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Infection during Chronic Epidural Catheterization: Diagnosis and Treatment

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A potentially serious complication of long-term epidural catheterization in cancer patients is infection. The early signs of infection were studied in 350 patients in whom long-term epidural catheters were inserted. Three areas of the catheter track were found to be involved; exit site and superficial catheter track infection, and epidural space infection. The authors identified the early signs of infection in each area and the progress of the infection from the deep track to include the epidural space in four of these patients. All 19 patients who developed deep track or epidural infections were successfully treated with antibiotics and catheter removal. None of the patients required surgery for spinal cord decompression. Catheters were replaced in 15 of the 19 treated patients who requested them after treatment with no recurrent infections. It was concluded that use of long-term epidural catheterization is associated with a definable epidural infection rate. The use of epidural opioid analgesia is an effective and safe means of obtaining pain relief for terminally ill patients when patients are monitored for possible infection and receive prompt treatment when the diagnosis is established. (Key words: Analgesics, epidural: morphine. Anesthetic techniques, epidural: complications. Epidural: infection. Pain, intractable.)

OVER THE PAST 5 yr, there has been increased interest in the use of long-term epidural opioid analgesia for the management of cancer pain.[1–5] Complications related to this prolonged therapy have not been well addressed as most reports cover small patient populations using a variety of clinical approaches.[2–5] Infection has always been a major concern of epidural analgesia, but studies and reports of infection have been limited to case reports or retrospective reviews. Large retrospective reviews by Dawkins[6] and Baker *et al.*[7] indicated the rare occurrence of epidural infections associated with epidural anesthesia. However, prospective clinical studies by Barreto[8] and Hunt *et al.*[9] revealed an incidence of positive cultures from routine epidural catheter cultures as high as 22% and positive skin cultures after aseptic procedures with no signs of epidural infection at the time of culture or during follow-up. Fine noted the inconsistency between the positive catheter cultures and the low incidence of epidural infections.[10] He further questioned the lack of reported infections during long-term postoperative analgesia and the rarity of epidural infections in the immunocompromised cancer patient.[10] No reports in the literature have described what factors may impact the natural history of epidural space contamination or quantified how many catheter contamination events actually lead to clinically detectable infections. These factors have limited us from establishing the risk and diagnostic criteria of epidural infection during long-term epidural catheterization. If left untreated, the infection may progress to abscess formation, which may result in vascular compromise and irreversible neurologic deficit.[11,12]

The increased use of temporary catheters (extended use) and long-term, externalized epidural catheters has given us the opportunity to learn more about epidural infections, and their incidence and relationship to duration of catheterization.[5–10,13–14]§ We previously reported on 55 patients (also included in this report) who received long-term, silicone rubber epidural catheters and who had none of the classical signs of intraspinal infection.[4] In retrospect, two of these patients had early signs of infection, but no cultures were obtained. Positive cultures taken during the autopsy on one of these patients were thought to have been contaminated (not included as an epidural infection in this report due to the question of contamination). Although there was no obvious abscess, epidural adhesions and tissue reaction were present. The questionable culture alerted us to the possibility of infection, and we began to take frequent catheter aspiration cultures when abnormal symptoms or epidurograms were present. This report presents our experience with long-term epidural catheterization for opioid analgesia, our frequency of catheter-related infections, diagnostic criteria of infection, and the results of treatment.

Materials and Methods

All patients referred to the Pain Consultation Service and in whom permanent epidural catheters were inserted

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§ Nickels HJ, Poulos JG, Chaouki K. Risks of infection from short term epidural catheter use. Regional Anesthesia 14:88–89, 1989.

were included in the review. Patients were screened before catheter placement based on the following criteria: terminal disease (cancer or acquired immune deficiency syndrome [AIDS]); estimated duration of survival greater than 2 months; intractable pain unrelieved by oral or parenteral opioids; pain or opioid-induced sedation limiting desired lifestyle; and neurolytic or neurosurgical procedures considered.

Each patient received either bolus opioid doses or infusion of opioid alone or in combination with bupivacaine. Patient instruction, medications, and infusion pumps were supplied by three different home infusion therapy companies after discharge. All dose changes, therapeutic adjustments, and analgesic medications were prescribed by the authors during the total period of epidural catheter use, with the exception of four patients who received care in a distant state from their own physician who used the authors for consultation. Specific patient follow-up was accomplished in this closely held population of patients through constant communication between the authors and the seven referring oncologists who saw each patient on a weekly or bi-weekly basis. Patients were scheduled to see one of the authors by request or if analgesia difficulties or catheter problems occurred, but most patients preferred to limit physician visits as much as possible.

Data from the 350 patients were included until death, catheter removal, or loss to follow-up (two patients) terminated their involvement in the review. Externalized, silicone rubber epidural catheters (Du Pen® catheter, Davol Inc., Cranston, RI; FDA-approved for long-term implantation) were inserted in 350 terminally ill patients for a total treatment period of 32,354 catheter-days the two-part epidural catheter system was placed using a paravertebral incision for both epidural needle insertion and catheter connection and a long catheter tunnel to the anterior thoracic-abdominal junction with the Dacron cuff 2 inches inside the exit site.[4] Each patient received a postoperative epidurogram to confirm catheter position, show volume spread of fluid within the space, and establish a baseline for future comparison. Repeat epidurograms were obtained during treatment to evaluate patency and position of the epidural catheter when problems were suspected.

When an infection involving the deep catheter track or the epidural space was suspected, the presence, extent, and progress of infection were defined by the following:

1. Complete physical and neurological examination.
2. Culture of the exit site.
3. Aspiration of the epidural catheter after removal of the filter and irrigation of the epidural space with 2 ml of normal saline. The aspirate was sent to the laboratory for a gram stain and culture (aerobic and anaerobic).
4. An epidurogram to determine the extent of epidural involvement as shown by the dye loculation around the epidural catheter tip. The retrograde flow along the catheter track from the loculated epidural space into a paravertebral, subcutaneous space may occur.
5. An magnetic resonance imaging (MRI) scan to evaluate the extent of the epidural abscess when aspiration from the epidural space returned a visible exudate or if nerve root pain was present.
6. A complete blood count and blood cultures if systemic symptoms were present.

Exit site and superficial track infections were treated by thorough daily cleaning with povidone-iodine. Topical or oral antibiotics were used depending upon the extent of involvement and response to treatment. Initially, deep catheter track infections were treated with intravenous antibiotics without catheter removal. In all these cases, the infection recurred and extended into the epidural space. All deep catheter track and epidural infections are now treated by catheter removal and parenteral antibiotic therapy. The duration of treatment was dictated by the organism cultured. Each patient was offered a replacement epidural catheter after completion of antibiotic therapy and after an MRI scan showed no further epidural involvement or inflammation.

Results

We diagnosed 30 exit site or superficial epidural catheter track infections, eight deep catheter track infections (internal from the Dacron cuff), and 15 epidural space infections (four with concomitant deep track infection) in our 350 cancer and AIDS patients (table 1). The 11 AIDS patients accounted for 9 infections (6 recurrent exit site infections, 2 deep track infections, and 1 epidural infection).

Differing clinical symptoms, physical findings, infection evolution, and response to treatment dictated the classification of the infections into three groups by the area of catheter involvement (fig. 1).

TABLE 1. Onset of First Catheter-Related Infection as Related to Duration of Therapy

	Days of Therapy					
Source of Infection	0–90	91–190	181–270	271–365	366–457	Total
Exit site and superficial catheter track	10	12	5	3	0	30
Deep catheter track (beyond Dacron cuff)	2	3	1	1	1	8
Epidural space	6	5	2	1	1	15
Total catheters in use:	350	126	44	21	6	350

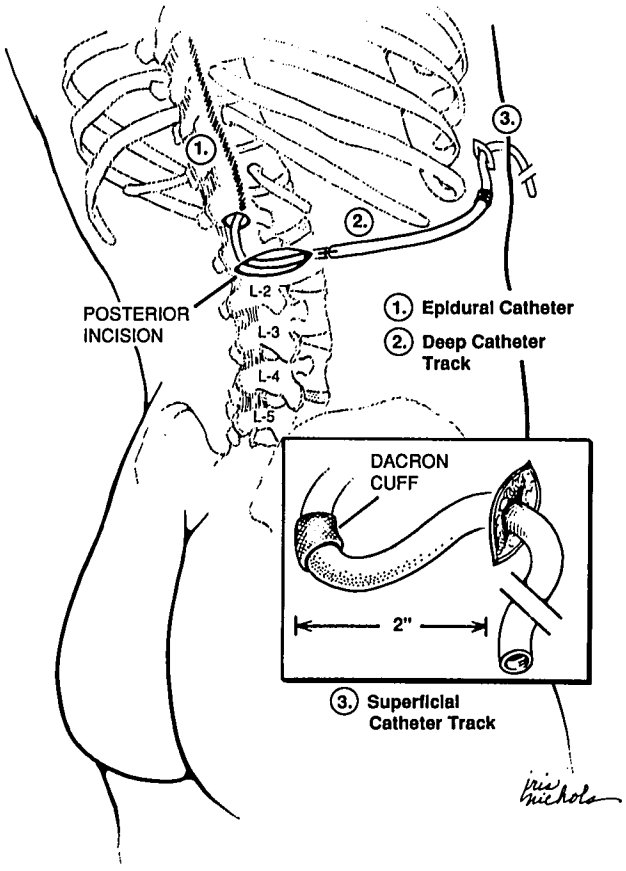

FIG. 1. DuPen® catheter placement through a small shallow incision. The divisions of catheter-related infection are shown.

1. Exit site and superficial catheter track infections. Inflammation and/or drainage from the catheter exit site with inflammation extending along the catheter to, but not beyond, the Dacron cuff.
2. Deep catheter track infections. Visible inflammation along the catheter track, extending internal from the Dacron cuff. Signs of epidural space infection may co-exist with deep track infections.
3. Epidural space infection. Pain during epidural injection (not previously present), a soft fluctuant fluid collection under the posterior incision site, decreased epidural analgesia even with increases of the opioid dose, and constant nonspecific back pain. None of the patients demonstrated meningismus, leukocyte counts elevation (WBC), fever, or neurologic signs of cord or nerve root compression.

The inclusion of superficial catheter infections was made for completeness and to show their complete resolution to cleaning and topical treatment unless therapy was started after infection progressed to the deep track. Deep track infections required catheter removal for full recovery, and epidural infections indicated the need to follow recovery closely to avoid abscess progression to neurologic compromise. The rate of epidural and deep track catheter-related infections was one in every 1702 days of catheter use in the 19 patients who were diagnosed as having deep track (8) or epidural (15) infections (Table 2). (Four patients had both deep track and epidural infections.) The onset of infections varied from the seventh to the 457th postcatheter placement day, and the onset of infection seemed to be unrelated to duration of catheter placement (table 1).

The bacteria cultured from the epidural space were most frequently from skin flora contamination: *Staphylococcus aureus* (6) and *Staphylococcus epidermidis* (4). Other organisms cultured included *Escherichia coli* (2), *Pseudomonas* (1), *Candida albicans* (1), and *Mycobacterium* (1). Skin bacterial contamination of the externalized catheter resulted in progressive inflammation along the catheter track to the epidural space (four cases). Contamination through the injectate was characterized by the onset of epidural inflammation without early track infection (eight cases). Direct extension or hematogenous spread of infection was implicated when the catheter was infected by the same bacteria previously cultured from blood or distant abscesses (three cases).

We removed the epidural catheters from all patients with gram stain and culture proof of deep catheter track or epidural space infection, with the exception of two patients who had major catheter track infections with negative epidural cultures. Both patients were treated with antibiotic therapy but subsequently developed recurrent infections that progressed to involve the epidural space. Therefore, following this observation, we removed all

TABLE 2. Silicone-Rubber Epidural Catheter Patient Data

Number of patients	350	
Duration range (shortest–longest) (days)	4–1,460	
Total days of use	32,354	
Infections	Patients with AIDS	Patients with Cancer
Exit site and superficial catheter track	6	24
Deep catheter track (beyond Dacron cuff)	2	6
Epidural space	1	14
Occurrence of epidural or deep track infections in 19 individual patients, (infections/days of use)	1/1,702	
Equipment failures	0	
Surgical technique errors	6	
Catheter replacements	15	
Total injections	99,239	

catheters from patients with infections that involved the epidural catheter internal to the Dacron cuff. The epidural catheters were replaced in 15 patients after antibiotic therapy. There were no recurrent epidural or track infections from the same organism after as long as 300 days of treatment through the replaced catheter. One patient, however, developed a second epidural infection from a new organism as a result of hematogenous spread from rectal tumor invasion 175 days after catheter replacement. Four patients did not accept catheter replacement because of their terminal condition or their request for a different mode of pain management.

Serial MRI scans showed both fluid collection and abscess size and were used to ensure resolution during treatment. In each case where an epidural abscess was diagnosed, the MRI was repeated weekly until full resolution of the abscess was determined. Computed tomographic (CT) scans with or without contrast did not consistently identify epidural abscesses. None of our patients required surgical decompression, died from complications related to the epidural infections, or showed MRI or epidurogram abnormalities after antibiotic therapy. Neurosurgical and infection disease consultations were obtained in all cases. Every patient with an epidural abscess had complete resolution of the abscess during antibiotic therapy (10–14 days for *Staphylococcus* organisms), but 6 months of antibiotic therapy was required for the mycobacterium-infected abscess.

Discussion

The symptom profile and diagnostic workup described in this clinical review are presented to enhance early diagnosis of infection in prolonged epidural catheterization. Although these patient were protected by a long catheter tunnel and the Dacron catheter cuff developed by the Hickman-Broviac vascular access technology,[15] there was still a nearly 5.4% incidence of infection. This rate of infection (1:1702 catheter-days) compares favorably with the published infection rate for the Hickman vascular access catheter (1:1045 catheter-days).[15] The site of infection along the catheter track and identification of the specific organism allow the clinician to determine the best and safest mode of therapy and appropriate monitoring of response to treatment.

Exit site and superficial catheter infection were all caused by skin flora contaminants and were usually successfully treated with exit site care, and the use of topical povidone iodine or antibiotic ointment. The more serious deep tack and epidural space infections were difficult to assess. These were found with or without the presence of superficial track infections, which implicated contaminated injectate or colonization from distant infectious processes when no track infection was detected. Epidural space and deep track infections were only successfully treated with catheter removal and parenteral antibiotic therapy. Serial MRI evaluation of epidural abscess response to therapy confirms response to therapy.

Given that exit site and superficial catheter track infection respond well to minimal "catheter sparing" treatment, consistent monitoring of the exit site and good cleansing techniques are important. A high level of infection awareness on the part of all involved in the care of the patient with a long-term epidural catheter is important in achieving our long-term goal of consistent and effective pain management.

The AIDS patients treated for 1–9 months were included in the review for completeness, but their 82% incidence of catheter-related infections did not significantly increase the overall deep tunnel and epidural infection rate (4.7–5.4%). The lack of rate change was due to the large number of resistant superficial tunnel infections in this population. The number of AIDS patients studied was too small to draw a therapeutic conclusion; however, the possible increased risk of infection should be viewed in conjunction with the benefits of pain relief and the alternative modes of pain management available.

The finding of abnormal epidurograms with tissue encapsulation of the epidural catheter was associated with late onset of pain during injection and epidural infection in all but one case. This patient had inadvertently received morphine containing phenol and formaldehyde during home care, and the epidurogram returned to normal only after the morphine preparation was changed.[16] We added these findings to our list of diagnostic signs of epidural inflammation, although this is in contrast to the findings of Coombs *et al.*[17] Coombs *et al.*[17] concluded from autopsy studies of silicone rubber epidural catheters and Durant and Yaksh[18] from rat studies that catheter encapsulation was a catheter-related reaction, but no cultures were reported and each investigator studied different catheter materials.

The lack of a clinically detectable epidural infection in Borreto's patients with 22% positive epidural catheter cultures indicates that not all epidural space contamination results in infection and validates the need for further studies to elucidate the true natural history of epidural space contamination.[8,19] It has been assumed[20] from one laboratory study reported in 1970[21] that the acidity of lidocaine and procaine resulted in a bacteriostatic environment that was assumed to protect the patient from epidural space infection. However, in our patients, four of the eight epidural infections without track involvement (inoculated through infusion) were in patients receiving a dilute infusion of opioid–bupivacaine. Thus, the use of acidic bupivacaine infusions of 0.10–0.25% probably has little protective effect.

This review has shown that even with the protection of the Hickman-Broviac technology, the risk of epidural and deep track infection with long-term catheterization is not only a real concern but is also a predictable reality. The diagnostic signs and therapeutic approach presented in this article have resulted in the successful diagnosis and treatment of a significant number of epidural infections without surgical intervention. Thus, the benefits of long-term epidural opioid analgesia for cancer and AIDS-related pain can now be balanced against the known risks of epidural infection. The extended use of temporary, unprotected, epidural catheters should result in an equal or greater incidence of epidural and track infections. Therefore, the use of epidural filters, careful catheter exit site hygiene, and close observation for the signs of catheter related infection are recommended for the prolonged use of epidural analgesia.

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