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Impact of bevacizumab chemotherapy on craniotomy wound healing.

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Abstract

OBJECT: The FDA approval of bevacizumab for recurrent glioblastoma has resulted in its increased use in this patient population. Phase II trials reported 4%-6% impaired wound healing for bevacizumab initiated postoperatively. The effect of preoperative bevacizumab on subsequent craniotomy healing has not been addressed.

METHODS: The authors retrospectively reviewed the cases of patients who underwent craniotomy for recurrent glioblastoma between 2005 and 2009, evaluating bevacizumab therapy/duration and healing complications (dehiscence, pseudomeningocele, CSF leak, and wound/bone infection). The Wilcoxon rank-sum test and Kruskal-Wallis test were used to compare continuous variables between groups. The Fisher exact test was used to assess for an association between categorical variables, including the comparison of wound-healing complication rates. Logistic regression models were used to estimate odds ratios of wound-healing complications while adjusting for baseline variables.

RESULTS: Two hundred nine patients underwent a second craniotomy (161 patients) or third craniotomy (48 patients) for recurrent glioblastoma. Twenty-six individuals (12%) developed wound-healing complications. One hundred sixty-eight patients received no bevacizumab, 23 received preoperative bevacizumab, and 18 received postoperative bevacizumab. Significantly more patients receiving preoperative bevacizumab developed healing complications (35%) than non-bevacizumab-treated patients (10.0%, $p = 0.004$). Postoperative bevacizumab was associated with 6% impaired healing, not significantly different from non-bevacizumab-treated controls ($p = 1.0$). Preoperative bevacizumab treatment duration (weeks) did not influence healing (OR 0.98, $p = 0.55$). More healing complications occurred in patients receiving preoperative bevacizumab than in non-bevacizumab-treated controls before the third craniotomy (44% vs 9%, $p = 0.03$).

CONCLUSIONS: Although subject to the limitations of a retrospective study, we demonstrate that preoperative bevacizumab treatment resulted in impaired healing after a second and third craniotomy, compared with minimal effect of postoperative bevacizumab. This effect is more striking for the third craniotomy and for a shorter delay between bevacizumab and surgery. These complications should be acknowledged as increased bevacizumab use results in more post-bevacizumab-treated patients in whom surgery for recurrent glioblastoma is considered. Based on these results, the authors recommend performing repeated craniotomy more than 28 days after last administered dose of bevacizumab whenever possible.

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