Evaluation of Vasospasm Secondary to Subarachnoid Hemorrhage with Technetium-99m-hexamethyl-propyleneamine oxime (HM-PAO) Tomoscintigraphy

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Vasospasm of intracranial vessels is difficult to diagnose on clinical ground alone. Still, a clear diagnosis is important because it can impact on surgical timing; and also because it can help evaluate new treatments. Fifteen patients with sub-arachnoid hemorrhage secondary to aneurysm rupture were submitted to a total of 26 tomographic technetium-99m-hexamethyl-propyleneamine oxime (^{99m}Tc-HM-PAO) brain examinations that were correlated with temporally close (generally < 24 hr) angiography or transmission computed tomography (TCT). Nine of 10 angiographically confirmed episodes of spasm and 6 of 6 infarcts seen on angiography or TCT were correctly diagnosed with ^{99m}Tc-HM-PAO. One normal scintigraphic exam was angiographically doubtful, one positive ^{99m}Tc-HM-PAO study was normal on angiography (sub-radiologic spasm?), one technically poor scintigraphy was positive for spasm on angiograms, and eight exams were normal for spasm with all modalities. We had agreement between tests in 23 of 26 series of exams (88%) obtained in 15 patients. We think that ^{99m}Tc-HM-PAO tomography should be useful for the evaluation of patients with suspected vasospasm.

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Intracranial aneurysms are a major health problem in the United States and manifest themselves through a yearly incidence of ~10 cases of subarachnoid hemorrhages (SAH) for every 100,000 inhabitants. In a fully equipped neurosurgical center, no more than 50% of those patients who suffer from a ruptured aneurysm have a successful outcome if they survive to be admitted (*1–5*).

Two major dramatic complications can occur after an initial non-lethal rupture, namely rebleeding and vasospasm. Vasospasm is a term which refers to the vascular narrowing seen on angiogram, or to the clinical condition of delayed cerebral ischemia. Vasospasm may be seen in as many as 36% of all patients and most often occurs from Day 4 to Day 16 post-hemorrhage. Although its physiopathology is still unclear, a few treatments are now available. Thus, its detection and follow-up are clinically important.

Angiography is presently the most common method used to study vasospasm. Its invasiveness has led some authors to evaluate other less traumatic methods. Many techniques such as magnetic resonance imaging (MRI), computed tomography (CT), transcranial doppler, cerebral blood flow (CBF) evaluation with xenon, and recently studies with iodine-123-HIPDM have shown some promises (*6–15*).

Technetium-99m-hexamethyl-propyleneamine oxime (^{99m}Tc-HM-PAO) is a CBF marker that has only recently been made available; it is usually employed with single-photon emission computed tomography (SPECT) (*16–18*). After an intravenous (i.v.) injection, it is rapidly taken up by the brain, essentially on its first passage, according to local CBF. The potential of this agent in the field of vasospasm has already been suggested by different authors (*19–21*). We present here our own experience with ^{99m}Tc-HM-PAO tomoscintigraphy of brain perfusion for the detection and follow-up of vasospasm secondary to subarachnoid hemorrhage.

MATERIALS AND METHODS

Fifteen patients (8 females, 7 males, mean age: 51 yr) who were admitted soon after an aneurysmal SAH were entered in

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this study. All cases of SAH were confirmed by the presence of xanthochromic cerebro-spinal fluid and/or CT showing blood in the sub-arachnoid spaces, and the source of bleeding was verified by angiography.

Computed tomography was performed on the patient's admission and was repeated as necessary. A total of 59 CTs were done in this population during hospitalization. Patients also underwent angiography, initially to localize the source of bleeding, and subsequently depending on the patient's clinical condition. A total of 79 examinations (some of those representing injection of multiple vessels during one session) were performed in these 15 patients.

Technetium-99m-HM-PAO tomoscintigraphies were performed 20 min after the injection of 925 MBq of ^{99m}Tc-HM-PAO using a rotating gamma camera interfaced with a dedicated computer (Scintronix 464 system, Edinburg, Scotland, UK). A total of 64 projections (64×64 matrix) of 20 sec each were acquired over 360°; on average, 30K counts are acquired per projection (close to 2 million counts per study). Tomographic sections were obtained as a series of horizontal, coronal, sagittal, and oblique slices permitting a full three-dimensional reconstruction. Twenty-six rCBF studies with ^{99m}Tc-HM-PAO were performed on the 15 patients and were compared with arteriography and/or transmission computed tomography (TCT) obtained concomitantly (see Table 1).

RESULTS

Vasospasm

Ten angiographic examinations showed vasospasm of at least one vessel. On ^{99m}Tc-HM-PAO tomoscintigraphy, nine of these cases showed abnormalities of their rCBF pattern which corresponded to the vascular territory involved on angiography. Figure 1 illustrates one of these patients (#7). She suffered a SAH caused by rupture of a left posterior cerebral artery aneurysm and developed vasospasm, 6 days post-SAH, of the left middle cerebral and peri-callosal arteries as demonstrated by angiography (Fig. 1A). Tomoscintigraphy shows hypoperfusion in territories matching those showed by angiography (Fig. 1B). A subsequent examination after spasm had resolved clinically was normal (Fig. 1C-D).

One patient showed vasospasm on angiography but this could not be confirmed by tomoscintigraphy because the exam was technically suboptimal—the patient moved during the acquisition of data.

TABLE 1
Comparison of ^{99m}Tc-HM-PAO, Anteriography, and TCT rCBF Studies

Patient	Sex	Age	Symptoms	Study series	TCT date	Angio date	HM-PAO date	Aneurysm
1	M	70	no	1	sh-6/22/87	N-6/30/87	N-7/2/87	L Post Com
				2	—	N-7/10/87	N-7/8/87	
2	F	50	yes	3	sh-6/10/87	S-6/15/87	S-6/17/87	R Perical
				4	—	?-6/22/87	N-6/22/87	
3	F	64	no	5	—	S-7/17/87	S-7/14/87	Basilar
4	F	37	yes	6	st-2/13/87	N-2/18/87	st-2/19/87	L Mid Cer
				7	st-4/28/87	—	st-5/6/87	
5	M	35	no	8	sh-5/15/87	S-5/9/87	?-5/12/87	L PICA
6	F	51	no	9	sh-5/28/87	S-5/23/87	S-5/25/87	Ant Com
				10	sh-5/5/87	N-5/5/87	-N-5/6/87	
7	F	47	no	11	—	S-5/11/87	S-5/12/87	L Post Cer
				12	—	N-5/27/87	N-5/25/87	
				13	—	N-6/10/87	N-6/22/87	
8	M	43	no	14	—	N-6/1 & 8/87	S-6/3/87	Ant Com
9	F	68	yes	15	—	st-6/12/87	st-6/11/87	Ant Com
				16	st-6/17/87	—	st-6/23/87	
10	F	65	no	17	sh-7/30/87	S-7/27/87	S-7/27/87	R PICA
				18	—	N-8/14/87	N-8/11/87	
11	M	52	yes	19	sh-8/25/87	S-8/24/87	S-8/26/87	Ant Com
				20	st-9/4/87	—	st-9/2/87	
12	M	44	no	21	sh-2/9/87	S-2/3/87	S-2/3/87	R Mid Cer
				22	—	S-2/9/87	S-2/12/87	
				23	—	N-2/23/87	N-2/24/87	
13	M	55	—	24	sh-5/4/88	N-5/5/88	N-5/6/88	L Post Com
14	M	32	—	25	st-8/23/88	—	st-8/25/88	L Mid Cer
15	F	42	—	26	sh-8/10/88	S-8/8/88	S-8/9/88	None found

s = spasm; sh = sub-arachnoid hemorrhage as shown by the presence of blood in the sub-arachnoid spaces; N = normal; ? = doubtful result (technical or interpretational problem); and st = stroke.

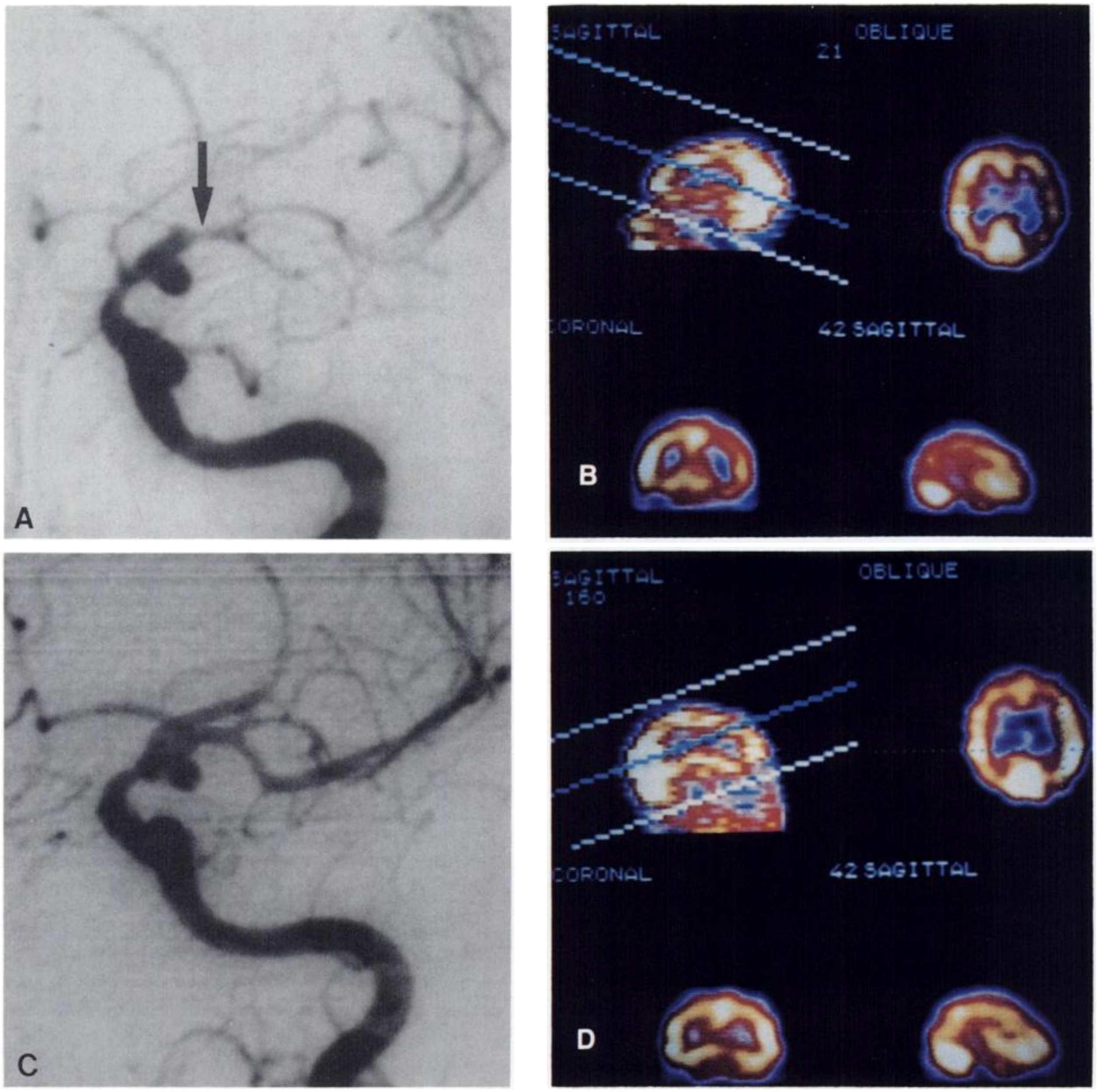

FIGURE 1
(A) Initial angiogram showing both the aneurysm and the area of vasospasm (arrow). (B) Initial ^{99m}Tc-HM-PAO study shows decreased perfusion of the left sylvian territory. (C-D) Three weeks later, both the angiogram and tomoscintigraphy show normalization of perfusion.

Infarcts

Six ^{99m}Tc-HM-PAO tomoscintigraphies suggested infarcts as they showed regions of profound hypoperfusion or luxury perfusion, sometimes with cerebellar diaschisis. They correlated well with six proven strokes (five by TCT, one by angiography). Figure 2A illustrates the tomoscintigraphy of a 52-yr-old male patient (#11) who developed a stroke 5 days post-SAH in the right fronto-parietal and left parieto-occipital territories. It corresponds well to the lesions shown by TCT (Fig. 2B).

Normals

Nine ^{99m}Tc-HM-PAO tomoscintigraphies were considered normal; eight of these had TCT and/or angiography which were negative for spasm. One exam was interpreted as normal on ^{99m}Tc-HM-PAO but was doubtful on angiography (of two neuroradiologists interpreting this study, one reported it as possibly positive for spasm while one considered it to be normal). Finally, another ^{99m}Tc-HM-PAO was considered as showing abnormalities compatible with spasm, but the angio

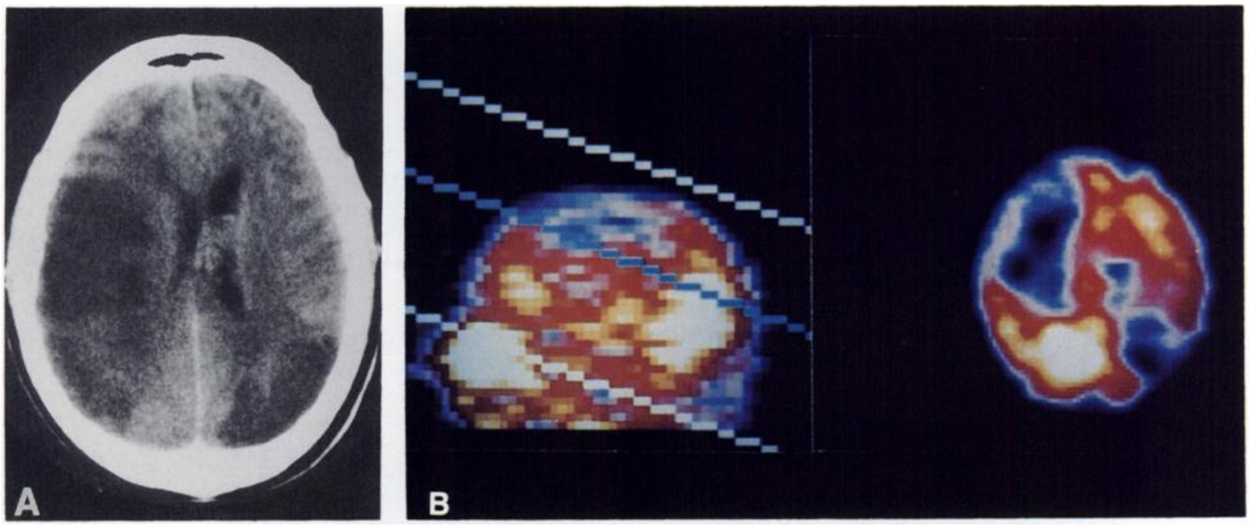

FIGURE 2
TCT study showing infarcts in multiple territories (A) and ^{99m}Tc-HM-PAO scintigraphy showing profoundly hypoperfused areas in same areas, interpreted as strokes (B).

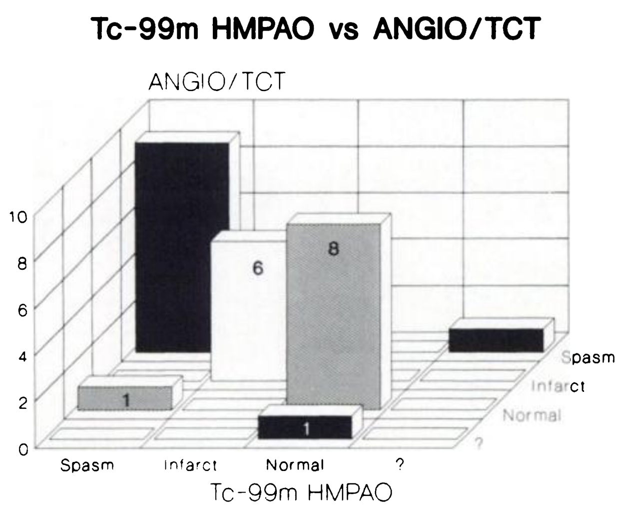

FIGURE 3
Technetium-99m-HM-PAO scintigraphy versus angiography/TCT: comparative results.

was negative (see discussion). Figure 3 summarizes those observations.

DISCUSSION AND CONCLUSIONS

Aneurysmal SAH is a devastating illness as only one-third of those having this disease recover totally and as many as two-thirds are disabled or die (*1*). Rebleeding is a feared complication which can actually be prevented by early operation and, if feasible, by antifibrinolytic therapy (*1,22–27*).

Vasospasm, the etiology of which is still uncertain, is a major problem occurring in close to 40% of patients. Many studies have been done on its prevention and management, and some treatments are actually available, e.g., volume overload and calcium-blockers administration (*1,2,28–30*). The diagnosis of this condition remains difficult as vasospasm seen angiographically is not always matched by clinical findings and vice-versa. Furthermore, angiography is invasive and not without morbidity.

In order to evaluate better treatments presently used, to establish the ideal timing of surgical intervention (delayed versus early), or to test new treatment modalities, a noninvasive, widely available diagnostic and follow-up test is thus necessary. Angiography still remains the "gold standard" for the diagnosis of spasm, and other methods will be compared to it. Many have been used with some success, such as TCT, transcranial Doppler studies of flow velocity, rCBF measurement by xenon inhalation or [^{123}I]HIPDM tomoscintigraphy.

Technetium-99m-HM-PAO, a recently developed rCBF marker, has been used successfully in combination with SPECT technology to study many cerebral diseases such as stroke, epilepsy, and dementia. Vasospasm was an obvious candidate for application of this approach.

In our study, we compared TCT, angiography, and ^{99m}Tc-HM-PAO brain tomoscintigraphy in post-SAH patients suspected of having vasospasm. We found an excellent correlation between the presence of spasm on angiography and rCBF abnormalities on ^{99m}Tc-HM-PAO. In only one case was the ^{99m}Tc-HM-PAO doubtful and the angiogram positive, and even then, this was due to technical problems. Additionally, one patient was described as having alterations compatible with spasm on ^{99m}Tc-HM-PAO but was negative on angiography. Further studies should help us understand if such cases represent sub-radiologic spasm, and, if so, whether or not this would have any significant hemodynamic effect and be clinically significant.

Stroke may complicate the outcome of SAH patients, often as a consequence of vasospasm. Our study demonstrates that this complication can also be evaluated by ^{99m}Tc-HM-PAO since we had an excellent correlation with findings on TCT and angiography.

Vasospasm has also been studied with other modalities (*6–15,19–21*). Studies with TCT have shown a significant correlation between the amount of blood present in the cysterns and the degree of vasospasm. TCT is noninvasive, but the evaluation of vasospasm is only indirect. Transcranial doppler, also a noninvasive method, has been shown to be valuable in the follow-up of these patients since it can demonstrate the hemodynamic effect of spasm before it becomes clinically evident. It is limited by the fact that few arteries are readily accessible and thus it does not give a global picture of cerebral blood perfusion.

Angiography, although invasive, will remain essential in the evaluation of these patients in order to localize the cause of bleeding and to define the surgical approach. However, ^{99m}Tc-HM-PAO tomoscintigraphy, a good tool to evaluate rCBF, can give global information about the cerebral perfusion status of the patient. Our study demonstrates that it should be a valuable mode of follow-up in these patients, either to decide on the appropriate time for intervention, or to help evaluate the efficacy of nonsurgical treatments.

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