolated Horner syndrome extend less often toward the vessel lumen and thus cause less often stenosis with hemodynamic impairment compared with patients with sICAD causing cerebral or retinal ischemia.\textsuperscript{1}

In our study, smokers, patients with a history of migraine without aura and those with neck pain were less likely to present with falsely normal ultrasound findings. However, also in these subgroups ultrasound was normal in several patients and therefore did not reliably exclude sICAD.

The low sensitivity of ultrasound in sICAD patients with isolated Horner syndrome is of particular importance in every day clinical practice, because emergency physicians may tend to use a widely available and less expensive examination technique such as neurovascular ultrasound especially in patients without ischemia, whereas patients with cerebral ischemia are more likely to be hospitalized and investigated with cranio-cervical MRI and MRA.

Our study is limited by its observational character even though data were collected prospectively. Another drawback of this study is that the mean interval from symptom onset to ultrasound was 11 days; therefore, some false-negative ultrasound findings may have resulted from early recanalization of the dissected vessel.\textsuperscript{2,13} However, the mean interval from symptom onset to the initial ultrasound examination did not differ significantly between patients with normal and abnormal ultrasound findings. Furthermore, all patients were examined within 24 hours of admission, and the delay from symptom onset to examination has been caused by patient’s delay to seek medical attention and thus reflects every day practice. Finally, patients were included over a long period and examined with different ultrasound equipment. However, the frequency of false-negative ultrasound findings did not differ over time.

In conclusion, nearly one third of patients with Horner syndrome as the only clinical sign of sICAD showed normal ultrasound findings at presentation. These results indicate that ultrasound is not a reliable method to diagnose sICAD in patients with isolated Horner syndrome examined within 30 days of symptom onset.

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Disclosures
None.

References


