NEUROLOGIA medico-chirurgica
Vol. 4, pp. 105-111, 1962

LOWER NEPHRON NEPHROSIS ASSOCIATED WITH BRAIN TUMOR*

Kazuo TAKEUCHI, M. D.** and Tetsuo SHIMAMINE, M.D.

Departments of Neurosurgery and Clinical Pathology,
Toranomon Hospital, Tokyo, Japan

Lower nephron nephrosis, described by Lucké[14] in 1946, is acute insufficiency or renal function, frequently associating with shock, trauma, burns, blood transfusion etc., one of the major causes of which has been thought by many authors to be disturbance of renal blood flow.

Recently we experienced a fatal case of lower nephron nephrosis in which renal vasoconstriction might have been caused by a central origin, namely, it occurred following general convulsive seizure after decompression and radiation against glioblastoma of the left frontal lobe mainly infiltrating in the posterior orbital surface.

CASE HISTORY

K. T., a 17-year-old female, was admitted to the Neurosurgical Department of the Toranomon Hospital on October 31, 1960, in comatose state following general convulsions occurring suddenly a day previous to the admission. Since the end of April 1960 she had been complaining of headache and at the end of May she was diagnosed as having a brain tumor by an ophthalmologist, but further examination was not performed at that time. At the end of September malaise, nausea, and blurred vision on the left side appeared gradually and on October 29 attacks of vomiting repeatedly occurred.

Examination. The patient was comatose at the time of admission, but on November 2 she regained consciousness with the administration of hypertonic glucose solution, PVP solution and Oxygen inhalation.

Positive neurological findings were: signs of increased intracranial pressure, bilateral oculomotor and left abducent palsies and right homonymous hemianopsia. Choked disc was more marked on the right side.

Electroencephalogram showed a slow-wave focus in the left frontotemporal

* *Read before the 3rd Annual Meeting of the Japanese Society of Neurology, Nagoya, Japan, April 5, 1962.*

** *Address: Toranomon Hospital, 2 Akasaka-Aoi Cho, Minato-ku, Tokyo, Japan.*

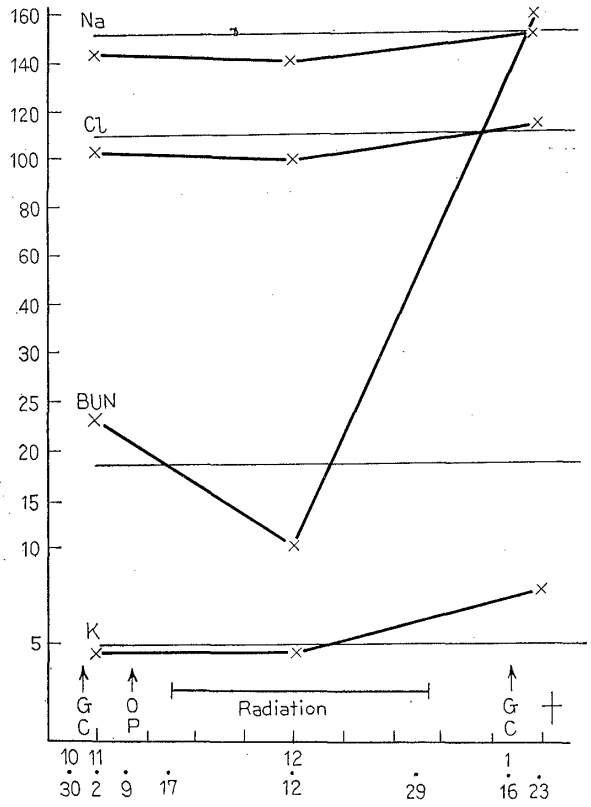

Fig. 1. Blood chemistry during the hospitalization. Marked elevation of serum sodium, chloride and potassium and blood urea nitrogen in the terminal stage, can be recognized.

region and random negative spikes were seen in the left frontoparietal region. Left carotid arteriography (lateral and anteroposterior views) confirmed the presence of an expanding, space-occupying lesion suggesting malignant tumor in the left frontal region. Blood chemistry will be described above (Fig. 1).

Operation. On November 9 a left frontal craniotomy was performed under endotracheal anesthesia. The frontal cortex was markedly edematous and hyperemic; tumorous infiltration, grey-yellow in color and about 2 cm in diameter, was found in the medial portion of the frontal lobe. Examination of the frozen section of the tumorous tissue revealed that the lesion was a glioblastoma. Then the bone flap was removed for decompression and the dura mater and scalp were closed.

Postoperative Course. Recovery was uneventful and tele-cobalt radiation was begun on November 17. During one week in the middle of November polydipsia and polyuria appeared temporarily, but they disappeared without any special treatment. When the irradiation dose reached 9,000r at the end of December, her general condition improved very much and she stayed at home for one week during the holiday season. Arteriographic regression was also noted at that time.

Bulging of the craniectomized area was not observed at all.

Since her admission anticonvulsant drugs have been taken intermittently, because of her very unco-operative character, probably due to the frontal lobe invasion. On Jan. 16, 1961 a sudden generalized convulsive seizure followed by status epilepticus occurred and she became comatose again. On the next day the convulsions disappeared completely, but she was still unconscious. In spite of sufficient administration of fluid and electrolytes by nasal feeding and intravenous infusion, anuria appeared after the convulsions. She ceased on January 24th in a uremic state.

Chemical analysis of the urine just after admission, during radiation and uremia revealed, as shown in Fig. 1, marked elevation of serum sodium, chloride and potassium and blood urea nitrogen in the terminal stage.

Autopsy. There was a poorly demarcated tumor, a hen's egg in size, in the posterior orbital surface of the left frontal lobe. The left inferior orbital and olfactory gyri, insular cortex and lenticular nucleus were invaded by the tumor. A very slight infiltration was observed in the right olfactory gyrus (Fig. 2). The optic chiasm and left optic nerve were buried by the tumor. There was a marked ischemic change in the "Sommer's Sector" and Purkinje's cell had disappeared fairly completely. The tumor was glioblastoma.

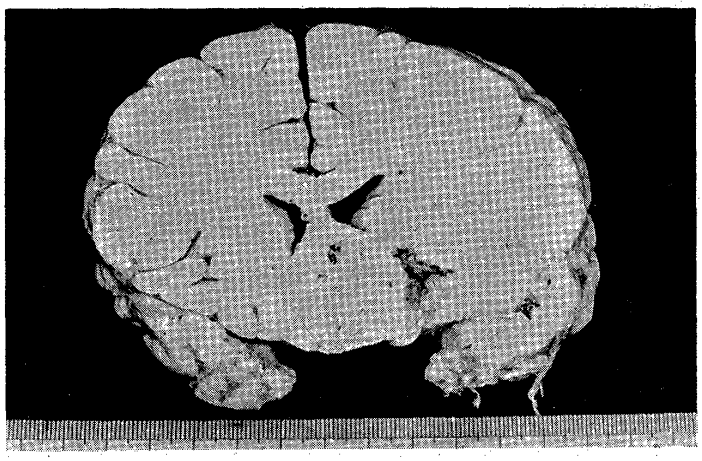

Fig. 2. Frontal section through the brain with a tumor (glioblastoma) in the posterior orbital area of the left frontal lobe.

Marked anemic swelling of the renal cortex was observed (Weight of the kidney: left 300 grm; right 240 grm). Cortical architecture was not clear, but it was not severely disordered. Histologically there were slight fibrosis and infiltration of lymphocytes in the edematously dilated interstitium. The lumen of the tubules was dilated and the epithelium was flattened and degenerated. There were protein-like casts which are hemoglobin-negative, in the distal side of the tubules. However, there was no remarkable change in the glomeruli. Those findings mentioned above,

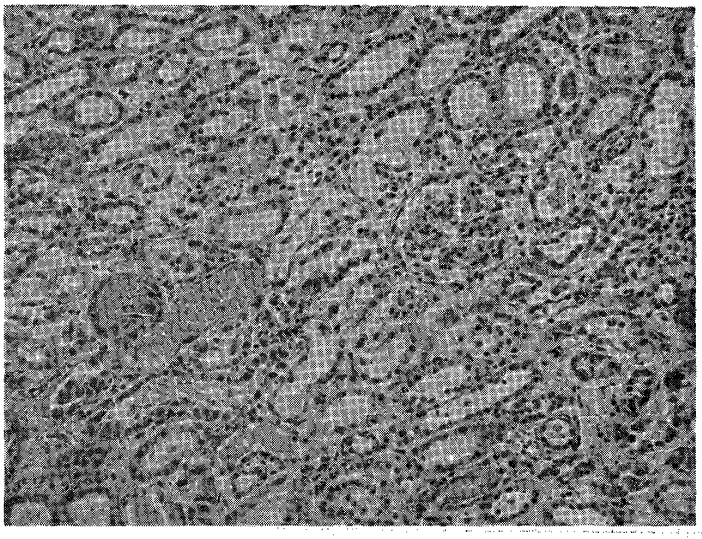

Fig. 3. Histological finding of the kidney. Marked dilatation of the renal tubules with flattened epithelium. Protein casts in the distal tubules. Interstitial edema. No remarkable changes in the glomeruli.

were similar to the lesions in the kidneys of so-called "Lower nephron nephrosis" (Fig. 3).

Comment

Lower nephron nephrosis was reported by Lucké[14] in 1943 in a study of 538 fatal cases occurring among military personnel. It was already discovered during World War I and again during the last World War it was found to be the most frequent fatal disorder of the kidneys among military personnel. According to Lucké the syndrome was seen under the following conditions: (1) severe or mild trauma to muscle; (2) non-traumatic muscular ischemia; (3) burns; (4) transfusion with incompatible blood; (5) heat stroke; (6) toxemia of pregnancy; (7) uteroplacental damage; (8) sulfonamide intoxication; (9) alkalosis; (10) poisoning with certain vegetable and chemical agents.

The major pathogenesis heretofore explained is lowering of renal blood flow caused by arteriolar vasoconstriction of the kidneys resulting in ischemia of the kidney and uremia.

Though the nature of the existing brain tumor is very malignant, surgical and radiological treatments had been rather successfully performed. However, the patient ceased from status epileticus followed by anuria and uremia in an unexpectedly early stage. In this case no peculiar cause of lower nephron nephrosis was found by postmortem examination. Therefore, it is natural that any relationship between the renal changes and existence of brain tumor in the posterior orbital area or occurrence of general convulsive seizures followed by status epilepticus, is suspected.

Table 1. Relationship between the central nervous system and renal function

Brobeck, J. R. et al.[2]	(1943)	Experimental hypothalamic lesion (rats) → Chronic glomerulonephritis with albuminuria and hematuria.
Lucké, B.[14]	(1946)	Lower nephron nephrosis
Livingston, R. B. et al.[13]	(1948)	Electrical stimulation of the Area 13 → Renal cortical ischemia.
Goodman, L.[5]	(1950)	Two cases of L. N. N. after electroconvulsive therapy.
Weinberg, S. J. et al.[23]	(1950)	Pneumoencephalography → Change of renal function; albuminuria and hematuria.
McLady, T.[15]	(1950)	Prefrontal lobotomies (bilateral lesion of the Area 47) → Death from uremia.
Hoff, E. C. et al.[8]	(1951)	Long continued stimulation of the cerebral cortex (cats) → L. N. N. with uremia.
Hoff, E. C. et al.[9]	(1951)	Stimulation of the anterior sigmoid gyrus (cats) → Renal cortical ischemia.
Silver, M.[19]		Canine epilepsy → All stages of renal damage due to prolonged central vasomotor stimulation.
Scheibert, C. D.[18]	(1961)	Intracranial lesions → Impaired renal function.
Gilbert, G. J. et al.[4]	(1961)	Lesions of the mid brain and diencephalon → Disturbance of natural regulation of water and salt metabolism.
Takeuchi, K. et al.	(1962)	Glioblastoma of the posterior orbital area → L. N. N. with uremia.

It has been known that the orbital surface of the frontal lobe is closely connected to the various autonomic nervous functions. Especially, there have been many articles on relationship between this area and circulatory functions (Bailey & Sweet[1], Delgado & Livingston[3], Kaada et al[10], Kaada[11], Wall & Davis[22], Livingston[13], Takeuchi[21]).

As to the relationship between the central nervous system and renal function, about 10 reports could be collected as shown in Table 1. According to these reports, stimulation or destruction of the posterior orbital area (Area 13 & 47) of the frontal lobe is followed by renal cortical ischemia which is thought to be a major cause of the lower nephron nephrosis. Besides electroconvulsive therapy or epilepsy may cause lower nephron nephrosis, clinically and experimentally.

It is felt that the mechanism of the severe renal change in this case is a neural transmission of impluses from the left posterior orbital area, invaded by glioblastoma, through the hypothalamus, brain stem and lateral spinal cord resulting in renal cortical ischemia with irreversible and fatal damage in the bilateral kidneys, similar to the lower nephron nephrosis frequently seen among wounded military personnel.

However, in this case general convulsive seizures followed by status epilepticus cannot be neglected as a responsible cause of the occurrence of lower nephron nephrosis, because anuria and uremia developed just after the seizures. Peripheral vasoconstriction has been observed in epilepsy, especially before seizure (Takeuchi[20]), and ischemic myocardial changes have been observed in postmortem examination of cases that have died from epileptic attacks (Neubürger[16,17], Hochrein[7], Gruber and Lanz[6]). The possibility of the occurrence of vasoconstriction of the kidneys during epileptic seizure cannot be denyed according to Goodman[5] and Silver[19]. However, Goodman thought the electric current used for electroconvulsive therapy is capable of setting into motion factors leading to the development of progressive renal insufficiency.

Summary

A fatal case of lower nephron nephrosis following status epilepticus in a case of left frontal glioblastoma is reported. In this case the renal change is felt to be caused by a central origin, i.e., invasion of the left posterior orbital area by glioblastoma, confirmed by the postmortem examination.

References

1) Bailey, P. and Sweet, W. H.: Effects on respiration, blood pressure and gastric mortility of stimulation of orbital surface of frontal lobe, J. Neurophysiol., 1940, **3**: 276–281.
2) Brobeck, J. R., Tepperman, J. and Long, C. N. H.: Experimental hypothalamic hyperphagia in the albino rat, Yale J. Biol. Med., 1943, **15**: 831–853.
3) Delgado, J. M. R. and Livingston, R. B.: Some respiratory, vascular and thermal responses to stimulation of orbital surface of frontal lobe, J. Neurophysiol., 1948, **11**: 39–55.
4) Gilbert, G. J. and Glaser, G. H.: On the nervous system integration of water and salt metabolism, Arch. Neurol., 1961, **5**: 179–196.
5) Goodman, L.: Lower nephron nephrosis following electroconvulsive therapy. Report of two fatalities, J. Nerv. Ment. Dis., 1950, **112**: 130–151.
6) Gruber, G. B. und Lanz, H. F.: Ischemische Herzmuskelnekrose bei einer Epileptiker nach Tod im Anfall, Arch. f. Psychiat. u. Nervenkrhten., 1920, **61**: 98–102.
7) Hochrein, M.: Der Coronarkreislauf. Physiologie: Pathologie: Therapie. Berlin: Julius Springer, 1932, 108 pp.
8) Hoff, E. C. and Kell, J. F., Jr.: Disorders of renal function produced by cerebral stimulation, Federation Proc., 1951, **10**: 65–66.
9) Hoff, E. C., Kell, J. F., Jr., Hasting, N., Sholes, D. M. and Gray, E. H.: Vasomotor, cellular and functional changes produced in kidney by brain stimulation, J. Neurophysiol., 1951, **14**: 317–332.
10) Kaada, B., Pribram, K. and Epistein, J.: Vascular and respiratory responses from stimulation of the temporal, insular, orbital and cingulate cortex in monkeys, J. Neurophysiol., 1949, **12**: 347–356.
11) Kaada, B. R.: Somato-motor autonomic and electrocorticographic responses to electrical stimulation of "rhinencephalic" and other structures in primates, cat and dog. A study of responses from the limbic, subcallosal, orbito-insular, piriform and temporal cortex, hippocampus-fornix and amygdala, Acta Physiol. Scand., **24** (Suppl. 83).

12) Liberson, W. T., Scoville, W. B. and Dunsmore, R. H.: Stimulation studies of the prefrontal lobe and uncus in man, EEG. Clin. Neurophysiol., 1951, **3**: 1–8.
13) Livingston, R. B., Fulton, J. F., Delgado, J. M. R., Sachs, E., Jr., Brendler, S. J. and Davis, G. D.: Stimulation and regional ablation of orbital surface of frontal lobe, Res. Publ. Ass. Nerv. Ment. Dis., 1948, **27**: 405–420.
14) Lucké, B.: Lower nephron nephrosis (The renal lesions of crush syndrome, of burns, transfusions, and other conditions affecting the lower segments of the nephrons), Milit. Surg., 1946, **99**: 371–396.
15) McLardy, T.: Uraemic and tropic deaths following leucotomy: Neuroanatomical findings, J. Neurol. Neurosurg. Psychiat., 1950, **13**: 106–114.
16) Neubürger, K.: Herz, Epilepsie, Angina Pectoris, Klin. Wschr., 1933, **12**: 1355–1357.
17) Neubürger, K.: Ueber die Herzmuskelveränderungen bei Epileptikern und ihre Beziehungen zum Angina pectoris, Frankfurt Ztschr. f. Path., 1933, **46**: 14–42.
18) Scheibert, C. D.: Intracranial lesions as a cause of impaired renal function, J. Neurosurg., 1961, **18**: 182–187.
19) Silver, M. cited by Kell, J. F., Jr.: J. Neurosurg., 1961, **18**: 186–186.
20) Takeuchi, K.: Peripheral blood circulation of epilepsy (Plethysmographic studies on the cerebral lesions, Part 2.), J. Jap. Surg. Soc., 1954, **55**: 251–273.
21) Takeuchi, K.: Changes of the cardiac rhythm caused by lesions of the posterior orbital area of the frontal lobe, Brain & Nerve, 1958, **10**: 171–178.
22) Wall, P. D. and Davis, G. D.: Three cerebral cortical system affecting autonomous function, J. Neurophysiol., 1951, **14**: 507–517.
23) Weinberg, S. J., Goodman, J. R. and Bushard, M. C.: Alterations in renal function, including hematuria, in man during intracranial air studies. Alterations in cardiac function, Arch. Intern. Med., 1950, **86**: 857–871.