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MR Screening for Brain Stem Compression in Hypertension

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PURPOSE: To determine the clinical usefulness of MR imaging to screen for vascular compression of the lateral medulla, considered by some to be responsible for neurogenic hypertension. **METHODS:** MR images and clinical records of 120 adults who had received brain MR imaging for any reason were divided into two groups: group 1 (n = 60) consisted of patients with essential hypertension and group 2 (n = 60) included patients who lacked a diagnosis of hypertension. No patient manifested symptomatic cranial neuralgias. The root entry zone of cranial nerves IX and X into the left lateral medulla was examined by MR imaging for proximity to the ipsilateral vertebral artery or its branches. Images lacking any contact between visible vascular structures and the root entry zone were recorded as normal. Vascular compression was graded according to the degree of proximity to the root entry zone. Lateral medullary contact only (grade I), contact and depression (grade II), or lower brain stem displacement or rotation (grade III) of the root entry zone were recorded in both hypertensive and normotensive patients. Among hypertensive patients, additional data were gathered from electrocardiographic, echocardiographic, and urinary protein reports. **RESULTS:** We found compression in 34 (57%) of the patients from group 1 and in 33 (55%) of the patients from group 2. Compressions in group 1 were grade I in 22 (37%) of the patients, grade II in 8 (13%), and grade III in 4 (7%). Among group 2 patients, grade I compressions were found in 27 (45%), grade II in 4 (7%), and grade III in 2 (3%). There were no statistically significant differences in MR findings between the two groups. Among group 1 patients, MR grading did not predict end-organ changes in the heart (left axis deviation and left ventricular hypertrophy) or kidneys (proteinuria). **CONCLUSION:** Vascular compression of the root entry zone of cranial nerves IX and X into the left lateral medulla is not an adequate lesion to produce systemic hypertension. This finding is as common among normotensive patients as among hypertensive populations. Neither the presence nor the severity of changes in the root entry zone on MR images increases the occurrence of common end-organ responses in the heart or kidneys among hypertensive patients. MR screening is not warranted among hypertensive patients lacking symptomatic cranial neuralgias.

Index terms: Brain stem, magnetic resonance; Hypertension

During the 1970s, case reports began to appear describing structural lesions affecting the lower brain stem on the left, associated with systemic (but not intracranial) hypertension (1,

2). By the mid-1980s, Jannetta et al had studied 53 hypertensive patients with symptomatic cranial neuralgias, 51 of whom had compression of the left lateral medulla by arterial branches of the left vertebral artery (3). Of these 51 patients, 42 underwent vascular decompression, of which 36 were judged to be surgically adequate. The blood pressure normalized in 32 (89%) of these and improved in the remainder, allowing a reduction in hypertensive medication usage. Among these hypertensive patients, none was found to have arterial compression of the right lateral medulla (3). Of the 36 patients whose decompressions were deemed adequate, 30 were still available for follow-up 7 years later, and 26 (86%) were either normotensive or had

improved control of their hypertension (4). Similar outcomes have been reported by others (5–8).

Animal models were established by using balloons applied against the left lateral medulla that distended with each heartbeat, thus simulating natural arterial pulsations. Baboon models produced increases in blood pressure, heart rate, cardiac output, and the thickness of the left ventricular wall (4). Canine models produced increases in blood pressure, but without changes in cardiac output (5). Deflated nonpulsatile balloon implants did not produce hemodynamic changes (4).

Thus was born a school of thought that has promoted primary neurogenic mechanisms for essential systemic hypertension, whereby interruptions of cardiac and baroreceptor afferents disturb the homeostasis between the brain stem vasomotor center and its complex interactions with suprasegmental neurons and autonomic efferent pathways (3, 4, 7, 9). There is a growing body of evidence that the central nervous system (CNS) regulates cardiovascular tone, and that dysfunctional central autonomic responses to humoral and afferent inputs can produce or propagate systemic hypertension (10–13).

Cardiovascular baroreceptors are found in the aortic arch and the carotid sinus. Afferent signals from the aorta travel in the glossopharyngeal nerve (cranial nerve IX), whereas afferents from the carotid sinus travel in the vagus nerve (cranial nerve X). The left vagus nerve also carries afferent signals from mechanoreceptors in the wall of the left atrium. These afferent fibers traveling in cranial nerves IX and X converge upon the nucleus tractus solitarius (NTS) of the medulla, which serves as the primary CNS terminus for baroreceptor afferent fibers (9, 11, 13). The baroreceptor reflex involves efferent autonomic responses to such NTS stimuli, which are then carried by vagal and sympathetic pathways. This reflex modulates cardiac inotropic and chronotropic effects, peripheral vascular resistance, renal sodium excretion, and renin secretion (11, 13–16). Sinoaortic deafferentation in animal models by surgical lesioning of the afferent pathways can affect these efferent responses and result in neurogenic hypertension (9, 14, 17). Disturbances in CNS regulation may also contribute to the perpetuation of hypertension of renal origin. Angiotensin II receptors are present within the circumventricular organs of the brain, to include the area postrema, the anteroventral region of the third ventricle, the organum vasculosum of the lamina terminalis, and the subfornical organ (9, 11). Each of these areas lacks a blood-brain barrier, allowing the CNS to monitor circulating humoral concentrations.

Lesions of the NTS result in neurogenic hypertension similar to sinoaortic deafferentation, and surgical disconnections between the NTS and the circumventricular organs may prevent this hypertensive response (9). Acute or chronic administration of angiotensin-converting enzyme inhibitors attenuate the hypertensive response induced by sinoaortic deafferentation (18). Similarly, lesions of the lateral and medial rostral ventral medulla can prevent neurogenic hypertension after sinoaortic deafferentation (9). Hence, the NTS must regulate and balance excitatory and inhibitory influences from suprasegmental, intramedullary, and peripheral nerve sources.

Guyton has argued that experimental neurogenic hypertension does not sustain chronically because of renal adaptability (19). Others argue that disturbed neural tone may become less critical to the maintenance of chronic systemic hypertension as vascular hypertrophy develops (16). Indeed, Jannetta's study includes five patients with chronically intractable (medically refractory) hypertension, only two of whom normalized after microvascular decompression of the left root entry zone of cranial nerves IX and X. Jannetta concludes that the more severe the hypertension and the longer it has persisted, the less likely it is to improve after microvascular decompressive surgery (4).

If such vascular lesions represent the physiologic equivalent of surgical sinoaortic deafferentation in animal models, then early identification of patients with such lesions could affect therapeutic decision making. Imaging data assessing the root entry zone of cranial nerves IX and X into the left lateral medulla in hypertensive populations are sparse. One series established the bony landmarks for the left root entry zone in 10 cadavers, and then extrapolated the position of the root entry zone to vertebral angiograms previously obtained in 99 hypertensive and 57 normotensive patients (20). Vascular structures were found in the vicinity of the left root entry zone in 81% of hypertensive and 42% of normotensive patients. We thought that magnetic resonance (MR) imaging could be a
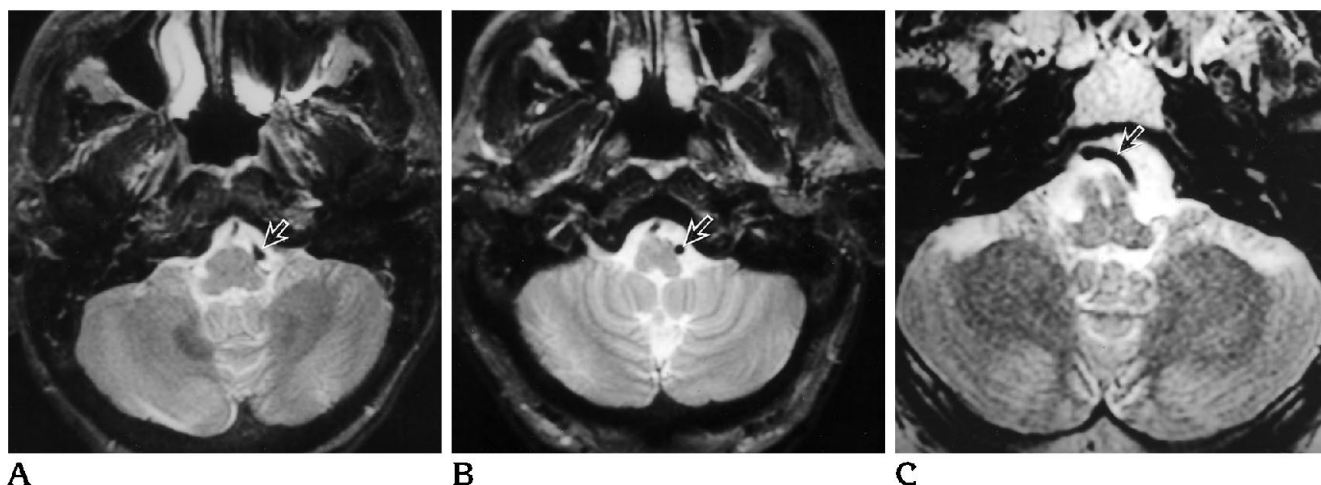
Fig 1. A–C, Axial T2-weighted spin-echo MR images (2800/80) were used to assess vascular compression (*arrows*) against the left lateral medulla. Findings were defined as grade I (contact with the root entry zone) (A), grade II (contact with the lateral medullary depression) (B), and grade III (displacement or rotation of the lower brain stem) (C).

more sensitive and less invasive technique by which to assess such relationships between vascular structures and the root entry zone.

Materials and Methods

Patient Selection

Patients under therapy for hypertension were identified by an audit of computerized medical records, and were then cross referenced for having received MR imaging of the brain. Patients with renal or endocrine sources of hypertension were excluded. Sixty patients were so identified over an 18-month period during 1993 to 1994 (group 1). Similarly, 60 nonhypertensive patients who had undergone brain MR imaging were identified (group 2). The indication for the brain MR examination did not enter into the selection process.

Study Design

The MR studies from both groups were concurrently reviewed by two neuroradiologists with a resultant single consensus reading. The reviewers were not blinded to the hypertensive status of the cases. The hypertensive patients' (group 1) records were reviewed in regard to electrocardiographic, echocardiographic, and urinalysis data.

Measurements

The glossopharyngeal nerve exits the lateral medulla at the upper-middle level in the retroolivary sulcus running between the olive and the inferior cerebellar peduncle, close to the rootlets of the vagus nerve. Together they traverse the basal cisterns to enter the jugular foramen. MR imaging is quite sensitive in the assessment of this area (21, 22).

Each patient's MR images included as a minimum an axial spin-echo T2-weighted sequence (2800/80/0.75 [repetition time/echo time/excitations]) through the posterior fossa with 5-mm sections at 7-mm intervals. Most patients also had T1- and T2-weighted sequences in other planes, but the axial T2-weighted images were used for grading determination. The vertebral artery and its most cephalad branch, the posterior inferior cerebellar artery, were assessed for proximity to the root entry zone of the left glossopharyngeal and vagus nerves. Images lacking contact with the root entry zone were recorded as normal. Vascular compression was graded according to the degree of vessel proximity to the root entry zone. Contact only (grade I), contact and depression of the lateral medulla (grade II), and displacement or rotation of the medulla (grade III) were recorded (see Fig 1). Proteinuria, left ventricular hypertrophy, left axis deviation, hypertension, and hypertensive therapies were defined in accordance with published criteria (23).

Statistical Analysis

MR results were compared between the two groups. Among group 1 patients, left ventricular hypertrophy, left axis deviation, and proteinuria were compared against the MR results. Fisher's Exact Test was used to assess statistical significance.

Results

MR images showed vascular compression of the left root entry zone for cranial nerves IX and X in the majority of patients from both groups. Higher-grade compressions (grade II and grade III) were twice as prevalent among hypertensive (group 1) patients, but this was not a statistically significant outcome. Table 1 summarizes the MR findings for both groups. No statistically

TABLE 1: MR Findings

Category	Group 1, n = 60 (%)	Group 2, n = 60 (%)
No compression	26 (43)	27 (45)
Compression*	34 (57)	33 (55)
Grade I	22 (37)	27 (45)
Grade II	8 (13)	4 (7)
Grade III	4 (7)	2 (3)

Note.—*P* value was greater than .05 (not significant) using Fisher's Exact Test when comparing hypertensive patients (group 1) with normotensive patients (group 2).

* Contact only (grade I), depression (grade II), and displacement or rotation (grade III) of the root entry zone of the left cranial nerves IX and X.

significant pattern could be determined when MR grading was compared with sex (Table 2).

Among hypertensive (group 1) patients, left ventricular hypertrophy and proteinuria were found more often in those who had compression. Left axis deviation was equally common among patients with or without compression. These results are summarized in Table 3. However, none of these findings is statistically significant.

Discussion

Compression of the root entry zone of cranial nerves IX and X in animal models produces systemic hypertension only when the left root entry zone is affected (4, 5). Humans with left-sided hemifacial spasm have an almost twofold increase in the prevalence of hypertension as compared with right-sided or matched general populations (6). Sustained reduction of hypertension has been achieved in patients with symptomatic hemifacial spasm, trigeminal neuralgia, or glossopharyngeal neuralgia when the left root entry zone has been adequately decom-

TABLE 2: MR Compared with Sex Demographics

Characteristic	Group 1		Group 2	
	M (n = 40)	F (n = 20)	M (n = 31)	F (n = 29)
Mean age, y	63	61	53	50
(range)	(27–84)	(38–84)	(31–83)	(32–78)
MR grading*				
Normal	17	9	13	14
Grade I	15	7	14	13
Grade II	5	3	2	2
Grade III	3	1	2	0

* In comparisons between the hypertensive (group 1) and normotensive (group 2) patients, all *P* values were greater than .05 using Fisher's Exact Test (not significant).

TABLE 3: Comparison Between MR Findings and Presence or Absence of Left Ventricular Hypertrophy, Left Axis Deviation, and Proteinuria in Group 1 Patients

	Normal MR Findings	Grade I	Grade II	Grade III
Left ventricular hypertrophy (n = 41)				
Present	4	1	3	1
Not present	13	13	4	2
Left axis deviation (n = 40)				
Present	5	3	0	2
Not present	11	12	6	1
Proteinuria (n = 53)				
Present	9	9	2	1
Not present	15	9	5	3

Note.—*P* value was greater than .05 (not significant) when compared against MR results using Fisher's Exact Test.

pressed (2–5, 7, 8). Our study shows that vascular compression of the left root entry zone per se is not an adequate lesion to result in hypertension. However, none of our patients had symptomatic cranial neuralgias.

One hypothesis to explain the paroxysmal nature of symptoms in such cranial neuralgias is that the local irritation caused by the pulsating vessels results in ectopic excitation, generating spontaneous action potentials and nonsynaptic (ephaptic) transmissions among adjacent axons (24–26). Such cross-talk by ephaptic transmissions may explain the presence of surgically reversible hypertension in patients with cranial neuralgias. Anatomic similarities (vascular compression) but functional differences (the absence of ephaptic transmissions) could explain the similar prevalence of compression among our two patient groups lacking cranial neuralgias. Ephaptic transmissions to the NTS could explain why the CNS appears unable to maintain normotension in hypertensive patients who have both symptomatic cranial neuralgias and left root entry zone compression. The surgical series do not reflect experience in decompressing the root entry zone in hypertensive patients who lack symptomatic cranial neuralgias.

Prospective clinical monitoring will be required to determine any increased risk of eventual hypertension, with or without symptomatic cranial neuralgias, among normotensive patients identified by MR imaging as having left root entry zone vascular compression. Any effect of hypertension per se upon the development of vertebrobasilar ectasia and brain stem compression could be assessed by serial im-

ages of both study groups. Among our hypertensive patients, higher-grade compressions (grades II and III) were twice as prevalent as those found in our normotensive group, suggesting that hypertension may increase the degree of vascular compression.

MR screening for medullary compression has been conducted in a similar study in Japan (27). Among 32 patients with essential hypertension, unilateral left-sided medullary contact was found in 22 (69%). This prevalence is similar to the 57% of patients with left-sided compression observed in our 60 hypertensive patients. The Japanese study did not distinguish between contact only or degree of medullary deformity. Interestingly, among their 18 normotensive control subjects, only three (17%) had neurovascular compression on the left side, compared with 55% of our 60 normotensive patients. This lower prevalence among the Japanese normotensive control group may be a result of their smaller sample size and use of asymptomatic volunteers, whereas our normotensive control subjects all had symptomatic brain disorders prompting the MR examinations. As in our study, none of the patients had symptomatic cranial neuropathies.

Our study would suggest that MR screening for left root entry zone compression is not warranted among hypertensive patients in the absence of symptomatic cranial neuralgias. Neither the presence nor severity of root entry zone changes on MR images increase the occurrence of common end-organ responses in the heart or kidneys among hypertensive patients.

Acknowledgments

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