Title: PATHOLOGIC ANATOMY OF CONSTANT MORPHINE INFUSION BY INTRASPINAL SILASTIC CATHETER

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Introduction. Constant infusion of analgesic agents either epidurally or directly into the cerebrospinal fluid may provide relief without systemic side effects in patients with otherwise intractible pain.[1] Six of the initial group of patients with intractible metastatic carcinoma and intractible pain that were treated with epidural or intrathecal infusion of morphine via Silastic® catheters died of their underlying disease and came to autopsy. This provided opportunity to search (1) for anatomical evidence of morphine toxicity to the nervous tissue of the spinal cord, (2) for silastic catheter toxicity to the dura and its vessels, and (3) for catheter-borne infection of the spinal cord or its coverings.

Methods. Where complete autopsy permission was granted, a full autopsy was performed to define the extent of underlying tumor, particularly in the brain, around the spine and in the pelvis and deliniate the histotoxic effects of chemo- and radiotherapy. In all cases where permitted, the spinal cord was removed within the spinal column by the method of Hughes.[2] In cases where limited autopsy permission was granted, cords were removed from the spinal column by a posterior approach (by the method of Hughes[2]) or an anterior approach by the method of Chason.[3] Spinal cords were fixed within intact dural sacs suspended in 10% buffered formalin for three weeks before sectioning. At sectioning, cross-sections of the caudia equina and cord with the overlying dura were examined from levels (a) below the entry of the silastic catheter into the spinal column, (b) at the level of the catheter's entry, (c) along the catheter's course, (d) above the catheter tip and (e) in the cervical cord. Where permitted, peripheral nerve roots and ganglia were also sectioned. All these sections were stained, after routine dehydration and paraffin embedding, by hemotoxyalin and eosin and luxol blue stains. The following pathologic changes were looked for: The pattern of necrosis around the Silastic catheter, the pattern of inflammation and fibrosis surrounding the catheter, the condition of the dura distant from the tract, the condition of the meningeal vessels (particularly regarding the presence or absence of vasculitis), and the presence or absence of necrosis, gliosis, inflammation or demylenation in the cord itself.

Results. In cases where catheters had remained in place for up to six months, the Silastic catheter was found surrounded by a layer of acellular necrosis which in turn was ringed by a dense fibrosis in which foci of lymphocytes and plasma cells and foci of calcification were embedded. This fibrotic process did not occlude the catheter lumen and resembled the quiescent response seen in long indwelling ventriculoperitoneal shunts used to treat hydrocephalus.[4] The dura distant from the tract appeared slightly thickened. The meningeal vessels showed no evidence of inflammation, thrombosis or sclerosis. There was no evidence of catheter-borne infection. In two cases, however, posterior column degeneration (demyelnation and vasculation of the posterior column of the cord was demonstrated. This change was not associated with a myelitis.

Discussion. In our review of autopsy material we found no evidence of dural or meningeal toxicity from the Silastic catheter which induced only a quiescent fibrotic response. This finding encourages belief that intraspinal chronic catheterization is feasible.[5] We found no evidence of meningeal inflammation or vasculitis associated with the catheters. As placed by our current protocol, the catheters do not appear to have been conduits of infection. The possibility of morphine toxicity to the spinal cord is raised by the finding of posterior column degeneration in two of our patients. The paucity of anatomic pathologic studies of spinal cords in metastatic carcinoma patients with chronic intractible pain who have been treated with radio- and chemotherapy makes it difficult to determine the prevalence of posterior column degeneration among patients who present to us. An association between continuous spinal morphine administration and posterior column degeneration remains, thus, a matter of speculation. To answer this question arising from our review of autopsy findings we conclude by advocating initial and sequential testing of posterior column neurophysiological function in all patients receiving intraspinal morphine by indwelling catheters as well as continued neuropathologic monitoring of the spinal cords not only of treated patients but also of the background population of patients with metastatic carcinoma treated by radio- and chemotherapy.

References.

1. Coombs DW, Saunders RL, Gaylor MS, Pageau MG, et al: Continuous epidural analgesia via implanted morphine reservoir. Lancet 2:425-26, 1981.
2. Hughes JT: The pathology of the spinal cord. Saunders:Philadelphia, 242-47, 1978.
3. Chason JL: The removal of the spinal cord. The Bullitin of Pathology. September 1968.
4. Sugar O, Baily O: Subcutaneous reactions to silicone ventroperitoneal shunts. J. Neurosurg. 71:367-71, 1974.
5. Yaksh TL: Spinal opiate analgesia: Characteristics and principle of action. Pain, 11:293-340, 1981.

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