Anesthesiology
76:943–947, 1992

# *Epidural Blood Patch in the HIV-positive Patient*

## *Review of Clinical Experience*

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**To characterize the natural history of autologous epidural blood patch (EBP) in human immunodeficiency virus (HIV)-seropositive patients, records from an ongoing longitudinal study of the neuropsychological manifestations of HIV infection were retrospectively reviewed. Of 252 participants (218 HIV-seropositive, 34 HIV-seronegative) who underwent at least one diagnostic lumbar puncture, 9 (7 seropositive, 2 seronegative) required EBP for post–dural puncture headache. After EBP, 6 of the seropositive subjects underwent serial neuropsychological evaluations over periods ranging from 6 to 24 months; none of these six subjects had a decline in neurocognitive performance or other adverse neurologic or infectious sequelae. We were unable to identify morbidity attributable to EBP in the HIV-seropositive patient followed for as long as 2 yr. (Key words: Anesthetic techniques, epidural: blood patch. Complications: post–lumbar puncture headache. Infection: human immunodeficiency virus.)**

WITH THE RECOGNITION of early central nervous system (CNS) involvement in human immunodeficiency virus (HIV) infection, the need has increased for cerebrospinal fluid (CSF) sampling in diagnostic and investigative studies. Our institution is conducting a longitudinal study of the CNS manifestations of HIV infection. This has included collection of CSF samples *via* lumbar puncture (LP). A small number of our patients developed prolonged post–dural puncture headache (PDPH).

Epidural blood patch (EBP) is generally accepted as the definitive procedure for treatment of prolonged PDPH unresponsive to conservative treatment.[1,2] Its safety in the HIV-seropositive patient has been debated,[3–5] and many clinicians, fearing infectious complications, are reluctant to perform EBP in this population.

Beginning with a patient requiring EBP on two separate occasions separated by 36 months, we review our experience with EBP in an additional six HIV-positive men, all but one initially neurologically asymptomatic, who underwent 1) neuropsychological testing and diagnostic LP, 2) EBP for subsequent PDPH, and 3) repeat neuropsychological testing and neurologic examination 6–24 months after EBP.

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Received from the Department of Anesthesiology, University of California, San Diego, Medical Center, San Diego, California. Accepted for publication March 6, 1992. Supported by National Institute of Mental Health grant 5-P50-MH45294.

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### Case Report

A 36-yr-old man with a 6-month history of chronic headaches, first known to be HIV-positive at age 30 yr, underwent diagnostic LP with a 25-G Quincke-point needle with gentle manual aspiration of CSF by syringe in the left lateral decubitus position. No technical difficulties were encountered. Forty-eight hours later he developed a headache with a postural component—not his typical headache—and he began to experience neck stiffness. There was no nausea, vomiting, diplopia, or fever. He was advised to increase his oral intake of fluids and caffeine and was producing dilute urine every 2 h on this regimen. His symptoms initially improved for 24 h and then worsened. Acetaminophen with codeine, oral fluids, and oral caffeine (20–30 cups of coffee per day, or twice his usual consumption) failed to alleviate the postural headache and neck stiffness. He was referred to the Department of Anesthesiology for further treatment 7 days after the LP.

The patient's past medical history was significant for chronic headaches during a 3-yr period. Neurologic examination prior to the LP was normal. The headaches were dull, encompassing the entire head without radiation to the neck, and lasted 10 min to 5 h. They occurred two to three times per week. The patient was unaware of precipitating factors, and the headaches were relieved with Fiorinal. Three years previously, the patient had had a diagnostic LP followed by PDPH and EBP. Six months previously, the patient had developed HIV-related myopathy that was responsive to steroids. He had been enrolled in a research protocol on the CNS effects of HIV (see Materials and Methods) since age 35 yr.

At the time of presentation to the Department of Anesthesiology, the patient's neurologic examination revealed postural headache and neck stiffness with mild proximal weakness. The remainder of the physical examination was normal. Medications were zidovudine 100 mg five times per day, fluconazole 200 mg orally every day, theophylline 300 mg orally three times per day (for reactive airway disease), and sulfasalazine/trimethoprim one double-strength tablet every day. The patient was not experiencing his typical chronic headache at this time.

We concurred in the diagnosis of PDPH and discussed

the risks and benefits of EBP, including our relative lack of knowledge regarding the safety of EBP in HIV-positive patients. The patient agreed to undergo EBP. He was placed in the left lateral decubitus position, and the lumbar area was prepared and draped in sterile fashion. After local infiltration of the L2–L3 interspace with 1% lidocaine, an 18-G Tuohy needle was introduced with loss of resistance noted on the first attempt. No CSF or blood was seen. Eighteen milliliters of blood was drawn under sterile conditions from the left antecubital vein and instilled slowly into the epidural space without apparent complications.

Within 30 s, the patient noted substantial relief of his headache, and was symptom-free after 10 min. Four days later, the headache had not returned.

The apparent lack of progression of this patient's neurologic symptoms in the 3 yr since his first EBP, together with recent solicitations by clinicians for experience with EBP in HIV-positive patients,[3–5] prompted us to review our experience with this problem.

## Materials and Methods

Patients were selected retrospectively from participants in an ongoing longitudinal study on the CNS effects of HIV. The study recruited HIV-seropositive volunteers and HIV-seronegative controls from the San Diego area and from the United States Navy, where personnel are routinely screened for HIV. Eligible participants were men aged 18–49 yr with no history of previous non-HIV-related nervous system disease. All participants gave informed consent before entering the study.

HIV serostatus was rechecked with enzyme-linked immunosorbent assay and confirmed by Western immunoblot. Thirty-four participants were seronegative for HIV; the remaining 218 were HIV-seropositive. Participants underwent yearly physical examination for determination of clinical stage (Centers for Disease Control [CDC] class; table 1)[6] and for detection of neurologic complications of HIV infection. Neuropsychological testing consisted of an expanded Halstead-Reitan battery[7,8] composed of standardized tests of eight major ability areas: memory, abstraction, attention, language, learning, verbal, motor, and sensory skills. Raw scores on each test were converted to T-scores to correct for age and education.[7] An experienced neuropsychologist, blinded to subjects' HIV serostatus, made clinical ratings of neuropsychological functioning for each ability area (1 = excellent; 2 and 3 = average; 4 = borderline; 5 = mildly impaired; 6 = mild-to-moderate impairment; 7 = moderate impairment; 8 = moderate-to-severe impairment; and 9 = severely impaired). An overall clinical global rating of neuropsychological test performance ranging from 1 to 9 (as above) was then formulated, taking these subscores into consid-

TABLE 1. Neuropsychological Test Results for HIV-seropositive Patients

| Patient Number | Age at EBP (yr) | Months after EBP | CDC Class | Global Score | | Neurologic Findings | Antiviral Prescription |
|---|---|---|---|---|---|---|---|
| | | | | Expanded | Limited | | |
| 0* | 33 | 0 | Unknown | NA | NA | Normal | AZT |
| | 36 | 0 | IVc2 | 4† | | Normal | AZT |
| 1 | 41 | 0 | III | 6 | | Normal | AZT |
| | | 12 | IVc2 | 4 | | Normal | AZT |
| | | 18 | IVc2 | | 3 | Normal | AZT |
| | | 24 | IVc2 | 2 | | Normal | AZT |
| 2 | 29 | 0 | III | 3 | | Normal | None |
| | | 6 | III | | 3 | Normal | None |
| | | 12 | III | 2 | | Normal | None |
| 3 | 24 | 0 | III | 4 | | Normal | None |
| | | 6 | III | | 3 | Normal | None |
| | | 12 | IVc2 | 4 | | Normal | None |
| 4 | 25 | 0 | III | 2 | | Normal | None |
| | | 12 | III | 2 | | Normal | None |
| 5‡ | 39 | 0 | IVc2 | 4 | | PN | DDI |
| | | 6 | IVc1 | | 3 | PN | DDI |
| 6 | 36 | 0 | IVa | 5 | | Normal | None |
| | | 6 | IVa | | 3 | Normal | None |

CDC class: 0 = seronegative; I = acute HIV infection; II = asymptomatic; III = lymphadenopathy; IV = AIDS or AIDS-related complex (ARC); IVa = constitutional symptoms; IVb = neurologic symptoms; IVc1 = opportunistic infections (major); IVc2 = minor opportunistic infections (*e.g.*, thrush); IVd = opportunistic tumors; IVe = other conditions.

Global score: Global rating of neuropsychological test performance ranging from 1 to 9: 1 = excellent; 2 and 3 = average; 4 = borderline; 5 = mildly impaired; 6 = mild-to-moderate impairment; 7 = moderate impairment; 8 = moderate-to-severe impairment; 9 = severely impaired.

EBP = epidural blood patch; CDC = Centers for Disease Control; NA = not assessed; AZT = zidovudine (azidothymidine); PN = peripheral neuropathy; DDI = dideoxyinsone.

* Subject of case report; not initially enrolled in study.

† Twelve months before second EBP, score was 4, and at time of second EBP, score was 4.

‡ Died of preexisting cytomegalovirus infection 14 months after lumbar puncture/EBP without developing further neurologic complications.

eration by previously described procedures.[8] A global rating of 5 indicates mild impairment clinically predictive of a cerebral disorder and implies mild impairment in at least two of the eight ability areas. Participants underwent the full battery, requiring 6–8 h of testing at enrollment and every 12 months thereafter; semiannually, a limited study requiring 90 min of testing was also performed to yield a global performance score only. This briefer standardized battery detects any major change in the patients' functioning.[7,8] It includes selected tests from the larger battery.

A total of 325 LPs were performed with Quincke-point needles on 252 participants as a baseline portion of a longitudinal study of neuropsychiatric manifestations of HIV infection. Four participants had 4 LPs; 3 had 10 LPs; 41 had 2 LPs; and 197 had a single LP. Repeat LPs were done annually on subjects who consented. In the 1st yr of the study, 80 LPs were done with a 22-G needle; thereafter, a 25-G needle was used with manual aspiration of CSF by syringe.[9] Subjects remained recumbent for 1 h postpuncture.

Participants who developed PDPH as defined by Tourtellotte *et al.*[10] were treated with hydration, caffeine, and oral analgesics. A total of nine participants (seven seropositive, including the subject of the case report, and two seronegative) had PDPH refractory to conservative treatment and were referred to the Department of Anesthesiology for treatment of PDPH. All nine received EBP between 5 and 13 days after LP.

## Results

The incidence of PDPH refractory to conservative treatment in our population was 2.8% (9 of 325), 2.5% (7 of 281) in HIV seropositive subjects and 4.5% (2 of 44) among seronegative subjects. Seven of the 80 LPs (8.8%) performed in 80 patients with 22-G needles resulted in PDPH, and 9 of 245 (3.6%) done with 25-G needles caused headache. No patient suffered from a localized spinal column space infection or developed signs of meningitis.

Neuropsychological results for the seven seropositive patients are shown in table 1. Patients 1–6 had an initial neuropsychological evaluation immediately prior to LP and EBP, followed by one or more further evaluations at least 6 months later. Patient 0, the subject of the Case Report above, underwent two EBPs 3 yr apart, but only the second LP and EBP was accompanied by neuropsychological evaluation.

Four of the six patients who had post-EBP neuropsychological follow-up had comprehensive follow-up evaluations 12 months after EBP (patients 1–4). Of these, two patients showed no change in neuropsychological functioning after 12 months, whereas two patients performed somewhat better at follow-up.

Two of the above four patients were unchanged in severity of disease (CDC class) during the evaluation period. Patient 3 progressed from CDC class III to IVc2 and underwent no change in neuropsychological performance. Patient 1, who progressed from CDC class III to CDC class IVc2, also had the greatest improvement in neuropsychological performance. In fact, he also showed continued neuropsychological improvement over the 2nd-yr post-EBP (table 1).

Two patients (patients 5 and 6) did not complete a comprehensive neuropsychological evaluation 12 months after EBP. Patient 5 died of preexisting cytomegalovirus infection following his semiannual brief neuropsychological examination but before his comprehensive 12-month follow-up. His semiannual brief neuropsychological exam revealed no progression of deficits. His CDC class, however, progressed from CDC class IVc2 to IVc1. Until his death, he developed no further neurologic complication. Patient 6 dropped out of the longitudinal study after his first semiannual neuropsychological examination, which showed no new or increased deficits.

In the larger study from which these patients were selected, 218 seropositive males had a median global neuropsychological performance score of 4.0 at the initial visit and a median score of 4.0 at the 1-yr follow-up. Eighteen percent of HIV-infected subjects in the larger study were found to have increased neuropsychological impairment at the 1-yr follow-up.

In terms of neurocognitive performance, none of the EBP patients declined in global score during the 6–24 months of follow-up (table 1). Overall, in the present HIV Neurobehavioral Research Center study, approximately 18% of HIV-positive subjects followed for 1 yr were rated worse after that interval.

## Discussion

Our study identified no increased CNS morbidity that could be related to EBP in six HIV-positive patients who were followed for periods ranging from 6 to 24 months. The sequelae of long-term EBP may never be fully understood, however, because of the high frequency of neurologic complications of HIV and the large numbers of LPs necessary to generate a small series of EBPs. Two lines of evidence suggest that the long-term risks of EBP in HIV-positive individuals may be small: 1) the nature of HIV infectivity and 2) human and animal studies of bacteremia and CNS infection.

HIV infection is associated with a variety of neurologic disorders.[11,12] Many, such as toxoplasmosis mass lesions, CNS lymphoma, cryptococcal meningitis, and cytomegalovirus retinitis, are secondary to HIV-induced immunocompromise and not attributable to EBP. Other neurologic disorders, however, are attributable to the direct action of HIV itself: the acquired immune deficiency syn-

drome (AIDS) dementia complex (ADC), acute or chronic "aseptic" (nonbacterial) meningitis,[13,14] chronic headaches without meningeal signs,[14] vacuolar myelopathy, and polyneuropathy.[11,15,16] By the time HIV has progressed to AIDS, the incidence of clinical neurologic disease is approximately 40%; AIDS autopsy studies show a 70–80% incidence of neuropathologic changes.[11]

The natural history of HIV CNS infectivity is under active investigation. A growing list of studies suggests that HIV can infect the CNS early in the clinical course—often before any symptoms appear.[11,13,14,17–20] EBP is thus unlikely to introduce HIV to an uninfected CNS. The likelihood of CNS inoculation by a small amount of viremic blood, introduced *via* EBP or LP, remains uncertain.

Theories on the natural history of HIV CNS infection invoke various mechanisms of HIV entry, including infiltration of CNS tissue by HIV-infected monocytes, sequestration of HIV in brain macrophages (perhaps due to altered immune lymphocytic action), and infection of brain capillary endothelial cells with subsequent budding of virus into the CNS. Many of these mechanisms require genetic mutations of HIV for survival in the CNS, and it is not clear that blood-borne HIV would be viable in the CNS.[21–25]

The clinician contemplating EBP in an HIV-positive patient must decide whether to introduce a CNS-infectious agent into the epidural space—and perhaps, inadvertently, into the subarachnoid space. For bacteremic patients, epidural injection, epidural catheterization, and LP have all been the subjects of investigations or clinical reports. There is a lack of consensus about EBP when blood cultures are negative but fever is present.[26] Relatively little is known about viremic patients, and we are unaware of any findings about these procedures on HIV-positive patients. The risk of infectivity from secondary pathogens in the CSF of an HIV-immunosuppressed patient is also unknown, although bacterial meningitis after diagnostic LP in an HIV-positive patient has not been reported.

The combined experience of Bromage[1] and Usubiaga[27] noted only five cases of subarachnoid (bacterial) infection possibly complicating epidural anesthesia, and although the origin of these infections remained unestablished, the signs of subarachnoid infection were obvious and distinctly different from epidural infection. Ready and Helfer,[28] presenting two obstetric cases of epidural catheter-associated bacterial meningitis in 1989, commented that Usubiaga's and Bromage's cases all were from the "early era" of epidural anesthesia and noted that the only intervening reports of epidural catheter-associated subarachnoid infections have been in cancer patients who were immunosuppressed.[29]

Regardless of whether bacteremic or viremic blood in the epidural space *per se* poses a danger to the CNS, the prime concern of many clinicians is the possibility of inadvertent dural puncture during an attempted EBP. Even in the absence of macroscopic evidence of CSF contamination with blood in the presence of a dural puncture, it appears likely that microscopic amounts of blood from epidural veins or other tissues may enter the CSF along with the needle.

Since 1919 it has been recognized that bacterial meningitis may develop after a normal LP.[30,31] Petersdorf *et al.*[32] showed in 1962 that dogs who received an intravenous bolus of $10^9$ pneumococci frequently developed meningitis after (but only if) they underwent LP. Eng and Seligman,[33] on the other hand, concluded that bacterial meningitis after clinically indicated LP in 1,089 adult humans was "rare enough to be clinically insignificant." Such findings may be reconciled with Petersdorf's "convincing animal data"[32] by noting that his bacteremia levels of $> 10^3$ organisms/ml are not commonly attained clinically, except in infants.[34]

Berman and Eisele[35] observed that "it is surprising how rarely bacterial meningitis [after dural puncture in adults] is reported, especially in view of the very frequent utilization of spinal analgesia in urologic procedures." Indeed, large series of spinal anesthetics, including those of Dripps and Vandam[36] in 1954 and Moore and Bridenbaugh[37] in 1966, have been entirely free of this complication.

Although the above data tend to support the safety of LP in bacteremic adult humans, many clinicians avoid spinal anesthesia in this setting, if only because of the possible medicolegal consequences of a spontaneous CSF infection. In any case, the value of extrapolating these findings to the HIV-positive patient is dubious. For example, most patients undergoing urologic procedures receive preoperative antibiotics; no such prophylaxis is available to the HIV-positive patient (an appropriate antiviral would have to cross the blood–brain barrier).

Because of the current uncertainty regarding EBP in HIV-positive patients, we are careful first to offer these patients the alternative treatments that are generally available for PDPH. Bed rest, analgesics, and oral hydration are the mainstays of conservative therapy for PDPH.[1,2] Intravenous caffeine sodium benzoate in doses of 500 mg has been shown to alleviate (but not necessarily eliminate) PDPH in about 70% of patients.[38]

Another reported alternative to EBP is the epidural injection or infusion of normal saline.[39–41] With bolus injection, large volumes of fluid (40–60 ml) are required for relief, and patients frequently complain of unpleasant sensations of warmth and tightness down the legs during the injections.[39] Finally, EBP with banked fresh heterologous blood might be an option in HIV-positive patients, but we are not aware of any clinical experience with this technique.

In summary, we present six HIV-positive patients who received EBP without apparent adverse neurologic se-

quelae, by examination and by neuropsychological testing, 6–24 months later. We offer this report as additional information regarding the role of EBP in the growing population of HIV-positive patients.

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