SOME COMPLICATIONS OF VERTEBRAL ANGIOGRAPHY

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As the use of cerebral angiography has become widespread, there are increasing numbers of case reports of complications.\(^7\),\(^8\),\(^10\),\(^11\),\(^13\),\(^16\) These are most valuable in trying to set standards for selection of patients for this diagnostic procedure. The similar stories from the 3 cases reported here are intended for this purpose.

CASE REPORTS

Case 1. H.W., 48 years old, a doctor’s mother, had “migraine” attacks for several years beginning at the age of 28. The severe left-sided headaches were preceded by blurred vision and numbness in the right hand. Six months prior to entry in St. Luke’s Hospital, there was return of severe left frontal headache following blurred vision; the pain lasted 6 to 12 hours, and recurred every week or two. Two weeks prior to admission, there was numbness and tingling of the right hand. A few days later, the usual headache began, but the blurred vision persisted when the headache disappeared.

Examination. On admission on Nov. 27, 1948 there was a complete right homonymous hemianopsia (without macular sparing). Right biceps and knee reflexes were slightly increased. Ankle reflexes were equal. There was no other neurological disturbance. Findings on lumbar puncture were normal. Roentgenograms of the skull showed a midline pineal calcification. B.P. was 144/98.

Angiography. Because of the possibility of aneurysm, left carotid and left vertebral angiograms were done with 35 per cent Diodrast (iodopyracet) under general anesthesia. Unfortunately, the total quantity of Diodrast was not noted.

Course. The patient was returned to her room in good condition, with B.P. 128/90. Two hours later, at 4:30 p.m., she was still unconscious; B.P. was 186/110, and pulse was irregular in quality and at a rate of 84 per min. At 8:00 p.m. she moaned and moved her arm occasionally. At 3:00 the next morning, the pulse rate was 100, respiratory rate 30, and B.P. 172/112. At 5:00 p.m., the B.P. suddenly dropped from 164/112 to 110/38; pulse 100, respiration 40. At 5:27 she was turned on her back; pulse 80, respiration 20 and very shallow. Two minutes later, she stopped breathing. There was a poor pulse at 70 per min. In spite of oxygen, coramine and artificial respiration, she died.

The left carotid angiograms were normal. The vertebral angiogram (Fig. 1) shows a number of filling defects in the vertebral and basilar arteries typical of arteriosclerosis. Marked resistance to flow because of arteriosclerosis could explain the discontinuities in the posterior cerebral circulation.

Autopsy (Dr. Edwin Hirsch, Department of Pathology, St. Luke’s Hospital).

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There was an old liquefied infarct of the calcarine area of the cerebrum. There were marked atheromatous changes in the basilar vessels. The left vertebral artery was occluded for 0.8 cm. by an old atheromatous plaque in the distal 1 cm. before its junction with the right vertebral artery.

Histologic study confirmed the ancient nature of the softening and there was hyalinization of small vessels in this area.

Case 2 (Research and Educational Hospital No. 405-635). L.M.B., aged 69, had onset of generalized epileptic seizures, midfrontal headaches, and disturbances of memory 1 year before hospitalization on Aug. 22, 1953.

Examination. The patient was an obese woman who was occasionally confused. B.P. was 186/136 mm. Hg. Retinal arterioles were “silver-wired.” There was a grossly evident left homonymous hemianopsia and depression of visual acuity (unable to count fingers at 6 feet). The deep tendon reflexes in the left leg were increased and a Babinski sign was elicited on this side. Blood count and urinalysis were normal. Spinal puncture yielded clear fluid with 51 mg. protein, under normal pressure. X-rays of the skull were normal but chest films showed a mediastinal widening suggesting neoplasm. Metastatic intracranial neoplasms were suspected.

Angiography. An intravenous test dose of Diodrast 35 per cent was well tolerated so the patient was anesthetized and intubated. The right vertebral artery was injected with three 10 cc. portions of Diodrast, and when no mass lesions were seen, a single 10 cc. injection was made into the right carotid artery. No mass lesion was
The tracheal tube was removed 75 minutes after induction of anesthesia (pentothal, nitrous-oxide-oxygen, and trichlorethylene). At this time she responded to painful stimuli, but 20 minutes later she did not, although the blood pressure was 160/110 and the color was good.

Course. At 3:30 p.m., the pressure was 140/100 and the color was good. She was found dead 20 minutes later.

Review of the axial and lateral angiograms (Fig. 2a) shows mural filling defects in the basilar artery, which is otherwise of good caliber. However, the superior cerebellar and posterior cerebral arteries appear very small, and there are marked constrictions at their origins.

Autopsy showed generalized arteriosclerosis (especially severe in the brain and heart), atherosclerosis of the aorta and its major branches, and right and left ventricular dilatation. In the brain all large vessels showed atherosclerosis. This was especially marked in the vertebral, basilar, and posterior cerebral arteries. Cross-sections of the posterior cerebral and superior cerebellar arteries showed marked narrowing of the lumina (corresponding to the thin column of contrast material in the angiogram). There was no evidence of antemortem thrombosis, at least at the origins of these vessels. There was marked softening of the inferior aspect of the temporo-occipital area bilaterally. This was more marked on the right, where it extended to the tip of the occipital pole (Fig. 2b). Another small softening was found in the right internal capsule and caudate nucleus.

Histologic study showed that the area of encephalomalacia in the right occipital
lobe had progressed to a precystic stage. Evidence of arterial and arteriolar arteriosclerosis was everywhere apparent, and in the basal ganglia there was actual necrosis of vessel walls. A section of the basilar artery showed calcific plaques, splitting of the elastic media and necrosis of all the vessel layers.

Case 3 (Chicago Memorial Hospital No. 134894).* M.M., a woman, was born in 1897. During the 8th month of her third pregnancy (1919) she suddenly fell, was unconscious and subsequently had a right facial weakness. Blood pressure was said to have been very high, and there was albuminuria. However, this child and a fourth were born without further incident. In 1941, she complained of headache, weakness and dizziness. In spite of several thorough investigations at various hospitals and clinics, nothing abnormal was found until after severe headache, vomiting and semistupor developed on Nov. 26, 1943.

On Dec. 3, 1943, she was hospitalized and, following ventriculography, a large midline meningioma arising from the under surface of the tentorium was removed. On the 11th postoperative day, the patient having hitherto done quite well, difficulty in speaking developed, which led to a severe expressive aphasia within the next 24 hours. She was unable to write, although she could read. Pressure of the spinal fluid was 85 mm. of clear yellow fluid. About a week later, the aphasia began to improve and by the time of discharge, Dec. 24, 1943, it had disappeared.

She remained well thereafter until 1952, when bitemporal pain and generalized headaches appeared, relieved by aspirin. These persisted into late 1953. Examination by an ophthalmologist in September, 1953 revealed left homonymous hemianopsia with macular sparing. The headaches diminished, but the visual loss persisted, and she was hospitalized on Dec. 9, 1953.

Examination. X-rays of the head showed no abnormalities except the surgical defect in the occipital bone. B.P. was 124/78. There were no abnormal neurological findings aside from left homonymous hemianopsia.

Angiography. On the next day, under intravenous sodium pentothal anesthesia and intranasal administration of oxygen, three injections of 6 cc. each of Urokon (35 per cent) were made into the right carotid artery. No abnormalities were seen, so 10 cc. of Urokon were injected into the right vertebral artery. The artery could be followed only to the foramen magnum (Fig. 3). Because of the belief that the exposure had been made too soon, subsequent injections of 10 cc. and 6 cc. were made, but the resulting films were unchanged.

Course. Three hours after completion of angiography, the patient was awake and responding well. Seven hours after angiography, she became lethargic, but could move all extremities on request. B.P. was 110/70 mm. Hg, pulse rate was 54 per min., and she vomited on several occasions. An hour later, the right pupil was found to be larger than the left, but both reacted well to light.

On the following morning, she was still lethargic and the right pupil was still dilated. Lethargy increased and on December 12, the speech was slow and unintelligible, and at times she would not respond when spoken to. Pulse varied from 48 to 62 per min., B.P. from 118–140/55–75, and respirations 18–20 per min. When examined at noon on this day, she had a complete right 3rd nerve palsy and left Babinski sign; there was a questionably positive right Babinski sign as well. She became less stuporous and at 12:30, 10 cc. of 1 per cent procaine were injected for a right stellate ganglion paralysis. This was produced, and within 15 minutes, she was talking coherently. That afternoon she was alert and asked for food. By the

* Case history of meningioma previously reported by Russell and Bucy.11
next day her pupils became equal and only a slight right ptosis remained.

On Dec. 15, 1953, she was found to have a left homonymous hemianopsia. The right pupil was smaller than the left, there was a slight right ptosis, and the right side of the face was slightly drier than the left.

On December 16, she was discharged to take Papaverine (0.1 gm.) four times daily. She has continued well except for persisting left homonymous hemianopsia. This is now attributed to thrombosis of the right posterior cerebral artery, and it is believed that she also has a partial occlusion of the right vertebral and basilar arteries.

Probably the most important lesson to be learned (or relearned) from these cases is that cerebral angiography is not without hazard, and Diodrast and Urokon are not innocuous materials. The most puzzling aspect of the problem of complications of angiography is the wide divergence in incidence in different clinics. This must be because of differences in technic (unless there is some hidden factor in the genetic make-up of different national groups). Among these must be included the different contrast media used, the quantities of dyestuff, the timing of successive injections, and the type of anesthesia. Most of the reports of low incidence of complication come from the Scandinavian countries, where Umbradil and Perabrodil are used. These, like Diodrast, are solutions of various salts of crystalline iodine compounds (3,5 diiodopyridone-N-acetic acid). It is not probable that it is the
sodium or diethanolamine salts that are responsible for the differences. It does appear that the smaller the total dose of contrast medium used, and the smaller the individual doses for each injection, the less numerous are the complications. However, serious complications have been reported with one 10 cc. injection of Diodrast, and Radner's patient had only 9 cc. of Umbra-dil. Experimental evidence indicates that a relatively long wait between successive injections is safer than making injections in rapid succession. A minimum wait of 10 minutes has been suggested, during which time it should be possible to examine films resulting from previous injections. If there are signs of vascular occlusion, arteriosclerosis, or marked delays in circulation through the brain, it would doubtless be wise to discontinue the procedure. Decker and Holzer suggest that films always include the tip of the needle, for they believe that injections into the vessel wall or just outside of it can cause such vasospasm as to make repeated injections of contrast material hazardous. (However, there is no evidence of any such complications here.)

Certainly if the injection is done under local anesthesia, and the patient shows an untoward effect of injection (coma, aphasia, hemianopsia, hemiparesis or hemiplegia), further injections are contraindicated. With general anesthesia such warnings pass unnoticed; hence, especial care must be used under these conditions to use small quantities of dye, well spaced injections, and, probably, very small amounts of solution with which to rinse the needle (for it seems likely that with some impairment of blood-brain barrier caused by the contrast medium, injection of large amounts of saline or glucose solution will produce rapid swelling of the brain). However, Perese et al. warn that local anesthesia is no guarantee that there will be warning of impending difficulty.

It is not clear just how angiography precipitates the neurological lesions. Thrombosis does not appear to be caused by the procedure. In Case 1, the thrombus in one vertebral artery found at autopsy was old, and no thrombi were found in the other case. Emboli from traumatized intima or from clots forming at the needle tip are unlikely in view of the large-bore needle and the intermittent washing through of small amounts of saline solution. Spasm of major cerebral vessels has been seen in many angiograms but was not evident here. The only obvious factors common to these 3 patients are atherosclerosis, with narrowing of the lumen of major vessels of the vertebral-basilar system, vertebral angiography, and general anesthesia. It is conceivable that the Diodrast could cause enough internal swelling to occlude a channel already narrowed by atherosclerosis. The ischemia (which we assume to be the basic cause of death) may be a relative one, and be caused by lowering of blood pressure during the angiographic procedure under general anesthesia. This hypothesis of relative hypotension has been discussed by Denny-Brown for basilar artery syndromes and by Corday et al. for lesions of the cerebral hemispheres.

In all events, the important factor appears to be atherosclerosis of the major cerebral vessels. It is roughly correlated with atherosclerosis else-
where in the body, but can exist independently. Retinal atherosclerosis (histologically proven) means a 4 to 1 probability that the basilar artery is arteriosclerotic, but unfortunately there is no good correlation between the histologic appearance of arteriosclerosis of the retina and this disorder as seen through the ophthalmoscope. Cerebral arteriosclerosis is more apt to be intense and to involve smaller vessels if there is co-existent hypertension, according to Fisher.

It is difficult to select patients for angiography who do not have arteriosclerosis, for many patients with tumors or vascular anomalies also have arteriosclerosis. Age is of little value as a criterion (beyond 40 years certainly); in this series, the patients were 48, 57, and 69 years old. The age span in the group of Perese et al. was 42-60, and 3 or 4 injections of 10 cc. of Diodrast were used. One of their patients had multiple metastases, in 1 case no autopsy was performed, and the other 4 patients who died had arteriosclerosis and thrombosis of the cerebral or basilar arteries with extensive softening (including 1 patient only 46 years old). Radner's patient was 66, admitted for right oculomotor palsy. She was known to have arterial hypertension and diabetes mellitus, with diabetic retinopathy. After carotid injection failed to show an aneurysm, one 9 cc. injection of Umbradil into the right vertebral artery filled both vertebral arteries and showed indentations of the vertebral, basilar, and both posterior cerebral arteries. There was no immediate reaction but in 45 minutes the woman became comatose; consciousness slowly returned 10 minutes later, with right-sided weakness, slurred speech, and difficulty in swallowing. In spite of antibiotic and anticoagulant therapy, the patient died on the 11th day. Autopsy showed severe generalized arteriosclerosis. Although the lumina were narrowed almost to the point of occlusion, there was no recent thrombosis. Old and recent softenings were found in the left occiput, both thalami, and the rostral part of the brain stem.

In the 162 vertebral angiograms done by Petit-Dutaillis et al., there were 4 serious accidents, 2 of which were fatal. One followed intra-arterial injection of procaine for failure to visualize the intracranial portion of the vertebral artery (and autopsy failed to reveal the pathology). The other occurred in an aged arteriosclerotic patient with right hemianopsia and hemiparesis, who died suddenly after the angiography (which had appeared to go without incident). Sjögren encountered only 1 complication in over 200 percutaneous vertebral angiograms with Umbradil; this was a transient syndrome of posterior inferior cerebellar artery insufficiency.

Occlusion of vessels supplying the brain is being reported with increasing frequency, but it is rare that the vertebral-basilar system is involved. In a large series of angiograms, Decker and Holzer found 97 instances of occlusion of vessels supplying the brain. Only 3 involved the vertebral and basilar system, whereas there were 35 occlusions of the carotid artery in the neck and 7 within the skull. The remaining 52 were occlusions of major cerebral vessels (including 42 of the middle cerebral artery and 1 of the posterior cerebral artery). In one autopsy, there was partial occlusion of the proximal end
of the basilar artery and complete obstruction of a segment of the posterior cerebral artery. Meningeal anastomoses were found in this patient. The authors offer the possibility that anastomoses between the muscular branches of the vertebral and occipital arteries protect the patient against occlusions of the vertebral arteries. Occlusions of the basilar artery are rarely compatible with life, but transient syndromes may be produced by stenotic lesions. Insufficiency of the basilar system may be completely unnoted until occlusion of a carotid artery interferes with collateral flow and precipitates infarction (and, conversely, occlusion of basilar flow may precipitate a middle cerebral artery syndrome if a carotid artery has been closed off some time before).

The cerebellar arteries usually have even better anastomoses than the cerebral ones, so that occlusions (except for the posterior inferior cerebellar artery) are rarely clinically evident. The superior cerebellar artery is rarely occluded, and then usually by embolus. Luhan and Pollack\(^9\) reported 6 cases of this disorder, 3 with autopsy. One was in a woman, 36, who was 7 months pregnant when she had a subarachnoid hemorrhage. Signs of posterior fossa involvement developed and a vertebral angiogram was done. It was normal. After she awakened from the anesthesia, she went into labor, had a major seizure, and aspirated vomitus. She died 24 hours after the arteriography. Autopsy disclosed a hemorrhagic softening in the mesencephalon, ascribed to a soft clot in one of the major subdivisions of the superior cerebellar artery. This was believed to have been caused by an embolus (site not disclosed by general autopsy).

Perhaps it would be wise to be especially cautious in patients with homonymous hemianopsia whose spinal fluid pressure and roentgenograms of the skull are normal. If dye study still appears indicated, and carotid angiography is done without revealing the lesion, it might be best to wait for a few days before doing the vertebral angiogram. In this way, one might avoid impairing the communications from the carotid to the basilar system and permit collateral flow in case there should be vascular insufficiency in the vertebral-basilar system. The vertebral angiography might well be done under local anesthesia providing that this is generously infiltrated into the region (including the periosteum) and providing that the needle for angiography is inserted from medial to lateral and always pointing upward (to avoid the roots of the brachial plexus). After a single injection of 8–10 cc. of Diodrast, the films should be inspected, and if signs of arteriosclerosis or occlusion are found, the procedure had best be discontinued. Measures to increase cerebral blood flow might then be undertaken (if no bleeding has occurred recently within the cranium); systemic or intra-arterial injections of Papaverine, carbon dioxide inhalations, and stellate block all have their proponents.

It might be argued that in virtually every case of complication of angiography because of arteriosclerosis, the procedure has merely hastened the inevitable in a patient who already has serious neurologic disease (else the
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procedure would not have been done). However, patients with arteriosclerosis can live with their symptoms for many years before natural processes put an end to life, and we do not believe that curiosity as to the cause of a disorder should be put above considerations of the patient's welfare.

SUMMARY

Death followed vertebral angiography in 2 patients, 48 and 69 years of age, in whom autopsy showed severe arteriosclerosis. In a third patient, aged 57 years, recovery occurred after the procedure had caused marked increase in neurologic symptoms. In each patient, there were headaches, homonymous hemianopsia, and other neurological findings, without evidence of raised intracranial pressure. In each instance, the angiograms revealed evidence of arteriosclerosis of the vertebral-basilar system.

The reduction in incidence of complications of vertebral angiography is discussed, with suggestions to limit the quantity of contrast medium and number of injections, to lengthen the interval between injections, and to look at each film exposed before making more injections.

REFERENCES