LETTER TO THE EDITOR

Effect of treatment with pegvisomant on meningioma growth in vivo

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Pegvisomant is a pegylated analogue of human growth hormone (GH) that functions as a GH receptor antagonist. Although its use is currently limited to patients with acromegaly (1), there exists considerable interest in the potential use of pegvisomant for the treatment of a variety of tumours whose growth may be promoted by insulin-like growth factor-I (IGF-I). We report the case of a 74-year-old woman with acromegaly, treated with pegvisomant, in whom we have documented the growth rate of a meningioma noted incidentally during the course of routine radiological imaging.

The patient’s acromegaly was diagnosed in 1992 on the basis of failure of suppression of serum GH during a 75 g oral glucose load (nadir serum GH 10 mU/l) and an elevated serum IGF-I concentration (489 ng/ml, age-adjusted normal range 109–269). Magnetic resonance imaging (MRI) of the pituitary demonstrated a 9 mm intrasellar pituitary mass lesion. She declined surgical adenomectomy or pituitary irradiation and was successfully treated with thrice-daily s.c. octreotide (serum IGF-I within age-adjusted normal range). In 1998, she enrolled in a 12 week placebo-controlled study of pegvisomant in the treatment of acromegaly (2) and was randomised to receive pegvisomant 10 mg daily. At its conclusion, she continued pegvisomant in an open-label study, but therapy was suspended after 9 months because of a shortage of drug. Eight weeks after cessation of pegvisomant, depot octreotide 10 mg four-weekly was commenced and continued for 26 months. In December 2001, she enrolled in an open-label study of patients with acromegaly converting from stable treatment with depot octreotide to therapy with pegvisomant and continued this drug at a dose of 10 mg daily until May 2004.

Regular surveillance pituitary imaging was performed during both clinical trials. Incidental note was made, at the start of the first trial, of a dural-based homogeneously enhancing mass related to the greater wing of the sphenoid, typical of a meningioma (Fig. 1A). She reported no symptoms referable to the mass and declined any surgical intervention. Axial, sagittal and coronal dimensions of the mass were recorded at each scan and the volume calculated, for a prolate ellipsoid, using the formula \( \frac{4}{3} \pi \left( \frac{\text{height}}{2} \right)^2 \left( \frac{\text{width}}{2} \right) \left( \frac{\text{depth}}{2} \right) \) (3). The volume of the meningioma increased from 470 to 4810 mm\(^3\) 5 years later (Fig. 1B), with no discernible inhibitory effect of pegvisomant therapy (Fig. 2).

Pegvisomant inhibits the functional dimerisation of cell surface GH receptors, thereby reducing IGF-I

Figure 1 Sagittal MRI scan showing a dural-based homogeneously enhancing mass related to the greater wing of the sphenoid in 1998 (A) and 2003 (B).
Evidence that growth of a variety of tumours is promoted by IGF-I has generated interest in the possible role of pegvisomant as an anti-cancer agent. In particular, data in nude mice indicate that pegvisomant inhibits growth of meningioma cells in vivo (5), leading to speculation that this drug may have a role in patients with inoperable or recurrent meningioma (6). To the best of our knowledge, this is the first report of the effect of pegvisomant therapy on growth of a non-pituitary tumour in vivo in a human subject. No inhibitory effect of pegvisomant therapy on meningioma growth was evident, emphasising the need for caution in extrapolating in vitro and animal data to therapy in human subjects. Further reports of the effect of pegvisomant therapy for acromegaly on coincidentally noted non-pituitary tumours are encouraged.

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References

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