

Primary CNS lymphomas in the elderly: state of art and advances in management

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Primary central nervous system lymphoma is a rare brain tumor, accounting for 3-6 % of all primary brain tumors . The median age of immunocompetent patients diagnosed with PCNSL is 60 years of age with the peak incidence rate occurring in the eighth decade of life . Up to 20 % of patients are aged 80 years or older .Advanced age has emerged as a major negative prognostic factor associated with shorter survival and increased risk of both systemic and CNS toxicity after treatments. PCNSL in the elderly is already a challenging problem at the time of diagnosis due to an increased risk of biopsy in patients with comorbidities. Differential diagnosis includes more frequently glioblastomas and brain metastases. As the morphologic MRI is not specific, the use of MR spectroscopy and perfusion is increasingly advocated to support the diagnosis. The presence of a lactate peak on MRS when necrosis is absent on standard MR and a low CBV on MR perfusion are highly suggestive .The use of steroids in the diagnostic phase still represents an issue. Few trials for elderly patients with PCNSL have been performed so far. Various regimens consisting of high dose methotrexate , alone or in combination with other chemotherapeutic agents , represent the standard first-line treatment. Whole-brain radiotherapy is generally avoided as a consolidation treatment in patients achieving a complete response after induction treatment with methotrexate-based regimens, and a recent phase III trial has indicated that the omission of WBRT does not compromise the overall survival. The risk of severe neurotoxicity, including dementia, is high and progressive over time in patients with age more than 60-65 years. Memory disturbances, ataxia and urinary incontinence are often the most disabling symptoms. On MR a diffuse hyperintensity of the white matter on T2/FLAIR images is generally seen , sometimes with hydrocephalus, and cortical atrophy. Pathologically, a damage to small vessels is the predominant feature .Several studies have demonstrated in a significant proportion of patients severe white matter damage linked to a small vessel disease in patients receiving whole brain radiotherapy in combination with high dose methotrexate. No convincing therapeutic strategy is available for patients who either can not be treated with high dose MTX or unresponsive to this agent.

The activity of novel therapeutic agents, such as rituximab, is still under debate.

Overall , the prognosis is severe with median survivals that are inferior to that reported for the whole population of PCNSL(30 to 60 months) . The best results are reported from centers of excellence , while in population studies advanced age is associated with less therapy and still the use of WBRT alone .