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Cisternal Puncture Complications

Treatment of Coccidioidal Meningitis with Amphotericin B

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Of two patients who had acute neurologic damage from cisternal punctures, one died 17 hours following a tap which produced major subarachnoid hemorrhage, the other patient recovered from probable brain stem infarction associated with cisterna magna amphotericin injection.

Subarachnoid hemorrhage is the commonest major complication of cisternal puncture, with at least 30 reported fatalities. Other serious complications result from direct puncture of brain substance.

Cisternal puncture is not an appropriate alternative to a difficult lumbar puncture, and indications for its use are limited. The occasional required cisternal tap should be performed only by persons carefully trained in the technique, preferably utilizing fluoroscopic guidance, and only where neurosurgical assistance is readily available.

Post-puncture subarachnoid hemorrhage accompanied by progressive obtundation requires emergency evaluation and consideration of posterior fossa decompression.

INTRATHECAL AMPHOTERICIN B TREATMENT of coccidioidal meningitis has greatly increased the number of cisternal punctures performed in California and Arizona.

Ayer and other clinicians performing early percutaneous punctures of the cisterna magna stressed the importance of preliminary practice on cadavers and the need for exacting technique to avoid possibly disastrous complications, but recent descriptions are more inclined to stress patient acceptance, technical ease, and a low incidence of post-puncture headache.

The following two case reports illustrate the hazards of cisternal puncture.

CASE 1. A 31-year-old man with chronic renal failure secondary to glomerulonephritis had acute onset of severe low back pain radiating down both legs and increasing with any movement of the

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back. When seen the next day for a regular hemodialysis appointment, he had excruciating low back pain and body temperature of 39.4°C (103°F). He was admitted for evaluation.

On admission he had lower lumbar and sacral tenderness with paraspinal muscle spasm, straight leg raising limited to 30° bilaterally, and moderate nuchal rigidity. The abdomen was soft and without masses. On neurologic examination there were no abnormalities except for a previously documented chronic neuropathy with absence of lower extremity reflexes. The white blood cell count, serum amylase and liver function tests were within normal limits. Serum creatinine was 12.2 mg per 100 ml. Lumbosacral spine x-ray studies and tomograms were normal. Pain and fever persisted, and when staphylococcus aureus grew from the blood cultures, treatment with cephalothin and then amipicillin was instituted.

On the fourth hospital day a neurological consultant suggested the possibility of spinal epidural abscess. An emergency myelogram was performed through a cisternal puncture to avoid possible cerebrospinal fluid contamination. An uneventful myelogram revealed a complete block at the fourth lumbar level, but subsequent laminectomy revealed a fibrous extradural constricting band at the fourth-to-fifth interspace without evidence of infection.

The cerebrospinal fluid at the time of myelography showed 170 white blood cells and 30 red blood cells, protein content of 124 mg and glucose of 74 mg per 100 ml. Postoperatively the back pain and nuchal rigidity persisted, but no new neurologic signs developed. The temperature continued to spike and blood cultures remained positive, but no definite source of infection was found.

Eight days after operation a cisternal tap was performed to re-evaluate the cerebrospinal fluid. The puncture was performed without difficulty but midway through the fluid collection a few drops of blood were noted on readjustment of the position of the needle. (Microscopic examination showed 2,200 red blood cells, five neutrophils, and one mononuclear cell.) Shortly after the cisternal puncture, the patient complained of severe neck pain and nausea but no changes were noted on neurologic examination. Seven hours after the procedure the patient complained of "anxiety" in addition to continuing nausea and neck pain. Respirations were noted to be rapid but the pulse was 80 and regular, the blood pressure was 170/80

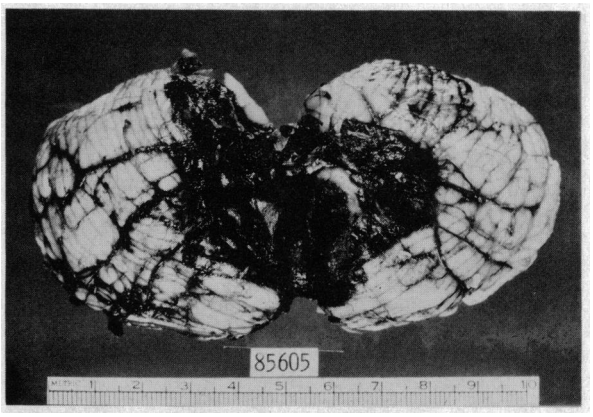

Figure 1.—Subarachnoid hemorrhage filling the cisterna magna (Case 1).

mm of mercury, and again no localizing neurological deficits were noted. Three hours later stupor developed and the patient rapidly became comatose, with loss of all brain stem reflexes. Cardiac arrest occurred 17 hours after the cisternal puncture.

Postmortem examination revealed subarachnoid blood filling the cisterna magna, diffusely coating the brain stem (Figure 1), and extending into the fourth and third ventricles. The site of the bleeding could not be identified. The spinal cord was normal, with no evidence of epidural abscess. Indeed, no evidence of infection anywhere in the body was discovered, although the vertebral bodies were not specifically examined.

Comment

A major subarachnoid hemorrhage followed cisternal puncture, with brain stem decompensation occurring ten hours later. The absence of localized neurologic signs engendered a false sense of security.

The patient's underlying meningeal reaction may have been secondary to occult lumbar vertebral osteomyelitis, but the possibility of uremic meningitis[1] unrelated to the sepsis cannot be excluded.

CASE 2. A 45-year-old woman was admitted in acute distress following a cisternal injection of amphotericin.

Nine months earlier the diagnosis of coccidioidomycosis had been established by skin biopsy when she presented with a six-month history of progressive verrucous back lesions and elephantiasis of the left lower extremity. The only neurologic complaint at that time was of mild headache but the coccidioidomycosis complement fixation titer of the

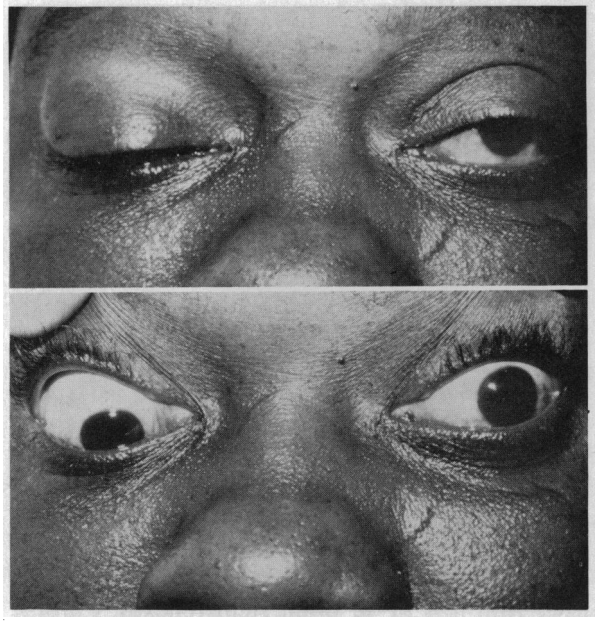

Figure 2.—Ptosis and skew deviation six hours after cisternal injection (Case 2).

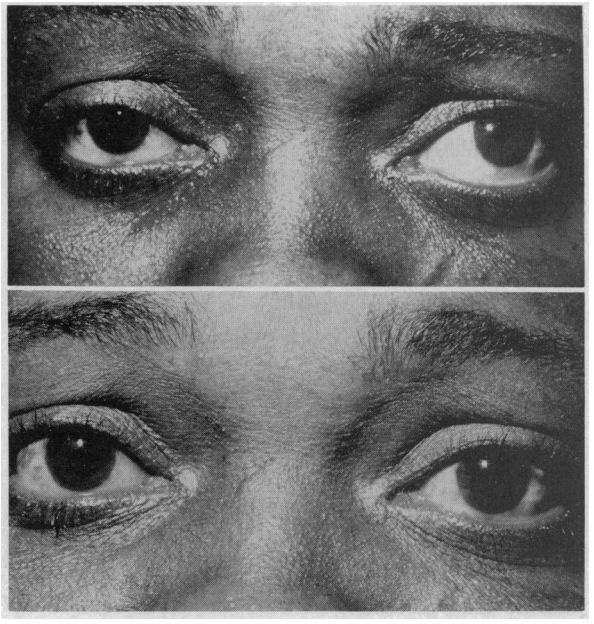

Figure 3.—Upper, 24 hours after injection (Case 2). Lower, two months after injection.

cerebrospinal fluid was 1 plus in a dilution of 1:16 and 4 plus in a dilution of 1:8.

Intravenous and intrathecal amphotericin B therapy was begun, but the initial biweekly lumbar subarachnoid injections of 0.10 mg soon proved too uncomfortable because of back pain, and after six injections an attempt was made to place an indwelling Ommaya reservoir-shunt to facilitate therapy. The attempt at ventricular cannulation was unsuccessful and resulted in a moderate left hemiparesis which slowly cleared over the next several months.

The intrathecal injections were then given cisternally and the patient received biweekly injections of 0.25 mg of amphotericin intracisternally and 50 mg intravenously. A total of 2,450 mg intravenously and 10 mg intrathecally was given without incident. The cerebrospinal fluid titer remained 4 plus positive at a 1:4 dilution, but no neurologic symptoms or signs developed.

On the thirty-seventh cisternal puncture blood appeared on the needle but the patient had no apparent ill effects. Immediately following the thirty-ninth injection of 0.25 mg of amphotericin with 20 mg of methyprednisolone acetate she complained of excruciating headache with severe nausea. After reclining for several hours, she attempted to go home but collapsed on arising. She regained consciousness after several minutes but progressive lethargy, dysarthria and right sided weakness followed and she was transferred to the neurology service.

On examination six hours after cisternal puncture the patient was stuporous and had severe dysarthria. The blood pressure was 150/80 mm of mercury, the pulse was 100, respirations 36, and the temperature 38.3°C (101°F). Although lethargic, she was well oriented and able to carry out commands. She could make sounds but few intelligible words even though her swallowing and tongue motion appeared normal. Bilateral ptosis, much greater on the right, was apparent, and a pronounced right hypotropic ocular skew deviation was present (Figure 2). The pupils were 5 mm, equal and reactive. There was mild right facial weakness and decided weakness of the right extremities, with hyperactive reflexes on the right side and a right extensor plantar response. Hypesthesia on the right side, including the face, and mild intention tremor of the left extremities were present.

Cerebrospinal fluid taken at the time of the cisternal tap showed 8 white blood cells and 24 red blood cells, while a lumbar puncture four hours after cisternal injection revealed a pressure of 270 mm of water, 800 white blood cells with 10 percent neutrophils, 70 red blood cells, protein content of 129 mg and glucose of 35 mg per 100 ml.

All the neurologic signs progressively cleared and on readmission two months later she had only minimal right ptosis (Figure 3), mild dysarthria and mild right hemiparesis with a nearly normal gait. Pneumonencephalography and RISA cistern-

ography with radioiodinated serum albumin demonstrated normal ventricular size without evidence of cerebrospinal fluid obstruction, and intrathecal amphotericin was not resumed.

Comment

The difficulties associated with intrathecal amphotericin administration are well illustrated by this case. Injection by lumbar puncture led to the expected back pain and radiculitis. The attempted change to ventricular catheter administration produced hemiparesis. The thirty-ninth cisternal injection was followed by acute brain stem damage.

The rapid onset of severe nausea and the subsequent anarthria suggest a direct medullary puncture, but the neurologic signs indicate brain stem damage that is bilateral and present at several levels. When the delayed progression is considered, it seems most likely that the chemical meningitis, documented on lumbar puncture, produced sufficient vasospasm which caused scattered brain stem infarcts.

The absence of blood on lumbar puncture dictated conservative therapy.

Discussion

Percutaneous puncture of the cisterna magna had been performed in animal studies for several years before Ayer published the first clinical series in 1920.[2,3] In a report of 43 punctures in 20 patients, he stressed relative safety but emphasized the need for preliminary practice of technique on cadavers.[3] There were no complications in his patients, but injury to the medulla occurred in ten of 1,186 preliminary punctures done on cats.[2]

In its early days, cisternal puncture was widely used in the diagnosis and treatment of lues, in serum treatment of meningitis, and in subarachnoid perfusion. Relatively few complications were reported; probably most went unreported. It seems generally agreed, however, that the test was relatively safe in very experienced hands.

Two major types of cisternal puncture complications are reported—subarachnoid hemorrhage and direct puncture of brain tissue. Aside from those attributed to grossly improper technique, most incidents occur in patients with anatomic variations of the posterior fossa, including large midline posterior inferior cerebellar artery branches, congenitally small posterior fossas, and inferior displacements of the brain stem and cerebellar tonsils.

In cases involving subarachnoid hemorrhage, the patients usually present with immediate headache, agitation, and stiff neck. Within minutes to several hours, or rarely after several days, progressive obtundation and various brain stem signs occur. In the cases examined at operation or autopsy, the hemorrhage fills the cisterna magna, acting as an acute mass to compress the brain stem directly and obstruct fourth ventricular outflow. Relief of this mass effect by posterior fossa decompression has seemed of value in the limited number of surgical cases.

Direct puncture damage usually involves the medulla, but occasionally the cerebellar tonsils or the pons are damaged. Symptoms of coughing, vomiting, generalized weakness, "electric" sensations of one side of the face or body, and respiratory dysfunction typically occur immediately. Fewer deaths have been related to direct puncture injury than to subarachnoid hemorrhage.

The first report of fatal complication was published by Nonne[4] in 1924. The patient, 79 years of age, died of subarachnoid hemorrhage from puncture of a tortuous arteriosclerotic posterior inferior cerebellar artery.

The following year Ebaugh photographically demonstrated subarachnoid blood surrounding the medulla and pons of a patient with tuberculous meningitis who died following perforation of a posterior spinal vein during a cisternal puncture performed by an inexperienced intern.[5]

By 1929, Saunders and Riordan could report experience with more than two thousand cisternal punctures.[6] They described a patient with numbness on one side of his body for a week following puncture. After reviewing the seven reported deaths, two references to deaths, and the nine reported cases of probable medullary puncture with recovery in the literature at that time, they concluded that the procedure was safe in skilled hands but dangerous when attempted by the untrained.

Two deep puncture wounds of the medulla with bleeding into the fourth ventricle were demonstrated on pathologic examination by Vonderahe and Haberman[7] in a patient who became stuporous following an "unsuccessful" cisternal tap and died four hours later.

Goodhart and Savitsky[8] reported the case of a 24-year-old man with syphilis who felt "a shock like 10,000 volts" on his right side during cisternal tap, with subsequent extremity numbness, dizziness and headache. He was admitted the next day with pain and hyperthesia in the first division of

the right fifth nerve and subarachnoid hemorrhage was demonstrated by lumbar puncture. The patient recovered promptly. The authors conjectured direct damage to the trigeminal descending tract in addition to the hemorrhage.

Dandy[9] described a 47-year-old man with general paresis who had headache with restlessness soon after a bloody cisternal tap and an hour later slipped into coma with Cheyne-Stokes respiration. At posterior fossa exploration six and a half hours after the tap, the cisterna magna was full of blood, which obstructed fourth ventricle outflow. An actively bleeding branch of the left posterior inferior cerebellar artery traversing low cerebellar tonsils was coagulated and the patient recovered completely. Dandy briefly mentioned a second case in which direct medullary puncture caused death within several minutes in a patient whose brain stem was displaced by tumor.

By 1949 Kehrer[10] was able to find 28 reports of death following cisternal puncture—most of them in the European literature. Two of the deaths resulted from definite medullary puncture and 21 involved subarachnoid hemorrhage. Kehrer added a further three cases of fatal hemorrhage and reported his own experience of four deaths in 8,835 punctures.

In Stender's case[11] the appearance of blood tinged cisternal fluid was followed by delayed progressive obtundation. At posterior fossa exploration, cisternal subarachnoid blood occluding the fourth ventricular foramina was removed and the patient had excellent recovery.

The patient reported by Schlorhaufer[12] experienced severe neck pain and sudden inability to speak during cisternal puncture but recovered over several days.

A 42-year-old man reported in the Swedish literature recovered from probable direct right medullary injury as well as subarachnoid hemorrhage requiring posterior fossa decompression in association with a cisternal puncture performed by an inexperienced physician.[13]

In 1964 Burzaco and Schisano[14] reported eight cases of severe post-puncture subarachnoid hemorrhage and noted three previous reports of surgical treatment in the literature.[9,11,15] Posterior-fossa decompressions were undertaken in all eight patients, with three surviving. In four of the cases bleeding came from ruptured branches of the posterior inferior cerebellar artery, and in the other four the site could not be demonstrated. The authors emphasized that some bleeding was evident in perhaps 5 percent of cisternal punctures and that progressive obtundation was the best guide to the presence of life-threatening hemorrhage. In one of their cases and several reported in the literature, the patients presented with late decompensation evidenced by pupillary changes, cranial nerve palsies, and obtundation three to eight days after puncture.

Zealear and Winn[16] described a probable cisternal puncture complication in a young man with coccidioidal meningitis who developed "deviation of the left eye laterally, increased deep tendon reflexes, nuchal rigidity and headache . . . at the time of . . . bloody cisternal and lumbar tap." He died four months later following an intraventricular amphotericin injection which produced lethargy, fever, nuchal rigidity and right facial paralysis. Besides evidence of active meningitis, diffuse subarachnoid hemorrhage was present at autopsy.

Intrathecal Amphotericin

The success of intravenous amphotericin B in the treatment of coccidioidal meningitis was demonstrated in several cases shortly after introduction of the drug.[17-19] To increase cerebrospinal fluid amphotericin levels without additional renal damage, Winn and others soon began combined intravenous and intrathecal treatment.[20] Winn came to favor the cisternal intrathecal route because of its more proximate location, and, although the injections were often attended by headache and vomiting in association with chemical meningitis, he felt the cisternal site preferable to lumbar injection with its arachnoiditis and frequent radiculopathy. The combined intravenous and cisternal approach has been widely accepted in treating coccidioidal meningitis and is occasionally used in other kinds of fungal meningitis.

There is no doubt of the efficacy of this treatment in suppressing infection, but there is little data on the precise benefits of the additional intrathecal administration. Frequent systemic infection precludes uses of intrathecal therapy alone, but several exacerbations of fungus meningitis have apparently responded to amphotericin given solely intrathecally.[20,21]

Current intrathecal amphotericin schedules vary considerably but Atkinson and Bindschadler's study of amphotericin cerebrospinal fluid levels in a single case suggests that the usual spacing of administration two or three times a week is suboptimal and that daily administration is required to maintain cerebrospinal fluid drug levels.[22]

Use of an Ommaya subcutaneous reservoir and intraventracular catheter is a technically appealing method of frequent intrathecal drug administration, but the complications of hemiparesis (as in Case 2), seizures, shunt blockage and secondary infection produce significant morbidity.[23]

All in all, the difficulties of intrathecal amphotericin administration by any route are sufficient to stimulate further inquiry into whether such therapy is virtually always required in coccidioidal meningitis or, in at least some cases, the disease could be adequately treated entirely intravenously pending discovery of a less toxic substitute for amphotericin.

Despite the risks of cisternal puncture, there will still be occasional need for a cisternal tap. When there is such need, only persons well trained in the technique should perform such procedures—preferably under fluoroscopic guidance—and only with ready access to emergency neurosurgical care.

Present evidence suggests that major post-puncture subarachnoid hemorrhage with progressive obtundation should be considered as an indication for emergency decompression of the posterior fossa.

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