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SEPTIC SHOCK WITH HYPERGLYCEMIA INDUCED BY HYPOTHALAMIC DYSFUNCTION AFTER REMOVAL OF LARGE PARASAGITTAL MENINGIOMA

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ABSTRACT

Septic shock (Klebsiella pneumoniae infection) accompanied with chronic hypokalemia and postoperative hyperglycemia was induced by surgical and infectious stress in a 64-year-old female patient with a large parasagittal meningioma that compressed the hypothalamic area. We concluded that a dysfunction of the compressed hypothalamus had some relation to the grave prognosis after surgical removal of the tumor.

Key words: Septic shock, Hypokalemia, Hyperglycemia, Hypothalamus, Intracranial tumor

INTRODUCTION

In spite of prophylactic treatment with antibiotics in patients with postoperative infections, sepsis followed by septic shock results in high mortality. We encountered a rapidly deteriorating course of sepsis in a postoperative patient and speculated that it resulted from a dysfunction of the hypothalamus due to stress after the removal of a large, long-standing tumor in the intracranial space.

CASE REPORT

The patient was a 64-year-old farm woman whose past history was not contributory. Several years ago, she had fallen down while working in a field, after which time she had a tendency to fall to the right and had a slowly progressive increment of sensory disturbance on the same side. In April, 1979, complaining of right hemiparesis, she visited a general practice physician and was referred to our clinic for further neurosurgical examination and treatment.

Neurologically the patient showed light hemiparesis including sensory disturbance of light touch sensation on the right side extremities. Her grasping power was 12 kg on the right and 20 kg on the left in spite of her right-handedness. No signs of increased intracranial pressure were found.

Laboratory examination showed that the preoperative treatment caused her hypokalemia level

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to rise from 2.4 mEq/L to 3.0 mEq/L. Electrocardiographic findings showed a prolongation of QT interval including some flattening of T wave. Chest X-ray film was normal. The value of fasting blood glucose was 95 mg/dℓ. No glucosuria, keton body, or protein appeared on urine examination. Other data in the blood chemistry were within normal limits. No data suggesting a failure of the renal function were found either.

Radiologic findings for the skull showed increased density of the inner table at the left coronal suture. Cerebral angiography on both sides was performed. By left cerebral angiographies, a round shift of the anterior cerebral artery to the right side and a downward displacement of an anterior part of the Sylvian groups of the middle cerebral artery were demonstrated. A group of lenticulostriate arteries as well as the anterior choroidal artery were poorly visualized on the left side. Hypoplastic finding of both the posterior communicating artery and the anterior choroidal artery on the left side were shown. Arteries feeding the tumor from the meningeal arteries including the precentral arteries formed the tumor stainings in a late arterial phase. These shadows were also detected in an early venous phase. Computed tomography(CT)

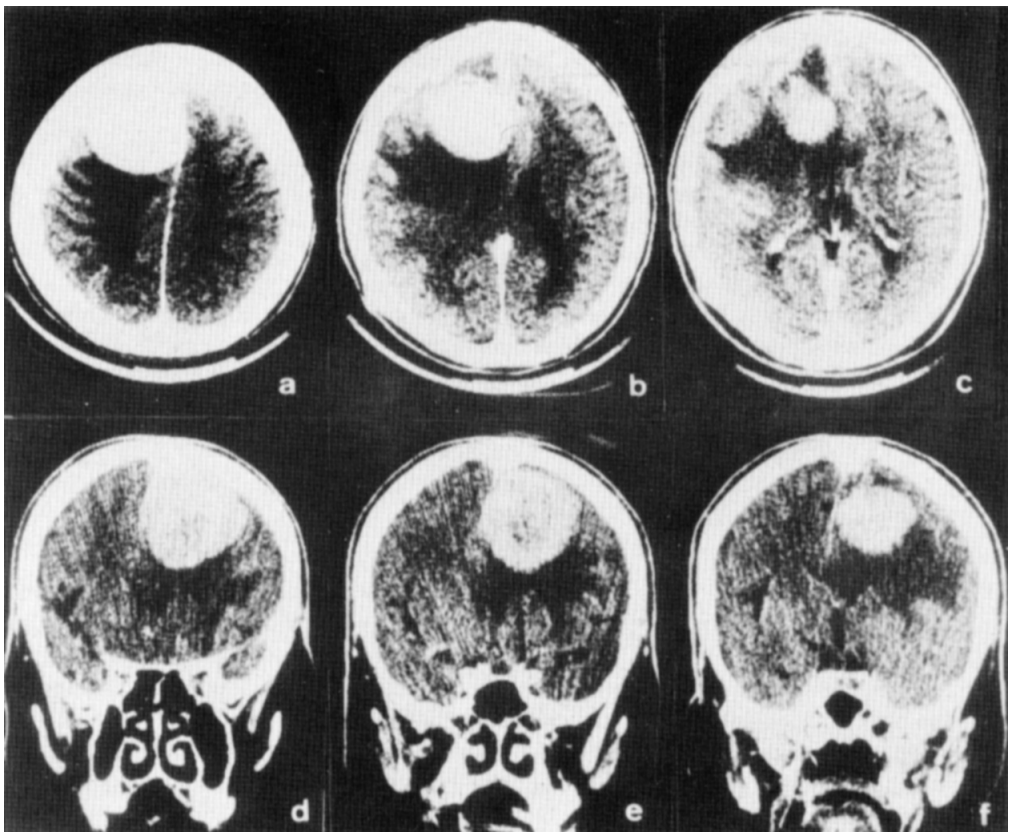

Fig. 1a–f Infused computerized tomography (CT) of horizontal (a–c) and coronal (d–f) scans.
A round, well-enhanced mass in the left parasagittal area with large low density and a shift of the compressed third ventricle to the antitumor side are noted.

showed a large, 5×4 cm, round, homogenously enhanced mass near the falx in a large, diffuse fronto-centro-parietal area of low density on the left side (Fig. 1a–f). The septum pellucidum was shifted to the right side. An anterior horn of the lateral ventricle on the left side was also markedly compressed downwards by the tumor. The third ventricle was compressed and shifted away from the tumor (Fig. 1d–f).

A left parasagittal meningioma was diagnosed and was confirmed as a meningotheliomatous type by the following operation.

OPERATION AND POSTOPERATIVE COURSE (Fig. 2)

On September 7, 1979, a left frontoparietal craniotomy was performed for the left parasagittal meningioma. Cortical sulci and gyri between frontal ascending veins and those from the central area were narrowed and flattened, showing an underlying large mass. A small part of a large pinky tumor appeared between the cortex and the falx. The total removal of the tumor was performed and the resulting defect was repaired.

The patient awakened immediately and oriented well postoperatively. Motor activity of her right upper limb remained unresponsive but the right lower limb showed withdrawal response to painful stimuli immediately after the operation. This condition continued on the second postoperative day as well, and the state of right hemiparesis was slightly improved. However, on the third day the patient became excited and confused.

In the evening of the third day the patient's temperature rose to 38°C and although she seemed drowsy, her hemiparesis remained unchanged. From the fifth postoperative day a high fever of 39°C continued until the eighth day. Although urine volumes were above 2000 cc/day until the fifth day, the specific gravity of the samples indicated normal variations (1.017 to 1.021). The level of serum sodium remained at a slightly high level (Fig. 2). By CT examination on the third day, there were only spotty small high density areas at the site from which the tumor had been removed. A air shadow in the left frontal surface was observed and the midline shift was decreased but remained. Neither postoperative bleeding nor massive edema was found. On the fifth day the patient's systemic blood pressure(BP) fell slightly to 120–70 mmHg and cardiac arrhythmia was noticed, rapidly followed by progressive hypotension of BP and high fever. Blood gas analysis revealed a hypoxic state. A tracheostomy was performed because of a progressive upper respiratory obstruction due to a decrease in the patient's level of conciousness; two hours later, a focal epileptic attack lasting 5 sec began from the right upper limb. In spite of vasopressor treatment, BP went down progressively to 80–50 mmHg, accompanied with high fever (Fig. 2).

Dexamethasone was given intravenously at 30 mg per day for the treatment of postoperative brain edema. However, because of an infection suspected to have arisen from the high fever, the dosage of corticosteroid were gradually decreased after the third postoperative day (Fig. 2).

On the fifth postoperative day, the last day of the gradual decrease in steroid administration, a blood glucose level of more than 300 mg/dℓ was detected in spite of normal glucose metabolism in this patient during preoperative examinations. Although regular insulin was injected, blood glucose values remained abnormally high. The value of blood glucose was unresponsive to repeated administrations of insulin and rose above 500 mg/dℓ on the sixth day, despite the termination of steroid treatment (Fig. 2). Although an infection of Klebsiella(K.) pneumoniae was diagnosed by the blood culture and although sensitive antibiotics were administered, the patient suddenly fell into septic shock on the fifth day. The state of septic shock was not corrected; the patient died on the eighth postoperative day of irreversible septic shock. An autopsy was not performed.

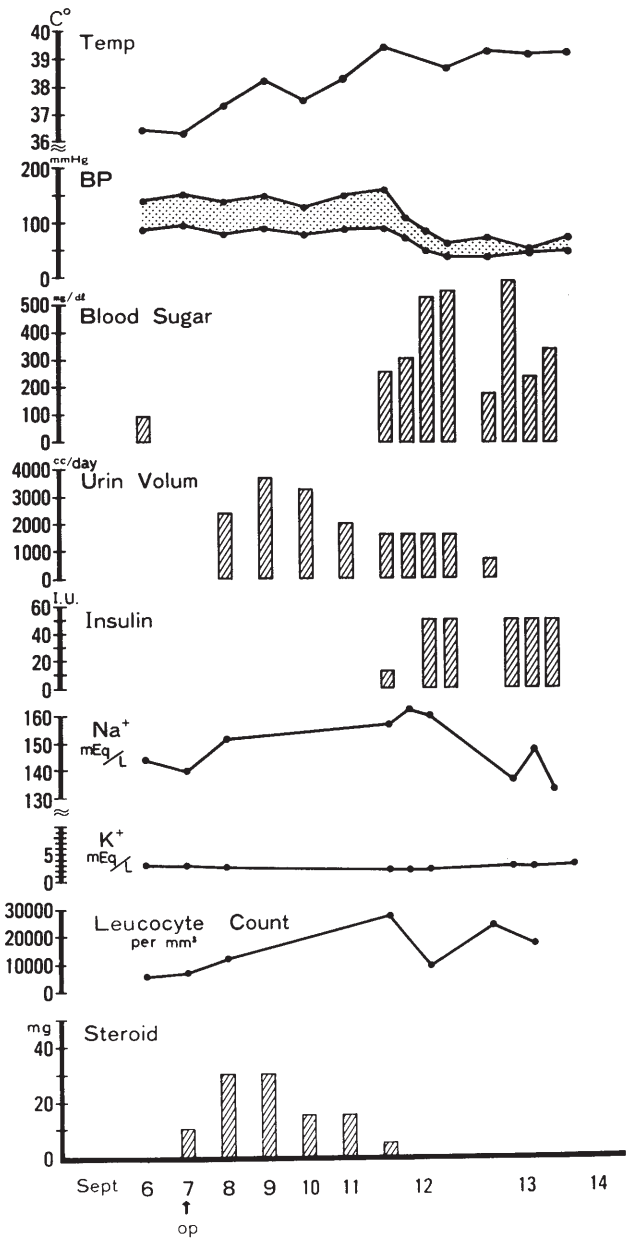

Fig. 2 Summary of data and treatment in the present case.
Temp.: body temperature; BP: systemic arterial blood pressure. Patient's temp. rose gradually to 38°C on the 3rd day and to more than 39°C after the 5th day, while BP remained normal and fell acutely to below 90 mmHg on those days, respectively, followed by decreasing urine volume. Leucocytosis showed a maximum on the 5th day. A high blood sugar value was detected just before the hypotensive state and was controlled on the 6th day by insuline injection which was, however, noneffective after the 7th day. Hypokalemia continued, while some hypernatremia was noticed from the 3rd day. On stopping steroid treatment, the hypotensive state with hyperglycemia was outstanding.

DISCUSSION

It is well known that a hypothalamic-pituitary dysfunction rarely occurs after an operation such as the removal of a tumor like that in the present case. In contrast, cases in which the patient suffers from meningitis frequently show a dysfunction of the hypothalamus.[1) 2)] Klebsiella pneumoniae infection seems to aggravate the occulting dysfunction of the hypothalamus. Our case demonstrated a fluminant course of sepsis followed by death after a craniotomy for the removal of a tumor in the parasaggital region. Similar to the report by Jeppsson et al., our patient showed an irritable or confused state on the third postoperative day. This symptom was supposed to originate from the tuberal region of the hypothalamus.[3)] However, cases similar to the present case cannot be found in the literature. Our speculations about the pathophysiology, although they may not be totally accurate, are largely supported by the clinical symptoms as well as by the laboratory findings.

In our patient, who had a large and long-standing intracranial space-occupying lesion, the tolerance of the hypothalamus coexisting with hypokalemia might have been pathologically lowered against various kinds of stress. It is also supposed that the microcirculation of the hypothalamus became unstable in the postoperative period of stress-strain redistribution of the intracranial structures after being released from the compression caused by such a large mass. Hypoplastic findings of the anterior choroidal artery as well as of the posterior communicating artery may also have some relation to the abnormal circulation of the hypothalamus. These microcirculatory changes may cause severe hypoactive states of the hypothalamus against invading circulatory[4)] and metabolic stress. Cerebral vasospasmus is induced not only by aneurysmal surgery but also by various kinds of intacranial manipulations in the postoperative period.[5)]

Thus microcirculation in the hypothalamus during this period is thought to be easily impaired by such stresses. Patients with such a condition must therefore be carefully treated throughout the postoperative period to prevent a hypoxic state from developing. However, the hypoxic state in our patient seems, retrospectively, to have been induced by the occulting Klebsiella pneumoniae infection of the lung. A state of transient hypoxia on the fifth postoperative day associated with a focal convulsion may have amplified factors like the stress of surgical intervention and infection that aggravate the hypofunction of the hypothalamus after the period of operative insult.

When the patient's BP first showed a shock level, a mildly high level of serum sodium was detected in spite of slightly increased urine volume. This indicates abnormal water excretion caused by hypothalamic dysfunction of the antidiuretic hormone secreting system. The state suddenly changed into hyperglycemia with hyponatremia associated with a hypotension of BP. In part, these findings demonstrate a failure of an adjustment mechanism to regulate the glucose level through the hypothalamus[6) 7)]; thus the patient fell into a fulminant course of irreversible septic shock.

Miller[8)] reported that the reaction to steroids in endotoxine shock was variable in its time course. Millis[9)] reported that a corticosteroid treatment was effective in the early state of septic shock.[10)] Glyconeogenesis was intensified by surgical stress[11)] and by large-dose steroid therapy; steroid treatment thus induces a high blood glucose level. However, in the present case, hyperglycemia at the final stage was unrelated to steroid administration.

There have been widely accepted opinions that the mechanisms of abnormal glucose metabolism are somewhat better understood in the extracranial tissue. Serum hypokalemia of unknown etiology had already been revealed by preoperative examinations in the present case, but the patient's fasting blood glucose value was not abnormal.

Examination of a patient with hypokalemia should begin with an evaluation of glucose

metabolism. Spergel et al.[12] reported a notably poor response to an increasing insulin level in a glucose tolerance test in hypokalemic animals. The state of hypokalemia was probably indicated by disturbances of glyconeogenesis in liver cells as Dodgen et al.[13] reported in their experimental work. Therefore, the glucose tolerance test would be important as a preoperative examination for a pathologically lowered level of serum potassium as recognized in the present case.

Dahn et al.[14] speculated that as a result of lowered levels of insulin in sepsis, glucose increased with the release of epinephrine, which inhibits the secretion of insulin from the beta cells of the pancreas as also suggested by Conn.[15] Hinshaw et al.[16] further suggested that the binding capacity of insulin in the peripheral tissue was weakened by sepsis.

Berk[17] reported that in 58% of patients with endotoxic shock, hyperglycemia changes into hypoglycemia especially in the terminal stage of the disease. The glucose concentration in blood increased at an early stage and then hypoglycemia was noted well into the later stages of endotoxic shock.[8] Thus hypoglycemia was due to an inability to maintain adequate glyconeogenesis after a depletion of glycogen store. Hinshaw et al.[16] also suggested that glucose administration for the treatment of hypoglycemia could prevent death in endotoxic shock as well as ensure good prognosis. Although these observations could not be confirmed in our case because of the rapid intolerance of the systemic circulation, they should be taken into consideration. These peripheral effects on abnormal glucose metabolism can probably be ruled out in our case by preoperative examinations.

A glucose level regulation conducted in the ventromedial hypothalamic neurons has also been reported.[7] We could not say which of the above two played a more important role in this grave pathological state. However, from the clinical symptoms as well as from the unusual course of hyperglycemia without hypoglycemia, the mechanisms of septic shock in our patient seemed mainly to involve the serious dysfunction of both the hypothalamus and the cardiovascular system. Although some degree of encephalopathy was seen in the patient on the third day, no abnormalities were revealed by CT. The confused state on the third day likely suggests the neurological changes induced by an invasion of endotoxin into the central nervous system.[18]

The failure of cardiovascular function and the impaired regulation of glucose metabolism by the hypothalamus via neurohumoral and neural mechanisms[6] may also have been caused by endotoxin in our case. The state of hypokalemia in our case suggested an occulting disturbance in the homeostasis of electrolyte balance via the hypothalamus. This was strongly supported by normal findings in preoperative laboratory tests of renal function.

We conclude that, progressive deterioration of metabolic regulation of glucose and an acute failure of circulatory controls in the hypothalamus are most likely to appear rapidly in a septic patient with hypokalemia after an intracranial decompression.

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