Reviewer's report

Title: The expression of Cytoglobin as a prognostic factor in gliomas: a retrospective analysis of 88 patients.

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Reviewer: Thomas Klonisch

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The manuscript by Xu et al. studied the PI3K-AKT pathway, presence of cytoglobin, TNFa, IL6, VEGF and assessed intratumoral microvessel density in glioma tissues from 88 patients (41 high grade and 47 low grade gliomas) and compared expression levels to histological grade and survival of patients. The authors report that the expression of tumor suppressor gene cytoglobin was inversely related to survival of these glioma patients and conclude that cytoglobin is a suitable new predictive marker for survival of glioma patients. Although the authors report a positive correlation between PI3K-pAKT, IL6, TNFa, VEGF and intratumoral microvessel density with overall patient survival in univariate analysis, only the inverse correlation between cytoglobin and overall patient survival was confirmed as an independent prognostic factor in multivariate analysis.

Major criticism

The authors demonstrate an interesting and potentially clinically relevant new finding. However, the discussion of the data is too speculative; e.g., in the discussion part on Cygb and IL6 and PI3K-pAKT it is not clear what the rationale for their conclusions is. This is particularly difficult when no references are provided to support their claim. The manuscript would benefit from a discussion that is shorter and more focused on the reported data.

The authors claim the existence of a Cybg-PI3K-AKT pathway in gliomas simply based on correlative data. This section should be removed since their data sets do not provide a causal link.

No negative controls are provided for the immunohistochemical images. These should be included as inserts.

The authors show a gender difference for the Cygb expression. They should provide information as to the gender effect on Cygb expression in different histological grades of glioma.

Minor comments

No page and figure numbers are provided in the manuscript.

The authors should consult a native speaker for the English.

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
none to all