Failure of bromocriptine to maintain reduction in size of a macroprolactinoma

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Abstract

A patient with a macroprolactinoma was treated with bromocriptine 15 mg daily. Both the size of the tumour as shown by computed tomography and the serum prolactin concentration decreased over several months but then increased. The dose of bromocriptine was increased to 40 mg daily but tumour growth continued, and the tumour was resected. Production of prolactin by cultured cells was not inhibited by high concentrations of bromocriptine, suggesting that regrowth of the tumour was due to cells resistant to dopamine agonist action.

This case of regrowth of a prolactinoma during bromocriptine treatment after an initial reduction in size indicates the need for close surveillance especially of patients whose serum prolactin concentration fails to fall into the normal range with bromocriptine treatment.

Introduction

Treatment with bromocriptine reduces the size of macroprolactinomas and is advocated as the initial treatment of choice. Clearly, the tumour may enlarge when bromocriptine treatment is stopped, but no case has been reported in which the size of the tumour decreased initially with bromocriptine treatment but subsequently increased despite continuing treatment. We now report such a case.

Case report

A 47 year old man presented in November 1981 with a history of failing vision for five months and headaches for one month. Libido and potency had waned over the past five years, and he had had diminished energy and cold intolerance for several months. On examination he had reduced visual acuity (right 6/24, left 6/36) and bitemporal hemianopia. Both tests were soft and 12 ml in volume. X-ray examination of the skull showed an enlarged and eroded pituitary fossa. A computed tomograph of the head showed a large contrast enhancing pituitary tumour with suprasellar extension (fig A). Serum prolactin concentration was 135 000 mU/l (normal < 500 mU/l). Serum follicle stimulating hormone concentration was 2 IU/l (normal 3-20 IU/l), luteinising hormone concentration 3 IU/l (normal 5-20 IU/l), and testosterone concentration 3 nmol/l (0.87 ng/ ml) (normal in men 10-35 nmol/l (2.9-10.1 ng/ml)). Serum thyroxine concentration was 40 nmol/l (3-1 mg/100 ml) (normal 60-150 nmol/l (4.7-11.7 mg/100 ml)), free thyroxine index 31 (normal 50-140), and serum thyroid stimulating hormone concentration 1 mU/l (normal < 4 mU/l). Plasma cortisol concentration was 47 nmol/l (1.7 μg/100 ml) (normal value at 0800 > 150 nmol/l ( > 5.4 μg/100 ml)).

Adrenal and thyroid hormone replacement was begun. Bromocriptine treatment was started at 2.5 mg daily increasing to 15 mg daily in divided doses over one week; this was continued uninterrupted throughout his care. Subjective visual improvement occurred within...
48 hours, and improvement in visual fields was recorded within three weeks, when visual acuity in each eye was much improved (right 6/5, left 6/9) and serum prolactin concentration had fallen progressively to 31,000 mU/l. Reduction in the size of the tumour was shown by computed tomography over several months (fig B) and was maintained at least until August 1982, when the serum prolactin concentration reached a nadir of 5020 mU/l. Steroid and thyroid replacement treatment were withdrawn, and he remained well with biochemical euthyroidism (serum thyroxine concentration 92 nmol/l (7·1 µg/100 ml), free thyroxine index 87).

Discussion

This patient clearly responded to treatment with bromocriptine initially, with a fall in the serum prolactin concentration, improvement in visual acuity and peripheral fields, and shrinkage of the tumour shown by computed tomography. At no time, however, did prolactin concentrations fall into the normal range. Subsequent recrudescence of tumour and rise in serum prolactin concentrations occurred during continued bromocriptine treatment and persisted despite an increase in the dosage of bromocriptine. The inability of high concentrations of bromocriptine to suppress production of prolactin by cultured tumour cells suggests that regrowth of the tumour was due to a population of cells resistant to dopamine agonist action.

One previous report described transient visual loss with suprasellar enlargement of a prolactinoma in the fifth month of bromocriptine treatment, ascribed to pituitary apoplexy. In our case, however, neither the computed tomograms nor the operative findings were compatible with a haemorrhage into the tumour being the cause of the expansion but indicated instead actual tumour growth.

Regrowth of a macroprolactinoma during continuing bromocriptine treatment, after an initial reduction in size due to the bromocriptine has not to our knowledge been described previously. The incidence of this event is unknown. It was not seen in a recent series of 29 patients, five of whom were treated for over one year. Nevertheless, although such a course may be uncommon, it represents an additional potential problem in the long term management of macroprolactinomas with bromocriptine and emphasises the need for close surveillance, especially of patients whose prolactin concentration fails to normal during bromocriptine treatment.

We thank Dr John Game and Professor Keith Bradley, who initiated the case; Dr Isla Williams for repeated visual field charting; Mr K Sui for operating; Dr Peter Fuller for tissue culture; and Miss H Hammond for typing the manuscript.

ADDENDUM—Since acceptance of our paper our attention has been drawn to a paper by Dallabonzana D, Spelta B, Oppizzi G, et al, entitled “Reenlargement of macroprolactinomas during bromocriptine treatment: report of two cases” (J Endocrinol Invest 1983;6:47-50). We believe that our case is still unique as the first case described by Dallabonzana et al is that of pituitary apoplexy during bromocriptine treatment and the second showed only transient expansion, possibly related to accelerated bromocriptine clearance caused by spironolactone treatment. In neither case was there sustained tumour growth during continued bromocriptine treatment nor was resistance to bromocriptine shown in tissue culture.

References


(accepted 17 May 1983)