Effect of post-operative infections on glioblastoma outcomes

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Abstract

Glioblastoma multiforme (GBM) is the most aggressive primary brain tumour with a poor prognosis. The risk of developing a post-operative infection after craniotomy is the highest in GBM patients. Historical beliefs suggest that post-operative infections render a survival advantage in GBM patients, however recent clinical neurosurgical reports involving large multicentric patient cohorts do not support this claim. Nonetheless, the relationship has not been extensively studied which poses the need for further large, scaled studies to determine the association between post-operative infections and survival benefit in GBM patients.

Keywords: Surgical site infections; glioblastoma surgery; survival time.

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Introduction

Glioblastoma multiforme (GBM) is the most aggressive primary brain tumour with a 5-year survival of 5% after initial diagnosis.[1] Patients with GBM have the highest risk of infections after craniotomy with the incidence of post-operative infections ranging from 3% to 27% in several studies.[2] (Figures 1&2)There is a long history of speculation into post-operative bacterial infections prolonging survival in cancer patients including patients with GBM.[3] Various theories have been presented which explain the beneficial effect of bacterial infections on the survival of GBM patients. One theory is that the infection generates an immunological cross-reactive attack that is not only directed towards the infection but also the tumour, resulting in an antitumour effect. Several initial reports suggested improved survival in patients with post-operative infections. Here-in we have reviewed the existing evidence on this topic.

Review of evidence

We reviewed the online database on PubMed and

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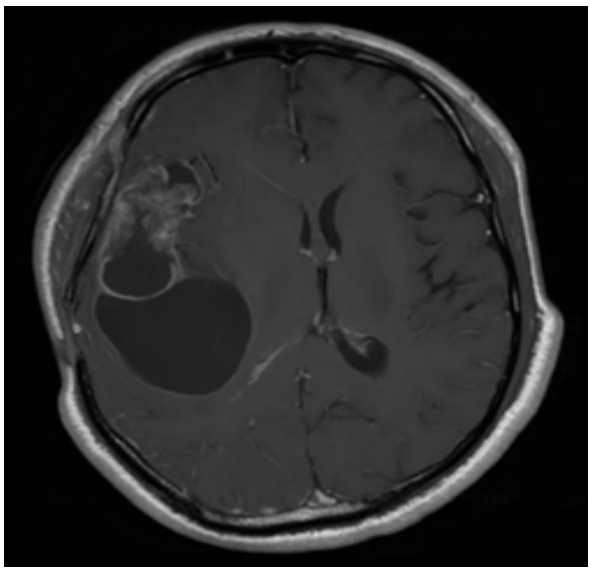

Figure-1: Axial section of T1 post-contrast MRI brain showing heterogenously enhancing cystic cum solid intra-axial lesion in the right fronto-temporal region. The lesion is causing effacement of ipsilateral lateral ventricle. Previous surgery scar can be seen on scalp. The lesion had been reported as Glioblastoma grade IV at time of first surgery.

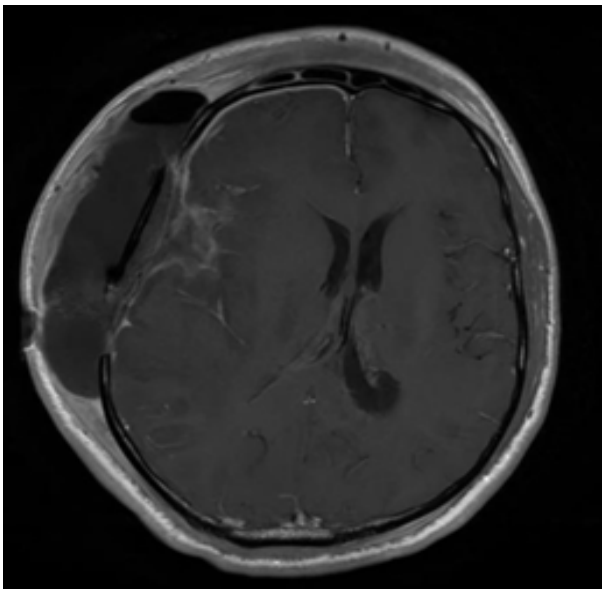

Figure-2: Axial section of T1 post-contrast MRI brain showing resection of the recurrent lesion with post-surgical changes. There is fluid collection under scalp with some air. The patient had developed meningitis, and fluid cultures had grown Staphylococcus aureus. The patient underwent wound debridement and received intravenous antibiotics.

Google Scholar for relevant literature. Salle et al., conducted a multicentric study to evaluate the effects of surgical site infections (SSI) after GBM surgery. Data of 64 SSI cases and 58 non-infected patients (controls) was collected and analyzed from 14 French neurosurgical centers. SSI cases included patients who had surgery for primary tumours (group I) and those who had surgery for a recurrent tumour (group II). The median overall survival (OS) times for group I, group II and the control group were 381, 633, and 547 days respectively. The authors reported a significant difference in the OS time between group I and the control group ($p = 0.029$) and also surprisingly between groups I and II ($p = 0.013$) with patients in group I having a significantly shorter survival compared to the other two groups ($p < 0.05$). Additionally, the overall median survival time after SSI diagnosis was 248 days with no significant difference between the two groups (0.45). On multivariate analysis, implantation of wafers was the only significantly associated risk factor for the development of SSI. Despite the small patient cohort, the results of the study highlight the significant impact of SSI on the survival time of GBM patients as patients with SSI had 30% shorter median overall survival compared to the control group, and 50% of patients died within a year following SSI diagnosis.[5]

Chen et al., analyzed the effect of post-operative infection in patients with GBM using the linked Surveillance, Epidemiology, and End Results (SEER) – Medicare database. This is the most comprehensive report on this topic so far. The authors identified 3784 patients with GBM over a 13-year period, of which 369 (9.8%) of the patients developed a post-operative infection within a month of GBM surgery. The primary outcome of the study was survival after diagnosis. When compared with patients with no infections (median 5 months), patients who had infections (median 6 months) had no significant difference in survival time ($p = 0.17$). Additionally, the study did not report any significant difference between the patients who had developed an infection and those who did not in terms of age, Gagne comorbidity score, race, extent of surgery, diabetic status, and smoking status. This is the first large-scale study to report that post-operative infection does not confer a survival benefit in patients with GBM.[6]

Kazim et al., reviewed and analyzed the existing clinical data on the survival advantage of post-operative infections in GBM patients in 2021. The authors reported seven studies which included 4 retrospective case control studies and 3 case series. They concluded that the available data did not demonstrate a definitive association between post-operative bacterial infection and prolonged survival in GBM patients. Of the three retrospective case control studies, Debonis et al., reported a significant survival advantage. The authors studied 10 GBM patients with postoperative infections and reported that multivariate analysis showed the infection group had a significant advantage in the median survival: 30 months vs 15 months for the patients without post-operative infection.[6] Furthermore, Kazim et al. identified the methodological constraints that likely explained varying results from the clinical studies. Several variables such as peri-operative steroids, adjuvant chemo-radiation, immune modulators and severity of infection can be expected to confound the survival advantage of post-operative infections in GBM patients. Interestingly, the authors also reported that immunobiology literature encourages the development of genetically modified bacteria as part of multimodal regimen against GBM.[7]

Conclusion

Although historical reports suggest that post-operative infections have a survival benefit in patients with GBM, clinical neurosurgical reports do not provide a definitive relationship between post-operative infection and prolonged survival. However, owing to the growing interest in the topic, further large scaled retrospective studies are required to further investigate the possibility of postoperative infections having a survival advantage in patients with GBM.

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