CEREBROSPINAL FLUID ENZYME STUDIES
AN AID IN THE SURGICAL MANAGEMENT OF INTERNAL CAROTID ARTERY OCCLUSION

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RECENTLY, attempts have been made to alleviate occlusive disease of the internal carotid artery by reconstructive surgery or a shunting procedure. The results of such therapy are difficult to evaluate, since a certain number of patients with thrombosis of the internal carotid artery recover spontaneously. Moreover, the maximal time interval between the onset of symptoms and operation that is compatible with a favorable result is not clearly defined. Lyons and Galbraith suggested that a subclavian-internal carotid shunt was of value in relieving neurologic symptoms if performed before a cerebral infarction was developed.

It is difficult, in many cases, to differentiate clinically between intermittent cerebral ischemia without infarction and infarction. An objective laboratory determination that aided in this differentiation would be of value in selecting those patients with internal carotid artery disease who might best benefit from surgical treatment. The measurement of certain enzyme activities in the cerebrospinal fluid may constitute such a prognostic aid.

We, and others, have reported elevated glutamic oxalacetic transaminase and lactic dehydrogenase activities in the cerebrospinal fluid of patients with cerebrovascular disease. The levels of these enzymes in the cerebrospinal fluid appeared, in several cases, to parallel the amount of brain-tissue destruction observed at autopsy. It was thought that serial determinations of glutamic oxalacetic transaminase or lactic dehydrogenase activity in the cerebrospinal fluid might indicate the occurrence of a cerebral infarction, and foretell the end result of a surgical attempt to re-establish the circulation in a case of internal carotid artery occlusion. Accordingly, the cerebrospinal fluid enzyme activities of 3 patients operated on for thrombosis of the internal carotid artery were determined, and the relationship between the changes in these activities and the clinical courses will be the subject of this report.

MATERIALS AND METHODS

Cerebrospinal fluid was removed by lumbar puncture from each patient as soon after admission to the hospital as practicable, and before arteriography. The lumbar puncture was repeated every few days, and occa-

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sionally daily if warranted by a change in the patient's hospital course. Each sample of cerebrospinal fluid studied had a normal cell content and a negative serologic test for syphilis.

The glutamic oxalacetic transaminase and lactic dehydrogenase activities in the cerebrospinal fluid were each determined by spectrophotometric methods at 37°C. These methods have been described in detail elsewhere. Normal glutamic oxalacetic transaminase activity, as determined in this laboratory, averaged 43 ± 12 μM. of oxalacetate formed per hour, per 100 ml., ranging from 25 to 62. Normal lactic dehydrogenase activity ranged from 31 to 87 μM. of lactate formed per hour, per 100 ml., with a mean of 68 ± 15.

CASE REPORTS AND RESULTS

Case 1. The first patient studied was a 59-year-old right-handed man who was admitted because of the abrupt onset of complete aphasia and right hemiparesis. One year before, he had suffered an almost identical attack, from which he made an excellent recovery.

Examination revealed an obese, aphasic man who was unable to move his right extremities. There was a marked facial weakness. Lumbar puncture yielded clear cerebrospinal fluid under a pressure of 150 mm. Percutaneous left carotid arteriography disclosed a block at the bifurcation of the common carotid artery.

Surgical exploration of the left carotid system, 12 hours after the onset of symptoms, revealed a firm thrombus in the common carotid artery at its bifurcation. The artery was opened, and the clot was found to extend into the internal carotid throughout its entire length in the neck. Since the thrombus reached at least to the foramen lacerum, no corrective procedure was thought possible.

The postoperative course was uneventful. No improvement was noted in either the hemiparesis or the aphasia. Periodic re-examinations conducted during the following 9 months revealed no change in his neurologic deficit.

The cerebrospinal fluid enzyme changes are shown in Fig. 1. It will be noted that the initial level of lactic dehydrogenase activity was high, and reached a maximum on the 5th day, then gradually declined. The glutamic oxalacetic transaminase activity, after rising slowly in the first week, had not yet reached a peak value on the 15th day. The cerebrospinal fluid protein varied between 35 and 45 mg. per 100 ml., in a random fashion.

Fig. 1. Case 1. Enzyme activities of cerebrospinal fluid. S indicates time of surgery. The upper limits of normal for glutamic oxalacetic transaminase and lactic dehydrogenase are 62 and 87 μM. respectively.
Case 2. A 45-year-old right-handed man became aphasic and a right hemiparesis developed over a period of 8 hours.

On examination, a severe right hemiparesis and a nearly complete aphasia were noted. He failed to improve during the following week. Left carotid arteriography, performed on the 8th day of the illness, demonstrated an occlusion of the left internal carotid artery close to its origin.

On the same day, the artery was opened, and a clot 2 cm. long was removed.

No improvement resulted from this procedure. When last seen, 6 months after operation, he was little changed in respect to his neurologic disabilities.

The glutamic oxalacetic transaminase levels in the cerebrospinal fluid of this patient are shown in Fig. 2. The initial value was normal; the activity then climbed to 130 $\mu$M. at the time of surgery. A sustained rise followed the operation. The total protein concentration in the cerebrospinal fluid was consistently normal.

Case 3. A 54-year-old right-handed housewife was admitted because of a partial aphasia. The speech difficulty had existed for 24 hours. Two months before admission she had complained of numbness and weakness of the right arm.

Examination disclosed a mild right-sided weakness and a receptive (sensory) aphasia. Lumbar puncture revealed clear fluid with a pressure of 160 mm. On the third day left carotid arteriography showed thrombosis of the internal carotid artery.

A few hours later a clot with much cholesterol-like material was removed from the left internal carotid.

She received heparin and Dicumarol, beginning 24 hours after surgery. Because of bleeding from the incision in the neck these were stopped on the 8th postoperative day. There was then a worsening of her condition, manifested by an increase in her speech disturbance. She improved during the next few days and was discharged. This patient maintained a steady rate of improvement and was able to return to her usual duties. The aphasia cleared completely.
The glutamic oxalacetic transaminase activity of the cerebrospinal fluid (Fig. 3) was normal at the time of operation and remained within normal limits except for one determination performed after anticoagulant therapy had suddenly been discontinued. This latter elevation correlated well with an increase in her speech impairment. The glutamic oxalacetic transaminase activity returned to normal and she improved clinically. The protein content of all cerebrospinal fluid samples was normal.

**DISCUSSION**

The cerebrospinal fluid enzyme levels correlated well with the clinical fate in the 3 cases presented. The first patient, who had a thrombosis of the internal carotid which was not amenable to surgical treatment, showed no improvement. The lactic dehydrogenase activity in the cerebrospinal fluid of this patient was elevated initially. The glutamic oxalacetic transaminase activity rose slowly, and continued to increase after the lactic dehydrogenase returned to normal. In Case 2, although the thrombus in the internal carotid artery was removed, this was accomplished on the 8th day of the illness. At this time, the glutamic oxalacetic transaminase activity in the cerebrospinal fluid was more than twice the normal value obtained shortly after admission. No improvement was noted clinically, and the glutamic oxalacetic transaminase continued to increase. The third patient had a normal glutamic oxalacetic transaminase activity at the time of surgery. The glutamic oxalacetic transaminase level rose after anticoagulants were stopped, corresponding to a worsening of the neurologic deficit. It returned to normal before discharge. This patient recovered.

The improvement in Case 3 may not have resulted solely from the surgical procedure. The initial symptoms of the patient were not severe, and for a short time she had received anticoagulants. The favorable course suggests that she had not sustained an extensive cerebral infarct. The glutamic oxalacetic transaminase levels in her cerebrospinal fluid, consistently normal with one exception, confirm this impression. It is possible that the removal of the thrombus prevented infarction and elevation of glutamic oxalacetic transaminase.

While definite conclusions cannot be drawn from so few cases, the data
suggest that in the absence of enzyme elevations on repeated sampling of the cerebrospinal fluid, irreversible cerebral infarction has probably not occurred. In support of this concept are 5 patients, previously reported, who recovered from a neurologic deficit within 24 hours of the onset. The glutamic oxalacetic transaminase activity in the cerebrospinal fluid was normal in each case.

Surgical attempts to alleviate the effects of internal carotid occlusion may be indicated while the enzyme activity of the cerebrospinal fluid remains within normal limits, before a cerebral infarct is developed. Postoperative determinations may be of value in predicting the final outcome.

SUMMARY

Serial determinations of glutamic oxalacetic transaminase, and in one case of lactic dehydrogenase activity were done on the cerebrospinal fluid of 3 patients undergoing thrombo-endarterectomy for occlusion of the internal carotid artery. The levels of these enzymes proved of value in predicting the results of the surgery. The elevation of enzyme activity in the cerebrospinal fluid may indicate the occurrence of a cerebral infarct. Conversely, normal activity suggests that surgical therapy may be indicated, since irreversible changes have probably not yet occurred.

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REFERENCES