The effects of octreotide in a patient with Nelson's syndrome

Fahrettin Kelestimur, Cengiz Utaş, Ömer Özbakir, Ahmet Selçuklu, Olcay Kandemir, Nevzat Özcan

Summary

We have administered octreotide, 100 µg tid, to a 27-year-old man with Nelson's syndrome. After seven days of therapy, adrenocorticotropin levels fell to 54% of initial values, and some shrinkage of the tumour was observed. This study indicates that octreotide therapy may have a role in the treatment of Nelson's syndrome.

Keywords: octreotide, Nelson's syndrome

Nelson's syndrome is a rare condition now as a result of the advent of pituitary microsurgery for Cushing's disease. These tumours are rather invasive and need urgent treatment. Pituitary surgery is the first line treatment, although pituitary irradiation has been suggested as primary or secondary therapy.¹ Some tumours are not responsive and carry a poor prognosis. Somatostatin has been shown to be effective in the inhibition of adrenocorticotropin release by the cultured pituitary cells in a patient with Nelson's syndrome.² However, there are a few reports about the effects of the long-acting somatostatin analogue octreotide (SMS 201-995) on adrenocorticotropin secretion in Nelson's syndrome. Recently we had the opportunity to investigate the effect of octreotide on adrenocorticotropin secretion and tumour size in a patient with Nelson's syndrome.

Case report

A 27-year-old man who underwent total bilateral adrenalectomy for Cushing's disease in 1987 in another hospital was admitted to our hospital because of skin pigmentation. He had been on prednisolone, 5 mg a day, since 1987. He had recently noticed increased pigmentation and muscle weakness. On physical examination, blood pressure was 100/60 mmHg, pulse rate 80 beats/min. He was hyperpigmented. Laboratory investigations showed fasting blood glucose 3.9 mmol/l, sodium 125 mmol/l, potassium 6.3 mmol/l, chloride 91 mmol/l, serum urea 4.9 mmol/l, creatinine 88.4 mmol/l, liver function tests within normal limits. Baseline hormone levels were as follows: prolactin 4.50 µg/l (3.3–10); follicle-stimulating hormone 5.63 IU/l (4–10); luteinising hormone 3.01 IU/l (1–8); free

triiodothyronine 2.24 pmol/l (2.1–6.1); free thyroxine 17.24 nmol/l (10–25); thyroid-stimulating hormone 2.32 mU/l (0.6–4.6); adrenocorticotropin 56.4 pmol/l (0–8.1), repeated 84.3 pmol/l. Computed tomography (CT) scan of the pituitary fossa showed suprasellar extension of the pituitary tumour. The diameter of the tumour was 18.7 mm (figure 1). We decided to treat the patient by transphenoidal microsurgery which is the first choice of therapy, but before surgery we administered octreotide to investigate its effectiveness in decreasing adrenocorticotropin secretion and tumour size. Before the administration of octreotide, blood samples for adrenocorticotropin detection were taken every 15 minutes for one hour in the morning between 8 and 9 am. The patient was then given octreotide at a dose of 100 µg tid subcutaneously for seven days, after which blood samples for adrenocorticotropin were again taken, as mentioned above. A second CT scan of the pituitary tumour was also taken (figure 2). The tumour was then successfully removed by the transphenoidal route. Using immunohistochemical techniques the tumour was found to stain strongly for adrenocorticotropin but not for growth hormone, follicle-stimulating hormone, luteinising hormone, or prolactin. Histopathologic and immunohistochemical examinations confirmed Nelson's syndrome.

Mean plasma adrenocorticotropin levels before and after octreotide therapy were 66.7 pmol/l and 36 pmol/l, respectively, a

Figure 1 CT scan of pituitary tumour before treatment with octreotide

Erciyes University
Medical School, 38039
Kayseri-Turkey
Department of
Internal Medicine
(Endocrinology)
F Kelestimur
C Utaş
Ö Özbakir
Department of
Neurosurgery
A Selçuklu
Department of
Pathology
O Kandemir
Department of
Radiology
N Özcan

decrease of approximately 54% (see table). Octreotide therapy also led to a 3-mm reduction in tumour diameter (as shown in figures 1 and 2).

Discussion

The treatment of Nelson’s syndrome is difficult. Although pituitary microsurgery and/or irradiation have been reported to be effective therapeutic interventions, some cases still carry a poor prognosis.¹ Somatostatin, dexamethasone, bromocriptine and cyproheptadine significantly inhibited adrenocorticotropin release by cultured pituitary cells in a patient with Nelson’s syndrome.² In another study Shibasaki and Masui showed that somatostatin-14 and somatostatin-28 suppressed the secretion of propiomelanocortin-derived peptides by the adenoma obtained from a patient with Nelson’s syndrome.³ Some studies have shown infusion of native somatostatin to be effective in Nelson’s syndrome. In one of them, Thyrell *et al* infused 500 µg somatostatin in one hour to five patients with Nelson’s syndrome which resulted in a sustained progressive fall in plasma adrenocorticotropin levels to 40–71% of the basal values with a return toward initial levels after cessation of the infusion.⁴ They also concluded that somatostatin receptors are not functional or present in normal pituitary tissue, but are present in Nelson’s syndrome. The degree of decrease in adrenocorticotropin level was similar to our result, ie, 48% and 54%, respectively. Octreotide has been used successfully in pituitary and neuroendocrine tumours of the gut.^{5–7} There are some reports of the effects of octreotide in patients with neuroendocrine tumours producing ectopic Cushing’s syndrome.⁷ The results of these studies suggest that octreotide produces striking improvements in the syndrome of ectopic adrenocorticotropin secretion. In patients with pituitary-dependent hypercortisolism octreotide treatment resulted in no change in blood adrenocorticotropin or cortisol levels.⁸ It was reported that *in vitro* autoradiography did not demonstrate the binding of octreotide to the tumour tissue in a patient with an adrenocorticotropin-secreting pituitary adenoma.⁹ In contrast, the secretion of excess adrenocorticotropin in patients with pituitary adenomatous development (Nelson’s syndrome) following bilateral adrenalectomy

Figure 2 CT scan of pituitary tumour after treatment with octreotide

Table Adrenocorticotropin levels before and after administration of octreotide

Time (min)	Adrenocorticotropin (pmol/l)	
	Before	After
0	72.7	24.9
15	68.0	20.4
30	65.2	53.9
45	60.6	44.8

has been shown to be suppressed by octreotide in one patient. Visual field defects were improved after six weeks of treatment despite the absence of tumour shrinkage on CT scan and continued suppression of adrenocorticotropin levels was demonstrated over two years.⁸ We think that variability in the concentrations of somatostatin receptors in adrenocorticotropin-secreting tumours may explain the variations in response to octreotide. In our patient octreotide worked well and decreased adrenocorticotropin levels by at least 50% after seven days of treatment (100 µg tid). This fall in adrenocorticotropin levels may be related to the lack of negative feedback mechanism which was due to bilateral adrenalectomy, as adrenocorticotropin release by normal corticotrophs appears to be sensitive to somatostatin only in the absence of the physiological peripheral feedback regulation by glucocorticoids.¹⁰

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