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DIABETIC MYELOPATHY

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Neurological complications of diabetes mellitus have been recognized for nearly a hundred years (de Calvi, 1860) and during the present century the orthodox teaching has been that diabetes mellitus may result in a symmetrical polyneuritis expressing itself largely by tenderness of the legs, loss of knee- or ankle-jerks, ataxia, sensory loss in the feet, and perforating ulcers, constituting the picture of diabetic pseudo-tabes. Martin (1953) has said that neuropathy is "characterized by a diffuse and ill-localized pain, vasomotor disturbances, thermal paraesthesiae, changes in tendon-reflexes, and often an alteration in pain sensibility in the feet without much impairment of touch or pressure. If the disorder progresses shooting pains develop, vibration sense is lost and, lastly, sense of touch and position as well as motor power becomes involved." These statements accord well with textbook descriptions (Gowers, 1893; Collier, 1926; Brain, 1951) and are supported by the literature of the past fifty years.

Rudy and Epstein (1945), after an analysis of 100 examples of diabetic neuropathy, stated that pain and sensory disturbances were the commonest manifestations, and neither they nor Rundles (1945), in an exhaustive survey of this subject, make any mention of a purely motor form of diabetic neuropathy. Jordan (1936) and Woltman and Wilder (1929) also emphasized that the neurological changes in diabetes mellitus are mainly sensory and that motor disturbances are rare. Although there are many casual references to weakness and wasting of muscles in association with sensory disturbances, the important observations of Bruns (1890) have been overlooked or dismissed as irrelevant. He described three patients, aged 58, 59, and 70, suffering from diabetes mellitus of short duration; all three developed severe pain in the hip and thigh followed by weakness and wasting of leg muscles without objective sensory loss, and each recovered fairly quickly following dietary restriction.

The reality of diabetic neuropathy without objective sensory loss has become apparent to us from clinical observation of the following patients; the case histories are presented in the order in which the patients came to our attention.

Case 1

A man aged 56 was first seen by one of us (H. G.) on March 14, 1950. He gave a two-months history of pain in the lumbar region and down the back of the right leg to the heel and toes, with less severe pain down the back of the left leg, getting steadily worse, and numbness down the back

of the thighs and calves. There was no specific complaint of weakness, but there had been polyuria and polydipsia for one year, with loss of 28 lb. (12.7 kg.) in weight. He had diffuse and severe wasting and weakness of all the muscles of the right leg, including the gluteus maximus, with loss of the right knee-jerk and both ankle-jerks. There was no sensory loss. The blood pressure was 150/80 mm. Hg. He was found to have glycosuria, and was admitted to hospital. The diabetes was well controlled by a diet of 10 black, 8 red (10B, 8R) Lawrence lines, and 10 units of zinc-protamine insulin (Z.P.I.) daily.

Investigations.—The cerebrospinal fluid (C.S.F.) protein was 68 mg. per 100 ml.; Lange 0013331000; fasting blood sugar, 350 mg. per 100 ml. Radiography of the lumbar spine was normal.

When seen again on June 8 he was still taking tab. codein. co. to relieve pain. His disability was stationary or increasing, and the left knee-jerk was now seriously depressed. On readmission to hospital on August 15 there was considerable weakness of most muscles of the left leg and he was only just able to walk. C.S.F. protein, 105 mg. per 100 ml. Lange 1233310000.

In December, 1950, both knee- and ankle-jerks were absent and the plantar responses were extensor. He did not begin to improve until early 1951; by April he could walk with one stick, and in November he was walking quite well. In May, 1952, his urine was constantly sugar-free on 12 units of Z.P.I. daily. By July he was walking very well unaided, the knee- and ankle-jerks were still absent and the right plantar response was extensor, but the left was now flexor—he said himself that there was "almost incredible improvement."

Electromyogram (D. T.)—On September 25, 1952, strength-duration curves were normal except for slight partial denervation changes in the right tibialis anticus muscle. Needle electrodes in both tibialis anticus and quadriceps muscles showed a decreased sustained pattern of motor-unit activity on voluntary contraction, with prominent single units superimposed, which in places amounted to discrete motor-unit activity. There was no spontaneous activity.

In January, 1953, there was only a little aching in the legs. He was walking quite well without sticks and was just able to jump off the ground. There was no demonstrable weakness or wasting of leg muscles and tone was normal. The knee-jerks were just present, but the ankle-jerks were still absent. The plantar responses were both flexor. There was no sensory loss. The diabetes was fully controlled, and he had gained 50 lb. (22.7 kg.) in weight.

Case 2

A man aged 63 was first seen by one of us (H. G.) on June 1, 1950. There had been pain in the left buttock, radiating down both back and front of the left leg to the ankle only, for two months. The pain was improving and

was said to be better when walking. The leg felt generally weak and he had fallen several times. There were no symptoms in the right leg. He claimed to have known that his knee-jerks had been absent all his life. There was patchy weakness and wasting of the left leg muscles, with depression of the left ankle-jerk and absent knee-jerks. He could walk only with a stick and was quite unable to jump off the ground. There was no sensory loss. He was admitted to hospital and found to have glycosuria.

Investigations.—The glucose-tolerance test showed impaired sugar tolerance. The C.S.F. protein was 139 mg. per 100 ml.

Treatment was begun with a 14B 9R Lawrence line diet together with 20 units of soluble insulin and 20 units of Z.P.I. daily, which was later reduced to 16 units of soluble and 16 units of Z.P.I. daily. He was fitted with a left toe-raising spring.

He began to improve rapidly, and by September had gained 14 lb. (6.4 kg.) in weight. On January 25, 1951, he was able to hop on one foot, and in April his insulin dosage was reduced by half.

Electromyogram (D. T.).—On September 18, 1952, strength-duration curves from both quadriceps and both gastrocnemii showed slight partial denervation. Needle electrodes in these muscles revealed irregular spontaneous motor-unit activity which was polyphasic in places. On voluntary contraction the motor-unit pattern was decreased, but superimposed isolated motor units gave an appearance approximating to that of discrete motor-unit activity.

When he was last seen, on February 19, 1953, the diabetes was controlled and the weight steady, though there was still some aching pain in the legs. The knee-jerks were absent, but the ankle-jerks were brisk; there was little weakness and he was walking normally.

Comment.—It was felt at this stage that both this patient and Case 1 were examples of a diabetic neuropathy of an unfamiliar type.

Case 3

A man aged 58 was seen by one of us (H. G.) in July, 1952, and diagnosed as another example of diabetic neuropathy similar to Cases 1 and 2. He had been attending a diabetic clinic for nearly two years, and at various times had been diagnosed as suffering from sciatica or motor neurone disease, with auricular fibrillation and hepatomegaly. In 1948 he developed a left external rectus palsy which recovered in six months. During 1950 he slowly developed pain in the right hip and down the right thigh to the knee, which was worse on walking but was unaffected by coughing. Early in 1951 he noticed polyuria and polydipsia, and glycosuria was detected. He became slowly worse, and by the spring of 1952 he could not walk more than 100 yards without a stick; in July he was unable to stand or sit up without help. There was weakness and wasting of the spinal muscles, with diffuse weakness and wasting of the legs, especially the right quadriceps, and some fasciculation of the left quadriceps. The knee- and ankle-jerks were absent. There was no sensory loss. The blood pressure was 105/60 mm. Hg.

Investigations.—The C.S.F. protein was 109 mg. per 100 ml.; Lange 0001210000; glucose-tolerance test showed evidence of impaired tolerance.

He was then admitted to Pinderfields Hospital, Wakefield, and given a 16B 8R Lawrence line diet and 10 units of Z.P.I. daily, together with suitable active physiotherapy. He began to improve rapidly.

Electromyogram (D. T.).—The patient was examined on three occasions during the second half of 1952. Strength-duration curves revealed widespread partial denervation of the leg muscles. Needle electrodes showed scanty fibrillation activity and widespread spontaneous motor-unit activity, often polyphasic in type, in the leg muscles. On voluntary contraction there was discrete motor-unit activity in the tibialis anticus (Fig. 1) and quadriceps muscles on both sides, but the surviving motor-units were of normal ampli-

tude. A short burst of low-frequency repetitive activity was detected in the left tibialis anticus muscle. In November, 1952, there was definite improvement in the electrical activity of the affected muscles.

On November 3 he was free from pain and gaining weight, and the urine was sugar-free. There was slight diffuse weakness of both legs with wasting, especially of the thighs, marked hypotonia, and absent knee- and ankle-jerks. Fasciculation was no longer apparent. He was just able to jump off the ground. On December 29 he could hop on his left foot, and the ankle-jerks were brisk. On February 23, 1953, there was still wasting of the thighs and calves, more marked on the left than the right, with slight weakness of all leg muscles. The right knee-jerk had returned and the plantar

FIG. 1.—Record of electrical activity during full voluntary contraction of the right tibialis anticus muscle of Case 3 (concentric needle electrode). Note the large discrete motor units standing out from a background showing little activity. Time: 10 msec.

responses were now extensor. Auricular fibrillation was still present, but was controlled. When last seen, on April 20, his condition was stationary and there was still no objective sensory loss.

Case 4

A woman aged 60 was first seen by one of us (D. T.) on October 5, 1952. There was a three-months history of severe aching pain radiating down the back of the left thigh and leg from the buttock to the outer malleolus and toes, worse when resting but unaffected by coughing or straining, and a two-months history of weakness of the left leg, causing her to fall several times. She had noticed polyuria and polydipsia for six months. There was slight wasting and marked weakness of the rotators and flexors of the left hip, left quadriceps, and extensors of the left foot and toes. The wasting was difficult to estimate because of obesity, but the left thigh diameter was 1½ in. (3.8 cm.) less than the right, and the left calf 1 in. (2.5 cm.) less than the right. There was no sensory impairment. The right knee-jerk was brisk, the left absent, the ankle-jerks were sluggish, and the plantar reflexes were flexor. The urine contained sugar but no acetone.

Investigations.—Radiography of the lumbar spine was normal. On October 10 the C.S.F. protein was 34 mg. per 100 ml. The glucose-tolerance test on October 13 showed impaired sugar tolerance.

Electromyogram (D. T.).—On October 17 the left quadriceps and left tibialis anticus muscles showed a greatly decreased pattern of motor-unit activity on voluntary contraction. Large isolated motor units were superimposed on this background activity, giving a picture approximating to discrete motor-unit activity. Similar but less marked changes were found in the right quadriceps and tibialis anticus muscles. There was no spontaneous activity.

The diabetes was controlled with a diet of 12B 8R Lawrence lines and 30 units of soluble insulin twice daily. She was given remedial exercises and improved steadily on this regime. On January 12, 1953, the pain, weakness, and wasting were less marked. Both knee-jerks and the left ankle-jerk were absent; the right ankle-jerk was just present. The plantar responses had become extensor. She was just able to jump off the ground. On February 14 she had improved still further. The pain was now slight and she could walk more easily. The physical signs were unchanged and the diabetes was under control. When last

seen, on April 16, she was still improving. The right knee-jerk was absent, but the left knee-jerk and both ankle-jerks were present. The plantar responses were still extensor, and there was no objective sensory disturbance.

Case 5

A man aged 73 was seen by one of us (H. G.) on November 9, 1952, at Scunthorpe at the request of Dr. Derek Millar. The history was unreliable, but the patient had noticed white stains on his shoes after micturition during the winter of 1951. Glycosuria had been detected by his general practitioner in the spring of 1952, but no therapeutic action had been taken until August, 1952, when he had been admitted to the Scunthorpe Memorial Hospital for stabilization. On admission he had ketonuria, which rapidly disappeared with a diet of 2,000 calories and the daily injection of 10 units of Z.P.I. His urine remained sugar-free, and numerous blood-sugar estimations varied from 120 to 168 mg. per 100 ml.

During the summer of 1952 the patient began to complain of pain about the left knee, with steady deterioration of gait, which was more pronounced on the left side than on the right. When seen in November he complained of diffuse pain in the left leg, excluding the foot, which was unaffected by posture; the pain was thought to be causing insomnia. He said that in 1944 he had had a precisely similar attack, but restricted to the right leg; at that time there was foot-drop with absent knee- and ankle-jerks, but no diagnosis was made and no investigations were performed. At first he could walk only with a calliper and crutches, but he slowly recovered during the next three years. All the tendon jerks in the legs had returned by August, 1952. He said that two of his brothers, aged 29 and 49, had died of diabetes in the pre-insulin days. Simple tests suggested early senile dementia. There was slight wasting of the left thigh and calf. Muscle-testing in the left leg was handicapped by pain, but there was unequivocal weakness of all muscles of the left thigh and normal power below the left knee. There was slight weakness of all muscles below the right knee. The left knee-jerk was absent, but the other tendon-jerks in the legs were present. The plantar responses were equivocal. There was no sensory loss, tenderness, or fasciculation. The blood pressure was 150/80 mm. Hg.

Investigations.—The C.S.F. protein was 120 mg. per 100 ml. The blood-sugar level was never higher than 168 mg. per 100 ml.

The patient refused further investigation and treatment. In January, 1953, his condition was stated to be about the same.

Comment.—It was felt that this was the fifth example of diabetic neuropathy without objective sensory loss; an important feature was the earlier history, which strongly suggested a previous attack between 1944 and 1947.

Discussion

It seems fairly certain that these five patients were suffering from the same syndrome. The youngest was 56 and the oldest 73. They all had diabetes of relatively short duration, varying from three years to six months. Although some had lost a great deal of weight and all showed impairment of glucose tolerance, none had very high blood-sugar levels or had ever been in coma. None had been treated with insulin before the onset of the neuropathy, although one had been under the supervision of a diabetic clinic. When first seen the duration of the neuropathy varied from one to fifteen months. All complained of pain in the legs, usually severe, always asymmetrical, and sometimes unilateral. The pain, though diffuse, tended to be maximal in the hip and thigh. All showed some degree of wasting of the leg muscles and loss of the tendon reflexes in the legs, again patchy and asymmetrical. At some stage three (Cases 1, 3, and 4) showed unequivocal extensor plantar responses, and in a fourth (Case 5) they were doubtful. In none was there any objective sensory disturbance, tenderness, or perforating ulcers. In spite of their ages it was

striking that all had normal vibration sense at the ankles. In all the patients the blood pressure was within normal limits. Four of them showed a high protein level in the C.S.F.

In the four patients on whom electromyography was performed a similar and severe abnormality was found. Strength-duration curves showed varying degrees of partial denervation of the leg muscles. There was some spontaneous motor-unit activity, but a striking absence of fibrillation potentials except in Case 2, and here they were scanty. There was a decreased pattern of motor-unit activity on voluntary contraction which amounted to discrete motor-unit activity in many areas. It is thought that these findings are compatible with, although certainly not diagnostic of, a cord lesion. They are unlike the usual

FIG. 2.—Record of electrical activity during full voluntary contraction of the left gastrocnemius muscle of a diabetic woman aged 65, with the typical clinical manifestations of polyneuritis (concentric needle electrode). Note the decreased but still sustained pattern of motor-unit activity and short duration and low amplitude of the individual motor units. Time: 10 msec.

findings in peripheral neuritis (Richardson, 1952), and bear no resemblance to the changes seen by one of us (D. T.) in other patients suffering from diabetic neuropathy of the recognized pattern (see Fig. 2). Here there is evidence of widespread denervation of the affected muscles with profuse fibrillation activity. The motor-unit pattern on voluntary contraction is well sustained, but there is a reduction in the amplitude and duration of the motor units.

Each patient was at once treated by means of a suitable diet, insulin, and active physiotherapy. Case 1 continued to deteriorate for some months, but ultimately made a complete recovery; Case 5, the oldest and least co-operative, showed no change at the time of writing, four months after he was first seen; the other three improved rapidly after the institution of treatment.

It is clear that the five cases we have described are identical with those recorded by Bruns (1890), and one of them (Case 5) had previously had a similar attack with spontaneous recovery, a point also noted by Bruns. The only important difference was that his patients recovered on dietary restriction alone, although this would no doubt be more drastic than is the practice to-day. It seems possible, however, that the natural history of this syndrome is one of spontaneous improvement, irrespective of the treatment employed. In Cases 2 and 3 improvement coincided with the institution of thorough control of the diabetes, but in Case 1 the condition deteriorated steadily for nearly a year, in spite of good control of the diabetes. The role of physiotherapy is also difficult to assess, but it would appear that vigorous active physiotherapy is of value, at any rate once spontaneous improvement has begun. It was noteworthy that considerable functional recovery could occur while the physical signs persisted unchanged or even deteriorated.

The peripheral site of the lesion in diabetic neuropathy has apparently been tacitly accepted for many years, but there are a number of references to cord lesions in the literature. Chromatolysis of anterior horn cells and degenerative changes in the posterior roots are mentioned by Courville (1945). Griggs and Olsen (1937) found degenerative lesions of the posterior and lateral columns in the cervical and mid-thoracic regions of the spinal cord. The most extensive modern study was reported by Woltman and Wilder (1929). In addition to changes in peripheral nerve fibres and the intraneural vessels they found

degeneration of the posterior columns and anterior horn cells in the spinal cords from three diabetic patients. Similar changes were described by numerous investigators at the turn of the century (Pryce, 1893; Nonne, 1896; Marinesco, 1903; Williamson, 1904; Bramwell, 1907).

Pathological studies have not been possible on the present series of patients, but there are clinical features which suggest that lesions may be present in their spinal cords. Not only is the disturbance limited to motor function but the distribution of the affected muscles is not compatible with the known distribution of peripheral nerves or nerve roots. The presence of extensor plantar responses in three, perhaps four, of the patients is unequivocal evidence of a central lesion. It is noteworthy that the plantar responses became extensor while the patients were under observation and were being treated. In Case 1 they became flexor again after some months. It may well be that the cord changes are secondary to atheromatous degeneration of the spinal arteries, but the patients all had normal blood pressures and there was no clinical evidence of arterial degeneration in their fundi or limbs. In this connexion the duration of the diabetes is probably of little importance. In the present series this has varied from six months to three years, calculated on the basis of the length of history of diabetic symptoms. This method, although obligatory, is probably fallacious in the case of middle-aged mild diabetics, and the duration of the disease may well be longer in our series (cf. Case 5). It seems to be agreed that the symptoms of the "classical" diabetic neuropathy usually develop in diabetes of long standing (Rundles, 1945), but this is not invariable. In Jordan's (1936) series of 120 diabetic patients with severe "neuritis" the condition preceded the onset of diabetes in 4, was coincident in 7, and in 28 developed within a year of the onset of diabetes.

Whatever the nature and cause of the lesion in these patients we feel that the existence of motor disturbances without objective sensory loss in diabetics, as described by Bruns over 60 years ago, is a fact of clinical importance. These patients are being misdiagnosed as suffering from other, often more serious, neurological conditions.

Summary

Attention is drawn to a form of diabetic neuropathy previously described 60 years ago but forgotten.

The syndrome consists of asymmetrical pain, weakness, muscle-wasting, and areflexia in the legs, without objective sensory disturbance, in middle-aged patients with diabetes mellitus of relatively short duration. The protein content of the C.S.F. is usually raised.

The plantar responses are often extensor and the electromyographic changes in the affected muscles are compatible with a myelopathic lesion.

Five new examples of the syndrome are described and the literature is reviewed.

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DIABETIC NEUROPATHY

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The changes which occur in the nervous system in diabetes were carefully studied in this country and in France before the end of the last century (Bouchard, 1884; Pavy, 1885; Auché, 1890). Williamson (1907, 1911, 1924) added further material. The subject was then neglected until interest was revived by the work of Jordan (1936). A considerable literature has accrued since then in the United States, but little has derived from this country.

On a routine examination of diabetic patients in hospital we found that neurological abnormalities were more the rule than the exception, and that acute nervous diseases were by no means rare. We have collected these acute cases and have also examined a consecutive series of 100 diabetic out-patients. For comparison, we studied 100 unselected chronic in-patients.

The present communication records the illnesses we encountered and attempts to analyse the significance of our findings.

Of the 100 diabetic out-patients, 57 showed neural abnormalities and three had an acute neurological illness at the time of examination. These figures agree with those of Jordan (1936), who found similar changes in 45.3% of his cases, with 2.5% suffering from "real neuritis." Rundles (1945) found neuritis in 4.5% of his cases but excluded abnormalities related to hyperglycaemia and also those which cause no symptoms. The incidence rates of diabetic neuropathy recorded in the literature vary from nil to over one-half. Such variation is explained only by the fact that the lesions discussed have often not been defined.

To reach a fuller clinical assessment of acute neuritic illness occurring in diabetes we have studied a further group of 50 patients. These were specially selected from among hospital in-patients, and therefore the findings in this group carry no indication of the incidence of the condition.

Classification and Terminology

We think that the comprehensive term "diabetic neuropathy" may be used to include all neurological changes occurring in diabetic subjects in whom there is no evidence of any alternative aetiological factor. Our cases have fallen most naturally into a scheme similar to that proposed by Grube (1899) in a neglected contribution. He wrote: "We have therefore three manifestations of nervous disturbance caused by the increase of sugar in the blood: (1) cramps or an acute irritation of the nerves; (2) neuritis or an acute inflammation of the nerves; and (3) a slow degeneration or nutritive change in the nerves."

No classification of the conditions under review has been generally accepted. The earlier schemes (Bernard