reaction to each of three drugs, unrelated in structure or metabolism, but having the common property of killing mycobacteria.

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Spontaneous hypoglycaemia in active acromegaly and its response to bromocriptine

Although a quarter of acromegals have definite diabetes mellitus and a further quarter decreased glucose tolerance, spontaneous hypoglycaemia has never been reported. Here we describe reactive hypoglycaemia in a patient with active acromegaly, and his symptomatic and metabolic response to treatment with bromocriptine.

Case report

A 39-year-old man diagnosed as acromegalic 11 years previously and taking replacement doses of thyroxine, cortisone acetate, and testosterone presented with attacks of sweating, shaking, dizziness, and hunger. The attacks had occurred about every two weeks over the preceding two years. They usually occurred in the midmorning after brisk exercise and were relieved by food. In one attack the blood glucose concentration was recorded as 2.0 mmol/l (36 mg/100 ml). He had no symptoms to suggest diabetes mellitus and no family history of diabetes or any other endocrine disease. On examination he was typically acromegalic, 180 cm tall, and weighed 113 kg; photographs of him showed that his facial features were still changing.

After a three-day fast the whole-blood glucose concentration (measured by the glucose oxidase method) was 2.5 mmol/l (45 mg/100 ml), and plasma insulin 13.5 mU/l. He was symptom free. Three hours' walking on a treadmill at 5.5 km/h after a normal breakfast provoked no symptoms, and the lowest blood glucose concentration recorded was 3.5 mmol/l (63 mg/100 ml). He had symptoms of hypoglycaemia when his blood glucose concentration was lowered to 1.9 mmol/l (34 mg/100 ml) by giving him fish insulin, but throughout the test his endogenous insulin production was appropriately suppressed, which excluded a pancreatic β -cell insulinoma.¹ His symptoms resembled those he experienced during spontaneous attacks.

The table shows the whole-blood glucose, plasma immunoreactive insulin, and serum growth hormone concentrations in three 50 g oral glucose tolerance tests carried out when the patient first presented and after he had been treated with a low-calorie diet and bromocriptine (for the first month 10 mg and thereafter 20 mg daily in four divided doses). In the initial glucose tolerance test the peak plasma insulin concentration was very high (702 mU/l) and the serum growth hormone moderately raised (mean 36 mU/l).

Blood glucose, serum growth hormone, and plasma insulin concentrations during glucose tolerance tests in an acromegalic man before treatment and when taking first 10 mg and then 20 mg bromocriptine daily

Body weight (kg)	Treatment	Measurements	Time (min) after 50 g oral glucose										
			0	30	60	90	120	150	180	210	240	270	300
113	Pretreatment	Blood glucose (mmol/l)	2.9	3.7	5.5	2.9	3.9	4.4	3.3	3.1	3.0	3.1	
		Plasma insulin (mU/l)	48.6	119.0	702.0	224.0	86.3	102.7	32.4	27.2	27.8	18.1	13.0
		Serum growth hormone (mU/l)	47.6			22.2	23.7	27.3	30.1	38.0	41.3	46.9	46.1
108	10 mg bromocriptine daily	Blood glucose (mmol/l)	3.4	4.3	3.4	4.1	4.5	2.8	3.4				
		Plasma insulin (mU/l)	10.8	258.0	43.9	87.3	318.0	32.7	42.7				
		Serum growth hormone (mU/l)	23.5	25.7	21.2	18.7	16.9	15.9	18.2				
107	20 mg bromocriptine daily	Blood glucose (mmol/l)	4.4	5.0	5.2	5.3	5.1	5.0	4.7	4.3	4.7	4.8	3.0
		Plasma insulin (mU/l)	7.1	30.1	25.8	11.4	11.5	14.0	9.4	34.0	34.4	31.8	7.1
		Serum growth hormone (mU/l)	25.2	23.2	21.0	19.6	21.0	20.6	18.6	23.0	23.5	18.1	19.5

Conversion: SI to traditional units—Glucose: 1 mmol/l $\approx$ 18 mg/100 ml.

When the patient was taking 10 mg bromocriptine daily the mean serum growth hormone concentration was reduced to 20 mU/l and the plasma insulin peak was earlier and lower (258 mU/l). When he was having 20 mg bromocriptine daily the mean serum growth hormone concentration was 21 mU/l and the plasma insulin concentration had fallen to within the normal range (peak = 30 mU/l).

Comment

Acromegaly is not known to be one of the endocrine disorders that produce hypoglycaemia, but an increase in the endogenous insulin response to intravenous glucose has been noted in acromegalic patients.² The impaired peripheral action of insulin,³ however (which is perhaps due to alterations in insulin receptors⁴), is thought to prevent reactive hypoglycaemia.

We have little doubt that in this case the attacks were due to spontaneous reactive hypoglycaemia, although we did not observe one during investigation. We suggest that before treatment massive overproduction of insulin in response to breakfast followed by brisk exercise led to the patient's hypoglycaemia. His obesity may have added to the insulin antagonism, and hyperinsulinism. At presentation his weight was 40% above the standard for a large-framed man, though the usual weight charts are not entirely appropriate in acromegaly.

The table shows the interesting metabolic response to bromocriptine. Probably the primary action of bromocriptine was to reduce insulin antagonism by lowering growth hormone concentrations. Certainly, we have no evidence that bromocriptine has a direct effect on the secretion of insulin in acromegaly.⁵ Dietary restriction and weight reduction may have contributed also to the fall in plasma insulin concentration. In 18 months taking 20 mg bromocriptine daily the patient has had no further attacks, growth hormone concentrations are suppressed, and glucose tolerance and plasma insulin remain normal.

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