A-45. Analysis of Factors Contributing to Acute Brain Swelling

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It is generally accepted that acute brain swelling developes under the variety of pathological conditions of the brain and is primarily due to the augmentation of cerebrovascular blood volume. Although this seems to be cuased by the impairement of cerebrovascular tone, there exists a controversy whether neural or metabolic factor is playing more important role in the mechanism of vasoparalysis. In the present study, acute brain swelling were produced by different ways of methods under the monitoring of intracranial pressure (ICP) and cerebral blood flow (CBF). Impairement of CBF and high ICP observed in acute brain swelling were modified by the administration of specific chemical agents to the experimental animals and alterations thus occured were carefully compared in the different models in order to demonstrate two main factors cotributing the pathogenesis of acute brain swelling.

A first model of acute brain swelling was produced by the epidural compression as described previously.[1] Critical level of increased ICP in cat was sustained for 3–4 hours. Immediately after the deflation of balloon, ICP is normalized transiently.

Secondary rise of ICP, however, started to occure shortly thereafter and acute brain swelling developed. This form of increased ICP could not be lowered by administration of hypertonic solution such as mannitol. On the other hand, an appropriate amonts of norepinephrine infused intravenously demonstrated considerable effects to lower ICP and to improve CBF. We felt this therapeutical effect of norepinephrine was probably due to restoration of the impaired cerebrovascular tonicity, is an essential pathomechanism of acute brain swelling.

In a second model acute swelling was produced in cat by small bilateral lesions of posterior hypothalamus using stereotaxic technique. As was shown in the previous papers, posteror hypothalamus in cat controls cerebrovascular tone in normal condition.

Rapid increase of ICP and reduction of CBF developed soon after the completion of electrocautery and elevated ICP was associated by the impaired CBF. Although intravenous administration of small amount of norepinephrine were not beneficial to improve CBF and ICP in this model, appropriate amount of THAM infused intravenously had shown potent effect to lower ICP with concomitant improvement of CBF in slight degree.

Thirdly, another type of acute brain swelling was produced by the transient cerebral ischemia.[2] Cats were submitted to 15 minutes of complete cerebral ischemia by clamping the innominate and subclavian arteries and lowering the systemic blood pressure (BP) simultaneously. Recirculation of brain was accomplished by releasing

the clamp of arteries and also administering the small amount of norepinephrine.

Shortly after the recirculation, changes in ICP and CBF depend passively upon the alteration of BP. As the administration of norepinephrine repeated, however, changes of ICP and CBF became almost independent to the alteration of BP. That is, stepwise decrease in ICP associated with increase in CBF occured regardless the level of systemic BP. These changes of ICP and CBF seem to be directly related to the degree of restoration of vascular tonicity by the administration of norepinephrine.

In the same experimental model the administration of THAM was made instead of norepinephrine. In this case improvement of ICP and CBF were noticed, but their changes were less conspicuous as compared with that induced by norepinephrine.

From these results, it seems reasonable to assume that impairement of cerebrovascular tonicity observed in acute brain swelling can be restored by norepinephrine, provided posterior hypothalamus, namely cerebral vasomotor center remains intact.

Since the effects of THAM is not well understood, following studies were further carried out. Acute brain swelling was induced by the reduction of posterior hypothalamus in cats as mentioned above. When increased ICP and simultaneous impairement of CBF developed considerably, the experimental animal was submitted to either hyperventilation or respiration with air containing 5% of CO_2.

Inhalation of CO_2 resulted in additional increase of ICP, which was synchronous to a rise of BP. On the contrary, virtually no alteration in CBF was seen during this period. Appropriate amount of THAM was given to the animal under this condition and transient but prominent decline of ICP with concomitant improvement of CBF resulted.

If CO_2 inhalation was reapplied thereafter, the rate of increase of ICP became less obvious that observed before administration of THAM. Furthermore, improvement in CBF was also found when both BP and ICP rised.

The same line of experiment was carried out in the experiment model of transient cerebral ischemia. When inhalation of CO_2 was given shortly after the recirculation, increase of ICP occurred passively to the increase of BP. On the contrary inhalation of CO_2 after THAM had been administered was followed by the stepwise increase of base line of CBF. On the other hand, change in ICP not associated with the elevation of systemic BP became less obvious. From these experiments it can be said that THAM demonstrates some beneficial effects in the any type of brain swelling induced either metabolically or by the destruction of hypothalamus. Since the pharmacological action of THAM was not interfered with the elimination of hypothalamic function, THAM and norepinephrine seem to be different in their pharmacological actions.

Although these hypothesis is still largely speculative, we can conclude from our experiments as follows. Acute brain swelling is produced by impairement of autoregulation in the cerebral vasculartur e. The mechanism of autoregulation is maintained not only by metabolic factors but also by the neural controls in which posterior hypothalamus is playing key role. For this reasons these two factors should be further analyzed in future in order to develop a new therapeutic means against acute brain swelling.

1) S. Shozo, Head Injury Conference proceedings. ed. by Caveness, W. F. and Walker A. E., Lippincott, Philadelphia & Tront. 276-299, 1966.

2) K. A. Hossmann & K. Sato, Science, vol. 168, 375-376, 1970.