Barium-Impregnated Fibrin Glue: Application to a Bleeding Duodenal Sinus

A 64-year-old man with Crohn's disease who had undergone repair of an ileovesical fistula and ileoileostomy had numerous postoperative complications related to sepsis and wound healing. Subsequently, upper gastrointestinal bleeding developed, and the site was identified as a duodenal sinus. Medical management was unsuccessful in controlling the bleeding. Because of the considerable risk associated with reoperation in this seriously ill patient, approval was obtained from the Food and Drug Administration to use fibrin glue in an attempt to prevent further bleeding. The glue was mixed with barium and placed in the duodenal sinus under endoscopic guidance. The barium-impregnated glue facilitated follow-up surveillance with abdominal roentgenography. The patient had no further gastrointestinal bleeding. Further clinical and experimental studies should be conducted to determine the mechanism of action and the efficacy of this application of fibrin glue.

Fibrin glue, a mixture of fibrinogen and thrombin, is available in Europe for use as a hemostatic adjunct and a biologic adhesive. Its effectiveness as a hemostatic agent has been reported in many publications, but currently it is not commercially available in the United States because clinical trials have not been completed. With the approval of the United States Food and Drug Administration, we used it on a "compassionate basis" to avoid operation in a seriously ill patient. This is the first report of the clinical use of fibrin glue ("Tisseel"; ImmunoAG, Vienna, Austria) in the United States.

REPORT OF CASE
A 64-year-old man with panhypopituitarism (secondary to transsphenoidal hypophysectomy performed in 1983 because of a nonfunctioning adenoma) came to our medical center for treatment of an enterovesical fistula on Mar. 23, 1986. His medical history included surgical treatment of perforated diverticulitis and multiple subsequent surgical procedures for septic complications and poor wound healing. At the time of admission, his medications included endocrine replacement with levothyroxine sodium, testosterone, and prednisone.

On Mar. 25, he underwent repair of the ileovesical fistula and ileoileostomy. Pathologic findings were consistent with Crohn's disease. Postoperatively, multiple complications related to sepsis and wound healing ensued: anastomotic dehiscence, wound dehiscence, pneumonia, urinary candidiasis, and abdominal wall abscess.

On Apr. 23, upper gastrointestinal bleeding developed. Subsequent upper gastrointestinal endoscopy and barium study (Fig. 1) disclosed a long bleeding sinus tract that originated from the first portion of the duodenum and extended posteriorly behind the pancreas, possibly from Crohn's disease. Endoscopic laser treatment of a small adjacent ulcer was unsuccessful in slowing the bleeding, and angiography was performed. A bleeding...
site from the gastroduodenal artery was identified within the sinus tract, but the anatomy was unfavorable for embolization or selective infusion of vasopressin. During maximal medical management, including corticosteroids (for possible exacerbation of Crohn's disease), systemic vasopressin, antacids, sucralfate, cimetidine, and maintenance of normal coagulation measurements, the patient continued to have intermittent, occasionally brisk, upper gastrointestinal bleeding that necessitated transfusion of 15 units of blood during a period of 9 days. Because of the substantial risk associated with reoperation in this patient, endoscopic sealing of the bleeding vessel with use of fibrin glue to fill the bleeding sinus was proposed.

Consent to use fibrin glue on a "compassionate basis" was obtained from the Food and Drug Administration, the Mayo Institutional Review Board, and the patient. On May 2, a double-lumen catheter (Fig. 2) was endoscopically guided into the duodenal sinus. No active bleeding was noted at that time. Then 7 ml of fibrin glue was placed in the sinus along with 6 ml of a cryoprecipitate and thrombin mixture to which aprotinin (a fibrinolysis inhibitor) had been added. No glue extruded into the duodenum, and the sinus was approximately two-thirds filled. The patient had no further gastrointestinal bleeding, but a roentgenographic contrast study with use of meglumine diatrizoate on May 5 showed that the glue was no longer present and that the sinus appeared unchanged.

In an effort to prevent further bleeding, the patient again underwent endoscopy for additional placement of fibrin glue on May 6. The thrombin component of the fibrin glue was reconstituted with dilute barium (three parts thrombin and one part barium) for roentgenographic visualization, and 18 ml of fibrin glue was placed in the duodenal sinus under endoscopic guidance. Fluoroscopy demonstrated the barium-impregnated glue filling the sinus, and the outline of the glue in the duodenal sinus was clearly visible on a flat-plate roentgenogram (Fig. 3). On May 7, a flat-plate roentgenogram showed resorption of most of the glue; a rim of glue on the sinus wall was still visible on May 9. The patient had no further gastrointestinal bleeding and was dismissed from the hospital on May 20.

After the patient returned home, septic complications but no further bleeding developed. He refused further treatment and died on May 30, 1986. Autopsy was declined.

**COMMENT**

This patient posed a challenging problem with an unusual source of upper gastrointestinal hemorrhage. On the basis of previous experience, it was evident that he could not tolerate major surgical intervention to control the bleeding. The decision to use fibrin glue was based on its theoretic applications for hemostasis weighed against the
small risk of transmission of hepatitis or acquired immunodeficiency syndrome (AIDS).\textsuperscript{5,6} The use of fibrin glue in this patient was unique in several respects. First, fibrin glue has occasionally been used to seal gastrointestinal anastomoses,\textsuperscript{7-9} but to our knowledge, this is the first report of its use inside the gastrointestinal tract. Second, although fibrin glue has been mixed with metrizamide for intravascular embolization,\textsuperscript{10} we are unaware of any published report of mixing barium into the fibrin glue. For our patient, the barium-impregnated fibrin glue facilitated surveillance of the disappearance of the glue by abdominal roentgenography. Third, the commercial product we used incorporates an antifibrinolysin, aprotinin, to delay degradation by local tissue proteases. In the duodenum, this product theoretically provided an advantage over the autologous fibrin glue\textsuperscript{11} and cryoprecipitate-thrombin mixtures\textsuperscript{12} that investigators in the United States have used while awaiting results of the Food and Drug Administration studies.

The efficacy and mechanism of action of this application of fibrin glue remain unclear. Theoretically, the glue may seal vessels or may merely provide a tamponade effect. On the basis of this case report, further experimental and clinical investigation seems warranted.

CONCLUSION
Endoscopically placed fibrin glue mixed with barium may be a nonsurgical treatment option for very ill patients with persistent bleeding from a duodenal sinus. The barium-impregnated glue is easily detected and thus facilitates follow-up with subsequent abdominal roentgenograms.

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REFERENCES