

wk history of polyuria and polydipsia. Past medical history was positive for hypertension and negative for diabetes mellitus, neurologic, thyroid, or liver disease. Medications included a thiazide diuretic and alpha-methyl dopa. Physical examination revealed an alert, oriented woman in no acute distress. Pulse was 72 beats/min and blood pressure was 136/88 mm Hg. The patient exhibited choreoathetotic movements of the right face, tongue, arm, and leg, and increased tone in the right upper and lower extremities. The serum glucose concentration was 584 mg/dl. Serum electrolytes, blood urea nitrogen, creatinine, calcium, phosphate, thyroid, and liver function tests were within normal limits. A CT scan of the brain revealed bilateral, 1-mm calcification of the caudate nuclei. The EEG was within normal limits. The choreoathetotic movements abated with return of the serum glucose to the 200–300-mg/dl range with insulin and hydration. The patient was discharged on haloperidol, intermediate-acting insulin, and the same antihypertensive regimen. Haloperidol was subsequently discontinued due to excessive sedation.

The patient did well for ~1 yr without any abnormal movements and serum glucose concentrations between 150 and 275 mg/dl when she presented with a 2-wk history of polyuria and a 3-day history of involuntary movements of the left face, tongue, arm, and leg, but no abnormal movements of the right side. The remainder of the examination was unchanged. The serum glucose level was 622 mg/dl. Serum electrolytes, calcium, phosphate, thyroid, and parathyroid hormone levels were within normal limits. CT scan of the brain revealed increasing calcification of the posterior head of the caudate nuclei bilaterally. EEG was again within normal limits. The choreoathetotic movements abated after the serum glucose level was normalized with insulin. The patient was discharged on intermediate-acting insulin and has had no further abnormal movements with continued good control of hyperglycemia.

#### DISCUSSION

Acquired paroxysmal choreoathetotic movement disorders arise from hypoparathyroidism, hyperthyroidism, and several neurologic diseases.<sup>2,3</sup> A review of the etiologies of acquired paroxysmal choreoathetosis revealed that 60% of the cases are unilateral, 30% are bilateral, and the remaining 10% are alternately unilateral and bilateral.<sup>2</sup> Our case demonstrates that choreoathetotic movements associated with diabetes mellitus may be alternately unilateral during periods of hyperglycemia and be successfully managed by restoring normoglycemia with insulin. Insulin therapy and hydration have been shown to be effective therapies for other neurologic manifestations of hyperglycemia and hyperosmolarity, including focal seizures and transient ischemic attacks,<sup>4</sup> by reestablishing previous osmotic gradients.

The choreoathetotic movements and basal ganglia calcification reported in this case are also seen in idiopathic hypoparathyroidism, a rare disorder in which neurons in the basal ganglia damaged by anoxia or vascular insufficiency are

predisposed to reversible dysfunction during hypocalcemia. The calcification of the basal ganglia is felt to represent an irreversible process of pericapillary deposition of acid mucopolysaccharides, iron, and calcium that follows an anoxic, vascular, or encephalitic injury.<sup>5</sup> In several autopsy studies in diabetic individuals, areas of calcification correspond to severe sclerosis of basal ganglia vasculature with resultant encephalomalacia and loss of neuronal parenchyma.<sup>6</sup> These histopathologic findings have not been correlated clinically with the presence of a movement disorder since only 25% of patients with basal ganglia calcification will develop extrapyramidal deficits.<sup>5</sup> The infrequent reporting of choreoathetosis with diabetes mellitus would indicate that both preexisting neuronal degeneration of the basal ganglia and the acute metabolic effects of hyperglycemia are required to produce a clinical picture of alternating choreoathetosis.

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## Remission of NIDDM After Irradiation of Metastatic Cervical Lymph Nodes

Remission of overt diabetes mellitus (DM) after removal of invasive epidermoid carcinoma of the tongue was reported by Rex and Duckworth<sup>1</sup> in 1984. Diabetes in the 54-yr-old man was detected when he was admitted for sore throat, dysphagia, and weight loss of 4 mo duration. Examination revealed a 2-cm exophytic lesion at the base of the tongue

extending to right vallecula. There was no palpable lymph node in the neck. He required 35–40 U exogenous insulin for control of hyperglycemia. After surgery, he received tele cobalt therapy, a tumor dose of 6000 rads to the base of the tongue. Glucose tolerance tests (GTT) done 1 yr later and 2 mo after discontinuing insulin were completely normal.

We report a similar case. A 60-yr-old man with a history of DM for 3 yr and mild hypertension for 11 yr was admitted to our institution on December 3, 1983, with a provisional diagnosis of carcinoma nasopharynx with metastatic left cervical lymphadenopathy. He had difficulty swallowing, resulting in reduced food intake and loss of weight (3.0 kg). Mass in the upper neck was first noted 3 mo before his admission and had gradually increased in size. It was 3.0 cm in diameter, partially fixed, and not tender. All efforts made to locate the primary site by various procedures were unsuccessful. Radical neck dissection was performed on December 6. Histopathology of the mass showed "(A) Tumor replacing the lymph nodes consists of large cellular masses of non-keratinised squamous cells having prominent anaplasia. (B) The salivary tissue and associated lymph nodes are unremarkable. Diagnosis: Metastatic grade III squamous cell carcinoma in cervical lymph nodes." He made an uneventful recovery and was discharged from the hospital on December 13. He was followed with radiation therapy as an outpatient using 60 cobalt from December 19, 1983 to February 8, 1984. A dose of 6500 rad was delivered to the supposed primary site of nasopharynx using three portals and 5000 rad to the cervical lymph nodes by parallel opposing antero-posterior and postero-anterior portals in 30 fractions.

In 1980, the patient was diagnosed to be diabetic after a GTT. Initially, he was put on chlorpropamide, but as his periodic (3–4 mo) fasting and/or 2-h postprandial blood glucose values persistently remained >14.0 mmol/L (250 mg/dl), he was switched to glibenclamide, and then insulin was added to the regimen. He came under our observation when admitted to the hospital. At that time, the patient was taking a single dose of 40 U lente insulin before breakfast and 15 mg glibenclamide daily, one 5-mg tablet at breakfast, lunch, and dinner. For hypertension, he received a single tablet containing 0.1 mg reserpine, 10 mg dihydralazine sulfate, and 10 mg hydrochlorothiazide. He received no other medication. His blood pressure was maintained at ~150 mm Hg systolic and 90 mm Hg diastolic. Glibenclamide was omitted on December 3, and the patient was put on two doses of insulin; split dose of regular plus intermediate-acting insulin before breakfast and intermediate-acting insulin before dinner. His blood glucose was monitored four times daily to adjust the insulin dose to maintain his plasma glucose levels between 8.0 and 11.0 mmol/L (140–200 mg/dl). He was stabilized on a total dose of 36 U insulin per day. His insulin dose was increased to 48 U/day with increased food intake after surgery. He was followed regularly as an outpatient. Periodic plasma glucose examinations thereafter persistently showed fasting value <5.6 mmol/L (100 mg/dl), 2-h postprandial <6.7 mmol/L (120 mg/dl) with glycosylated hemoglobin (GHb) <6.5% (normal range 5.4–7.0%). No hypoglycemic episodes were reported. His insulin dose was gradually de-

creased and insulin finally omitted on May 23, 1984, i.e., after 6 mo. The patient regained his normal weight. Follow-up at 3-mo intervals thereafter showed similar plasma glucose values. GTT done on March 4, 1985 (i.e., 10 mo after omission of insulin) was normal as per National Diabetes Data Group Criteria<sup>2</sup> and showed the following plasma glucose values: fasting, 5.2 mmol/L (94 mg/dl); 1 h, 9.6 mmol/L (175 mg/dl); 1½ h, 9.0 mmol/L (162 mg/dl); and 2 h, 7.0 mmol/L (137 mg/dl). On this occasion his GHb was 8.4%.

At present, the patient has no complaints and is fairly active with no evidence of recurrence of malignancy. He regained 3.0 kg of weight loss soon after surgery and continues to maintain his normal weight of 53.0–54.0 kg. The patient states that he has maintained this weight for ~10 yr. Therefore, in this case remission cannot be attributed to changes in weight. His blood glucose was noted to be high on several occasions before admission. Also, in the hospital before surgery and after he was on normal diet, elevated plasma glucose concentrations were noted, even though the patient received insulin twice daily (Table 1). Hence, he continued to be diabetic from diagnosis until radiotherapy was initiated.

Remission in non-insulin-dependent diabetes is uncommon.<sup>2</sup> It can occur after weight loss, gestational diabetes, or after correction of certain endocrine disorders.<sup>2,3</sup> None of these factors was operative in both cases discussed in this report. Some patients may be normoglycemic after withdrawal of sulfonylurea,<sup>4,5</sup> although our patient needed insulin for 6 mo after omission of glibenclamide. Unlike the patient of Rex and Duckworth,<sup>1</sup> our patient had diabetes for 3 yr before the onset of the malignancy. Hence, development of diabetes or its remission cannot be attributed to tumor growth or its removal. However, both patients had (1) squamous cell carcinoma in the head and neck, and (2) radiation therapy with 60 cobalt delivered to the primary site and the neck. Insulin requirements began to fall soon after radiotherapy. In both patients, a fall in fasting blood glucose to <5.6 mmol/L (100 mg/dl) was noted soon after initiation of radiation therapy. It is difficult to explain this total remission, and all explanations must be considered speculative. We believe radiation therapy with 60 cobalt directed to the primary site and the neck may have contributed to remission of diabetes. This

TABLE 1  
Plasma glucose values as measured by autoanalyzer

Date	Sample	Plasma glucose (mg/dl)	Comment
December 4, 1983	Fasting	106	December 3, glibenclamide omitted December 6, operated. On i.v. fluids; oral feedings after 10:00 p.m.
	Prelunch	180	
December 5, 1983	Fasting	225	
	2 h postlunch	250	
December 8, 1983	Fasting	262	
December 10, 1983	Predinner	124	

theory must be investigated critically to see if this coincidence is significant, or if radiation therapy to the neck helps in any way to decrease insulin resistance, a feature of non-insulin-dependent diabetes.

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## Standard EKG: A Useful Screening Method for Diabetic Autonomic Neuropathy

Cardiovascular tests based on heart rate and blood pressure responses to various stimuli are generally used in the diagnosis of diabetic autonomic neuropathy.<sup>1</sup> As reduced spontaneous heart rate variation is a predominant feature of cardiac autonomic nervous involvement,<sup>2,3</sup> we decided to measure the R-R interval variation in routine EKG recordings from a group of diabetic and healthy subjects in order to evaluate the usefulness of the standard EKG as a screening method for diabetic autonomic neuropathy.

The series consisted of 122 subjects with type I diabetes, aged 15-63 yr (mean 29), and 40 healthy subjects, aged 16-50 yr (mean 28). The mean duration of diabetes was 12 yr (range 0-33) and 55 diabetic patients had microvascular complications. None had any other diseases or received any medication known to interfere with autonomic nervous function.

Heart rate responses to deep breathing and to standing up (the 30:15 ratio) were determined using a Hewlett-Packard (Andover, Massachusetts) 8812 A-rate computer following a standard technique.<sup>1</sup> Standard 12-lead EKGs (rate 50 mm/s) without any maneuvers were recorded by the laboratory staff according to the regular hospital routine with the subjects lying quietly in a supine position. The difference between the longest and shortest R-R interval was determined from these EKG strips (of ~12 s duration) in order to obtain the R-R interval variation in the EKG.

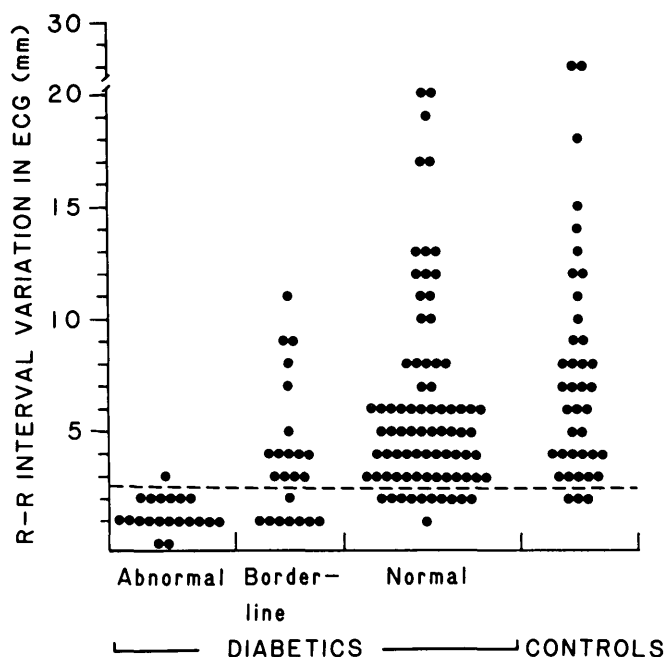


FIG. 1. The R-R interval variation in the EKG in diabetic subjects with abnormal, borderline, and normal autonomic nervous function tests and in healthy controls (see text).

The diabetic subjects were grouped using the generally accepted normal values for autonomic nervous function tests.<sup>1</sup> Twenty diabetic subjects had abnormal heart rate responses to deep breathing, nine also had abnormal 30:15 ratios, and one had symptomatic postural hypotension. Seventy-nine diabetic subjects had normal cardiovascular reflexes and 23 had borderline responses to deep breathing. Two controls had borderline responses to deep breathing.

Figure 1 plots the R-R interval variation in the EKG in the diabetic and control subjects. The mean R-R interval variation plus two standard deviations ( $=2.7$  mm) in the diabetic subjects with abnormal autonomic nervous function tests was taken as the borderline above which autonomic neuropathy was considered unlikely. A standard EKG strip thus had a sensitivity of 95% and specificity of 81% in diagnosing diabetic autonomic neuropathy. The positive predictive value of the EKG was 49% and the negative predictive value, 99%.

The reproducibility of the reduced R-R interval variation in the EKG was estimated in 10 patients with abnormal cardiovascular reflexes by measuring the R-R intervals in a total of 25 EKGs taken at later dates. The mean R-R interval variation in these recordings was 1.1 mm (range 0-2).

Regular EKG checks are recommended for diabetic subjects in order to reveal latent coronary artery disease, which is common among these patients.<sup>4</sup> Our findings show that a routine EKG also provides a useful screening for diabetic autonomic neuropathy. A marked R-R interval variation in the EKG rules out autonomic neuropathy and makes further testing unnecessary (as in 70% of the present diabetic subjects). On the other hand, a blunted R-R interval variation