Delayed Cerebral Ischemia Following Arteriography

MARK FISHER, M.D.,* RODNEY SANDLER, M.D.,† AND JOHN M. WEINER, Dr.P.H.‡

SUMMARY Cerebral ischemic events associated with arteriography are usually attributed to catheter-induced emboli. We present three patients with cerebral ischemia occurring 6 to 48 hours post-arteriography. We suspected that alternate pathogenic mechanisms were in effect. To evaluate the possibility that sustained platelet activation occurs in association with arteriography, we measured the platelet-specific protein beta-thromboglobulin (BTG) prior to and 24 hours following arteriography in two groups of patients. Group I had arteriography performed shortly after venipuncture, while Group II patients did not have arteriography between samples. Seven of eight Group I patients had an increase of BTG on day two, compared with two of eight group II patients (p < .05). When compared to Group II changes, Group I had a significant increase of BTG on day two (p < .05). We conclude that cerebral ischemic events associated with arteriography may occur on a delayed basis, and that platelet activation, manifested by increased BTG levels, may be one mechanism contributing to this phenomenon.

CT OF EXTRACRANIAL CAROTIDS/Culebras et al


References

From the Departments of Neurology, * and Medicine, † University of Southern California School of Medicine, Los Angeles, California.
This was supported in part by a grant from the Professional Staff Association, LAC-USC Medical Center (#2507 RR05466-15).
This paper was presented in part at the Ninth International Joint Conference on Stroke and Cerebral Circulation, February 16-18, 1984, Tampa, Florida.
Dr. Fisher is recipient of the Teacher-Investigator Development Award #1K07-NS00884-01.
Address correspondence to: Mark Fisher, M.D., Department of Neurology, Unit I, Room 5641, USC School of Medicine, 1200 North State Street, Los Angeles, California 90033.
Received July 23, 1984; revision accepted October 24, 1984.

Cerebral ischemic events represent a significant source of morbidity among patients undergoing arteriography for occlusive cerebral vascular disease.1 The pathogenesis of these complications is usually attributed to either thrombus formation on catheter tips with subsequent injection into the intracranial circulation, or dislodgement of atherosclerotic plaques by the catheter.1 These result in sudden neurological deficits, usually occurring while the patient is on the angiography table. We report three patients who experienced cerebral ischemic events beginning 6 to 48 hours following performance of arteriography. We suspected that alternate pathogenic mechanisms were in effect and thus investigated the relationship between cerebral angiography and platelet activation. We used plasma beta-thromboglobulin (BTG) prior to and 24 hours following arteriography in two groups of patients. Group I had arteriography performed shortly after venipuncture, while Group II patients did not have arteriography between samples. Seven of eight Group I patients had an increase of BTG on day two, compared with two of eight group II patients (p < .05). When compared to Group II changes, Group I had a significant increase of BTG on day two (p < .05). We conclude that cerebral ischemic events associated with arteriography may occur on a delayed basis, and that platelet activation, manifested by increased BTG levels, may be one mechanism contributing to this phenomenon.

Case reports

Case 1  A 65-year-old female, admitted for evaluation of an abdominal aortic aneurysm, sustained a right hemisphere stroke nine years previously. At that time, she experienced an incompletely resolving sensori-motor deficit involving left arm and leg along with dysarthria. She had chronic hypertension and adult onset diabetes controlled with oral agents. General physical examination revealed a pulsatile abdominal mass. The cardiac exam was normal. Neurological examination showed a normal mental status. A cholesterol embolic fragment was noted on funduscopic exam of the right eye. There was mild weakness of the left iliopsoas, with left-sided hyperreflexia and a left Babinski. Admission laboratory evaluation was unremarkable.

The patient underwent an aortic arch study, which demonstrated an abdominal aortic aneurysm and occlusions of both superficial femoral arteries. There were non-ulcerated, non-flow-restricting plaques at both carotid bifurcations. Beginning 6 hours following the procedure, the patient experienced at least three episodes of transient right upper extremity sensori-motor deficit, each lasting minutes. These occurred...
over a 12 hour period and were unassociated with hypotension or arrhythmia. She never experienced similar symptoms previously, and at follow-up, 19 months later, there was no recurrence of these symptoms.

Case 2

A 35 year old female was admitted for the acute onset of the inability to speak. The patient had a similar episode several months earlier, resolving over three days without treatment. She had a three year history of hypertension and was using oral contraceptives for six years. General physical examination revealed a blood pressure of 224/128. The cardiac exam was unremarkable. On neurological exam, the patient exhibited a moderate nonfluent aphasia, right central facial weakness, and a right pronator drift. Routine blood chemistries and hematological evaluation were unremarkable. Serum VDRL and FTA were positive. The cerebrospinal fluid, including serology, was normal. Echocardiography showed no evidence of mitral valve prolapse. A computerized tomographic (CT) scan showed a low density region in the left parietal lobe, without contrast enhancement.

Nine days post-stroke, the patient underwent selective carotid arteriography. The study revealed a questionable intraluminal filling defect in a fronto-opercular branch of the left middle cerebral artery. 36 hours after the study, the patient experienced right upper and lower extremity weakness and sensory loss, with subtotal resolution over six hours. The patient had not experienced these symptoms previously. She was discharged on antiplatelet medications. Follow-up at 20 months revealed no recurrence of symptoms.

Case 3

A 56 year old female underwent cardiac catheterization for evaluation of chest pain. The cardiac study revealed normal coronary arteries and normal left ventricular function. 48 hours following the procedure, the patient suddenly lost vision in the left eye. She had no previous neurological symptoms. The general physical exam was normal and there were no carotid bruits. Neurological examination revealed left optic disc pallor with light perception only, along with a left Marcus-Gunn pupil. The mental status, sensory, and motor examinations were normal. Routine laboratory studies were unremarkable. A CT scan showed no evidence of infarction. Her diagnosis was a left central retinal artery occlusion, and she was discharged on anti-platelet therapy. Follow-up 14 months later revealed no change in visual function, but no new symptoms.

Methods

Two groups of patients with signs and/or symptoms of occlusive cerebral vascular disease were selected for the experimental study. Plasma was collected from these patients for BTG assay on two consecutive days at an interval of approximately 24 hours. Group I had selective carotid arteriography performed on day one of the study, shortly after collection of the plasma sample. Group II did not have arteriography between plasma samples. Plasma samples were collected using a modification of the method of Files et al. A solution of 1 ml acid-citrate-dextrose (ACD, NIH Formula A), 80 ul aspirin (180 mg ASA/ml ethanol), and 10 ul PGE,

among Group I patients, BTG levels on day one were 19.1 ± 8.1 ng/ml (mean ± SEM) and on day two were 22.5 ± 8.4 ng/ml. Among Group II patients, BTG levels on day one were 19.8 ± 1.8 ng/ml, while on day two the levels were 17.0 ± 2.2 ng/ml. The mean difference (day two minus day one) was significantly greater for Group I patients when compared to Group II patients (p < .05). Seven of eight Group I
patients had an increase on day two, compared to only two of eight Group II patients (p < .05). BTG levels for the three case report patients, with plasma collected two to nine months following the arteriographic episodes, were within normal limits.

Among Group I patients, there were no ecchymoses noted over femoral puncture sites. There were no significant increases of BUN (17.4 ± 2.7 mg/dl day one vs 17.0 ± 3.2 mg/dl day two, mean ± SD), creatinine (1.3 ± 0.3 mg/dl day one vs 1.2 ± 0.3 mg/dl day two), or cortisol (10.9 ± 2.6 mg/dl day one vs 7.6 ± 1.3 mg/dl day one). All but two Group I patients were fully anticoagulated with heparin prior to and shortly after arteriography or were taking aspirin. The patients receiving heparin or aspirin (n = 6) had a mean BTG increase of 2.8 ng/ml, while the patients taking neither medication had a mean increase of 5.0 ng/ml. Patients with unilateral carotid injections (n = 3), bilateral carotid injections (n = 4), and aortic arch study plus unilateral carotid injections (n = 1) had increases of 2.7 ng/ml, 3.5 ng/ml, and 5.0 ng/ml, respectively.

**Discussion**

Our case reports document episodes of cerebral ischemia occurring 6 to 48 hours following arteriography. Two patients had previously experienced cerebral ischemic episodes, while one was likely at risk for cerebral ischemia due to symptoms of myocardial ischemia. Nevertheless, it is of note that all three patients had new symptoms following arteriography, without recurrence at follow-up of 14–20 months. Thus, it seems reasonable to speculate that these symptoms were related to the arteriograms.

It is not immediately apparent what the mechanism might be for delayed cerebral ischemia following arteriography. Catheter-induced embolism or spasm would appear to be unlikely, due to the delay in onset of these episodes. Contrast media may cause marked alteration of the blood-brain barrier, with neurological symptoms usually consisting of cortical blindness. Postarteriographic CT scans in these patients may show extensive contrast enhancement. While our patients did not have such CT scans, the striking focal, delayed nature of their symptoms suggest an alternate mechanism.

Our experimental study indicates that increased platelet activation occurs in some patients 24 hours after cerebral arteriography. This supports the findings of Gawel et al., who, using an earlier collection procedure for BTG, described increased platelet activation following cerebral arteriography. In our study, the changes in platelet activation were demonstrated with a mean BTG increase of 3.4 ng/ml for Group I patients. In contrast, the control group showed smaller changes with a mean BTG decrease. One explanation for the diminished BTG for the control group lies in the fact that all but one patient had recent cerebral ischemic episodes. Diminishing platelet activation is known to occur following such episodes, and may account for the reduction in BTG seen here.

There are several possible mechanisms for platelet activation in association with arteriography. Measurable changes in BTG might result from arterial thrombosis following femoral puncture or platelet aggregation and thrombus formation on arterial catheters during arteriography. Contrast-induced hemorheological changes, consisting of increased blood viscosity and reduced erythrocyte aggregation and deformability, could induce altered platelet function. Additionally, interactions between platelet membrane and contrast agents might occur, similar to those between erythrocyte membranes and these ionic, hypertonic...
contrast agents, resulting in altered platelet function.

Elevations of BTG may represent a risk factor for stroke among patients with transient cerebral ischemia. The elevations in our study were smaller than those noted to be a significant risk for stroke. However, some trends seen in this study include the tendency for larger increases in platelet activation to occur in patients with more extensive arteriographic procedures and among those not taking anticoagulants or antiplatelet agents. While these trends clearly need to be studied in a larger patient population, they raise the possibility of the existence of a subset of arteriogram patients with increased levels of platelet activation comparable to those demonstrated to be at risk for stroke.

Based on the current study, we believe that ischemic episodes occurring within 48 hours following arteriography may be considered as possible complications of the procedure. The underlying mechanism for such episodes is unclear, but may include increased platelet activation superimposed on pre-existing vascular disease. Further studies are needed to determine how this increased platelet activation is modified by the extent of the arteriographic procedure and the administration of anticoagulant or antiplatelet medications.

Acknowledgments

We thank Angelina Morales for assistance in preparing the manuscript.

References


Delayed cerebral ischemia following arteriography.
M Fisher, R Sandler and J M Weiner

doi: 10.1161/01.STR.16.3.431

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1985 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/16/3/431