Neurosurgical Forum LETTERS TO THE EDITOR

Nonfunctioning pituitary macroadenoma

TO THE EDITOR: We read with great interest the article by Anderson et al.¹ (Anderson E, Heller RS, Lechan RM, et al: Regression of a nonfunctioning pituitary macroadenoma on the CDK4/6 inhibitor palbociclib: case report. *Neurosurg Focus* 44(6):E9, June 2018). In this study, the authors presented one case and concluded that palbociclib may represent a possible adjuvant therapy for the treatment of nonfunctioning pituitary adenomas, acting through the inhibition of the CDK4/6 pathway. The patient was a 71-year-old woman with an asymptomatic nonfunctional pituitary adenoma, meningioma, and breast cancer. While these findings might bolster the evidence for the medical management of a nonfunctional pituitary adenoma, we would like to convey some words of caution and quell any unjustified excitement that this finding may generate.

We disagree with the authors that “there is evidence to suggest that palbociclib might have affected tumor reduction in this case.”¹ The authors claimed that the tumor responded to palbociclib, just according to time priority. However, a time priority is not enough to suggest a cause-and-effect relationship, and further conditions are required. Furthermore, the images of the pre- and post-operative tumor do not indicate similar views on the same anatomical planes.

We would like to emphasize that neither definite pathological diagnosis nor biomolecular details are provided. Based on Fig. 1B, with consideration of the incongruity of mass periphery,¹ it seems that the stalk has also been involved; the thickness and enhancement of the stalk are unusual for a pituitary adenoma. Possibly the mass was a lesion that had metastasized from the patient's breast cancer to the pituitary gland; that is not a very rare incident. Thus, the response to medication might indeed be the shrinkage of the metastasis. As pointed out by the authors, “the pathways involved in the pathogenesis of this specific tumor are unknown.”¹ Therefore, the judgment about the genetic correlation of tumor and CDK4/6 pathway is just based on the presence of multiple primary tumors. Moreover, the risk of high-grade anemia and high-grade thrombocytopenia with palbociclib has been reported to be significant. Use of this drug without a confirmed pathology, therefore, may not be justified.³

Cystic pituitary adenomas that spontaneously regress

are not uncommon and would be encountered in routine practice.^{2,4–6} We wholeheartedly agree with the authors that “the pituitary adenoma could have spontaneously regressed in this patient.” Spontaneous regression of nonfunctioning pituitary macroadenomas has been reported in approximately 10% of tumors. It is our concern that the casual reader will misinterpret the overly simplistic conclusion that “inhibition of the CDK4/6 pathway by palbociclib contributed to adenoma regression in this patient.” We believe the conclusion should be qualified to state that although there is evidence to suggest spontaneous regression in an asymptomatic, nonpathologically confirmed cystic pituitary adenoma, palbociclib might have affected tumor reduction in this case.

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Disclosures

The authors report no conflict of interest.

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Response

We appreciate the interest shown by Drs. Javadi and Zeinalizadeh in our article.

In their letter, they raise the possibility that the lesion characterized in our report is more consistent with a metastatic lesion than a pituitary adenoma. While the precise pathology cannot be certain without a tissue diagnosis, the behavior of this lesion was highly uncharacteristic of a metastasis. The patient in this report returned for a follow-up visit in our clinic in July 2018. At this visit, she had located an MRI study from 2008 that had previously been lost. This study showed the lesion to measure 8 mm in maximum height (Fig. 1A). At its largest, the tumor reached a maximum measurement of 14 mm in 2016 (Fig. 1B). This increase of just 6 mm over an 8-year span essentially excludes the possibility of its being a metastatic lesion, which would exhibit a more aggressive growth pattern.

At the latest follow-up visit in July 2018, the patient underwent a repeat MRI of the sella that demonstrated continued regression of the pituitary adenoma, now measuring 6 mm (Fig. 1C). The patient remains on palbociclib therapy and her pituitary adenoma continues to be asymptomatic. The steady and continuous involution of the adenoma suggests a medication effect rather than spontaneous regression.

We agree that novel inhibitors such as palbociclib are not to be administered without caution, particularly in cases in which tissue diagnosis and genetic testing of the tumor might not be available. Nonetheless, targeted immunotherapy is a growing field in oncology, and its applications to neurooncology should be embraced. We thank the editors for allowing us the opportunity to answer the questions raised regarding our report.

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FIG. 1. Sagittal MR images from 2008 (**A**, without gadolinium), 2016 (**B**, with gadolinium), and 2018 (**C**, with gadolinium) demonstrating the pituitary adenoma's growth from 8 mm in 2008 to 14 mm in 2016 and then its diminishment in size to 6 mm in 2018 after therapy with palbociclib.