Transient global amnesia and cortical blindness after vertebral angiography: further evidence for the role of arterial spasm.

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Transient Global Amnesia and Cortical Blindness after Vertebral Angiography: Further Evidence for the Role of Arterial Spasm

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Summary: We describe a series of six patients who experienced severe retrograde amnesia (five cases) or cortical blindness (one case) during selective vertebral angiography. All angiograms were obtained with the same nonionic contrast medium. Analysis of the contrast batch demonstrated no abnormalities, but investigation of the angiographic suite revealed a faulty contrast warming cabinet resulting in injection of contrast material above body temperature. The warming cabinet was withdrawn, and the complication has not recurred. We believe that these symptoms reflect ischemia caused by vertebral arterial spasm.

Index terms: Angiography, complications; Iatrogenic disease or disorder; Vasospasm

Transient global amnesia is a disorder of mental function characterized by acute attacks of retrograde amnesia without other neurologic abnormality (1, 2). The attacks are typically short lived and self-limiting, and recurrence is rare. Transient global amnesia can also occur as a complication of cerebral angiography and has a prevalence of 0.5% to 0.7% when ionic contrast media are used (3–5). Although an ischemic mechanism for spontaneous transient global amnesia is well accepted (6–10), the etiology of angiography-related transient global amnesia remains contentious. Underlying temporal lobe disease (11), cerebral ischemia (12, 13), cerebral embolism (2), arterial spasm (12), and contrast-induced neurotoxicity (11) have all been implicated. Since the introduction of nonionic contrast agents, four cases of transient global amnesia have been reported (12–15), and this has been cited as further evidence for the role of contrast toxicity. We have recently seen six cases of transient global amnesia related to cerebral angiography with the nonionic contrast agent iohexol. Our experience with these patients is reported here.

Case Reports

Over a 24-month period beginning January 1991, a total of 246 selective cerebral angiograms were obtained at the Manchester Royal Infirmary. All selective injections were performed by using iohexol (Omnipaque 300, Nycomed, Oslo, Norway) diluted with saline to an iodine content of 150 mg/mL. During the 4-month period beginning July 1992, six (17%) of 35 patients experienced complications of vertebral artery angiography as described below.

Case 1

A 42-year-old woman with a strong family history of aneurysmal subarachnoid hemorrhage was admitted for cerebral angiography. Computed tomography (CT) was normal, and there was no significant medical history. Bilateral carotid angiography was normal and without complications. The vertebral artery was selectively catheterized, and an initial test injection of 2 mL of contrast material was performed without complication. During the first formal angiographic run, 6 mL of contrast material was injected by hand, and the vertebral angiogram appeared normal. Within 1 minute of injection, the patient became confused and nauseous. Questioning revealed profound retrograde amnesia with no memory for events within the past week. The patient did not know where she was or why she was in the hospital, although long-term memory was intact. She was unable to retain the answers to her questions despite frequent repetition. The patient became extremely anxious and angiography was abandoned. Gradual improvement occurred over the next 24 hours, but 36 hours after angiography the patient had total retrograde amnesia for the 24 hours preceding the procedure. Long-term memory was normal, and there were no other neurologic abnormalities.

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Case 2

A 38-year-old woman was admitted from another hospital after a suspected subarachnoid hemorrhage. CT findings were normal, but lumbar puncture demonstrated mildly xanthochromic cerebrospinal fluid. Bilateral carotid angiograms were normal, although there was no filling of the posterior cerebral arteries from the carotid circulation. A right vertebral injection demonstrated bilateral filling of the posterior cerebral arteries and normal posterior fossa vasculature. After the vertebral injection the patient had complete loss of vision, which developed over a period of less than 1 minute. Visual testing demonstrated normal direct and consensual light responses in both eyes but with apparent total loss of vision. The patient was also noted to be mildly confused and unable to remember the details of her hospital admission. A diagnosis of cortical blindness and transient global amnesia was made, and angiography was abandoned. The patient's visual acuity returned to normal within the next 6 hours, although a mild confusional state persisted for almost 24 hours. The next day, full neurologic examination was normal, although the patient's memory of the procedure and the preceding 24 hours was absent. Another angiogram 1 week later showed no intracranial vascular abnormality and was without complication. A CT head scan 48 hours after angiography also was normal.

Case 3

A 61-year-old man was admitted with acute onset of headache. CT showed blood within the basal cisterns. Bilateral cerebral angiograms 24 hours after admission showed minimal spasm in the region of the right middle cerebral artery and a small right posterior communicating artery aneurysm. Catheterization of the left vertebral artery was performed without complication, but after an initial test dose of 2 mL of undiluted contrast material (300 mg I/mL), the patient had nausea and tinnitus. The symptoms were treated with Metochlorpropamide (10 mg, intravenously), but over the next 3 to 4 minutes he became increasingly confused and examination demonstrated a profound retrograde amnesia lasting at least 24 hours. He repeatedly questioned the radiologic staff as to where he was and what had happened to him and was unable to remember the answers to these questions even seconds later. The patient became extremely anxious and frightened and intravenous sedation (diazepam 10 mg intravenously) was required. Angiography was abandoned and the patient returned to the ward. He remained drowsy until the next day, and examinations at 24 and 48 hours after angiography demonstrated a residual retrograde amnesia for 12 hours preceding angiography. There had been no evidence of memory impairment before angiography, and the angiogram itself showed no evidence of vascular spasm in the posterior arterial circulation.

Case 4

A 32-year-old woman was admitted after sudden onset of headache. CT showed a perimesencephalic pattern of subarachnoid hemorrhage. Bilateral carotid angiography was normal. After an initial test dose of 2 mL of undiluted contrast material in the left vertebral artery, the patient had buzzing in the ears and mild vertigo. Over the next 1 to 2 minutes she became increasingly confused and anxious. Examination at this stage revealed amnesia extending back over a period of 1 week or more and an inability to form new memories. The patient was unable to remember being ill, the original event, or being admitted to hospital. Long-term memory was intact, and there was no other neurologic deficit. The symptoms resolved after 24 hours of conservative management, but the patient was left with a period of amnesia extending for 3 to 4 hours before the angiogram itself, although she did remember details of the original hospital admission. A repeat cerebral angiogram was normal and without complication, and repeat CT also was normal.

Case 5

A 64-year-old man was admitted with a 2-week history of a painful right third cranial nerve palsy. CT was normal, and cerebral angiography was performed to exclude a posterior communicating artery aneurysm. Right carotid angiography was normal. After the first angiographic injection into the right vertebral artery, the patient heard ringing noise in his ears and over 1 to 2 minutes became vertiginous and nauseous. He started retching and was treated with metochlorpropamide (10 mg, intravenously). Within 5 minutes of the initial angiographic injection he was confused and profoundly amnesic. All recent memory seemed to be absent for a period in excess of a week, and new memory formation and long-term memory were difficult to test because of confusion. Angiography was abandoned, and the patient was sedated with diazepam (6 mg intravenously) and returned to the ward for observation. Recovery was gradual over the next 48 hours; by discharge from the hospital 4 days later he still had profound retrograde amnesia extending over 48 hours from the time of angiography. He did not remember hospital admission or any subsequent event before waking from the angiogram. The angiogram itself was normal without evidence of vascular spasm in either the anterior or posterior circulation.

Case 6

A 56-year-old woman was admitted after acute onset of headache. CT showed blood in the basal cisterns, particularly on the right side, and a cerebral angiogram was performed 3 days after the original event. The patient was fully conscious and oriented although a little drowsy. Neurologic examination at this stage was normal. Right cerebral angiography showed a small right middle cerebral artery aneurysm at the trifurcation of the vessel but no

other abnormality. Left carotid angiography was normal, and there was no evidence of vascular spasm in the anterior circulation. A left-sided vertebral angiogram was also normal, but within 1 to 2 minutes after the first injection the patient had tinnitus and nausea leading to vomiting. Before treatment could be instituted, the patient became confused, extremely anxious, and had memory loss. Examination demonstrated no focal neurologic deficit except for profound retrograde amnesia extending back over the previous week. Angiography was again abandoned and the patient treated conservatively. The amnesia resolved almost completely over the next 24 hours, but the patient was left with a period of 2 to 3 hours before angiography of which she had no recollection. A head CT scan 56 hours after angiography was normal.

Investigations

Because all examinations were performed with the same batch of iohexol, this was withdrawn from use and analyzed by the manufacturers. Tests were performed on four random bottles, all of which had been subject to the same storage conditions. One of the bottles had been taken from the contrast warmer that was routinely used within the angiogram suite and one of the bottles was that used for the vertebral injection on the last patient. Analysis demonstrated a normal pH (7.27) and no evidence of significant ionized iodine content (8 μg/mL). Photoabsorbance and refractive index were also within normal limits. There was no evidence of microscopic particulate contamination.

Review of angiographic technique and of the films from the six patients demonstrated no particular anatomic abnormalities in the vascular system and no evidence of problems of vertebral catheterization. However, it was noted that the contrast warming cabinet had a faulty thermostatic control and was prewarming contrast material to a temperature just over 40°C. A sample of contrast material diluted with room-temperature saline, as used for angiography, had a temperature of 38.5°C. The cabinet was withdrawn from use, and cerebral angiography was subsequently performed with contrast material at room temperature. Since this time there has been no recurrence of these complications in a series of over 50 selective cerebral angiograms, and we believe that these complications relate to the injection of contrast material above body temperature.

Discussion

Transient global amnesia is a condition of sudden onset characterized by loss of memory for recent events and an inability to retain new memories (1, 2, 15–17). Spontaneous transient global amnesia is a rare disorder whose clinical features are rather stereotyped and remarkably similar to the six cases reported here. The patient experiences sudden confusion, often associated with rather severe anxiety features. Examination reveals an inability to retain new memories that is characterized by repeated questioning even after the answer has been given. Recent memories formed in the hours or days before the acute event are also characteristically absent, although the consciousness level and other neurologic parameters are normal. The episode usually lasts 30 minutes to several hours, and after recovery there is retrograde amnesia extending over hours or days preceding the acute event and anterograde amnesia for the event itself. The attacks may recur, and there is an association with the risk factors for cerebrovascular disease and particularly with vertebrobasilar insufficiency.

The occurrence of transient global amnesia as a complication of cerebral angiography was first described by Hague (18) in 1954. Since then there have been a number of similar reports (2, 4, 5, 19), and transient global amnesia was subsequently shown to have a prevalence of 0.59% in a series of 1520 patients (4). Selective vertebral artery injections carry the highest risk, although carotid artery, aortic arch, and coronary artery injections have all been associated (2, 13). The vast majority of recorded cases have occurred as a complication of cerebral angiography with ionic contrast media. Before this report, four cases of transient global amnesia occurring after injection of nonionic contrast media had been recorded; all were associated with selective cerebral angiography (11, 12, 14).

The abnormality of memory seen in transient global amnesia appears to result from bilateral functional disturbance of the medial temporal cortex (2, 20). The mechanism by which cerebral angiography produces this disturbance remains unclear; epilepsy, ischemia, and direct neurotoxicity have all been implicated. The theory that transient global amnesia results from a focal epileptic discharge (21, 22) fell into disfavor after Miller et al (23) failed to demonstrate

any electroencephalographic abnormality in 13 cases. Several workers have favored a direct neurotoxic effect of contrast media as a cause of transient global amnesia (11, 24). Experimental studies have suggested that contrast media can alter the permeability of the blood-brain barrier by causing shrinkage of endothelial cells, allowing contrast material to enter cerebral interstitial tissue where it may have a direct neurotoxic effect (25, 26). Minuk et al (11) have suggested that the risk of neurotoxic effects might be increased by preexisting abnormalities of the blood-brain barrier and by repeated contrast injections. It is striking however that in the case described by Juni et al (12), in case 1 described by Giang and Kido (14), and in all six cases described here the onset of transient global amnesia occurred suddenly within 1 to 2 minutes after the first vertebral artery injection of contrast material. Furthermore, the suggestion of Minuk et al that the effect may be partly dose dependent is not in keeping with the cases presented here, where transient global amnesia followed vertebral injections of no more than 8 mL of dilute contrast material and in two cases followed test injections of only 2 mL of undiluted contrast material. The sudden onset of symptoms and the small contrast volumes make it improbable that a direct toxic effect of contrast material was the mechanism in these cases. In addition, none of the patients described here had any structural temporal lobe abnormality to suggest a preexisting deficit of the blood-brain barrier.

The close relationships between the risk factors for cerebrovascular disease and spontaneous transient global amnesia (6–10) and the description of infarcts on CT (27) provide strong evidence for an ischemic cause. Several reports have also linked arteriography-related transient global amnesia with clinical and arteriographic vertebrobasilar insufficiency (11, 13). The findings of very low rates of symptom recurrence (8, 27), completed infarction (10, 28), and associated atherosclerotic disease of the carotid systems (29) do not however support the suggestion that spontaneous transient global amnesia represents a form of atheroma-related transient ischemic attack. Wales and Nov (3) reported two cases of angiography-related transient global amnesia and suggested that microemboli resulting from intrinsic particles in the contrast media (30) might be responsible, although they were not able to analyze the contrast material used. In the cases described here, analysis of four samples of contrast material, including one sample from a bottle that produced symptoms, revealed no evidence of particulate contamination or of any other abnormality.

Arterial spasm has also been suggested as a causative mechanism in transient global amnesia (12). Several workers have implicated migraine in the genesis of spontaneous transient global amnesia (31, 32), and one study found migraine to be the only related cerebrovascular risk factor (33). A number of authors have also implicated migraine in the genesis of angiography-related transient global amnesia, particularly when the acute episode is delayed for some hours (12, 14). It should be noted that Shuaib and Hachinski (5) found only one case of transient global amnesia (0.67%) when reviewing 149 cerebral angiograms of patients with migraines; this is no different from the rate in an unselected group (0.59% [4]). Arterial spasm related to angiography or previous subarachnoid hemorrhage has also been described in cases of angiographically related transient global amnesia (12) and was present in our case 3.

We believe that arterial spasm related to the injectate temperature is the most likely mechanism of transient global amnesia in the cases reported here. Although the injectate temperature was not measured, the incidence of transient global amnesia was 17% over a 4-month period, and no other causative factor was identified. The rapid onset of symptoms and the small volume of injectate also support the suggestion of spasm as an underlying mechanism.

Review of all the reported cases of angiography-related transient global amnesia is frankly confusing. The cases described here, together with other reports, suggest that cerebral arterial spasm can be responsible, and the reports of delayed onset of transient global amnesia provide further support for this conclusion. At the same time, the arguments that transient global amnesia results as a toxic effect of contrast material in some cases are also convincing.

In conclusion, we believe that arteriography-related transient global amnesia results from an insult to the temporal lobes and that preexisting temporal lobe abnormality or cerebrovascular insufficiency can be a predisposing factor. The precipitating insult is often focal ischemia, which may result from immediate or delayed

arterial spasm. The roles of catheter- or contrast-related emboli and of direct contrast toxicity remain uncertain, but it seems probable that either may be responsible in individual cases.

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