Glioma accounts for a third of all primary brain tumors. The interplay between glioma cells and the systemic immune response has been of great research interest. Previous studies have established correlation between neutrophilia and higher-grade glioma, whereas increased number of tumor-infiltrating lymphocytes indicates better survival prognosis. Combining the two hematological findings, neutrophil-to-lymphocyte ratio (NLR) is computed as a systemic inflammation marker. Previous studies have established NLR>4 as a prognostic marker for glioblastoma grading and survival. Specific genetic alterations such as IDH1 mutation and MGMT promoter hypermethylation are also associated with better glioma prognosis.

Methods

Data was collected as part of the ongoing NCT00887146 clinical trial. Patients with grade III-IV glioma were recruited through Norris Cotton Cancer Center and 4 other sites. Subjects underwent neurologic surgery on day 0. Surgically resected tumors were tested for IDH1 and MGMT mutation. On day 14, subjects start a 6-week combined temozolomide (TMZ) and radiation therapy (RT). Blood samples were collected pre- and post-surgery. Compared with patients under the age of 50, patients older than 50 had a significantly higher pre-surgery NLR (p < 0.05). Patients with IDH1 wild type had a statistically significant decrease in NLR from pre to post-surgery (p < 0.001), whereas IDH1 mutated group did not. No group differences in NLR change were found for MGMT mutation status, sex, or tumor grade.

Results

A total of thirteen patients were included in this analysis (61.5% female, mean age 59, 69% grade IV). The mean decrease in NLR from pre- to post-surgery was 12.91 (t (12) = 5.85, p < 0.001).

Compared with patients under the age of 50, patients older than 50 had a significantly higher pre-surgery NLR (p < 0.05). Patients with IDH1 wild type had a statistically significant decrease in NLR from pre to post-surgery (p < 0.001), whereas IDH1 mutated group did not. No group differences in NLR change were found for MGMT mutation status, sex, or tumor grade.

Conclusion

NLR is a systemic marker for tumor burden and is drastically decreased following glioma surgical resection. Compared to wildtype IDH1 patients, patients with IDH1 mutation are generally younger and have lower pre-surgery NLR, and experience milder change in NLR after surgical resection. IDH1 mutated glioma cells produce a unique R2-hydroxyglutarate metabolite, which differs from alpha ketoglutarate by one hydroxyl group. Such difference manifests as a reprogramming of cellular metabolism. The current study indicates such altered cellular metabolism might be associated with an underlying variation in immunological responses. The team is currently analyzing plasma cytokines profile to better understand the shared pathway between altered cellular metabolism and systemic immune response. Limitation for this study is the limited subjects included.

References