Thalidomide

Thalidomide has been trialled in central nervous system tuberculosis due to its immunomodulatory and immune reconstitution effects, through inhibition of TNF-alpha. Despite animal models demonstrating dramatic improvement in survival, studies in paediatric patients have been associated with higher levels of mortality. The effects of thalidomide have not yet been studied in adults with CNS TB. This narrative case series guides clinicians through a range of CNS TB clinical cases seen in a large London teaching hospital, serving a region with a high TB incidence of 32 per 100,000, with 55% of TB manifesting as extrapulmonary disease.

Keddie et al., aim to illustrate the experiences of using thalidomide to treat a range of severe CNS TB complications.

Five inpatients at the Royal London Hospital, London, UK treated with thalidomide in addition to standard TB treatment are described in detail. The rationale for treatment initiation with thalidomide is explained.

The case examples are used to guide our reflections and lessons learnt regarding the use of thalidomide. Responses to treatment and functional outcomes suggest thalidomide may be a useful adjunct to standard TB therapy in selected adult cases.

The experience gained from using thalidomide in this small case series may provide evidence towards more research into using thalidomide to treat severe CNS TB [1].

Overexpression of pro-angiogenic molecules such as VEGF and basic fibroblast growth factor (bFGF) has been considered typical of high-grade glioma.

Thalidomide (N-phthalylglutamic acid imide) was found to inhibit VEGF and bFGF in an animal model. RTOG 9806 was a single arm study to evaluate safety and efficacy of daily thalidomide with radiation therapy in patients with newly diagnosed GBM. Thalidomide was delivered in 200 mg of the daily dose before sleep starting with the first fraction of radiation. The dose was increased every 1-2 weeks by 100 mg-200 mg to 1200 mg as tolerated and continued as 8 weekly cycles until disease progression. The primary endpoint was OS with secondary endpoints of PFS and toxicity. The median survival time was 10 months not different from the historical cohort with increased toxicity in the form of venous thrombosis, fatigue, skin reactions, encephalopathy, and neuropathy [2].

1)
Keddie S, Bharambe V, Jayakumar A, Shah A, Sanchez V, Adams A, Gnanapavan S. Clinical perspectives into the use of thalidomide for central nervous system tuberculosis. Eur J Neurol. 2018 Jun 23. doi: 10.1111/ene.13732. [Epub ahead of print] PubMed PMID: 29935038.

2)
Mallick S, Gandhi AK, Rath GK. Therapeutic approach beyond conventional temozolomide for newly diagnosed glioblastoma: Review of the present evidence and future direction. Indian J Med Paediatr Oncol. 2015 Oct-Dec;36(4):229-37. doi: 10.4103/0971-5851.171543. Review. PubMed PMID: 26811592; PubMed Central PMCID: PMC4711221.