

W.I. Schievink, MD
S.A. Georganos, MD
M.M. Maya, MD
F.G. Moser, MD
M. Bladyka, MD

ANAPHYLACTIC REACTIONS TO FIBRIN SEALANT INJECTION FOR SPONTANEOUS SPINAL CSF LEAKS

Spontaneous intracranial hypotension due to a spontaneous spinal CSF leak is an important cause of new-onset headaches, particularly in young and middle-aged adults.¹ Treatment has traditionally involved epidural blood patching or surgical CSF leak repair if conservative treatment, e.g., bed rest, fails.¹ Recently, percutaneous placement of fibrin sealant has emerged as an alternate therapy.¹⁻³ The fibrin sealant is injected through a large-bore needle into the epidural space at the site of the CSF leak. Allergic reactions following topical placement of fibrin sealants are caused by the presence of aprotinin, a proteinase inhibitor derived from bovine lung, but they are extremely rare (0.005% of applications).^{4,6} Fibrin sealants contain a small amount of aprotinin to prevent lysis of the clot. Allergic reactions following intravascular administration of aprotinin during cardiac surgery are more common, occurring in less than 0.1% of initial applications but in 3% upon re-exposure.⁶ In approving aprotinin, the Food and Drug Administration recommended against its routine intravascular use due to the risk of severe allergic reactions (<http://www.fda.gov/bbs/topics/NEWS/NEW00453.html>) and the manufacturer of the fibrin sealant warns against its intravascular application (http://www.baxter.com/products/biopharmaceuticals/downloads/Tisseel_PI.pdf). We report the common occurrence of allergic reactions to re-exposure to fibrin sealants delivered percutaneously for spontaneous spinal CSF leaks.

Methods. Among 94 consecutive patients with spontaneous spinal CSF leaks and intracranial hypotension (2001 to 2006), 30 patients underwent one or more fibrin sealant injections. Eight patients underwent two treatments, and two underwent three treatments. Two patients had anaphylactic reactions following injection of the fibrin sealant.

Results. *Patient 1.* A 42-year-old man presented with a 15-month history of positional headaches,

vertigo, and muffled hearing. Physical and neurologic examinations were normal. Brain MRI was normal. CT myelography showed multiple CSF leaks in the cervical and thoracic spine. He remained symptomatic in spite of four epidural blood patches. Fibrin sealant (Tisseel, Baxter Bioscience, Westlake Village, CA) was then injected at the site of the largest thoracic CSF leak. He tolerated the procedure well, but remained symptomatic. Twenty-four days later he underwent a second fibrin sealant injection for a cervical CSF leak. Within 10 minutes, while the thoracic spine was imaged in preparation for further fibrin sealant placement, he had pruritus and urticaria developed. The procedure was terminated, and diphenhydramine and corticosteroids were administered IV. He was admitted to hospital for observation without evidence of other complications.

Patient 2. A 29-year-old woman presented with a 7-month history of positional headaches, echoing in her ears, nausea, and vomiting. Physical and neurologic examinations were normal. Brain MRI showed enhancement of the pachymeninges. CT myelography showed a CSF leak originating from a thoracic meningeal diverticulum. She remained symptomatic in spite of two epidural blood patches. Fibrin sealant was then injected at the site of the diverticulum. She tolerated the procedure well with complete but temporary resolution of symptoms. Fifty-four days later she underwent a second fibrin sealant injection. She tolerated the procedure well with temporary resolution of symptoms. Eighty-six days after the second procedure, she underwent a third fibrin sealant injection. Within 30 minutes, pruritus, stridor, and urticaria developed. Diphenhydramine, corticosteroids, and epinephrine were administered IV with prompt improvement of symptoms. However, arterial hypotension developed (66/34 mm Hg) and pressors were initiated with good response. She was admitted to the intensive care unit. No further complications developed.

Discussion. Anaphylaxis occurred in 2 of 10 patients who underwent repeated applications of fibrin sealant. We suspect that inadvertent

intravascular delivery may have occurred during percutaneous placement in the epidural space. In spontaneous intracranial hypotension, spinal epidural veins are often dilated¹ and only a small amount of aprotinin is required for sensitization. Similar to three-fourths of reported cases,⁶ the anaphylactic reactions in our patients occurred within 3 months of initial exposure.

Percutaneous application of fibrin sealant has been important in the armamentarium to manage spontaneous spinal CSF leaks. Similar to cardiac surgery practice where aprotinin is given IV at high doses, the initial percutaneous application of fibrin sealant can be considered safe with minimal risk of a hypersensitivity reaction.⁶ However, a detailed history of possible previous exposure to aprotinin is mandatory.⁶ Aprotinin or fibrin sealant is used in various cardiac, craniospinal, otolaryngologic, and gastrointestinal procedures.⁴⁻⁶ For repeated fibrin sealant injections, we now wait 3 and preferably 6 months and treat prophylactically with H₁, H₂-receptor antagonists and corticosteroids. Patients are admitted to hospital for observation. For patients with multiple spinal CSF leaks, we now treat up to six sites in one setting rather than in a staged fashion. Consideration should be given to the use of new synthetic dural sealants, but none are yet suitable for percutaneous application.

e-Pub ahead of print at www.neurology.org.

From the Department of Neurosurgery (W.I.S.), Imaging Medical Group (S.A.G., M.M.M., F.G.M.), and Department of Anesthesiology (M.B.), Cedars-Sinai Medical Center, Los Angeles, CA.

Disclosure: The authors report no conflicts of interest.

Received April 25, 2007. Accepted in final form June 12, 2007.

Address correspondence and reprint requests to Dr. Wouter I. Schievink, The Maxine Dunitz Neurosurgical Institute, Cedars-Sinai Medical Center, 8631 West Third Street, Suite 800E, Los Angeles, CA 90048; schievinkw@cshs.org

Copyright © 2007 by AAN Enterprises, Inc.

1. Schievink WI. Spontaneous spinal cerebrospinal fluid leaks and intracranial hypotension. *JAMA* 2006;295:2286–2296.
2. Schievink WI, Maya MM, Moser FM. Treatment of spontaneous intracranial hypotension with percutaneous placement of a fibrin sealant. Report of four cases. *J Neurosurg* 2004;100:1098–1100.
3. Gladstone JP, Nelson K, Patel N, et al. Spontaneous CSF leak treated with percutaneous CT-guided fibrin glue. *Neurology* 2005;64:1818–1819.
4. Beierlein W, Scheule AM, Antoniadis G, et al. An immediate, allergic skin reaction to aprotinin after reexposure to fibrin sealant. *Transfusion* 2000;40:302–305.
5. Oswald AM, Joly LM, Gury C, et al. Fatal intraoperative anaphylaxis related to aprotinin after local application of fibrin glue. *Anesthesiology* 2003;99:762–763.
6. Beierlein W, Scheule AM, Dietrich W, Ziemer G. Forty years of clinical aprotinin use: a review of 124 hypersensitivity reactions. *Ann Thorac Surg* 2005;79:741–748.