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Ventriculostomy-related Cerebral Hemorrhages after Endovascular Aneurysm Treatment

Ian B. Ross and Gurmeet S. Dhillon

BACKGROUND AND PURPOSE: Recent evidence suggests that endovascular treatment of acutely ruptured aneurysms is equivalent, if not superior, to surgical treatment. Not all patients who undergo endovascular treatment do well, however. We have identified ventriculostomy-related hemorrhage to be a potential source of morbidity and mortality.

METHODS: Prospectively gathered data on patients ($n = 51$) admitted to a hospital for the endovascular treatment of acutely ruptured aneurysms during a 2.5-year period was analyzed.

RESULTS: Twenty-four patients had drains inserted, and three suffered symptomatic ventriculostomy-related cerebral hemorrhages. Two of the three patients were being treated with heparin, one of whom also received clopidogrel, and the third was being treated with low molecular weight heparin at the time. The latter had a normal platelet count, prothrombin time, and activated partial thromboplastin time. All cerebral hemorrhages were deemed to have occurred as a result of drain manipulation.

CONCLUSION: The risk of hemorrhage must be considered when using anticoagulation and antiplatelet therapy in patients requiring ventriculostomy. Interventionalists must not only work closely with neurosurgeons when it is anticipated that a ventriculostomy may be needed but also ensure that there is good communication with the neurosurgical team during the postprocedural period.

The recent finding of the International Subarachnoid Aneurysm Trial that the chance of disability-free survival is better after endovascular treatment than after surgical treatment is encouraging for physicians who specialize in endovascular treatment (1). At times, however, patients who receive endovascular treatment still do poorly. The causes of poor outcome, other than rebleeding, were not discussed in the International Subarachnoid Aneurysm Trial paper. Presumably, most were due to the initial brain injury, but other sources, including thromboembolism and vasospasm, were doubtless present (2–4). It is imperative that the reasons for poor outcomes be understood, so that results can be improved. We think that one overlooked but significant cause of morbidity and mortality among patients with subarachnoid hemorrhage who receive endovascular treatment is ventriculostomy-related brain hemorrhage because of the need for anticoagulant and antiplatelet agents. Antithetical therapeutic concepts are presented herein. The he-

mostatic needs of the surgeon are often at odds with those of the interventionist.

We present three patients whose ventriculostomy hemorrhages were attributable to drain manipulations while the patients were being treated with anticoagulants and antiplatelet agents. The aim is to increase awareness of this potential problem and, by extension, improve outcomes.

Methods

Between March 2000 and August 2002, a total of 51 patients were treated for aneurysmal subarachnoid hemorrhage by endovascular coil embolization at our institution. Twenty-four of the patients underwent ventriculostomy procedures. All except one of these patients received heparin at some point during aneurysm treatment. Heparinization during the procedure was always tailored to keep the activated clotting time to >300 s. Antiplatelet agents, including acetylsalicylic acid and clopidogrel, and low dose anticoagulants were also used frequently after coiling to treat or prevent clots in the vessels. Use of these agents is summarized in Table 1. Three patients who developed ventriculostomy-related cerebral hemorrhages are described below. One did well; one achieved a moderate outcome; and one died as a result of the hemorrhage.

Case 1

A 40-year-old woman presented with a subarachnoid hemorrhage. Her Hunt and Hess grade was III. Ventricular drainage effected an improvement in her clinical state, and the next day, a 6-mm aneurysm of the left internal carotid artery was

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Use of Anticoagulant and Antiplatelet Agents in Patients with Subarachnoid Hemorrhage who Undergo Aneurysm Coiling and Ventriculostomy (n = 24)

Medication	n	%
IV administered heparin, during procedure	23	96
IV administered abciximab, during procedure	2	8
SC administered heparin or enoxaparin, after procedure	7	29
PO ASA, after procedure	10	42
PO clopidogrel, after procedure	2	8

Note.—SC indicates subcutaneously; PO, per os; ASA, acetylsalicylic acid.

coiled. Transcranial Doppler velocities climbed to >200 cm/s within a week of the original subarachnoid hemorrhage. The patient remained clinically well, however, with a regimen of continuous ventricular drainage and aggressive fluid administration. Enoxaparin, 30 mg administered subcutaneously twice a day, and acetylsalicylic acid, 325 mg administered orally every day, were administered because of a perceived risk of thromboembolism arising from the coil mass of this wide necked aneurysm. Two weeks later, while the patient was still receiving these medications, the ventricular drain was removed. During the next several hours, the patient became somnolent and less responsive. CT revealed acute hydrocephalus, secondary to an intraventricular bleed. The next day, with normal prothrombin time, activated partial thromboplastin time, and platelet counts having been documented and 6 hr after the last dose of enoxaparin was administered, a new ventricular drain was inserted, this time in the left frontal region. The CSF was under considerable pressure, and drainage effected an immediate improvement in level of consciousness. Over several hours, however, the patient became aphasic, and CT revealed a new left frontal lobe hemorrhage, along the course of the newest ventricular drain. The patient's condition gradually improved, and she underwent permanent CSF shunt surgery 2 weeks later. Four months after the initial subarachnoid hemorrhage, her speech had returned to normal and she had resumed most of her regular activities.

Case 2

A 66-year-old woman presented to the emergency department with a grade IV Hunt and Hess subarachnoid hemorrhage. CT revealed a pan-ventricular hemorrhage with acute hydrocephalus. A ventricular drain was inserted. A 14-mm wide necked aneurysm at the bifurcation of the basilar artery was documented. The challenging anatomy of the aneurysm, the neurologic status of the patient, and comorbidity that included concurrent myocardial infarction and locally advanced breast carcinoma dictated that the aneurysm not be acutely repaired. After 2 weeks, however, the patient's condition had improved significantly and we elected to coil the aneurysm. Just before starting the procedure, the nonfunctioning right frontal ventricular drain was removed and a new one inserted on the same side of the head. Routine heparinization was used during embolization. Because of the large coil mass and concerns regarding the integrity of the proximal posterior cerebral arteries, the patient was kept fully heparinized to maintain an activated partial thromboplastin time of 60 to 80 s at the end of the procedure. Although she awoke from the procedure well and did not show any localizing signs, she did not completely resume her preoperative status, exhibiting lethargy and disinterest in her surroundings. CT performed 4 days after the procedure showed evidence of a bleed along the tract of the ventricular catheter. The heparin was discontinued. The pa-

tient eventually underwent shunting and achieved a slow recovery. Three months after the subarachnoid hemorrhage, her status was still only moderate. She was able to ambulate, converse, and perform basic activities of daily living but needed assistance with more complex tasks. She refused further treatment of her breast carcinoma and died as a result of the neoplasm 17 months after the subarachnoid hemorrhage.

Case 3

A 60-year-old woman presented with a Hunt and Hess grade I subarachnoid hemorrhage. Early hydrocephalus and a 3-mm anterior communicating artery aneurysm were present. The patient was taken to the angi suite to undergo coiling. Some extravasation of contrast material was noted from the aneurysm at the start of the case, and heparin was not used. Non-occlusive intravascular clots were noted in the proximal right A2 segment of the anterior cerebral artery at the end of the coiling procedure. We placed a ventricular drain on the right side, and approximately 0.5 hr later, the patient underwent heparinization. We also provided orally administered clopidogrel, 300 mg, to achieve an anti-platelet effect. The patient woke up well from the anesthesia and did well initially. Approximately 4 hr after the placement of the drain, the patient accidentally pulled out her ventriculostomy. CT performed soon thereafter showed a small right frontal hemorrhage. The patient's condition deteriorated during the next few hours, and she suffered a transtentorial herniation despite reversal of the heparin, transfusion of 6 U of platelets, and placement of a ventricular drain on the opposite side of her head. Repeat CT showed that the frontal hematoma had greatly enlarged. After discussion with the family regarding her prognosis, support was discontinued and the patient died.

Discussion

Chinese philosophy, specifically the yin-yang school of thought, is helpful in understanding and dealing with the hemostatic system. Opposite principles, namely anticoagulant/antiplatelet factors and clots/platelet aggregates, are at work. It may not be scientifically accurate to say that these "principles" produce one another and overcome one another, but there is no denying that one is never fully anti-coagulated, because anti-coagulation carries with it the principle of clot formation. And vice versa. These principles are also useful when one is pharmacologically altering the system. Artificial anticoagulation is necessary to perform aneurysm coiling, but clotting remains equally important. After acute rupture, clot formation in the coiled aneurysm forms the basis for early protection from rebleeding and also the later formation of a stable matrix within the coil mass.

There is, however, no avoiding the fact that good intraluminal clot prevention in interventional neuro-radiology is the prevailing principle. Large doses of heparin used during aneurysm embolization often are continued for some time after the procedure. Protocols are not uniform, although many groups treat patients who have undergone aneurysm coiling with the administration of low molecular weight heparin for 1 or 2 weeks. Acetylsalicylic acid also is usually administered to these patients, as is the more powerful agent clopidogrel.

Insertion of a ventricular drain is considered a neurosurgical procedure and, although many inter-

ventional radiologists have been trained in its performance, the surgeon is still the person to whom this task usually falls. The hemostatic requirements of the surgeon usually differ from those of the interventionist. A discussion of the hemorrhagic complications of ventriculostomy may seem out of place here. If the interventionist understands the issues facing the surgeon, however, a more intelligent dialogue can be entertained and, perhaps, patient outcomes improved.

Ventriculostomy is not especially dangerous for most patients. Guyot et al (5) reported a 3.28% cerebral hemorrhage rate for 274 ventriculostomies. Another group, who performed CT after all ventriculostomies, reported a 9.4% incidence of hematoma, although most were small and only 0.5% were symptomatic (6). The patient who receives endovascular treatment, however, will have a higher risk of cerebral hemorrhage because of exposure to anticoagulant and antiplatelet agents. Low molecular weight heparin, which does not affect the activated partial thromboplastin time, is sometimes used after the procedure (7) and can also increase the risk for a patient who requires a ventricular drain.

Neurosurgeons have always been cautious regarding the use of heparin. Evidence now exists that 5000 U of subcutaneous heparin administered twice a day is not dangerous to the CNS in patients undergoing major neurosurgical procedures (8–10). Evidence exists that when enoxaparin is started within the first 24 hr after a neurosurgical procedure, 40 mg administered subcutaneously once a day is safe (11). One of these papers does not provide much detail regarding the 872 patients studied other than to state that 152 underwent craniotomy (10). The other two papers studied only patients undergoing “major” spinal or cranial neurosurgical procedures.

The use of low molecular weight heparin has been advocated in many settings recently because of favorable dosing and administration regimens and lower risks of heparin-induced thrombocytopenia (12). Surgeons became interested in low molecular weight heparin when animal work suggested that it is associated with a lower hemorrhagic risk (13). This is apparently because of decreased heparin-associated platelet dysfunction and changes in microvascular permeability (14). Compounding the relaxed attitude regarding this class of drug is the fact that low molecular weight heparin does not generally elevate the activated partial thromboplastin time and current guidelines do not call for monitoring of anticoagulant activity. However, low molecular weight heparin does affect hemostasis, and this activity is measurable with an anti-factor Xa assay (15). The effect is dose dependent. Thus, although 40 mg of subcutaneous enoxaparin administered once a day may be safe for major neurosurgical procedures, the most widely prescribed dose of enoxaparin for the prevention of deep vein thrombosis—30 mg every 12 hr—results in 50% more anticoagulant activity and may be dangerous.

No literature is available regarding the effect of antiplatelet agents on neurosurgical procedures. Clo-

pidogrel, when combined with acetylsalicylic acid, however, has been found to increase postoperative bleeding and morbidity in patients who undergo coronary artery bypass grafting (16, 17). Interestingly, clopidogrel-acetylsalicylic acid therapy is routine premedication for patients undergoing endovascular coronary interventions, and the problem associated with these drugs arises when disease not amenable to endovascular treatment is found. It is intuitive that these drugs should increase the risk of ventriculostomy.

Neurosurgeons are, for the most part, exceedingly careful in assessing patients' hemostatic statuses before inserting ventricular drains. This is not always the case for the seemingly more benign procedure of drain removal, or replacement. In teaching hospitals, ventriculostomies are most often performed by the resident staff and subsequent manipulations delegated to junior residents or nurse practitioners. Awareness of these potential complications and good communication between team members are essential.

In North America, ventriculostomy is preferred over lumbar drain insertion for the management of hydrocephalus in patients who have suffered subarachnoid hemorrhage. This is not the case in other parts of the world. However, the hemorrhagic risks of either procedure in patients who have received anticoagulant and antiplatelet agents require equally serious consideration.

Conclusion

We are constantly in a tug of war, following the ebb and flow of clot formation and prevention in our patients. The endovascular treatment of aneurysms is made safer when anticoagulant and antiplatelet medications can be used. Unfortunately, these increase the risk of adverse events when ventriculostomy is required. In each patient, the specific clinical circumstances will determine what treatment scheme is appropriate.

We understand and accept that there is a yin-yang aspect to our practice. Good communication between the interventionist and neurosurgeon during the entire period of patient service is likely to help improve the present state of the art of acute ruptured aneurysm management and to minimize complications.

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