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Epidural Fibrin Glue Injection Stops Persistent Cerebrospinal Fluid Leak During Long-Term Intrathecal Catheterization

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The leakage of cerebrospinal fluid (CSF) during the initial phase of long-term intrathecal (IT) infusion of analgesics can be a bothersome complaint. A series of 98 cancer patients was treated with an IT catheter in this hospital in one year; 8% showed persistent leakage of CSF via the catheter tract. In a previous series, 26% of the patients had persistent CSF leakage (1). Treatment of CSF leakage can be undertaken with an epidural blood patch; however, in our experience, this is not always successful in cancer patients. Three patients in whom persistent CSF leakage was successfully treated with an epidural injection of fibrin glue (Tissucol®, duo 500, Immuno AG, Vienna, Austria) are described.

Case Reports

Patient 1

A 50-yr-old man complained of increasing pain and sensory disorders in his left leg. A sigmoid resection for adenocarcinoma had been performed 2 yr previously, and chemotherapy had been given. Using magnetic resonance imaging, compression of the S1-level cauda equina due to massive parasacral tumor growth was confirmed. As analgesia with acetaminophen, oral morphine, and amitriptyline was insufficient, a 20-gauge epidural catheter Perifix®; Braun, Melsungen, Germany) was inserted using a 18-gauge Tuohy needle by paramedian approach at the lumbar level. Pain relief improved significantly during IT infusion of morphine and bupivacaine (2). Leakage of CSF at the puncture site was observed 6 days after introduction of the IT catheter. The patient had no symptoms of postdural puncture headache (PDPH) or meningitis. An epidural blood patch with 10 mL autologous blood was performed at an interspace above the catheter entry site, but the CSF leakage continued abundantly, necessitating frequent changes of the dressings. As pain relief was adequate and the patient feared return of his symptoms upon cessation of IT infusion, treatment with an epidural injection of fibrin glue was suggested. A lumbar

epidural injection of 4 mL of fibrin glue was given one interspace cephalad of the original puncture level, with the IT catheter *in situ*. The CSF leakage stopped the same day. There was no increase in the neurological impairment of the patient. The IT infusion was continued until the patient's death due to respiratory insufficiency two weeks later, which was attributed to the natural progression of his disease and unrelated to our procedure.

Patient 2

A 59-yr-old woman presented with severe low back pain radiating to the thoracic region and the side of both legs despite oral morphine. Global hypesthesia was present from the groin down to the feet in both legs. Five years previously, a malignant hypernephroma with local spread had been resected. A year before starting IT treatment, multiple pathological fractures in both humeri and left femur had developed. All had been treated palliatively by osteosynthesis and radiotherapy. Because of the persistent severe back pain, a lumbar IT catheter was inserted using the same technique as described above (20-gauge catheter, Perifix®, Braun, Melsungen, Germany).

CSF leakage at the puncture site was observed after 8 days without signs of PDPH. Despite an epidural blood patch of 10 mL autologous blood at the lumbar region, the CSF leakage persisted in the consecutive days.

After a lumbar epidural injection of 4 mL fibrin glue, CSF leakage stopped within an hour. There was no aggravation of the neurological complaints. The IT infusion was continued until the patient's death 3 weeks later.

Patient 3

A 63-yr-old man complained of increasing back pain radiating into the anterior side of both legs despite large oral morphine (480 mg/day) intake. The pain was due to widespread bony metastases of prostate carcinoma. Diffuse vertebral metastases had previously been shown on a bone scan. Global sensory neurologic function was normal.

A 20-gauge epidural catheter was inserted through an 18-gauge Tuohy needle at the lumbar level. The pain was adequately relieved after commencing morphine and bupivacaine infusion.

CSF leakage started 1 week postpuncture, again without signs of PDPH. Three milliliters of fibrin glue was injected epidurally 14 days postpuncture, stopping the CSF leakage within hours. There was no increase in neurological symptoms. No CSF leakage occurred up to the time of his last visit

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to the outpatient clinic (10 mo later), and analgesia was adequate.

Discussion

In these patients, persistent CSF leakage unresponsive to an epidural blood patch responded favorably to epidural injection of fibrin glue. Fibrin glue is a preparation of pooled human plasma obtained from plasmapheresis. It is prepared by mixing two solutions. The first contains fibrinogen, factor XIII, fibronectin, aprotinin, and plasminogen; the second contains thrombin and calcium. When these solutions are mixed, fibrinogen is converted to fibrin monomers, which aggregate and form a gel (3). Fibrin glue has a high tensile strength and tolerates high-moisture environments. The fibrin clot forms a temporary biological seal of the dura until healing occurs (4). Fibrin glue is widely applied in otology and neurosurgery as a method of achieving a watertight dural closure (5). It has proven to be a satisfactory technique in stopping CSF leakage in a series of 20 consecutive craniofacial resections with dural defects (6). Percutaneous fibrin sealing has also been successfully applied in cases of subcutaneous CSF fistulae after operations of the brain and the spinal cord (7), thereby avoiding reoperation.

Using a product of biological origin implies a potential risk of viral infection. However, there has been no documented case of viral transmission by using fibrin glue (as manufactured by Immuno AG, Vienna, Austria). The manufacturer uses a recombinant DNA technique; exponential multiplication of a genome by polymerase chain reaction results in a very low level of detectable viral load (8). A CSF leak might be difficult to differentiate from infusate tracking back along the IT catheter. In the patients described, the observation of heavily soaked dressings in the presence of a low infusion rate (0.1–0.4 mL/h) allowed the diagnosis of CSF leak to be made.

The routine treatment of CSF leakage after dural puncture consists of initial conservative symptomatic treatment with progression to an epidural injection of autologous blood, which can be repeated if necessary (9–11). Since introduction of the epidural blood patch (12), it has been widely and safely applied. Alternative therapies proposed after a failed blood patch are continuous epidural infusion of saline (13,14) or epidural infusion of dextran (15). The theory behind these methods is that the establishment of a stable counter-pressure stops the leak, allowing the dura to heal.

The epidural blood patch was not effective in our first two patients. All three patients responded positively

to an epidural injection of fibrin glue, which was easily applied by injection through an 18-gauge Tuohy needle. The presence of an extradural tumor or metastatic mass (Patients 1 and 3) through which the IT catheter passed might explain the persistent leakage in those cases.

The epidural injection of fibrin glue should be considered in the treatment of persistent CSF leakage when other measures, including epidural blood patch, fail. It should be considered when further palliative treatment of patients with terminal disease necessitates continuation of the IT infusion. This technique is not recommended for other PDPH-related complaints.

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