COMPLICATIONS OF PANTOPOAQUE MYELOGRAPHY

CASE REPORT AND REVIEW*

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(Received for publication September 11, 1961)

MYELOGRAPHY, since its introduction by Dandy in 1919, has assumed universal acceptance as a diagnostic technique for pathology of the vertebral canal. Air was the original contrast agent and was used until 1922 when Sicard and Fores-tier reported the use of Lipiodol, an iodized oil which was used widely for years, providing excellent radiographic visualization of the subarachnoid space. Thorotrust was first used for myelography in this country by Nosik in 1938 but was abandoned because of radioactivity, retention by the reticuloendothelial system and difficulty in removal. Tyrodeg, a suspension of iodinated tyrosine in gelatin, proved unsatisfactory because of pronounced pleocytosis of the cerebrospinal fluid. Pantopaque was introduced clinically in 1944 by Ramsey et al. and Steinhausen et al. and is presently the most widely used contrast agent for myelography. Reasons for continued use of Pantopaque have been its ideal physical and radiographic properties and the infrequency of complications directly attributable to its use. We have carried out over 1500 myelograms during the last 15 years and have encountered virtually no complications, even minor, until the death of a young man following lumbar myelography. This prompted us to review and summarize the reported complications of Pantopaque myelography.

CASE HISTORY

G.T., a 31-year-old male truck driver, was admitted to Good Samaritan Hospital on April 10, 1959 because of pain in the left hip and leg of 5 weeks' duration. There was marked spasm of the left paravertebral muscles, limitation of movement of the back and atrophy of the left thigh and calf. The left patellar and Achilles reflexes were decreased and Lasègue's test was positive at 45° on the left. There was tenderness over the left sciatic nerve. Routine laboratory findings were within normal limits. It was felt that he had a protruded lumbar intervertebral disc on the left and that a myelogram should be made prior to operation. The patient was very apprehensive at the prospect of myelography and possible surgery, but consented to myelography even though he was warned by his relatives that a spinal tap would cause him to become paralyzed.

Myelography was performed on April 20, 1959, spinal puncture being carried out between L2 and L3. The spinal fluid was clear and colorless, with no cells, a negative globulin and Kolmer's test and contained a total protein of 49 mg. per cent. Nine cc. of Pantopaque were placed in the subarachnoid space without incident, fluoroscopy was completed and appropriate films were obtained (Fig. 1). While waiting for these films to develop the patient had an urge to defecate, complained of pain in the tailbone, became agitated and began to thrash about. The needle was withdrawn and the patient was placed on a bedpan. Following this the needle was reinserted and aspiration of Pantopaque was begun. However, he became hysterical, moved about violently and the needle again was removed. A third attempt at aspiration was only partially successful. He was taken to his room and given morphine for relief of severe low-back pain. That afternoon another attempt to remove the remaining Pantopaque again was only partially successful. It was estimated that 5 of the 9 cc. of Pantopaque were finally removed. The remaining 4 cc. were dispersed in the subarachnoid space and could not be collected for aspiration (Fig. 2A). This probably is evidence of a violent inflammatory reaction to the Pantopaque. The Pantopaque remained fixed in this position in the subarachnoid space as shown by a film taken 19 days later in an upright position (Fig. 2B).

After myelography the patient remained in bed making no effort to get up, and complained of headache, backache and pain in the lower extremities. We did not consider this significant because he was afebrile and his unusual personal-

* Presented in part to the Western Neurosurgical Society, Pebble Beach, California, October 25, 1960.
FIG. 1. Normal lumbar myelogram. The Pantopaque was in the lumbar subarachnoid space and flowed freely.

FIG. 2. (A) Roentgenogram taken about 5 hours after introduction of 9 cc. of Pantopaque, 5 cc. having been aspirated. The patient was in the upright position when the roentgenogram was made. (B) Roentgenogram taken 19 days after introduction of Pantopaque.
ity was the same as it was prior to myelography. Ten days after myelography he began to have difficulty emptying his bladder and finally weakness of the lower extremities was noted. Roentgenograms of the skull taken on May 11, 3 weeks after myelography, showed Pantopaque within the intracranial cavity (Fig. 3). An electroencephalogram on May 11 demonstrated diffuse and markedly abnormal activity. Lumbar puncture on May 12 was attempted at several interspaces but no fluid could be obtained. Although he remained afebrile until the 26th day after myelography, multivitamin and steroid therapy was started since it was felt he had a diffuse arachnoiditis of uncertain etiology. His condition did not improve and steroid therapy was discontinued.

Four weeks after myelography he was almost totally unresponsive, areflexic and at times cata-
tonic. Bilateral dilated pupils, paralysis of the 6th nerve and early papilledema on the left were noted. Another lumbar puncture was done on May 19 and a small quantity of thick yellow fluid was aspirated which clotted subsequently. Cultures for bacteria, tuberculosis and fungi produced no growth. A cisternal puncture was performed on May 25 with removal of 85 cc. of clear colorless cerebrospinal fluid. Replacement with air revealed a marked hydrocephalus (Fig. 4). The ventricular fluid contained no cells, total protein was 10 mg. per cent and all cultures were negative. Varidase was placed in the cisternal subarachnoid space. A ventriculopleural shunt to reduce intracranial pressure was carried out on May 27, 5 weeks after myelography. Subsequently the
papilledema subsided and throughout the rest of his life there was no evidence of increased intracranial pressure. We felt he was improving slightly with partial return of tendon reflexes. A tracheotomy was performed on July 6 because of respiratory difficulty. This was followed by a pyriform sinusotomy to facilitate tube feeding. Lumbar puncture was attempted 5 months after myelography but no fluid could be obtained. Six months after myelography he was able to respond to some verbal commands and periodically was moved into a chair beside the bed. Little change in his over-all condition was noted until Nov. 18, 1959, some 7 months after the myelography, when he died suddenly after being found in a diaphoretic state, breathing irregularly and without perceptible blood pressure.

Postmortem Examination. In addition to involvement of the central nervous system, tracheobronchitis and focal bronchopneumonia, there was generalized atrophy of the skeletal musculature.

There was complete obliteration of the subarachnoid space with a membrane, varying in thickness from 1–10 mm., which filled all of the sulci (Fig. 5). The membrane was adherent to both the underlying pia mater and to the overlying dura mater. In some areas the adherence was so dense that the membranes could be separated only by sharp dissection. There was maximal involvement in the posterior fossa, the membrane filling the basilar cistern and completely encasing the medulla and upper cervical cord. Cross sections through the hemispheres revealed symmetrical ventricles of normal size. Grossly there were no focal abnormalities in any portions of the hemispheric parenchyma. Sectioning through the pons, cerebellum and medulla disclosed complete obliteration of the foramen of Luschka and Magendie. Cross sections through the cord showed a completely encircling dense fibrous membrane forming a collar about the cord. In the region of the cauda equina there were adhesions between nerve roots and the meninges.

Microsections demonstrated fibrovascular proliferation of the arachnoid (Figs. 6–10). There was considerable variation with fibroblasts and delicate reticulin in some areas and a dense, almost collagenous, fibrous tissue simulating dura mater in other areas. Scattered inflammatory cells, including lymphocytes, plasma cells and macrophages, were present throughout all sections, while neutrophils and eosinophils were found in moderate numbers. In the lumbar subarachnoid space granulomatous foci were found consisting of round clear spaces bounded by histiocytes and inflammatory cells suggestive of a foreign body of lipoid nature. No bacteria, abscesses or areas of necrosis were noted. There was extensive vacuolization throughout the outer two-thirds of the spinal cord and portions of the cerebral hemispheres. Numerous fat-laden phagocytes in the parenchyma of the cord were seen in sections stained with Nile blue sulfate and Sudan IV.

DISCUSSION

Several possible etiologies of the pathologic process were considered. There was no evidence to suggest a bacterial leptomenigitis. The reaction was not caused by detergents used for cleaning needles and tubing since three other myelograms were carried out on the same day without incident and all myelographic packs were set up by the same nurse. All of our Pantopaque vials are immersed in methylene blue prior to use to check for defects in glass. Pantopaque from the same
carton was used on the other patients upon whom myelograms were done that day. We felt the diffuse aseptic leptomeningitis in all probability resulted from a hypersensitivity to Pantopaque and that death was caused by compression of the brain stem by the surrounding membrane.

In animals, it has been shown that Pantopaque in the spinal and intracranial subarachnoid space will cause a meningeal reaction with polymorphonuclear cells, round cell macrophages and fibrin resulting in fever and nuchal rigidity. The reaction progresses with time and hydrocephalus may result if a sufficient quantity of Pantopaque is used. Smith and Ross have shown that in rabbit
and guinea pigs the fibroblastic response of the meninges to Pantopaque may be suppressed by daily administration of intramuscular cortisone. Pantopaque becomes encysted within 6 weeks in dogs and is absorbed at a rate of 0.5 to 3 cc. per year. Interestingly, Pantopaque has been demonstrated to pass through the cribiform plate in dogs and into the lymphatics of the head. In man, transient mild meningeal reactions
sufficient to produce clinical signs and symptoms have been recorded by numerous authors. These have included fever, meningismus with nuchal rigidity, headache, malaise, ileus, increased counts of cells and elevated total protein in the cerebrospinal fluid. These findings occurred from 5 to 24 hours after myelography. Schnitker and Booth and Peacher and Robertson felt that meningeal reactions to Pantopaque occur more frequently when Pantopaque is left in the subarachnoid space, but that there is no direct relation of symptoms to the amount of Pantopaque left, while Ford and Key believed that postmyelographic reactions are more frequent with larger volumes of Pantopaque. In England, where it has been customary to leave Pantopaque in the subarachnoid space following myelography, the reported incidence of meningeal reactions varies greatly. Davies stated that nearly 60 per cent of patients in his series had postmyelographic reactions. Of 70 patients, 56 had immediate reactions and 14 had chronic symptoms. Early symptoms included headache, meningismus, nuchal rigidity, diplopia, nystagmus, retention of urine, pyrexia, diarrhea, shock and cramps of muscles. The late symptoms included chronic headache, cervical pain and stiffness, persistent severe backache, urinary frequency, hesitancy and incontinence, continuous pain in the legs, cramps and paresthesias. In contrast to this high incidence of reactions, Bering noted no clinical symptoms in 26 patients with 6 cc. of Pantopaque left in the subarachnoid space.

In addition to the early mild reactions, Luce et al. described 2 cases of delayed meningeal reactions occurring simultaneously with a flaring of Pantopaque skin wheals. The intradermal wheals were made prior to myelography to check for possible sensitivity to Pantopaque and in each case the reaction was negative initially. They felt testing of the skin is contraindicated because of the possibility of sensitization by this means.

More severe reactions to Pantopaque with

Fig. 10. Fibrous membrane under higher magnification. The membrane is becoming vascularized. Hematoxylin and eosin, X300.
resulting arachnoiditis and gross neurological involvement have been reported by Hurteau et al. In their series patients having normal myelograms initially, who had subsequent myelography with incomplete removal of Pantopaque, demonstrated at laminectomy an adherent arachnoiditis with a rope-like mass of nerve roots and encystment of Pantopaque. Similar cases were reported by Davies, Sarkisian described a patient with two normal myelograms whose symptomatology increased and a third myelogram demonstrated a complete block, which at operation proved to be an inflammatory lipoid granuloma.

Lumbar arachnoiditis has been described secondary to a number of etiologies other than Pantopaque, surgery for protruded disc, cleansing agents for needles and tubing, and spinal anesthesia being examples. Winkelman et al. felt that breaks in technique are more important than Pantopaque in production of arachnoiditis. This is substantiated by 2 deaths from purulent meningitis caused by faulty technique during myelography.

Taren reported a case of severe diffuse meningitis and ventriculitis following myelography in which 5 cc. of Pantopaque were left in the subarachnoid space. The patient became febrile and unresponsive, and had nuchal rigidity, a high count of white blood cells, papilledema and dilated fixed pupils. Trephination yielded cloudy ventricular fluid. The patient was placed on antibiotics and steroids and recovered 19 months later. It was not certain whether the reaction was caused by sensitivity to Pantopaque or by bacterial infection.

Erickson and van Baaren described a case in which a diffuse aseptic meningitis developed following myelography. The patient had signs of increased intracranial pressure caused by internal hydrocephalus and died 15 months after myelography despite surgical intervention. The sequence of events and findings were remarkably similar to those in our case.

Other infrequent complications of myelography are venous intravasation and pulmonary embolization of Pantopaque. Hin-
Pantopaque in the lumbar subarachnoid space and then pooling the oil in the posterior fossa. Considerable Pantopaque becomes trapped within the intracranial subarachnoid space. In 14 examinations there was 1 reaction with fever, meningeal irritation and a pleocytosis of 2500 cells/mm$^3$ in the cerebrospinal fluid.

We believe that Pantopaque is the most satisfactory contrast agent available for myelography. Large series, up to 3000 myelograms, with and without significant untoward clinical effects have been reported. A small percentage of people have individual hypersensitivity to Pantopaque and introduction of any quantity into the subarachnoid space will result in significant meningeal irritation with possible catastrophic results. Many patients who are not hypersensitive will undergo minimal meningeal reaction with pleocytosis and no significant clinical signs or symptoms. Malis, after evaluating Pantopaque for myelographic examination of the foramen magnum, stated "We feel that the so-called danger of intracranial Pantopaque and its relationship to continued syndromes after myelography has been grossly exaggerated, and, in fact, does not exist." Based on the experimental and clinical data of various authors as well as our own experience, we believe that every reasonable effort should be made to prevent Pantopaque from remaining in the intracranial subarachnoid space and that Pantopaque should be removed as completely as possible from the lumbar subarachnoid space at the conclusion of myelography.

**SUMMARY**

1. A case report of a patient who died following myelography is presented.
2. The patient died from a diffuse aseptic meningitis secondary to hypersensitivity to Pantopaque.
3. Experimental work dealing with meningeal reactivity to Pantopaque has been reviewed.
4. The various clinical complications reported have been considered.

5. We believe that Pantopaque should be removed as completely as possible following myelography.

**REFERENCES**

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