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LETTER TO THE EDITOR

Radiological response in an incidental meningioma in a patient treated with chemotherapy combined with CP-751,871, an IGF-1R inhibitor

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To the Editor,

Meningiomas arise from arachnoid cap cells on the outer surface of the meninges. They are one of the most common intracranial tumours. While benign, some may need treatment due to symptomatic compression of adjacent structures, when the treatment of choice is surgery or radiotherapy [1]. The treatment of recurrent or unresectable meningiomas is difficult. While there have been some reports of modest benefit from chemotherapy, and more recently from interferon alpha-2β [2,3], therapeutic options are limited.

Insulin like growth factors (IGF) are autocrine peptides which are important for mitogenesis, survival, and tumorigenesis. CP-751,871, a fully human IgG2 monoclonal antibody is a highly specific and potent inhibitor of the autophosphorylation of IGF-1R. This leads to a decrease in cell growth, inhibition of tumour proliferation, and increased apoptosis in cells treated with cytotoxic chemotherapy [4].

Case report

A 53-year-old woman presented with increasing dyspnoea and chest pain over several months. CT scans showed a spiculated soft tissue mass measuring 2.4 cm × 1.7 cm in the posterior segment of the right upper lobe with enlarged ipsilateral hilar and subcarinal nodes. Biopsy confirmed adenocarcinoma, which stained positive for TTF-1 consistent with a lung primary, final staging was T4N3 (stage IIIb).

She had a past history of well controlled epilepsy diagnosed six years previously and a parafalcine meningioma which was stable on serial MRI scans since then (Figure 1). She was enrolled in a phase 1 trial of chemotherapy (cisplatin and gemcitabine) in combination with an anti-IGF-1R antibody CP-751,871 for treatment of her non-small cell lung cancer. Treatment was planned for cisplatin and CP-751,871 three weekly in combination with gemcitabine on a day 1, day 8 schedule every 21 days.

Treatment achieved a partial response in her lung cancer with complete resolution of her adenopathy and she continued to six cycles of combination chemotherapy and CP-751,871. Her lung carcinoma remains stable on follow-up to date, without further therapy.

In conjunction with the expected toxicity associated with her treatment, the patient complained of an increase in seizure activity from her baseline and was further investigated with an MRI of her brain (Figure 2). This showed a decrease in the dimensions of her previously stable meningioma of 20% in greatest dimension from 21 to 17 mm and a 41% decrease in volume from 3.73 to 1.98 cm^3. Four months following completion of therapy an MRI showed an increase in the volume of the lesion to 2.49 cm^3. Repeat MRI six months later showed a longest diameter of 20 mm with a volume of 2.63 cm^3. These finding suggests a response in terms of a size reduction, while on therapy and an increase in size of the meningioma when therapy was discontinued.

Discussion

In spite of the advances in therapeutics and translational research in oncology in recent years, the molecular biology of solid tumours remains poorly

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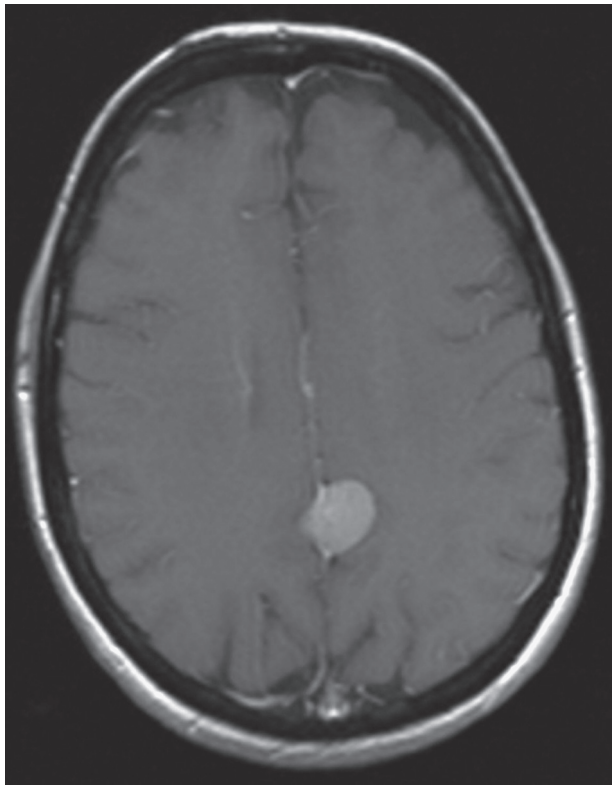

Figure 1. T1 post contrast axial MR scan showing the parafalcine meningioma two weeks before chemotherapy.

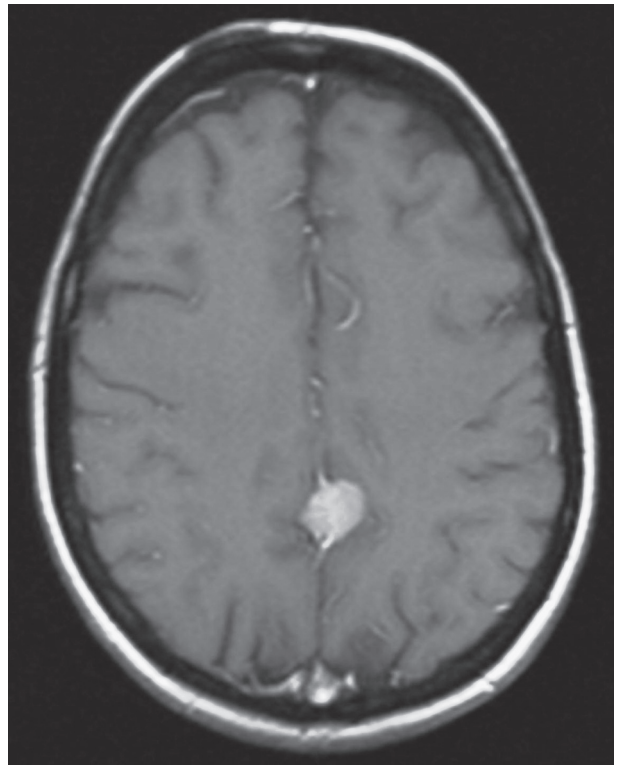

Figure 2. T1 post contrast axial MR scan showing the meningioma while patient was on chemotherapy.

understood. Meningiomas often display a benign behaviour, increasingly found as incidental findings with improved neuro-imaging. Many require no treatment, and patients remain asymptomatic. Some however may have a very aggressive clinical pattern.

IGFs bind to the type 1 IGF receptor (IGFR-1), a transmembrane receptor from the tyrosine kinase receptor family responsible for mediating the activation of multiple downstream signalling pathways [5]. These signals ultimately activate the phosphatidylinositol-3 kinase pathway and protein kinase B (PKB/Akt) and MAP kinase pathways. This has a promoter effect on cell growth, survival and proliferation and may offer a target for cancer chemotherapy.

Studies have shown a correlation between behaviour of meningiomas and expression of IGF-2 [6]. Higher levels of IGF-2 in tumour samples correlated with more aggressive tumours with an increase in peri-tumoural oedema. IGF-1R receptors have been found in many tumour types including non-small cell lung cancer, melanoma, breast cancer, and prostate cancer. CP-751,871 is a potent anti-IGF-1R antibody that inhibits the function of IGF-1R and has anti-tumour activity as a single agent or in combination with other cancer drugs [4,7].

While this is a case of a benign meningioma responding radiologically, and thus may not be applicable to more aggressive meningiomas, it does suggest an area for further study in aggressive, symptomatic or recurrent meningiomas. While this patient responded to treatment with a three drug combination, previous studies have shown little benefit in the treatment of meningiomas with chemotherapy and the role of the targeted agent is interesting. As with many of the newer targeted therapies in current clinical trials, there are often unexpected benefits and effects from treatment due to their complex and sometimes unpredicted interactions with downstream pathways, as our case illustrates.

Declaration of interest: Kenneth J O'Byrne is a member of the ADVIGO steering committee, has recieved honoraria from Pfizer, the maunfacturers of the targeted therapy and has recieved funding for a PhD student from Pfizer. Kenneth J O'Byrne does not feel these reflect a conflict of interest in this paper in particular.

References

[1] DeAngelis LM. Brain tumors. N Engl J Med 2001;344:114–23.
[2] Kaba SE, DeMonte F, Bruner JM, Kyritsis AP, Jaeckle KA, Levin V, et al. The treatment of recurrent unresectable and malignant meningiomas with interferon alpha-2B. Neurosurgery 1997;40:271–5.
[3] Marc C. Chamberlain MJG. Interferon-alpha for recurrent World Health Organization grade 1 intracranial meningiomas. Cancer 2008;113:2146–51.

[4] Cohen BD, Baker DA, Soderstrom C, Tkalcevic G, Rossi AM, Miller PE, et al. Combination therapy enhances the inhibition of tumor growth with the fully human anti-type 1 insulin-like growth factor receptor monoclonal antibody CP-751,871. Clin Cancer Res 2005;11:2063–73.

[5] Esparis-Ogando A, Ocana A, Rodriguez-Barrueco R, Ferreira L, Borges J, Pandiella A. Synergic antitumoral effect of an IGF-IR inhibitor and trastuzumab on HER2-overexpressing breast cancer cells. Ann Oncol 2008;19:1860–9.

[6] Sandberg Nordqvist A-C, Mathiesen T. Expression of IGF-II, IGFBP-2, -5, and -6 in meningiomas with different brain invasiveness. J Neurooncol 2002;57:19–26.

[7] Karp DD, Paz-Ares LG, Novello S, Haluska P, Garland L, Cardenal F, et al. Phase II study of the anti-insulin-like growth factor type 1 receptor antibody CP-751,871 in combination with paclitaxel and carboplatin in previously untreated, locally advanced, or metastatic non-small-cell lung cancer. J Clin Oncol 2009;27:2516–22.