Cancer Seeding Risk from an Epidural Blood Patch in Patients with Leukemia or Lymphoma

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Abstract

Introduction. Lumber punctures are a common procedure in patients with cancer. However, a potential complication of a lumbar puncture is a postdural puncture headache. The risk of neoplastic seeding to the central nervous system has led to concern over performing epidural blood patches (EBPs) for the treatment of postdural puncture headaches in patients with cancer. The goal of this retrospective study was to evaluate cancer seeding in the central nervous system in patients diagnosed with leukemia or lymphoma.

Methods. Institutional electronic records were queried over a 13-year period from 2000 to 2013 for patients with leukemia and/or lymphoma who received at least one EBP. Demographic and procedural data, cancer treatments, and mortality were all examined. Patient records were reviewed for evidence of new-onset neoplastic central nervous system seeding after an epidural blood patch.

Results. A total of 80 patients were identified for review. Eighteen patients had a diagnosis of leukemia, and 62 had lymphoma. Following an EBP, none of the patients experienced new cancer or cancer seeding in the central nervous system following an epidural blood patch at a median follow-up of 3.74 years.

Discussion. Though the risks of EBP in the cancer patient population have been hypothesized, no previous studies have assessed the risk of seeding cancer to the central nervous system. Based on our results, an epidural blood patch bears low risk of cancer seeding when used to treat postdural puncture headache that is unresponsive to conservative treatments.

Key Words. Epidural Blood Patch; Cancer Seeding; Cancer Risk; Leukemia; Lymphoma

Introduction

Cancer patients undergo lumbar puncture for anesthetic, diagnostic, and disease-monitoring purposes, as well as for intrathecal chemotherapy. A postdural puncture headache (PDPH) can occur in 10% to 40% of patients after a diagnostic lumbar puncture [1,2]. The classic PDPH is described as a positional headache that worsens in the upright position and improves in recumbent position. Associated symptoms may include photophobia, nausea, and shoulder and neck pain [3,4]. Often symptoms from the PDPH will resolve after one or two weeks with conservative management [5]. However, when associated symptoms are debilitating, an epidural blood patch (EBP) has a high success rate for symptom resolution [6–8].

The cancer patient presents dual risk with the use of epidural blood patch for the treatment of PDPH: circulating cancer cells and immunosuppression [9]. The risk of neoplastic seeding to the epidural space has led to concern over performing EBP in these patients [10,11]. The goal of this retrospective study was to evaluate cancer seeding into the central nervous system after epidural blood patch placement in patients diagnosed with leukemia or lymphoma.

Methods

This study was completed after approval by the Investigational Review Board of the MD Anderson
Cancer Center (Houston, TX, USA). A retrospective review of institutional databases was performed over a 13-year period (2000–2013). Inclusion criteria were patients diagnosed with leukemia or lymphoma and who underwent at least one EBP. Demographic and procedural data, cancer treatments, and mortality were also examined. Medical records were reviewed for evidence of new CNS seeding after EBP. New CNS space seeding was defined as cancer detected in the epidural space and/or brain following an EBP. In patients with pre-existing CNS lesions, new CNS space seeding was defined as new cancer detected at CNS sites other than the pre-existing lesions.

All epidural blood patch placements were performed under strict sterile conditions. EBPs were placed using a blind loss of resistance (LOR) technique or under fluoroscopic guidance. A blind LOR epidural blood patch was performed in the sitting position with a proceduralist performing the Touhy needle placement while another provider simultaneously withdrew autologous blood in a sterile fashion. The amount of autologous blood injected into the epidural space was at the discretion of the attending provider. EBPs placements under fluoroscopic guidance were performed in a dedicated procedure room in the prone position. Correct epidural needle placement was confirmed with a contrast injection of Omnipaque 300 and viewed under fluoroscopy in both anteroposterior and lateral views.

Following an EBP, patient radiographic and laboratory results were examined for evidence of new tumor involvement in the CNS. In addition, records of radiation treatment, chemotherapy, and follow-up were reviewed for evidence of treatments intended for potential neoplastic seeding.

Results

The retrospective review identified 80 patients who met our inclusion criteria. Of the 80 patients, 18 had leukemia and 62 had lymphoma at the time of EBP. Patients were an average age of 43 years, ranging from nine to 76 (Table 1). There were 45 male (56.3%) patients and 33 female (43.7%). Twenty-one (26.3%) patients had pre-existing epidural/spinal or brain lesions at the time of the epidural blood patch (Table 1). All of the EBP procedures were performed by attending anesthesiologists or resident anesthesiologists supervised by an attending. In all procedures, autologous blood was drawn from a peripheral vein in a sterile manner and injected into the epidural space under sterile conditions with use of a 17 g Touhy needle. There was a high success rate of the EBP, with improvement occurring in 96.2% of patients (Table 2). One patient had worsening of symptoms following the EBP.

Most patients (82.5%) were on systemic chemotherapeutic regimens at the time of the EBP or following the EBP, while 56.3% of patients received intrathecal chemotherapy following the EBP (Table 2). Upon review, post-EBP chemotherapy was associated with either a pre-existing care plan or related to a later cancer recurrence. None of the patients who received intrathecal chemotherapy received it as prophylaxis associated with the EBP. A total of six (7.5%) patients received radiation therapy to the spine, and five (6.4%) received radiation to the brain following the EBP.

Nineteen of the patients died during the study period; they survived a median 0.81 years following EBP. The 61 surviving patients had a median follow-up of 3.74 years (5.63 in leukemia and 3.73 in lymphoma populations), with a maximum follow-up time of 12.3 years following EBP (Table 2). In this study, none of the patients experienced new cancer in the CNS following an EBP.

Discussion

An epidural blood patch for the treatment of a postdural puncture headache has been in clinical practice for
The success rate of an epidural blood patch in providing immediate symptom relief has been reported to be as high as 90% [8]. The use of intrathecal chemotherapy and the need for diagnostic lumbar puncture in patients with hematological malignancies have led to an increase in requests for epidural blood patches. Though the risks of EBP in the cancer patient population have been hypothesized, no previous studies have assessed the risk of seeding leukemia or lymphoma to the epidural space and CNS.

There are several case reports of EBP used for treatment in cancer patients [11,12]. In a case report by Mergan et al., the authors used flow cytometry to screen for blast cells in circulating blood. In that case report, the patient showed no signs of neoplastic seeding in the three-month follow-up. There are concerns for possible increased risk of infection when placing autologous blood into the epidural space in a patient who is immunocompromised. In patients with HIV, Tom et al. did not find any adverse events after EBP after a two-year follow-up [13].

In patients with acute leukemia, the CNS is a common extramedullar site of disease invasion. Despite CNS-directed therapy, relapses occur in 2% to 10% of patients with acute leukemia [18]. Similarly, in non-Hodgkin’s lymphoma, the reported CNS relapse rates are 2.3% to 10% [19,20]. The pathophysiology of spread to the CNS is poorly understood. The blood brain barrier (BBB) separates the microvasculature from the brain tissue. The mechanism by which the cancerous cells bind and disrupt the tight junctions of the BBB has also been reported [17].

Table 2  EBP treatment characteristics post-EBP cancer treatment

<table>
<thead>
<tr>
<th>EBP</th>
<th>Leukemia (N = 18)</th>
<th>Lymphoma (N = 62)</th>
<th>Total (N = 80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume of injected blood, mL, median (range)</td>
<td>20 (2–30)</td>
<td>20 (10–30)</td>
<td>20 (2–30)</td>
</tr>
<tr>
<td>EBP technique, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blind loss of resistance</td>
<td>8 (44.4)</td>
<td>34 (54.8)</td>
<td>42 (52.5)</td>
</tr>
<tr>
<td>Injection thru pre-existing catheter</td>
<td>1 (5.6)</td>
<td>0 (0)</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>Fluoroscopic guidance</td>
<td>9 (50)</td>
<td>28 (45.2)</td>
<td>37 (46.2)</td>
</tr>
<tr>
<td>Patient headache following EBP, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement</td>
<td>18 (100)</td>
<td>59 (95.2)</td>
<td>77 (96.2)</td>
</tr>
<tr>
<td>No change</td>
<td>0</td>
<td>2 (3.2)</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>Worse</td>
<td>0</td>
<td>1 (1.6)</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>Post-EBP chemotherapy*, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic</td>
<td>12 (66.7)</td>
<td>54 (87.1)</td>
<td>66 (82.5)</td>
</tr>
<tr>
<td>Intrathecal</td>
<td>7 (38.9)</td>
<td>38 (61.3)</td>
<td>45 (56.3)</td>
</tr>
<tr>
<td>Post-EBP radiation*, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>2 (11.1)</td>
<td>3 (4.8)</td>
<td>5 (6.3)</td>
</tr>
<tr>
<td>Spine</td>
<td>2 (11.1)</td>
<td>4 (6.5)</td>
<td>6 (7.5)</td>
</tr>
</tbody>
</table>

Values are expressed as median (range) or N (%) unless otherwise specified. EBP = epidural blood patch.

*Post-EBP chemotherapy or radiation was included if the treatment occurred at any point after the EBP.

In addition to conservative strategies for the treatment of PDPH, other alternatives for injection into the epidural space exist as alternatives to autologous blood. The use of irradiated blood, saline, and fibrin can be considered. The use of irradiated blood is not well studied in the use for EBP. There is potential for increasing risk of graft vs host disease in an immunocompromised cancer patient. While the use of saline injection for treatment of PDPH is a consideration, it does not provide results comparable with EBP [14]. The injection of fibrin glue is an option for injectate into the epidural space, but may be associated with adverse sequelae such as viral or aseptic meningitis [15,16]. Other complications with the use of fibrin glue such as intravascular thrombosis and anaphylaxis, while uncommon, have also been reported [17]. Members of the vascular endothelial growth factor family (VEGF) are the essential mediators involved in tumor angiogenesis and lymphogenesis [21]. VEGF-A has been found to stimulate leukemic cell proliferation and migration. In one study by Tang et al., a higher CSF level of VEGF-A was closely related to CSF leukemia [22]. In addition, vascular adhesion molecules (VCAM), metalloproteinase-9, and chemokine ligand-2 levels in the CSF have also been implicated in predicting CSF leukemic metastasis [23]. VCAM-1 stimulates cell adhesion, while metalloproteinases can disrupt the tight junctions of the BBB [24,25]. For malignant cells to enter the CNS, the BBB must be breached by the theorized mechanisms. During the placement of an epidural blood patch, the BBB is not directly breached. Perhaps the stagnant blood placed for an EBP is placed into a potential space, not into a blood vessel; the dura is not breached, and angiogenesis cannot occur. Theoretically, an inadvertent dural puncture during an EBP placement presents a higher risk of CNS spread as potentially cancerous cells

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would be injected directly into the CSF. Likewise, a traumatic diagnostic lumbar puncture may theoretically have a higher risk of CNS spread as the microvasculature and the BBB are disrupted as the needle is inserted into the spinal space. In patients with leukemia or lymphoma, it is our current practice to perform EBP under fluoroscopic guidance and inject contrast media to ascertain that there is no leak into the CSF before injecting autologous blood.

While 26.3% of patients in our review had pre-existing CNS lesions, this constituted 21 actual patients. Sixteen patients were being treated for lymphoma. While the CNS relapse rates in leukemia and lymphoma are low, those patients with CNS relapse have poor median survival [26]. The median survival for patients with non-Hodgkin’s lymphoma ranges from two to five months [27]. Perhaps those patients with CNS disease did not live long enough for autologous blood from an EBP to cause additional disease. In those patients without pre-existing CNS disease, the authors can only theorize, as considered earlier, as to why potentially cancerous cells do not cause CNS spread during an EBP. In our review, no new lesions occurred during the median 3.74-year follow-up.

The authors do note several limitations to this study. First, the total number of patients with leukemia or lymphoma who received an epidural blood patch was low even over a 13-year period. Second, we were unable to evaluate for use of conservative strategies prior to epidural blood patch placement. Perhaps detailing the success of conservative management of PDPH in patients with leukemia or lymphoma would have added to this study. Lastly, while we documented patients on chemotherapy regimens at the time of EBP or having received port-EBP radiation treatment to the CNS, we can only speculate on its protective effects against cancer seeding into the CNS following EBP.

While our study demonstrates that the risk of neoplastic seeding is low, the decision to perform an EBP in a patient with hematological malignancies is one that should be made in consultation with the patient’s oncologist. Further study is warranted in other cancer populations, as well as to evaluate the potential protective effects of chemotherapy and radiation treatment.

References
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