CONTRAST MEDIUM INJURY TO THE SPINAL CORD PRODUCED BY AORTOGRAPHY

PATHOLOGIC ANATOMY OF THE EXPERIMENTAL LESION

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The acute pathologic changes in the central nervous system produced by intracarotid injection of toxic doses of contrast media in experimental animals are well known. The mildest lesion consists of a transient breakdown of the blood-brain barrier, demonstrable only by the use of dye indicator technics, and unaccompanied by other structural changes. Reactions of greater severity are manifested by edema, vasodilatation and stasis, and by punctate hemorrhages. Anatomic evidence of neuronal damage has been sparse, only a single experimental study reporting a significant structural change. This effect, seen in acute experiments productive of severe disturbances in cerebral electrical activity and of the toxic manifestations listed above, consisted of an advanced hydropic cytoplasmic degeneration of neurones. Other than this report, there is no evidence from experimental studies to suggest that the contrast media are capable of producing an irreversible neuronal lesion.

Beyond the immediate and acute pathologic changes resulting from contrast medium injury in animals, virtually nothing is known. The reported experimental studies have made no attempt to follow the complete evolution of the lesion, or even to allow sufficient time for the necrobiotic and reactive changes secondary to irreversible tissue injury to appear. That negative results have been obtained in chronic studies merely indicates that an irreversible lesion was not produced in such experiments. The scarcity of chronic studies may reside in part in the general focusing of interest upon the initial stages of the reaction, and in part in the inability of the severely brain-injured animals to survive beyond the acute phase of the injury. Recently, however, a method has been developed for the production of a central nervous system injury by contrast media allowing extended survival of the injured animals and providing an opportunity for the functional and anatomic study of all temporal phases of the contrast medium lesion. The anatomic features of the cord injuries are described in the present report.

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These have been reported by us elsewhere, but it is necessary to summarize them in detail here.

The method of injury consisted of the rapid intra-aortic injection of 7 to 20 cc. (approximately 1 cc. per kg.) of a contrast medium into dogs. Except for a few studies made with 70 per cent Diodrast (diethanolamine salt of 3,5-diiodo-4-pyridone-N-acetic acid) the contrast medium used was 70 per cent Urokon sodium (S-acetyl-amino-2,4,6-triiodo sodium benzoate).* The injections were made at one of three levels: just below the renal arteries, above the superior mesenteric artery, or in the mid-thoracic aorta. An 18-gauge needle was used, pointing obliquely cephalad, and the injection was given over a 5 to 10 sec. period. In all injections, the animal was anesthetized with Nembutal and the aorta was surgically exposed. In the mid-thoracic injection, the animals were positioned on their right side; otherwise they were in a supine position. A total of 41 dogs was used in these experiments; the animals were sacrificed at periods varying from 5 hours through 27 days following the injection.

At the conclusion of each study, the animal was sacrificed by an overdose of Nembutal, and the vertebral column was removed. The entire cord was exposed by a dorsal laminectomy and fixed in situ for a few hours in isotonic neutral formalin, following which it was removed and fixation was completed with the cord suspended in a 5000 cc. cylinder. Most of the cords were sectioned transversely at 0.3 to 0.5 cm. intervals, but a few cords were sectioned longitudinally in a horizontal plane. The gross features of the lesions were recorded and in some instances photographed. Sections at 1.5 cm. intervals from the caudal 15 cm. of cord and from other levels with grossly recognizable lesions, and at 5 cm. intervals from the remainder of the cord were chosen for microscopic study. The materials were embedded in paraffin and sectioned at 6 microns. The sections were routinely stained with hematoxylin-eosin and with a modification of the Klüver-Barrera stain developed in our laboratory. This method, which allowed a study of the cell picture, the myelin sheath pattern, and the vascular bed in a single preparation, consisted of Luxol fast blue MBS (du Pont) followed by the periodic acid-Schiff reaction and a hematoxylin nuclear stain.

As a correlative study the acute phases of the cord injury were compared with lesions encountered in a previous study evaluating certain contrast media used for cerebral angiography and observed only in their early stages of development. The cerebral lesions had been produced by the following agents: Diodrast 35, 50, and 70 per cent; Neo-iopax (3,5-diiodo-4-pyridoxal-N-methyl-2,6-carboxylic acid) 37.5 per cent; N-methyl nicotinamide hydrochloride 20 per cent, a normal body metabolite approaching the chemical structure of these agents; Urokon 30 per cent at pH 5.4 and 7.0; its non-iodinated homologue, 3 acetylaminobenzoic acid 20 per cent at pH 7.4; and the benzene derivative para-aminohippurate 20 per cent.

During these studies it soon became evident that anatomic features such as the blood supply of the spinal cord and its caudal position were of prime importance in determining the site and severity of the contrast medium lesion. Accordingly, a special study of these relationships was made in 14

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