Editorial

Bifocal germ cell tumors

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The finding of bifocal or synchronous germ cell tumors (GCTs) of the pineal and suprasellar regions, first described in 1974, is an uncommon event. Historically, reports of bifocal GCTs were limited to case reports or small case series. Previous authors have debated whether these tumors represented truly synchronous neoplasms or whether they represented metastatic disease from one location to another.

In this interesting manuscript, Phi and colleagues¹ report a relatively large series of bifocal tumors and make the argument that these tumors are metastatic rather than synchronous primary tumors. The authors dispel the notion that the finding of a bifocal tumor is pathognomonic for germinoma. They also demonstrate that patients with bifocal tumors have a poorer prognosis than those with either suprasellar or pineal GCTs alone. Their patients with bifocal tumors had overall survival and event-free survival that were statistically similar to those of patients with disseminated disease, a finding that should prompt more aggressive therapy.

The authors performed a retrospective review of their institution's database between 1998 and 2010 and found 181 patients with intracranial GCTs. Of these patients, 23 presented with bifocal GCTs, 5 of whom had mixed GCTs as determined by either CSF or serum markers. In one case, the patient had undergone MRI of the brain 7 months before presenting with bifocal tumors, larger in the suprasellar region than in the pineal region, suggesting a suprasellar primary tumor with metastasis rather than synchronous tumors.

Next, the authors hypothesized that if bifocal tumors represented metastases from a primary site, then the primary site should be the larger of the 2 tumors. Given this, they looked at the ratio of pineal to suprasellar tumors

and found a not dissimilar ratio in their bifocal series. They also noted that pineal tumors were found predominantly in males, suprasellar tumors were found predominantly in females, and that the bifocal tumors had a sex ratio between the other 2 ratios. When the authors looked at the number of patients with primary pineal and suprasellar tumors that had evidence of metastatic disease on MRI or cytology, they found that the patients with bifocal tumors had nearly 5 times the likelihood of metastatic disease than did either of the other groups, which they use to support the contention that these are large metastases rather than synchronous primary tumors.

Finally, when the authors looked at the overall and event-free survival of patients with pineal and suprasellar tumors versus those of patients presenting with disseminated disease, they found that patients with bifocal tumors had a worse outcome than even those with disseminated disease. Although their outcome was not statistically different from those with diffuse dissemination, it was notably worse than those with single-site disease, again supporting their hypothesis. Thus, although the authors cannot provide definitive proof that bifocal tumors represent metastatic disease, they provide a cogent and logical argument in support of their contention. More importantly, they demonstrate quite clearly that the finding of a bifocal tumor portends a poor prognosis and is likely to be associated with diffuse metastatic disease, and that these patients require more aggressive treatment than patients with either primary pineal or suprasellar GCTs.

I found this article to be very well written. Although the authors are quick to note that they do not have definitive proof that bifocal GCTs represent metastatic disease, they certainly support their contention with enough presumptive data that their hypothesis is difficult to refute. (<http://thejns.org/doi/abs/10.3171/2012.8.PEDS12357>)

Disclosure

The author reports no conflict of interest.

Reference

1. Phi JH, Kim SK, Lee J, Park CK, Kim IH, Ahn HS, et al: The enigma of bifocal germ cell tumors in the suprasellar and pineal regions: synchronous lesions or metastasis? Clinical article. *J Neurosurg Pediatr* [epub ahead of print November 30, 2012]. DOI: 10.3171/2012.10.PEDS11487]

Response

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We greatly appreciate Dr. Boop's positive and detailed comment on our study. Location specificity is one of the most interesting aspects of neurooncology. Intracranial GCTs show striking evidence of location specificity among brain tumors. Our study on bifocal GCTs deals with the uncommon but important presentation of GCTs in both suprasellar and pineal locations.

From the start of the study, we suspected that bifocal GCTs may be a metastatic spread from pineal GCTs because the proportion of male patients with bifocal GCTs was high, reminiscent of the sex distribution of pineal GCTs. However, analysis of the entire cohort of 181 patients (perhaps the largest patient cohort from a single institution) revealed that the proportion of male patients with bifocal GCT is between those of suprasellar and pineal GCTs. Therefore, we turned to the hypothesis that

bifocal GCTs originate from metastasis from either suprasellar or pineal location to the other. Tumor size measurement of suprasellar and pineal masses also supported the same hypothesis.

The metastasis hypothesis was further reinforced by the fact that bifocal GCTs were strongly associated with tumor seeding along the neuraxis. This implies that bifocal tumors may be an early manifestation of metastatic spread to amenable locations. We do not know the reason why the suprasellar and pineal regions are good soil for early metastasis of GCTs. Nonetheless, as Dr. Boop pointed out, this finding may have clinical significance in setting the level of treatment.

However, all the evidence presented in our study is indirect. Finding direct evidence of the metastasis hypothesis may be a difficult task at present, because the pathogenesis of GCTs is obscure and we do not have an animal model of the disease. As for intracranial GCTs, we think there are still more enigmas to be solved.

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