Experimental Hydrocephalus

Part 2: Gross Pathological Findings in Acute and Subacute Obstructive Hydrocephalus in the Dog and Monkey

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There is a general tendency to regard hydrocephalus of both the communicating and obstructive types as a chronic pathological process. This derives in part from the frequently insidious onset of the condition and in part from the chronic and inexorable manner in which the changes often progress. Little or no opportunity has been available to study the acute pathological changes in the human since in the early stages the condition is either unrecognized or at least not severe enough to provide substantial surgical or autopsy material for study. Experimental studies of hydrocephalus are few, but it is generally held that it takes as long as several weeks or even months for marked changes in ventricular size and remodelling of cerebral contour to develop.1,2,4,6,7

The current study examines the early pathological findings in experimentally-produced obstructive hydrocephalus. These early findings are of considerable interest, for it is likely that the manner in which the pathological process evolves is revealed in the acute rather than the chronic stages of the condition, and also that the sequence of these changes may provide information not only about the destructive processes that develop but about the compensatory alterations that occur, if any do occur. Questions fundamental to a study of the pathophysiology of hydrocephalus are: How quickly and with what severity do the changes in obstructive hydrocephalus appear? What are these changes and where are they most pronounced? What is the sequence of these changes? Do compensatory changes occur or does the pathological process progress as a linear function of time? These are some of the questions which this paper attempts to answer.

Materials and Methods

In this study we used 26 mongrel dogs ranging in age from 3 to 12 years and in weight from 25 to 40 lbs, in addition to the 230 rhesus monkeys (Macaca mulatta) mentioned previously in Part 1, which ranged in age from 1½ to 2 years and in weight from 4 to 6 lbs. Both dog and monkey groups had a roughly equal number of male and female animals.

Hydrocephalus was produced in all 256 animals by obstruction of the fourth ventricle and caudal aqueduct with an inflatable balloon. The technique has been discussed in detail in Part 1 (see pp. 385–389).9

The animals were painlessly sacrificed and perfused with 10% formalin solution according to a predesigned schedule covering an interval from 1 hour to 2 weeks after inflation of the balloon. After gross examination, the tissue was embedded in either paraffin or celloidin for microscopic examination.

Additional information, useful in documenting the rate and degree of ventricular enlargement, was obtained in a number of animals by ventriculography. These findings were not included in the reported pathological data to avoid possible variables, but x-ray films of interest will be referred to in passing. For the same reason, animals participating in correlative physiological studies, however simple, were excluded from this report.
Results

Clinical Observations. Although no significant alterations in pulse, blood pressure, or respirations were evident in the 256 animals included in this report, a number of other animals were excluded because of transient bradycardia, hypertension, or labored respirations occurring immediately after inflation of the fourth ventricle balloon. Most animals regained consciousness within 2 to 3 hours after light Sernylan anesthesia, but in none of the animals was there a return to normal alert wakefulness. This was the most prominent and consistent clinical finding and was observed in all animals without exception. Within 6 to 12 hours, most of the animals were up and about in their cages. They would sit quietly when left alone and frequently assumed a stooped posture with their heads upon their chests as though sleeping. When attended to or otherwise stimulated, the animals would respond and defend appropriately, but they were obviously lethargic and exhibited much less spontaneity than usual. Lethargy was prominent from the outset, and although this became more severe as time progressed, it did so at a very slow rate after the first 24 hours. In fact, with few exceptions, the animals that were not sacrificed early were still upright, self sufficient, and adequately nourished at the time of sacrifice 2 weeks later.

Cerebellar signs were evident in most animals for several days and included truncal ataxia, dysmetria of the extremities and, at times, intention tremor. These signs were generally transient and became progressively less prominent after 48 to 72 hours. Cranial nerve deficits were observed in a few animals immediately after surgery and included an occasional unilateral or bilateral abducens palsy or a decreased gag reflex with impaired facility for swallowing solid foods. Since these deficits generally improved and did not increase in severity, they were considered to be the result of the local lesion rather than increased intracranial pressure. Only a few animals developed abducens palsies secondarily; this was regarded as an unreliable sign in following the progression of early hydrocephalus. Vomiting also occurred rarely and was too infrequent a finding to be regarded as a reliable parameter of hydrocephalus. A summary of the fundoscopic findings will be presented elsewhere.

Gross Pathological Findings. Significant hydrocephalic changes were found in all 256 animals in which the fourth ventricle and caudal aqueduct had been obstructed. The ventricular dilatation developed at an unexpectedly rapid rate and was clearly recognizable as early as 1 hour; by 3 hours these changes had become advanced (Figs. 1 and 2). Thereafter, ventricular size continued to increase but at a much slower pace. So acute was this initial ventricular expansion that within 3 to 6 hours the size of the lateral ventricles was at least 50% of that reached in 2 weeks (Fig. 3). A curve of ventricular enlargement over the 2-week interval is represented in Fig. 4.

After allowing for obvious inaccuracies that come from approximating rather than quantitating ventricular size, it was nevertheless clear that when the obstruction of the ventricular system was complete, considerable dilatation occurred within a few hours. Figure 4 emphasizes that this initial enlargement did not progress evenly in a linear relationship with time. During the first 3 to 6 hours, ventricular expansion was precipitous. Thereafter and up to 24 to 48 hours, continued ventricular enlargement occurred at a substantial but considerably reduced pace. After 48 hours, ventricular enlargement occurred very slowly, and eventually assumed a rate that was roughly linear in relation to time.

In addition to enlargement of the lateral ventricles, flattening of the cerebral surface markings was an early gross finding in acute obstructive hydrocephalus. Although the surface changes were considerably less pronounced than the changes in ventricular size, these could, nevertheless, be distinguished within the first 1 to 3 hours. The findings consisted of flattening of the cerebral hemispheres, widening of the gyri, and narrowing of the sulci (Fig. 5). No obvious changes in the surface vasculature could be distinguished and there was little convincing evidence of either distension or compression of the cortical venous system.

The early enlargement of the ventricular system was characterized by expansion that preserved the angulated ventricular contours.