Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Letter to the Editor Regarding Effects of the COVID-19 Outbreak in Northern Italy: Perspectives from the Bergamo Neurosurgery Department, and the Role of Radiosurgery as a Minimally Invasive Procedure for Primary Central Nervous System Lymphoma in the Pandemic Outbreak

Letter:

Physician scientists around the world are working against COVID-19, and continuation of less invasive brain oncology treatments demands action now.[1,2] The effects of the COVID-19 outbreak in Northern Italy and the perspectives from the Bergamo Neurosurgery Department has been described by Bernucci et al.,[1] and we are writing to advocate for the use of minimally invasive urgent procedures and Gamma Knife radiosurgery (GKRS) as a first-line and/or palliative treatment in brain tumors, in specific, in primary central nervous system lymphoma (PCNSL).[3,4]

COVID-19 is extremely infectious, and as described in the article all hospitalizations for elective surgical procedures were stopped in Italy,[1] and currently worldwide, especially in the elderly population.[2,5] This pandemic is changing our lives radically: nations are working at home, mass transportation is shutting down, main central towns and worldwide cities are doomed.[6] Medicine practice is shifting too because many clinical providers and clinical resources are isolated, and specifically dedicated to the COVID-19 worldwide emergency.[2,6] Although neurooncologic treatment is changing in the senior population, avoiding prompt chemotherapy treatment and open surgery and/or invasive procedures in most cases could be a challenge.[7] Wherever possible invasive procedures should be delayed in the COVID-19 era. Surgical procedures may induce the immune response and may increase the risk of rising severe acute respiratory disease in patients with COVID-19.[6] Additionally, open approach should be avoided to reduce the length of hospital stay and potential postoperative morbidity, thus reducing in-hospital spread of nosocomial infections and COVID-19.[3,5,6]

In a recent systematic review analyzing current clinical studies in PCNSL, and in a level III, single-center, retrospective, nonrandomized, observational study, the authors found that life expectancy and patient-reported outcomes were found to be superior at 3-year follow-up when using GKRS combined with methotrexate compared with methotrexate only.[4] Although concerns have been raised regarding the use of GKRS, a systematic review published this year by Palmer et al.,[4] provides support for use of radiosurgery when encountering the challenging situation of multiple patient comorbidities, and the inability to proceed with chemotherapy due to systemic instability or the inability to receive in-patient medical treatment due to the COVID-19 outbreak.[5]

Standard treatment for PCNSL consists of different methotrexate-based chemotherapy regimens associated with whole-brain radiotherapy (WBRT).[1,7,8] Unfortunately, standard treatment requires high-dosage regimens that can result in methotrexate toxicity and a broad range of serious side effects, especially in elderly or immunocompromised patients.[3] Additional concerns have been noted for the use of WBRT. Increasingly, research has demonstrated the hazards of using WBRT.[8,9] Several studies and a recent systematic review have demonstrated that in patients diagnosed with PCNSL with multiple lesions (>5), there is a significantly higher rate of complications, especially in senior patients, due to chemotherapy and radiotherapy side effects.[4,8]

Concordantly, GKRS has proven to be an effective therapeutic option for the treatment of brain tumors, including both single and multiple smaller brain metastases.[6] The technique results in a reduction of adverse patient events, as well as an increased ability to attack surgically inaccessible lesions and achieve local tumor control.[3] Various studies have demonstrated the utility of stereotactic radiosurgery (SRS) in the treatment of central nervous system (CNS) lymphomas. Palmer et al.,[4] in a systematic review of 16 studies evaluating the use of SRS for the treatment of CNS lymphoma found that although many current studies using SRS lacked methodologic rigor, SRS provided favorable local control in patients with refractory CNS lymphoma. In a similar vein of inquiry, Shin et al.[5] demonstrated that the use of GKRS as a rescue therapy could enhance treatment outcomes for patients. In this study, 14 patients that had relapsed or were refractory to salvage SRS experienced local control of 95%, 91%, and 75% at 3, 6, and 12 months, respectively, post-SRS.[5]

The data evaluated in the systematic review are reliable with Palmer et al.[4] regarding the use of GKRS for the treatment of PCLS. In reports by Alvarez-Pinzon et al.[3] and Kasenda et al.,[7] no patients with CNS lymphoma treated with GKRS at various stages were noted to have a local recurrence at last follow-up, despite several instances of distal failure. Remarkably, response rates to GKRS were greater, with more than 80% of lesions diminishing or disappearing on magnetic resonance imaging follow-up, resulting in better cognition and overall clinical performance status.

Collectively, these data support the use of GKRS as a viable treatment for adults diagnosed with PCNSL. However, several questions remain to be answered, including what outcomes can be achieved through the use of GKRS in patients that have developed PCNSL due to HIV.[3,4] Immunocompromised patients have consistently been shown to have the highest mortality rates when provided with all existing treatments, and significantly higher adverse events with the use of whole-brain radiation and/or methotrexate.[6,9] Neurosurgeons and oncologists have a responsibility to utilize existing evidence-based information to improve the treatment outcomes and quality of life in these patients. In infectious disease outbreaks, such as COVID-19, providing counseling and information for potentially utilizing GKRS as a first-line treatment option in PCNSL is clearly warranted in light of this evidence, and minimizes the compromise of social distancing during cancer care delivery.

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