Changes in glucose tolerance and development of gall stones during high dose treatment with octreotide for acromegaly

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Ooctreotide, a longer acting analogue of somatostatin, growth hormone inhibiting hormone, lowers growth hormone concentrations in resistant acromegaly and is well tolerated by most patients. There have been reports of changes in blood glucose values and isolated reports of gall stone formation in people receiving octreotide. Patients with somatostatinomas often have diabetes and gall stones. We have studied prospectively both glucose tolerance and, by ultrasonography, gall stone formation in 10 acromegalic patients receiving high dose octreotide treatment.

Patients and methods

Ten acromegalic patients (mean age 45, mean duration 11 years) were treated with octreotide. All 10 had undergone surgery or irradiation, and eight had received bromocriptine (four of whom were intolerant). All had a baseline 24 hour profile of growth hormone measured every two hours, followed by a 75 g oral glucose tolerance test starting at 1000. The initial dose of octreotide was 100 μg subcutaneously at 0800, 1600, and 2400 for one month and was increased at monthly intervals by 300 μg a day to a maximum of 1500 μg/day if the mean of the 12 growth hormone measurements remained >=5 μU/ml. Treatment continued at this dose for a further seven months. The glucose tolerance test was repeated at six months. (One insulin dependent diabetic patient did not have a glucose tolerance test.) Seven patients had a baseline gall bladder ultrasound examination (Diasonic 400R with a 3-5 MHz probe), which was repeated at six months and one year.

One patient was withdrawn from the study because of persistent diarrhoea and another because of insulin resistant diabetes. Six were maintained on 1500 μg daily, one on 1200 μg daily, and one on 600 μg daily. Mean serum growth hormone fell from 36 (SE 10) μU/ml at the onset of the study to 8 (1) μU/ml and 8 (2) μU/ml (n = 8, p<0.05) after six and 12 months respectively. Of three patients with normal glucose tolerance initially, one remained normal, developed impaired glucose tolerance, and one became diabetic (by World Health Organisation criteria). Of four patients who had impaired glucose tolerance initially, two remained unchanged, one developed diabetes, and the other returned to normal glucose tolerance. One of the seven patients who had normal baseline ultrasonic appearances of the gall bladder had developed multiple small gall stones after six months of treatment, and another two developed similar findings after one year (fig). One patient did not have an initial examination but after four months of therapy had four gall stones, which remained unchanged at each assessment.

Comment

Octreotide successfully lowered growth hormone concentrations and was generally well tolerated. It had a heterogeneous effect on glucose tolerance. Three patients became more glucose intolerant, three showed no change, and one had improved glucose tolerance. As growth hormone induces insulin resistance and octreotide reduces both insulin and growth hormone secretion the relative change of each will influence glucose tolerance.

The high incidence of new gall stones found in our prospective study is a cause for concern. Previously
Lyme disease facial palsy: differentiation from Bell’s palsy

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Lyme disease is caused by the spirochaete Borrelia burgdorferi and is transmitted to humans by the tick Ixodes ricinus. Infection may affect the skin, nervous system, heart, and joints, and one presentation is of a facial nerve palsy that resembles Bell’s palsy. There are, however, differences that are important to recognise so that a palsy caused by infection with

B burgdorferi may be treated early and appropriately, which may lead to a more rapid and complete recovery.

I describe nine patients who presented with facial nerve palsies between February 1986 and August 1988. Eight of these had Lyme disease and one had Bell’s palsy.

Case reports

A woman aged 32 presented with painless erythema and swelling of the left side of her face. This became worse over the next 24 hours, resulting in considerable induration of her upper lip, pinna, and periorbital tissues. She developed a headache, pain down the side of her neck, and parasthesia of her left hand. Erythema of the left tympanic membrane and an early lower motor neurone facial nerve palsy were found on examination. Lyme disease was diagnosed, and she was treated with oral tetracycline for one week. She made a quick and full recovery. Serological testing with western blotting to detect IgM and IgG later confirmed the diagnosis.

The table summarises the clinical data on the eight other patients. All except one (case 5) presented in the summer, and all lived near land inhabited by deer (hosts for the ticks) or had recently walked in the New Forest. Only three patients, however, had evidence of having been bitten by a tick.

Four patients received treatment with oral tetracycline, but I found that unless this was started within 48 hours after the onset of the palsy it made no difference to the time taken to recover. All patients, with or without treatment, recovered eventually. Bell’s palsy was diagnosed in case 8 because the facial palsy was not associated with facial induration and swelling, and serological tests did not show antibodies to B burgdorferi.

There have been only isolated reports of gall stones occurring during octreotide treatment.1 Gall bladder contraction and cholecystokinin secretion in response to food are almost abolished by its administration2 and may contribute to stone formation. The high incidence of gall stones might have been due to the higher doses of the drug which we used. None of our patients had symptoms from the gall stones, and the correct management of the stones remains problematical.3 While further prospective studies of the incidence of gall stones during octreotide treatment are awaited we recommend the use of the smallest effective dose of octreotide.

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