Pathology & Oncology Research (2020) 26:1363–1364
https://doi.org/10.1007/s12253-019-00699-w

LETTER TO THE EDITOR

Aspirin Use and Risk of Glioma: a Double Track for a Single Goal?

Raffaella Mormile [1]

Received: 12 March 2019 / Accepted: 17 July 2019 / Published online: 22 July 2019

Gliomas represent the most common malignant primary brain tumors which are well-known for resistance to therapy [1]. Recently, aspirin use has been connected with a reduced risk of glioma [2]. COX-2 and survivin have been found to play an important role in the process of glioma carcinogenesis [2–5]. Higher survivin expression has been related to worse overall survival in patients suffering from glioma [3]. Patients with survivin-positive tumors have been demonstrated to experience a significantly shorter survival time compared with those who were negative for survivin [4]. It has been found that there is a critical positive association between levels of COX-2 and survivin expression in the glioma tissues [5]. Both survivin and COX-2 have been proposed as sensitive predictors of a negative clinical prognosis for patients affected by glioma [5]. On this regard, it has been indicated that COX-2 and survivin proteins appear to be valuable for biomarker studies to calculate glioma severity and patient prognosis [5]. COX-2 and survivin expression levels have been observed to be significantly negatively associated with the rate of survival [5]. COX-2 and survivin expression have been revealed to be positively associated with the pathological grade of a glioma [5]. It has been highlighted that COX-2 and survivin are overexpressed in glioma tissues, and higher expression levels have been detected in glioma tissues of histological grades III-IV in comparison to those in grade I-II tumor tissues [5]. The COX-2 pathway has been implicated in gliomagenesis by directly supporting systemic development of myeloid-derived suppressor cells (MDSCs) and their C-C motif ligand 2 (CCL2)-mediated accumulation in the tumor microenvironment where they limit infiltration of cytotoxic T lymphocytes (CTL) [3]. The chemokine CCL2 appears to play a critical role in migration of MDSCs towards the tumor microenvironment [3]. Aspirin has been reported to reduce the MDSC-attracting chemokine CCL2 in the tumor microenvironment through inhibition of the COX-2 pathway [3]. Inhibition of survivin has been suggested to have a major role in the antineoplastic effects of aspirin [6]. All these contentions led me to suppose that taking aspirin regularly might inhibit glioma cells proliferation by a double track for a single goal. I hypothesize that the protective action of aspirin as chemopreventive agent for glioma may be mediated by two mechanisms which operate parallel working independently one from the other. I speculate that inhibition of the COX2 - MDSC -CCL2 signaling pathway and down-regulation of survivin expression may be involved in the anticancer activity of aspirin against glioma in the newly diagnosed cancer patients and in those who have progressed. Further research should be performed to verify the relationship between aspirin use and glioma risk in terms of drug repositioning approach.

Compliance with Ethical Standards

Conflict of Interest The author declares no potential conflicts of interest.

References

1. Gusyatiner O, Hegi ME (2018 Aug) Glioma epigenetics: from subclassification to novel treatment options. Semin Cancer Biol 51:50–58
2. Amirian ES, Ostrom QT, Armstrong GN, Lai RK, Gu X, Jacobs DI, Jalali A, Claus EB, Barnholtz-Sloan JS, Il'yasova D, Schildkraut JM, Ali-Osman F, Sadetzki S, Jenkins RB, LaChance DH, Olson SH, Bernstein JL, Merrell RT, Wrensch MR, Johansen C, Houlston RS, Scheurer ME, Shete S, Amos CI, Melin B, Bondy ML (2018 Nov 27. pii: cebp.0702.2018) Aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), and glioma risk: original data from the glioma international case-control study and a meta-analysis. Cancer Epidemiol Biomark Prev. https://doi.org/10.1158/1055-9965.EPI-18-0702
3. Fujita M, Kohanbash G, Fellows-Mayle W, Hamilton RL, Komohara Y, Decker SA, Ohlfest JR, Okada H (2011 Apr 1) COX-2 blockade suppresses gliomagenesis by inhibiting myeloid-derived suppressor cells. Cancer Res 71(7):2664–2674

✉ Raffaella Mormile
raffaellamormile@alice.it

[1] Division of Pediatrics and Neonatology, Moscati Hospital, Via A. Gramsci, 81031 Aversa, Italy

4. Zhang S, Zhang C, Song Y, Zhang J, Xu J (2018) Prognostic role of survivin in patients with glioma. Medicine (Baltimore) 97(17):e0571
5. Zhang F, Chu J, Wang F (2017) Expression and clinical significance of cyclooxygenase 2 and survivin in human gliomas. Oncol Lett 14(2):1303–1308
6. Németh K, Szücs N, Czirják S, Reiniger L, Szabó B, Barna G, Karászi K, Igaz P, Zivkovic V, Korbonits M, Patócs A, Butz H (2018) Survivin as a potential therapeutic target of acetylsalicylic acid in pituitary adenomas. Oncotarget. 9(49):29180–29192