Cerebral Hemorrhage in Neonates with Coarctation of the Aorta

RICHARD S. K. YOUNG, M.D., * RICHARD R. LIBERTHSON, M.D., † AND EDWIN L. ZALNERAITIS, M.D. †

SUMMARY Coarctation of the aorta is an uncommon cause of cerebral hemorrhage in the full- or near-term infant. The clinical, radiologic, and neurologic findings of four infants with aortic coarctation and cerebral hemorrhage are presented. In all four infants, cerebral hemorrhage was associated with only moderate elevation of systolic blood pressure (90–110 mmHg).

**CEREbral HEMORRHAGE** is a recognized complication of coarctation of the aorta and may occur in as many as 10% of older patients with this disorder. However, cerebral hemorrhage in infants with coarctation is rare, and a review of the literature yielded only one such patient. In this report, we present the clinical history and management of four infants who had documented coarctation of the aorta and an associated cerebral hemorrhage.

**Patient 1**

This 3.2 kg boy was born at 36 weeks of gestation after a normal pregnancy, labor, and delivery. On the second day of life, he became lethargic, tachypneic, and tachycardic. Physical examination revealed a grade III/VI systolic ejection murmur, and blood pressures of 66/50 mmHg in the upper extremities. His lower extremity pulses were absent.

The clinical course was marked by oliguria, metabolic acidosis (pH 7.08; pO₂ 117 and pCO₂ 25 mmHg) and coagulopathy (prothrombin time, 21/12.5 seconds; partial thromboplastin time, 61 seconds). Cardiac catheterization showed severe periductal (adult type) coarctation of the aorta and a patent ductus arteriosus. On the fourth day of life, he underwent subclavian patch angioplasty repair of the coarctation and ligation of the ductus arteriosus. Following the operation, he was placed on dobutamine. The blood pressure was 90/60 in his upper extremities and 65/50 in the umbilical artery. Several hours later, he developed tonic seizures which were controlled with anticonvulsants. The cerebrospinal fluid was bloody. A computed tomographic (CT) brain scan showed intraventricular and subarachnoid hemorrhage, and scattered areas of low density in the white matter (fig. 1).

Both the neurologic and cardiac status gradually improved during the early postoperative weeks. However, at nine months of age he had microcephaly, spastic diplegia, and extensor plantar responses.

**Patient 2**

This infant male was one of twins born at 36 weeks of gestation to a healthy multigravida whose pregnancy, labor, and delivery were normal. The infant initially appeared well, but by the seventh day of life was mottled and tachypneic. Examination revealed retractions, hepatomegaly, and a grade II/VI apical systolic murmur. The neurologic examination was normal. On

**References**

the following day, the child abruptly became irritable, lethargic, and acidic (pH 7.17; pO₂ 73 and pCO₂ 33 mmHg). Suck, grasp, and Moro reflexes were absent. The serum and urine electrolytes reflected inappropriate secretion of antidiuretic hormone. A CT brain scan showed hemorrhage within the tentorium as well as several punctate cerebral parenchymal hemorrhages (fig. 2).

Because of oliguria and biventricular failure, dobutamine was administered. The pulses, which previously had been symmetric on physical examination, became bounding in the arms and unappreciable in the legs. Cardiac catheterization showed severe pericardial (adult type) coarctation of the aorta. A left subclavian angioplasty repair of the coarctation was performed. The tentorial hemorrhage was treated with fluid restriction, and both neurologic and cardiac status improved. The neurologic examination at 10 months of age showed mild delay in gross motor skills.

Patient 3

This 3.7 kg boy was the product of a full-term, uncomplicated pregnancy, labor, and delivery. At age 12 days he suddenly developed vomiting, seizures, and persistent crying. He became lethargic and apneic. On examination, there was a grade III/VI systolic ejection murmur, elevated upper extremity pulses (brachial blood pressure, 106 mmHg), but absent lower extremity pulses. A clinical diagnosis of coarctation of the aorta was made. There were no findings of heart failure. The anterior fontanelle was tense. There was intermittent right sided and generalized seizure activity, bilateral Babinski signs, and right hemiparesis. The pupils were 6 mm and reactive, but there was limitation of upgaze on oculocephalic reflex testing. A sample of cerebrospinal fluid was grossly bloody. CT brain scan showed massive intraventricular and left thalamic (fig. 3) hemorrhage. Right and left brachial angiograms did not demonstrate a vascular malformation or aneurysm. During the next three weeks, the neurologic status gradually improved. Secondary hydrocephalus was relieved with a ventriculoperitoneal shunt. The seizures responded to treatment with anticonvulsants. On follow-up examination at one year of life, his upper extremity systolic blood pressure is 90 mmHg. The neurologic examination is normal with the exception of persistent Babinski signs. In view of his stable cardiovascular status, both cardiac catheterization and surgical repair of the aortic coarctation were deferred.

Patient 4

This girl was the product of a full-term uncomplicated pregnancy and delivery. She fed poorly for the first two days, and then developed marked respiratory distress, cardiomegaly, hepatomegaly and metabolic acidosis (pH 7.07; pO₂ 108 and pCO₂ 10 mmHg). The brachial pulses were present, but the femoral pulses were not detected. Laboratory tests documented thrombocytopenia and elevation of prothrombin and partial thromboplastin times, and fibrin split products. On subsequent examination, she manifested decorticate posturing. A lumbar puncture revealed grossly bloody cerebrospinal fluid with xanthochromic supernatant. The seizures continued and the child died on the 11th day of life.

Postmortem examination revealed severe pericardial (adult type) aortic coarctation, and a bicuspid non-

Figure 1. Blood is present in both the lateral and fourth ventricles (arrows.)

Figure 2. Blood is present within the tentorial leaflets (arrows.)
stenotic aortic valve. Neuropathologic examination disclosed subarachnoid hemorrhage, intraventricular hemorrhage, small punctate cerebral parenchymal hemorrhages, and periventricular leukomalacia.

Discussion

Cerebral hemorrhage in patients with coarctation of the aorta has been attributed to both the frequent presence of associated aneurysms of the Circle of Willis and the presence of systemic hypertension. The actual prevalence of aneurysms in patients with coarctation is estimated at 2.5–50%. None of our patients had evident cerebral aneurysms on CT brain scan (3 patients), arteriography (1 patient), or postmortem study (1 patient). However, it is possible that small aneurysms may not have been detected by the above studies.

The diagnosis of aortic coarctation may be missed in infants with cerebral hemorrhage if there is not a high degree of suspicion. This is illustrated by the fact that in three of our infants aortic coarctation was not diagnosed prior to the onset of neurologic dysfunction. Meticulous attention to upper and lower extremity pulse and blood pressure evaluation is essential in the neonatal examination. The clinical presentation in our infants was similar. All demonstrated signs of neurologic dysfunction including lethargy, irritability, and seizures. Three infants also had heart failure and metabolic acidosis; two had coagulopathy.

In contrast to the one previously described infant with coarctation and cerebral hemorrhage who had marked systemic hypertension (200/100 mmHg), blood pressures in our four infants were only moderately elevated (90–110 mmHg systolic). The causal role of systemic hypertension in cerebral hemorrhage in infants with coarctation is thus not clear. Studies of the cerebral circulation of the newborn dog show that acute elevation of mean arterial blood pressure beyond 80 mmHg may exceed the upper limit of the autoregulatory plateau (the range of blood pressures throughout which cerebral blood flow is held constant). Lactic acidosis secondary to inadequate tissue perfusion may also contribute to increases in cerebral blood flow. These observations and our own clinical experience would suggest that extreme hypertension may not, therefore, be necessary for cerebral hemorrhage in newborns.

There are presently no management guidelines for the infant with coarctation of the aorta and severe systemic hypertension vis-a-vis early surgical correction. Management of infants with coarctation who have already had a cerebral hemorrhage must be individualized. If there is medically refractory heart failure, emergency coarctation surgery is necessary. Infants without heart failure should initially receive medical management for their hypertension. When their cerebral injury has healed, elective coarctation repair may then be carried out. Meticulous support of cerebral perfusion following the cerebral hemorrhage, and avoidance of extreme brady or tachycardia, hypo or hypertension, and hypovolemia is essential. In summary, because cerebral hemorrhage is such an unusual complication of coarctation of the aorta in the infant, a high degree of suspicion for the presence of coarctation is necessary when one is evaluating full- or near-term infants with cerebral hemorrhage.

Acknowledgments

The authors thank Dr. Cheston Berlin for his critical review of the manuscript and Jody Hower and Joan McAfoos for secretarial assistance. This work was done during the tenure of a Clinician-Scientist Award (Dr. Young) from the American Heart Association and with funds contributed in part by its Pennsylvania Affiliate.

References


Figure 3. A massive thalamic (arrow) and intraventricular hemorrhage is present.
The Effect of Incomplete Cerebral Ischemia on Prostaglandin Levels in Rat Brain

E. SHOHAMI, PH.D., J. ROSENTHAL, M.SC., AND S. LAVY, M.D.*

SUMMARY Rats were subjected to severe incomplete cerebral ischemia followed by recirculation. The levels of several of the cyclooxygenase products of arachidonic acid were measured at 5 and 15 minutes of ischemia and at 30 minutes of recirculation following 15 minutes of ischemia, PGE₂ accumulated during the first 5 min. of ischemia and its level declined at 15 min. and returned to control level at 30 min. of recirculation. TXB₂, on the other hand, increased during the whole time course of the experiment and at the end of the post ischemic period its level was 5 times higher than control. Treatment of the animals with indomethacin (4 mg/Kg, i.v.) prior to ischemia reduced the levels of these products without altering the pattern of their changes. During the ischemic period the EEG was isoelectric and the mean recovery time of electrical cortical activity after 15 min. of ischemia was 10.4 ± 3.5 min. in the control rats. The rats which received indomethacin recovered faster (4.3 ± 0.9 min) and were more resistant to the induction of ischemia. We suggest that the reversibility of cortical activity may be correlated to the accumulation of TXB₂ during ischemia and recirculation, and inhibition of its synthesis might improve the post-ischemic reflow.

CEREBRAL ISCHEMIA leads, among other biochemical changes, to the decomposition of membrane-bound phospholipids and a release of free fatty-acids, likely due to the activation of endogenous phospholipases.¹⁻⁵ This breakdown of structural lipids may interrupt membrane function and bring about the accumulation of free fatty acids. The increase in the level of fatty acids, in particular of arachidonic acid, the precursor of prostaglandins, leads to changes in prostaglandin level.⁶⁻⁸ An animal model for reversible incomplete ischemia has been developed and studied by Nordstrom et al.⁷ and Nordstrom and Siesjo.⁸ This (physiologically well controlled) model is based on the occlusion of both carotid arteries of the rat, combined with arterial hypotension. Removal of the clamps from the arteries followed by blood infusion restores the blood supply to the brain. During ischemia the cerebral blood flow in cortical tissue is reduced to less than 10% of normal,¹¹ the tissue is depleted of ATP following 2–3 minutes of ischemia, and the tissues pool of adenosine nucleotides falls rapidly, thus reducing the energy production of the tissue.¹² Recently, Rehncrona et al.¹³ reported a rapid increase in cerebral cortical content of free fatty acids after 5 minutes of ischemia, in the same model. The accumulation of these FFA is reversed during 30 minutes of recirculation. They also observed a marked (3-fold) increase in the relative content of arachidonic acid.

During the recirculation period following ischemia the neurophysiological and metabolic functions might be restored if no irreversible cell damage occurred. A prerequisite for recovery is an adequate perfusion, whereas immediate or delayed perfusion defects might be the cause for irreversibility of brain function.¹⁴⁻¹⁵ Hossmann²¹ reviewed various factors that may contribute to delayed hypoperfusion thus increasing the primary ischemic region. Among these factors are blood coagulation and vascular spasm.

The maintenance of normal tissue perfusion depends on a balanced interaction of two prostaglandins which have opposite effects at the blood-endothelial interface, namely thromboxane A₂ (TXA₂) and prostaglandin I₂ (PGI₂).¹⁷,¹₈ Both prostaglandins have the same precursor, cyclic-endoperoxide (PGH₂), but while TXA₂ is a potent platelet aggregator and vasoconstrictor,¹⁹ PGI₂ inhibits platelet aggregation and is a vasodilator.²₀ Thus, any interruption in the balanced production of these compounds which might result in an increase of TXA₂ could diminish local blood flow. Hallenbeck and Furlow²¹ have shown that dogs exposed to complete ischemia had low post ischemic blood flow with focal zones of greatly impaired perfusion. A significant increase in the blood flow during the post ischemic period was observed in animals receiving either indomethacin prior to ischemia or a combination of indomethacin and PGI, after ischemia. Gaudet and Levine have demonstrated that gerbils pre-
Cerebral hemorrhage in neonates with coarctation of the aorta.
R S Young, R R Libethson and E L Zalneraitis

Stroke. 1982;13:491-494
doi: 10.1161/01.STR.13.4.491
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1982 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/13/4/491

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/