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Case Report

Allogeneic Epidural Blood Patch in the Setting of Persistent Spinal Headache and Disseminated Coccidioidomycosis

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In most cases of post-dural puncture headache, the positional symptoms will resolve spontaneously within 2 weeks. Conservative therapies include oral analgesics and hydration, bed rest, and abdominal binders. For refractory cases, an autologous epidural blood patch remains the treatment of choice. However, in certain cases the use of autologous blood for the blood patch may place the patient at risk for infectious or malignant contamination of the central nervous system.

Coccidioidomycosis results from inhalation of the arthroconidia (spore) stage of the fungal lifecycle. The most common manifestation of coccidioidomycosis is acute pulmonary symptoms, while the most feared complication is meningitis. Immunocompromised patients are at increased risk of fungemia; therefore, introduction of fungal elements into the central nervous system can occur if autologous blood is used for an epidural blood patch.

We report a case of persistent dural-puncture headache in the setting of disseminated coccidioidomycosis. An autologous blood epidural blood patch was considered but deferred due to risk of coccidioidomycosis meningitis. Other epidural space interventions such as fibrin glue injection or saline infusions were judged to be too imprecise or ineffective. The patient was successfully treated with allogeneic blood donated by his wife, but only after testing of her blood as is required for any directed blood donation. Allogeneic epidural blood patches are an option for refractory dural puncture headaches when autologous blood may cause meningitis or malignant seeding of the central nervous system.

Key words: Epidural blood patch, post-dural puncture headache, Coccidioidomycosis, arthroconidia, acute pulminary symptoms

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Coccidioidomycosis (valley fever) results from inhalation of the arthroconidia (spore) stage of the fungal lifecycle. Although the most common manifestation is acute pulmonary symptoms, many of these patients must undergo lumbar puncture to rule out meningitis, which can lead to long-term neurologic morbidity or death (1,2). As in any patient, diagnostic lumbar puncture can result in a disabling orthostatic headache syndrome that persists despite conservative treatment. Autologous epidural blood patch (EBP) can be curative, but in the setting of disseminated coccidioidomycosis, the risks and benefits must be carefully weighed given the potential introduction of infection into the central nervous system (CNS). We present a case in which this risk was circumvented by performing an allogeneic EBP using the patient's wife as donor.

Case Report

A 37-year-old male with a 3-year history of prednisone treated sarcoidosis presented with several months of polyarthralgia. He was referred to rheumatology for evaluation of possible sarcoid arthropathy; however, the patient related a history of a recent upper respiratory infection that preceded new cutaneous lesions and a nodular lesion on his left foot.

This information led to an evaluation for possible disseminated coccidioidomycosis. Serologic testing demonstrated positive coccidioidomycosis by Enzyme Immunoassay (EIA) (IgG+, IgM-), by Immunodiffusion (ID) (IgG+, IgM+), and by Complement Fixation (CF) at 1:256. These results strongly supported a diagnosis of coccidioidomycosis. The patient subsequently underwent a biopsy of skin lesions on his abdomen that cultured positive for Coccidioides immitis/posadasii, as did a biopsy of his left navicular bone. The anti-fungal agent fluconazole was instituted at 800 mg orally per day and a diagnostic lumbar puncture was suggested to exclude CNS involvement.

Two bedside attempts at lumbar puncture using a 20-gauge Quincke needle were unsuccessful. The patient was transported to interventional radiology where fluoroscopic guidance was used to obtain 10 mL of clear cerebrospinal fluid (CSF) at the L2-3 level via a 20-gauge Quincke needle. Analysis and cultures of the CSF demonstrated an absence of fungal elements and otherwise normal cell, protein, and glucose content. Unfortunately, the patient subsequently developed a severe positional headache that was unresponsive to bed rest, over-the-counter analgesics, oral hydration, intravenous fluids and caffeine, and an abdominal binder. He was unable to work or participate in many other activities of daily living. A magnetic resonance imaging (MRI) scan demonstrated epidural CSF from the level of the lower thoracic spinal canal to L3, with a very small amount of CSF visible at the L4/5 level, supporting the diagnosis of CSF leak (Fig. 1). Because of concerns over an EBP seeding the CNS with coccidioidomycosis, the patient was not formally referred to the chronic pain clinic until 4 weeks after the lumbar puncture(s). At that point, it was felt that non-invasive therapies were unlikely to be effective and the orthostatic headache was unlikely to resolve spontaneously.

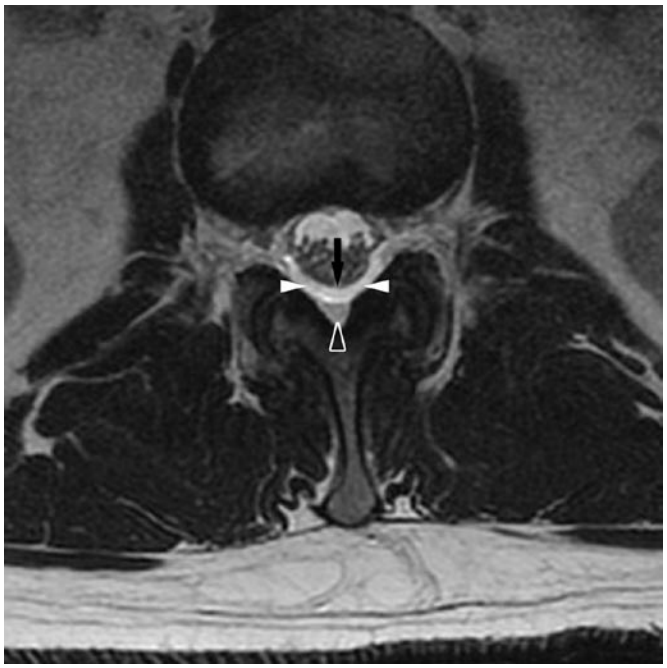

Fig. 1. *Axial T2-weighted image from lumbar spine MRI demonstrates an abnormal epidural fluid collection (white arrowheads) dorsal to the dura (black arrow) at L2-3. The fluid is slightly more hyperintense than the adjacent fat in the dorsal epidural space (open arrowhead). Because of the presence of this prominent epidural fluid collection, the decision was made to perform the epidural blood patch under CT-guidance.*

After a discussion of risks and benefits, and a signed, informed consent, initial interventional therapy included a single epidural injection of 30 mL of preservative free normal saline at the L2-3 level. This provided minimal, short-term benefit. An epidural saline infusion was deferred due to the low likelihood of success and risk of catheter-related infection in this immunocompromised patient. Neurosurgery consultation was obtained to discuss computed-tomography (CT)-guided epidural fibrin glue injection to seal the dural puncture(s). However, this option was not recommended as the location of the CSF leak(s) was not precisely known, and if an EBP was needed later, the fibrin glue might make it ineffective due to epidural space mass effect. An open surgical procedure to repair the dural leak(s) was also discussed but only as a "last resort."

Despite ongoing treatment with oral fluconazole, the patient's CF titer remained elevated at 1:256. An autologous EBP was not a viable option due to unacceptable risk of fungal seeding of the CNS. Therefore, an allogeneic EBP was discussed with the patient. His wife agreed to donate blood for the EBP, and written informed consent was obtained. The patient was found to be blood group A-positive, and his wife was found to be O-positive.

Following standard testing protocol for blood donors, the patient's spouse was found to be negative for Hepatitis B (HBV), Hepatitis C (HCV), West Nile virus (WNV), Chagas' disease, syphilis, human immunodeficiency virus (HIV), and human T-cell lymphotrophic virus (HTLV).

Six days after receipt of the negative results, and after confirmation that there were no interim donor health status changes including exposure to the infectious agents noted above, the patient underwent an EBP via an 18-gauge spinal needle at the L2-3 level. This level was chosen for the initial attempt as there was more CSF visible here than at the lower lumbar levels. Eighteen mL of his wife's blood were drawn aseptically from her antecubital fossa and immediately injected into the patient's epidural space. Skin puncture was performed where there were no visible coccidioidomycosis lesions. As CSF was present in his epidural space, CT-guidance was used to allow precise needle placement with contrast confirmation of epidural (and not intrathecal) injection of the blood. Unlike other directed blood donations, her blood could not be drawn and stored for use later, as this requires anticoagulation. Therefore, both donor and recipient were together in the CT-suite.

The first allogeneic blood patch provided only partial symptom relief, so 4 days later the procedure was repeated using 22 mL of his wife's blood, this time at the L4-5 level (Figs. 2A-B). The L4-5 level was selected as this was the presumed level of the unsuccessful bedside lumbar puncture attempts, although as noted above there was more CSF visible at higher lumbar levels. At follow-up 2 days later, he reported complete resolution of his headache, although he continues to require treatment for disseminated coccidioidomycosis.

Discussion

In most cases, post-dural puncture headaches will resolve within 2 weeks and no invasive therapy is needed (3). An autologous EBP remains the treatment of choice for persistent orthostatic headache symptoms after dural puncture. For patients who fail EBP, consideration can be given to percutaneous CT-guided epidural fibrin glue injection to seal dural puncture sites (4). Management of patients with infectious or malignant diseases and refractory positional headache presents a clinical dilemma, as an EBP may introduce the infectious agent or malignant cells into the epidural and intrathecal spaces (5).

Coccidioidomycosis is caused by the dimorphic fungus Coccidioides immitis. It is endemic to the southwestern United States, but tourists and migrant workers are at risk of exposure as well as the residents of Arizona and California (1,6). An estimated 150,000 infections occur per year, largely due to the rising population in the Southwest (7). Fortunately, most of these infections are subclinical; pulmonary symptoms, including pneumonia that presents 1 – 3 weeks after exposure, are the most common clinical presentation. However, any site in the body can be involved in disseminated disease, most commonly the bone, skin, and meninges. Single antifungal drug therapy is the mainstay of treatment, although multi-antifungal drug therapy may be indicated in some cases. Occasionally, surgical debridement is needed (7).

Immunocompromised patients, including those with chronic steroid dependence, are at increased risk of developing disseminated disease (8). In one series of 15 patients with coccidioidomycosis fungemia, 10 were receiving steroids at the time of fungemia diagnosis (9). The highest CF titer in this series was 1:128 and occurred in only 2 patients. Our patient was receiving steroids and had a persistent CF of 1:256,

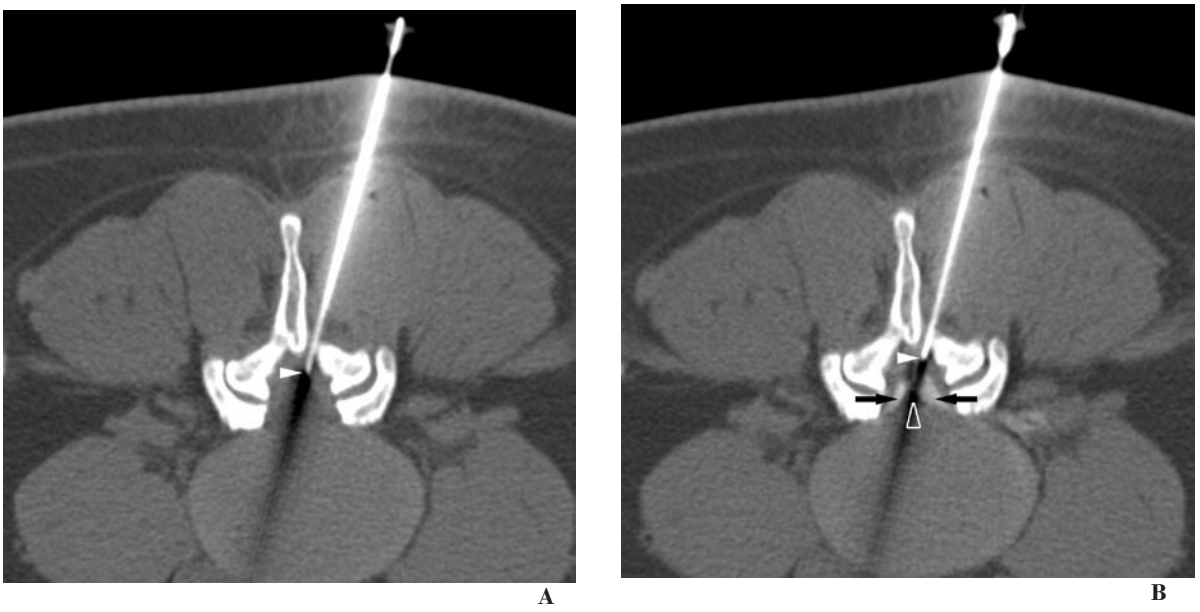

Fig. 2. (A) Axial CT image with the patient in prone position demonstrates placement of an 18-gauge Quincke spinal needle via a left paraspinous approach through the L4-L5 interlaminar space. The needle tip (white arrowhead) is just entering the dorsal epidural space. (B) Following completion of the allogeneic epidural blood patch (22 mL), the epidural blood (black arrows) is exerting mild mass effect on the thecal sac (open arrowhead). The blood appears brighter (more dense) than expected because iodinated contrast was added to allow for effective localization (0.5 mL Isovue-200 per 10 mL blood).

highlighting the risk of meningitis if an EBP had been performed with autologous blood. Coccidioidomycosis meningitis can lead to fever, meningismus, altered mental status, nausea and vomiting, and even death if untreated (2).

Anesthesiologists administer a significant portion of the allogeneic blood transfusions in the United States, with about two-thirds of the 10 million units transfused annually being given in the perioperative period (10). However, the use of allogeneic blood for an EBP is unusual.

We are aware of just one other report of an allogeneic EBP. Cesur et al (11) performed a successful EBP using allogeneic blood in a parturient 2 days after accidental dural puncture during epidural catheter placement for labor. The authors were reluctant as the patient had a post-partum fever, but she "begged for (an) epidural blood patch." Like our donor, the donor underwent testing for infectious diseases, although there was a small risk of transmission of prion disease (e.g. variant Creutzfeldt-Jacob or "mad cow" disease) to this patient in the United Kingdom (12,13). Arguably in this case, the EBP could have been deferred until the fever abated; or alternatively, the headache would have likely resolved spontaneously.

Martin et al (14) faced a similar dilemma in a patient with acute varicella infection and headache after diagnostic lumbar puncture. They performed an EBP with autologous blood without the development of meningitis, although the patient did suffer leptomeningeal irritation after the EBP, perhaps secondary to the varicella infection. Bucklin et al (15) chose not to perform an EBP in a parturient with a dural puncture headache and acute myelogenous leukemia, over fears of neoplastic seeding of the CNS. The headache resolved spontaneously in 10 days. Finally, Tom et al (16) reported on autologous EBP in human immunodeficiency virus (HIV) patients with no ill effects at 24-month follow-up.

The typical process of allogeneic blood donor testing gives assurance that the donated unit of blood is free of infectious disease. The risk of infection is

extremely small in the United States (HIV 1:2,000,000 units transfused; HBV 1:205,000; HCV 1:2,000,000; and HTLV-I/II 1:2,993,000) (17). Because stored blood is anticoagulated and therefore cannot be used for EBP, allogeneic blood patches must be performed with the donor present and willing to provide a small amount of blood for the procedure. They also must be willing to donate more than once, as more than one EBP may be necessary in refractory cases like ours where multiple dural punctures may have occurred. Blood donor testing performed at blood banks is usually batched. When all serologies and nucleic acid testing (NAT) are negative the results should be available within 24 to 48 hours. Any positive result will require confirmatory testing. Therefore, an obligatory delay will occur between testing of the donor's blood and the EBP. The donor should be reliable and questioned regarding any infectious exposures between the time of testing and donation, i.e. the testing guarantees the donor blood at the time it was tested, not at the time the EBP is performed.

Conclusion

In conclusion, we report on successful treatment of a refractory dural puncture headache in a patient with disseminated coccidioidomycosis using an allogeneic EBP. Conservative therapies had failed, and other epidural space interventions such as fibrin glue injection or saline infusion were judged to be too imprecise or ineffective. Allogeneic EBP is an option in this setting but only after careful testing of a reliable donor.

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