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An unusual electroencephalogram of a patient with diabetic acidosis

REPORT OF A CASE

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ELECTROENCEPHALOGRAPHIC evidence of changes in patients with diabetes mellitus is usually nonspecific, the changes being related to the state of consciousness. Specific abnormalities are usually attributed to an underlying condition other than diabetes mellitus. This paper presents the case history of a patient with long-standing brittle diabetes whose electroencephalogram had unusual features.

REPORT OF A CASE

A 59-year-old woman was first examined at the Cleveland Clinic in 1950 because she was unable to control the diabetes mellitus, which was diagnosed in 1947. She had been hospitalized for diabetic ketoacidosis five times during the three years after diagnosis, three times in the most recent four months.

In the 17 years in which her progress has been followed here, she has been hospitalized at least 25 times because of acidosis, with frequent trips to the Emergency Room for treatment of hypoglycemic reactions. Neurologic symptoms, which were present during the first few years, consisted of disorientation, incoherent speech, intermittent blurring of vision, headaches, and nausea. These symptoms were confined to periods of acidosis or of hypoglycemia. Results of neurologic examinations in the intervening periods were always within normal limits.

During 1958 she began to notice numbness in the backs of the legs. Neurologic examination revealed a decrease in vibratory sensation distally in the left leg, decreased perception of joint movement in the left great toe, asymmetry of deep-tendon reflexes, with the right knee jerk being greater than the left one, and a right extensor plantar response. The presumed diagnosis was that of myelopathy and peripheral neuropathy secondary to diabetes mellitus.

In 1961, while hospitalized for treatment of acidosis, the patient 'collapsed' several times while undergoing physical therapy, and on one occasion was incontinent of feces and urine while sitting in a chair. Her state of consciousness was not recorded. Neurologic examination revealed asymmetry of reflexes, but this time the left knee jerk was more active than the right one. Ankle jerks were absent bilaterally. The right plantar response was again extensor. Pinprick sensation was decreased in both ankles. Muscle wasting and weakness were noted in both legs, and were greater proximally than distally. The episode of collapse was thought not to be a seizure, despite the incontinence, as her mental state at the time was not known.

An electroencephalogram was obtained which showed slowing of the background pattern at from 7 to 8 cps, with an excessive amount of moderately high amplitude 4 to 5 cps theta activity seen predominantly in the central and frontal regions symmetrically. Brief runs of from 5 to 6 cps theta activity were seen which were not definitely paroxysmal

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bursts. This record demonstrated an increase in the slow theta activity, in comparison to a previous record obtained five years earlier. A lumbar puncture revealed crystal-clear and colorless fluid with 2 leukocytes, no erythrocytes, and 116 mg per 100 ml of protein. A psychologic evaluation revealed a low normal intelligence quotient, with poor abstraction of similarities. Seven days later an electroencephalogram revealed a pattern quite similar to that previously recorded. Electromyography was performed on the right arm and right leg, and the results were interpreted as compatible with myopathy. The conclusion was drawn that she had neuromyopathy secondary to diabetes, and some ill-defined type of diffuse cerebral degeneration.

Between 1961 and 1967 the patient continued to require periodic hospitalization at the Cleveland Clinic Hospital, for the control of diabetic acidosis. During those periods, she had various neurologic symptoms, including intermittent blurred vision, weakness, irritability, ataxia, numbness of fingers and midcalf regions, dysarthria, vertigo, nausea, anorexia, and headache. These symptoms were again related to periods of acidosis or of hypoglycemia, clearing with the control of diabetes. At times, when the blood sugar content was normal, episodes of confusion occurred. In October of 1964, her reports disclosed that headaches were occasionally associated with visual scotoma as well as photophobia. She was treated with ergotamine tartrate and caffeine, and dimenhydrinate, and reported regression of symptoms.

In March of 1966, her legs gave way and she fell, sustaining an intertrochanteric fracture of the right femur, which required open reduction. She did well postoperatively and was able to walk with the aid of a cane. No note was made as to her state of consciousness at the time of the fall.

On May 16, 1967, the patient was admitted to the Cleveland Clinic Hospital, in ketoacidosis, having been discharged just two weeks previously after a similar event of collapse. Her son stated that she had spent the majority of this interval lying in bed or on the couch because she was too weak to be up and about. She had lost her appetite and had become nauseated, vomiting during the two days before admission to the hospital. As the vomiting continued, she became progressively more lethargic. There was no prior trauma.

On admission to the hospital she was a well-developed, slightly obese woman, who was stuporous. She opened her eyes on command, but participated in little spontaneous activity. Blood pressure was 100/60 mm Hg; respirations were 32 per minute; oral temperature was 98.6 F. Her breath had an acetone odor. The lungs were clear; the heart rhythm was regular with no audible murmurs. The neck was supple, and the pupils were equal in size and reacted to light. The abdomen was soft and did not appear to be tender. The patient appeared to be dehydrated. An electrocardiogram showed changes interpreted as hyperkalemia. Venous pressure was 10 cm H_2O. Blood concentrations were as follows: glucose, 590 mg per 100 ml; carbon dioxide, 5.5 meq per liter; chloride, 100 meq per liter; sodium, 138 meq per liter; potassium, 7.0 meq per liter; urea, 69 mg per 100 ml; and hemoglobin, 11.6 g per 100 ml.

The patient received insulin and saline parenterally, and within 10 hours her responsiveness had increased. The following blood studies were then obtained: glucose content, 212 mg per 100 ml; carbon dioxide content, 15.5 meq per liter; chloride, 103 meq per liter; sodium, 139 meq per liter; and potassium, 3.4 meq per liter. Seventeen hours after admission to the hospital her blood glucose content was 138 mg per 100 ml and the carbon dioxide content was 26.5 meq per liter, and all other laboratory tests were normal. The blood glucose content continued to range from 125 to 350 mg per 100 ml, with normal electrolyte values, but the patient remained stuporous.

A neurologic examination revealed the patient to be semicomatose, responding poorly to spoken questions. Her speech was slurred, and she was disoriented in time. She resisted neck flexion briefly, but no firm nuchal rigidity was found. There was increased resistance to passive motion on the left side, increased deep tendon reflexes on that side, with the presence of Hoffmann's reflex. There were bilateral flexor plantar responses. The amount of obtundation was far out of proportion to the localizing signs, and it was concluded that the patient had a diffuse encephalopathy of undetermined origin.

Lumbar puncture revealed an opening pressure of 150 mm of cerebrospinal fluid with

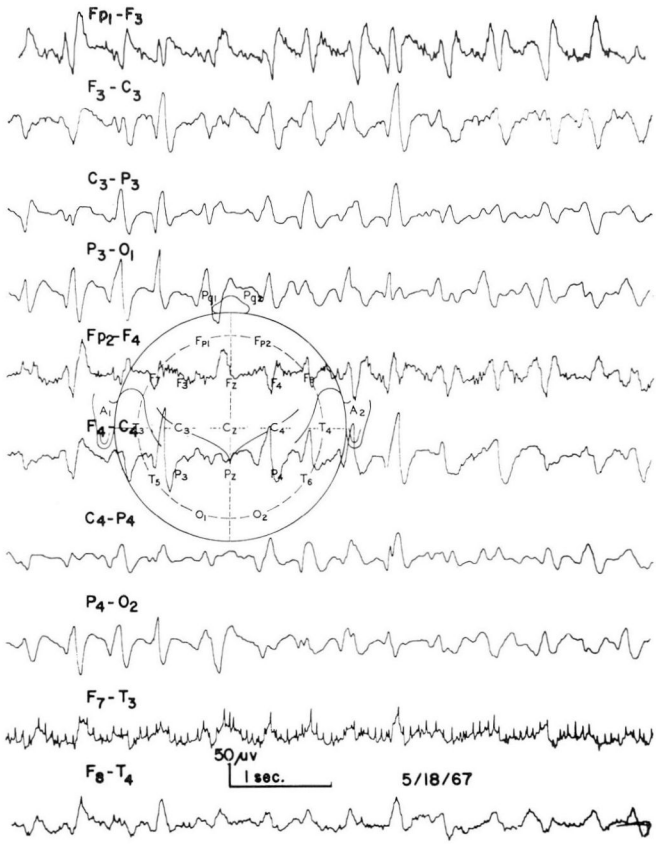

Fig. 1. Electroencephalogram obtained two days after admission to the hospital, when the patient was still in semicoma and blood values were normal except for a slight increase in glucose.

crystal-clear and colorless fluid, no blood cells; negative Pandy's test; total protein, 68 mg per 100 ml; glucose, 115 mg per 100 ml; and negative cytologic tests. Roentgenograms of the skull were normal. An electroencephalogram (*Fig. 1*) was obtained on May 18, 1967, two days after her admission to the hospital, when she was in the state of semicoma just described. This was reported as "An extremely abnormal record with continuous complex high voltage 'seizure-like' activity in an essentially diffuse, but somewhat variable distribution. Much of this was in the 2–4/sec range reaching several hundred microvolts, always detectable bilaterally, but with strict symmetry." * These high amplitude waves were not synchronous with electrocardiogram artifact.

The patient's course and treatment remained unchanged during May 18. On the morning of May 19, two full days after reported normal blood values, she was responsive enough to sit up in bed, smile, and eat breakfast without help. Her mental alertness continued to improve. Electroencephalography was performed again on May 20 (*Fig. 2*),

* *Interpreted by our colleague, Charles E. Henry, Ph.D., Electroencephalographic Laboratory.*

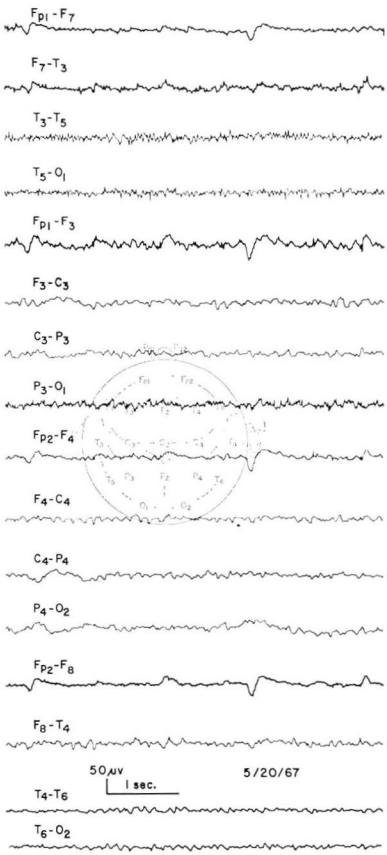

Fig. 2. Recording four days after admission to the hospital, at which time the patient was alert and responding appropriately.

at a time when the patient was responding in a relatively appropriate manner. This electroencephalogram showed a great improvement, with a loss of the periodic, high-amplitude, slow, sharp waves that were seen on the previous recording, and a return toward a relatively normal basic rhythmicity. Within several days the control of the diabetes was improved. Two more electroencephalograms (*Fig. 3 and 4*) were obtained during the remainder of the hospitalization. These showed "... continued improvement of the background pattern with a decrease in the amount of dysrhythmic theta activity occurring either maximally over the left temporal area or in a more diffuse bilateral and symmetric manner." * A psychologic evaluation revealed a woman with borderline-to-low normal intelligence who, although at times confused, has shown no evidence of a mentation defect. She was given physical therapy, and discharged from the hospital with the diabetes under good control.

DISCUSSION

The occurrence of various neurologic signs and symptoms in association with diabetes mellitus is well known. According to Garland,[1] 60 percent of

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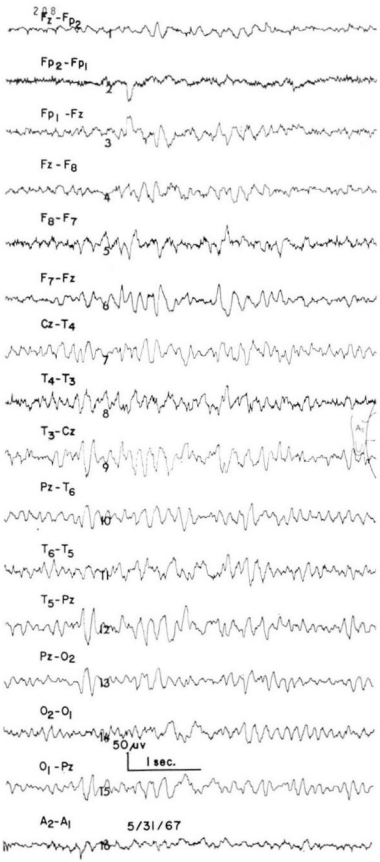

Fig. 3. Recording 15 days after admission to the hospital, showing continued improvement.

all patients with diabetes have neurologic complications at some time in the course of the disease. These complications usually consist of peripheral neuropathy. Cranial nerve palsies, and signs consistent with spinal cord involvement have been reported.[2-4] The possible existence of cerebral involvement in diabetes is a controversial matter. Some authors[3-6] believe that diabetic encephalopathy exists, and others[1] deny this. Some[2] believe that cerebral dysfunction (not related to hypoglycemia or acidosis) is due to a complication such as arteriosclerosis, rather than to the diabetes itself. DeJong[2] has noted an increased incidence of cerebrovascular disease in diabetic patients, whereas Garland[1] states "... the incidence of strokes in diabetics is not higher than in others when allowance is made for age and hypertension."

It is agreed that carbohydrate metabolism does have an effect on electro-

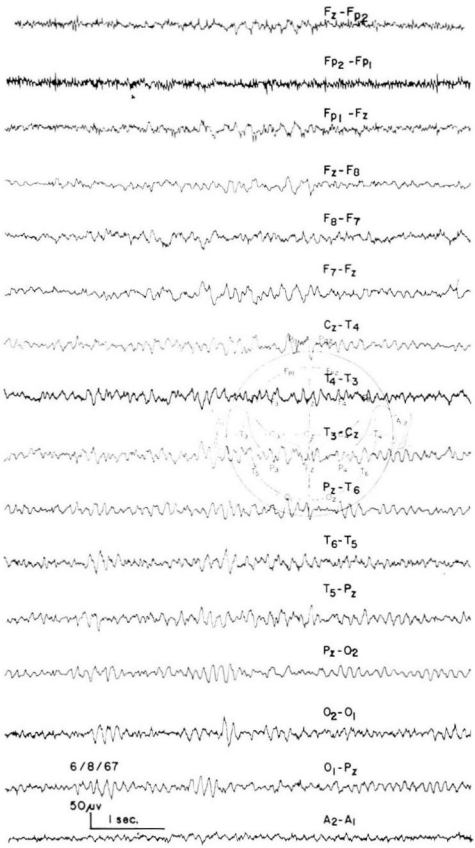

Fig. 4. Final recording 23 days after admission to the hospital, showing return to previous pattern.

cortical activity, and it is impossible to discuss the electroencephalographic changes in the patient we treated, without considering the diabetes, either directly or indirectly, as a possible etiologic factor.

In uncomplicated diabetes the electroencephalogram is usually normal.[4, 6, 7-9] Greenblatt, Murray, and Root[10] reported that of 40 adult patients with uncomplicated diabetes, three had abnormal electroencephalograms, a proportion that is similar to the incidence of cerebral dysrhythmia found in the nondiabetic population. Diabetic acidosis and hypoglycemia do produce electroencephalographic abnormalities. Acidosis produces progressive slowing of electric activity. This reduction in electric activity is related in degree to the depth of coma, and is indistinguishable from other causes of coma; it is not related to the hyperglycemia, but requires the

acidosis and the associated electrolyte disturbances.[7, 9] Initially, the alpha rhythm becomes disorganized, being eventually replaced by generalized theta activity and delta activity of moderate amplitudes. As the coma deepens, the delta activity becomes dominant. Hypoglycemia induces an increased instability of the electroencephalogram as one of its earliest changes, with bursts of bilateral, synchronous, slow activity appearing earlier, and more readily, than in the same individual with a normal blood glucose content. Further slowing of the alpha rhythm, followed by generalized theta activity, occurs with continued hypoglycemia. Eventually, if hypoglycemia persists, spontaneous activity ceases and a flat tracing ensues. Therefore, both in acidosis and in hypoglycemia the general pattern is that of diffuse, progressive slowing, advancing from alpha through theta to delta activity. This electroencephalographic pattern is common to many coma-producing situations, and is not specific for diabetes.

The pattern often fails to return to normal until several days after effective treatment has been started. With hypoglycemia, the slow activity may show some asymmetry, and occasionally a well-marked focal abnormality may be seen. Coma with acidosis is sometimes associated with 'mitten-like' patterns resembling those commonly seen in hepatic coma.[6] When diabetes is complicated by cerebrovascular disease, the electroencephalographic patterns are those from patients with cerebrovascular disease regardless of origin.

The electroencephalographic tracings obtained from the patient we treated are interesting in several respects. Severely abnormal tracings were obtained 48 hours after initiation of treatment, and 36 hours after the blood glucose and other values had been restored to normal. The abnormality was generalized, and of a type not usually seen in relation to diabetic acidosis.

The periodic, slow, sharp waves seen were similar to patterns associated with other diseases, such as hepatic coma, or Jakob-Creutzfeldt disease as demonstrated in *Figure 5*. Finding this pattern, in the encephalogram of the patient of this current report, prompted an initial impression of the fatal progressive neuronal degenerative Jakob-Creutzfeldt disease. However, two days later the electroencephalographic pattern was practically restored to acceptable limits, corresponding with the patient's remarkable clinical improvement. Further tracings revealed persistent mild abnormalities, but nothing approaching the severe deviations in the initial tracing.

That the abnormality was related to some cerebrovascular complication of diabetes is unlikely, as it was not the type of pattern of a patient with cerebrovascular disease. A metabolic cause could not be determined, as all blood values were within normal limits. There was no evidence of other

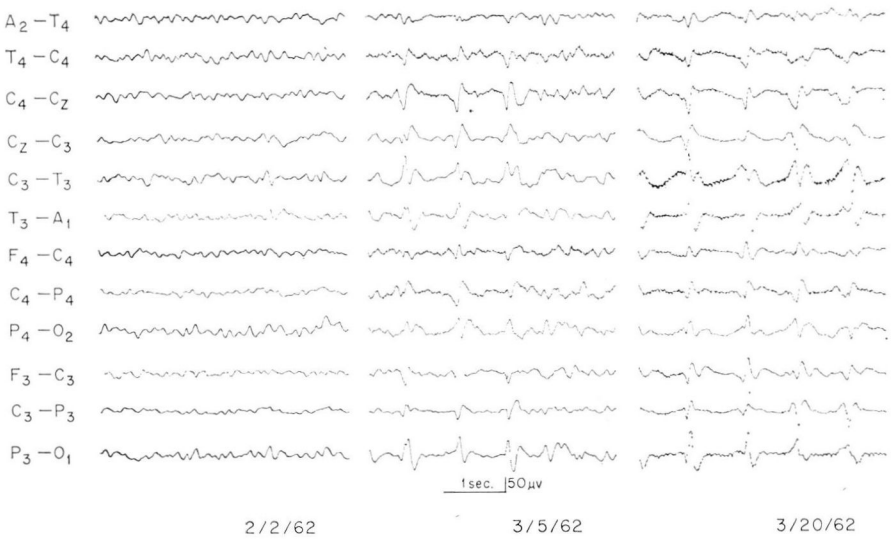

Fig. 5. Electroencephalographic tracings of a patient who subsequently died of Jakob-Creutzfeldt disease. Note the progressive development of periodic, slow, sharp waves in the recording of February through March, shortly before she died.

systemic disease, such as hepatic coma, which might be influencing the electroencephalogram. There was no evidence of a progressive degenerative process. Psychologic testing showed this woman to be actually clearer mentally than she had been at the time of her first examination six years previously.

The patient may have some type of subclinical seizure disorder, which was only manifested on the electroencephalogram at the time of decreased cerebral threshold, such as occurs with acidosis. Despite frequent comments in her chart noting episodes of confusion and disorientation, a tonic-clonic seizure was never observed, and the pattern was not that of a seizure discharge. Greenblatt, Murray, and Root,[10] found that 51 percent of 35 diabetic patients with frequent, severe, insulin reactions had abnormal encephalograms. Fabrykant[11] reported a series of severely labile diabetics among whom 80 percent were found to have abnormal electroencephalograms, 50 percent with severe abnormalities. Some of these patients had had clinical seizures, but many had what the authors termed "pseudo-hypoglycemic reactions" (the patients interpreted them as hypoglycemic reactions), consisting of episodes of nausea, fatigue, weakness, irritability, and temper tantrums. Blood glucose values when determined during these periods, frequently were normal or increased. The patients, under the

mistaken impression that they were suffering from a lack of sugar, would increase their dietary intake of sugar or take less insulin. The frequent result was ketoacidosis. It was postulated that these pseudo-hypoglycemic reactions were actually a type of seizure disorder, and seven of the patients were given a trial course of anticonvulsant drugs. The diabetes in five of the seven patients became easier to control, with fewer episodes of hypoglycemia and acidosis.

CONCLUSIONS

Neurologic disease is found in association with diabetes mellitus and is even considered by some to be a part of the disease process rather than a complication. The brain, spinal cord, and peripheral nerves are variously affected by the diabetes, either transiently or permanently, directly or indirectly. Much has yet to be learned about how the central nervous system reacts, including the effect of electric activity of the brain. This presents an atypical electroencephalographic pattern after diabetic acidosis.

SUMMARY

A patient with long-standing brittle diabetes had presenting symptoms of unusually slow recovery of mental abilities after episodes of ketoacidosis. The electroencephalogram demonstrated a severely abnormal pattern that is more often seen with progressive irreversible degenerative brain disease. The electroencephalographic pattern though, became more nearly normal as the diabetes became controlled. The patient's mentation returned to her previous normal state.

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