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Hypertension Does Not Cause Spontaneous Hemorrhage of Intracranial Arteriovenous Malformations

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The authors measured blood pressure changes non-invasively in 56 conscious, unpremedicated patients with cerebral arteriovenous malformations (AVMs) during preparation for proton beam therapy. The procedure requires six injections of local anesthetic and application of a stereotactic frame by fixation into the outer table of the skull, and has been used during the past 20 yr to treat over 1,000 patients with cerebral AVMs. No effort was made to control blood pressure. Blood pressure increased during administration of the local anesthetic and application of the frame. Maximum systolic and mean arterial pressures averaged 160 ± 17 and 118 ± 7 mmHg (mean ± SD), respectively. This represented an average increase of 44 mmHg (38%) in systolic pressure and 32 mmHg (37%) in mean blood pressure at some point during the procedure ($P < 0.01$ compared with pretreatment control pressures). Systolic pressure increased more than 60 mmHg in 21% of patients. Nevertheless, none of these 56 patients nor any of the more than 1,000 patients treated in similar fashion suffered a clinically evident AVM hemorrhage during the procedure. Since the treatment protocol has not changed materially during the past 20 yr, the authors assume that most patients treated in this fashion developed a similar degree of hypertension and conclude from this large clinical experience that moderate arterial hypertension does not precipitate spontaneous hemorrhage of intracranial AVMs. (Key words: Blood pressure: hypertension. Brain: arteriovenous malformation; hemorrhage. Complications, arteriovenous malformation: intracranial hemorrhage.)

IT IS WELL ESTABLISHED that arterial hypertension can cause rupture of an intracranial aneurysm, but whether hypertension contributes to spontaneous rupture of intracranial arteriovenous malformations (AVMs) is less clear. Although evidence from human or animal studies is lacking, clinicians often presume that arterial hypertension can precipitate spontaneous AVM hemorrhage and, consequently, prevention of hypertension is advocated in the anesthetic management of such patients.[1,2]

We have unique, extensive experience with a nonoperative treatment of patients with AVMs wherein the usual principles of blood pressure control appear to be violated. Yet, after 20 yr and more than 1,000 cases, no AVM has ruptured during the procedure. This suggests that arterial hypertension does not lead to spontaneous hemorrhage of these lesions, and it was this clinical impression that forms the basis of this report.

Methods

Over the course of 1 yr, we measured arterial blood pressure systematically in 56 randomly selected adult patients with intracranial AVMs undergoing Bragg-peak proton beam therapy.[3] Proton beam therapy[3] is a noninvasive stereotactic surgical procedure that capitalizes on the physical properties of protons such that small areas of tissue can be intensely irradiated while surrounding normal tissue is spared. This procedure is an alternative to surgery when the size or location of the AVM make surgical excision particularly risky or impractical.

The treatments took place at the Cyclotron Laboratory of Harvard University, located approximately 4 miles from the Hospital. Because hospitalized patients are typically transported to and from the Cyclotron by taxi and many individuals are treated as outpatients, we followed a protocol that has been used for 20 yr in patients undergoing this treatment. Specifically, the procedure was performed entirely under local anesthesia. Seizure medication was continued but no premedication was given and patients received no intravenous analgesic or sedative drugs. With the patient in a 45° head-up position, approximately 12 ml of 2% lidocaine with epinephrine 1: 200,000 was administered in four separate injections into the periosteum and subcutaneous tissues in the area of the maxilla and occiput. An additional 1–2 ml of 2% lidocaine (with or without epinephrine) was administered subcutaneously into the outer rim of each external auditory canal. Soon thereafter, the stereotactic frame was attached to the patient's head by skeletal fixation. This 10–20-min process involves inserting metal rods into the external auditory canals for temporary support and subsequently stabilizing the frame using drill rods inserted into the outer table of the calvarium. The remainder of the procedure, including treatment, lasts 1–2 h and is painless. It is important to emphasize that a single neurosurgeon (RKK) has treated over 1,000 patients with AVMs in this fashion over the past 20 yr with few modifications (except with respect to the stereotactic apparatus) in the treatment protocol.[3]

In the 56 study patients, blood pressure was measured noninvasively from an arm at three time points. Control

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TABLE 1. Demographics of AVM Patients Treated with Proton Beam Therapy

	Study Group (n = 56)	Total (n = 1,000)
Age (yr)	29 ± 15	31 ± 13
Sex		
Male %	56	50
Female %	44	50
Presenting symptom (% incidence)		
Hemorrhage	51	46
Seizures	12	22
Headache	25	21
Progressive neurologic deficit	12	11

blood pressure was obtained by averaging 1–3 days of sphygmomanometric recordings from the patient's hospital record. The patient's control mean blood pressure was then calculated using a standard formula (systolic + ⅓ pulse pressure). Several blood pressure measurements were obtained at the treatment facility just prior to treatment and then at approximately 2-min intervals during application of the stereotactic frame. The highest readings were used in the tabulation of results. An automated blood pressure device (Dinamap®, Critikon, Inc., Tampa, Florida) was used for immediate pretreatment and treatment measurements. This method was selected in order to reduce interobserver variability with sphygmomanometric readings. In addition, we used the automated device to record blood pressure 24 h prior to treatment in eight patients on the ward and found excellent agreement with pressures obtained by nurses using sphygmomanometry. The data were analyzed by analysis of variance and Dunnett's test for multiple comparisons.

Results

The study patients were 29 ± 15 yr of age and included nearly equal numbers of men and women (table 1). Hemorrhage was the presenting symptom in approximately 50% of the patients, but several presented with recurrent headaches, seizures, or a progressive neurologic deficit. Seventy-five percent of the study patients had a cerebral hemorrhage at some time prior to treatment. The demographic features of the 56 study patients are similar to those of the first 1,000 AVM patients treated with proton beam therapy at this facility (table 1).

TABLE 2. Maximum Blood Pressure Changes in AVM Patients during Preparation for Proton Beam Therapy

	Arterial Blood Pressure (mmHg)	
	Systolic	Mean
Baseline (range)	116 ± 9 (96–135)	86 ± 7 (71–98)
Waiting room (range)	131 ± 15* (102–173)	96 ± 12* (74–130)
Application of frame (range)	160 ± 17* (123–219)	118 ± 7* (94–154)

Data are mean ± SD for 56 patients with AVMs. The range for each measurement is given in parentheses.
* $P < 0.01$.

Prior to treatment, all patients were normotensive and only six were taking antihypertensive medication. As anticipated, blood pressure was increased in the waiting room and increased further during local anesthetic injection and application of the stereotactic frame (table 2). Systolic blood pressure increased an average of 44 mmHg (38%, $P < 0.01$) and mean arterial pressure increased 32 mmHg (37%, $P < 0.01$) (table 2) at some point during the procedure. Peak systolic and mean pressures averaged 160 ± 17 and 118 ± 7 mmHg, respectively, but the range of increases was broad. For example, 57% of patients experienced increases in systolic blood pressure of 41 mmHg or more and, in 12 patients (21%), systolic pressure increased more than 60 mmHg (fig. 1). Mean blood pressure increased more than 40 mmHg in 15 (27%) patients. One patient's systolic and mean pressure reached 219 and 154 mmHg, respectively (table 2). Blood pressure generally remained elevated throughout the 10–15-min period required for application of the stereotactic apparatus and returned toward baseline soon thereafter, but no systematic study of the time course was made. Since patients were in a semi-sitting position, blood pressure at the head would be lower by approximately 8–12 mmHg than the values reported here. However, although the absolute values may differ, blood pressure measured at the arm should accurately reflect the relative changes in pressure at the head.

Discussion

Arteriovenous malformations of the brain are uncommon congenital lesions characterized by the formation of direct arterial-to-venous communications without an intervening normal capillary bed.[4] These lesions account for roughly 9% of all subarachnoid hemorrhages and about 1% of strokes.[5,6] Although hemorrhage, which is often intraparenchymal, is the most common presenting symptom, seizures, recurrent headaches, and progressive neurologic deficits are also common.[5,6] The risk of hemorrhage appears to be about 2–3% per year regardless of whether the patient has suffered a previous hemorrhage.[4] Although hemorrhage from an intracranial AVM is usually not as devastating as that from an aneurysm, mortality from the first hemorrhage is 6–30% and serious morbidity varies from 15–80%.[5,6]

The factors that precipitate AVM hemorrhage are not clear and a direct relationship between arterial hypertension and spontaneous AVM hemorrhage has not been established. AVM vessels are viewed as fixed vascular conduits: they do not autoregulate in response to changes in arterial blood pressure and do not respond to chemical

stimuli such as arterial CO_2.[7] This suggests that increases in arterial blood pressure would be transmitted directly to AVM vessels. However, when the circulatory dynamics of these lesions are considered, the hypothesis that transient arterial hypertension does not cause an AVM to bleed is plausible. Most AVMs are high-flow, low-resistance shunts,[7] and mean blood pressure in the AVM is only about 45–60% of systemic MAP and is less pulsatile.[7,8] Moreover, blood flow is usually irregular and turbulent and, in a turbulent system, only the square root of the pressure change is transmitted to the vessel wall.[7] Thus, the impact of an abrupt increase in systemic arterial pressure should be attenuated in the AVM. This is supported by other clinical observations. For instance, the majority of AVMs rupture during sleep,[9] when hypertension is unlikely,[10] and there appears to be no relationship between chronic arterial hypertension and AVM rupture.[11] These data taken together with our own substantiate our assertion that there is probably little relationship between arterial hypertension and spontaneous AVM hemorrhage.

Of course, the statistical probability that hemorrhage would occur in any of our 56 patients during the treatment is very low. However, it seems reasonable to speculate that most, if not all, patients treated in this way over the years developed a similar degree of hypertension. Thus, based on the larger group of 1,000 patients with AVMs, we conclude that a procedure that violates generally accepted principles of blood pressure control and that precipitates moderate hypertension (*i.e.*, 20–30 mmHg increase in MAP) is associated with little short-term risk of clinically evident AVM hemorrhage. We believe this clinical experience is convincing, albeit uncontrolled and indirect, evidence that arterial hypertension of this magnitude and duration is unlikely to precipitate spontaneous hemorrhage of intracranial AVMs.

This information may be most useful under circumstances when prevention of hypertension is difficult to achieve, such as during a rapid sequence induction or awake tracheal intubation of a patient with an intact AVM (*i.e.*, no recent hemorrhages). Our clinical experience suggests that, in such situations, blood pressure control might be considered a secondary priority because a brief period of moderate hypertension is unlikely to cause rupture or rerupture of the AVM. Thus, although increases in blood pressure may be undesirable when intracranial compliance is compromised (*e.g.*, by an intracerebral hematoma) or when the AVM is being manipulated by the surgeon, we conclude that prevention of hypertension in patients with intact cerebral AVMs seems necessary only to the extent that it is a conservative and prudent management objective in any patient undergoing anesthesia and surgery.

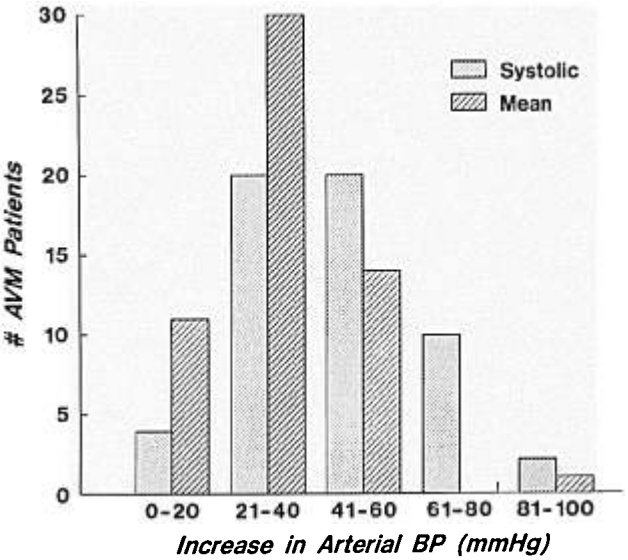

FIG. 1. Maximum increase in systolic and mean arterial blood pressure during application of the stereotactic frame for proton beam therapy in 56 patients with intracranial arteriovenous malformations.

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