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Primary intracranial malignant melanoma

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Primary Intracranial Malignant Melanoma

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Abstract

Primary intracranial malignant melanoma (PIMM) are rare brain tumours; more infrequent than melanomas metastasizing to the brain or those extending to the brain from adjacent structures such as the orbit. Complete surgical excision with adjuvant chemotherapy and radiation remains the mainstay of treatment. Herein, we have reviewed the literature to find the treatment modalities for PIMMs that can lead to longer overall survivals and better patient outcomes.

Keywords: Malignant Melanoma, Primary Intracranial Melanoma, Brain Tumour.

Introduction

Primary Intracranial Malignant Melanoma (PIMM)is an extremely rare tumour, accounting for not less than 0.1% of all brain tumours.[1-3] It may be argued that most PIMM may actually be metastatic, as at times the primary lesion may be difficult to locate. In most cases, they stain positively for the S100 protein, and malignant melanoma antibody (HMB-45).[2] Depending upon their pathological behaviour, they can be divided into 2 subtypes; diffuse, and solitary, nodular lesions.[3,4] While few studies have shown improvements in the overall survival with surgical resection and adjuvant radiotherapy and/or chemotherapy, a standard treatment protocol for PIMM is yet to be established. This can be contributed to the rarity of the tumour, difficult pre-operative diagnosis and a rather poor prognosis despite treatment.

Review of Evidence

Recent studies show an improvement in the survival potential of metastatic malignant melanoma (MMM) patients through targeted therapies against mutated BRAF proteins, and immunotherapeutic agents; the interleukins and anti-cytotoxic T-lymphocyte antigen 4.[2,5] The use of several chemotherapeutic agents, including dacarbazine, temozolomide, BRAF inhibitors such as vemurafenib, and intrathecal methotrexate have also been reported, without, however, any reports of an increased overall survival with any of them.[2] Paul et al., reported a significant reduction in CNS relapse in the temozolomide group compared with the dacarbazine group at 19-month follow-up.[6] However, its utility in the chemo resistant PIMM remains questionable. To the best of our knowledge, no large cohort studies or randomized controlled trials have been performed on the subject, with only a few case reports and series existing in the literature.

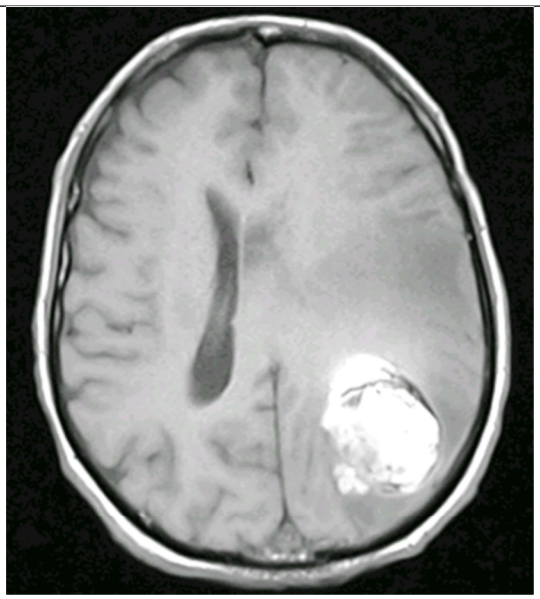

Figure-1: Axial section of MRI brain T1-weighted image showing heterogenous hyperintense signals in the left parieto-occipital region with mass effect. The lesion was reported as Malignant Melanoma on histopathology.

Nakagawa et al., reported three decades ago, a survival of 9.5 years in a patient with a solitary PIMM, having undergone three surgical resections and an adjuvant chemotherapy regimen composed of vincristine, methyl-CCNU, and no-cardia CWS (cell wall skeleton).[7] Another case report by Onal et al., shared a surprisingly long overall survival of 17 years in a patient after having undergone gross total resection of the solitary tumour, external beam irradiation to the tumour bed, and adjuvant chemotherapy with methyl-CCNU.[8] Martin et al., also published a case of a patient who underwent sub-total resection of a PIMM in the pineal region, followed by stereotactic radiosurgery (SRS). Follow-up scans at 12 and 52 weeks respectively,

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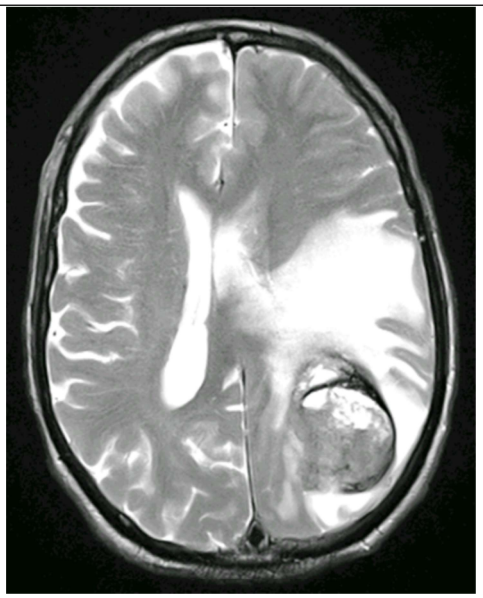

Figure-2: Axial section of MRI brain T1-weighted post-contrast image of the same patient, showing heterogenous hyperintense signals and subtle contrast enhancement.

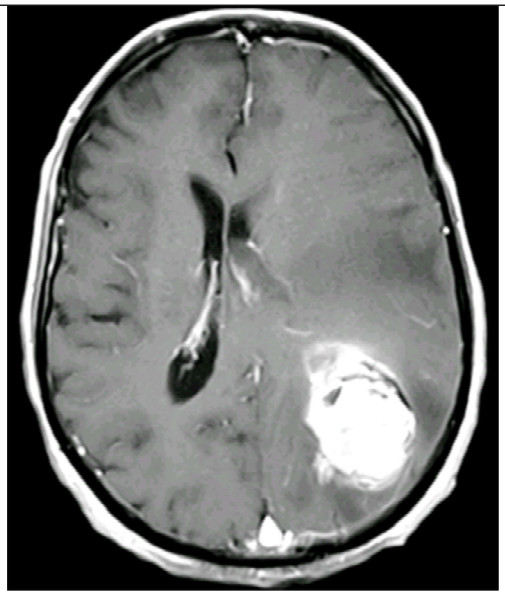

Figure-3: Axial section of MRI brain T2-weighted image of the same patient, showing heterogenous hypointense signals and significant per-lesional edema.

revealed no recurrence or progression of disease. However, at 63 weeks, the patient developed somnolence and gait ataxia, secondary to a tumour bleed. The patient later died at 65 weeks post-surgery, exhibiting a rapid progression of disease despite a favourable course over more than a year.[9]

Wang et al., retrospectively analyzed eight patients with PIMM in their series.[4] Gross total and sub-total surgical resection was achieved in six and two patients, respectively. Postoperatively, seven patients showed improvement in symptoms, while one remained the same at the time of discharge. Six patients received radiation after surgery. The mean follow-up period was 13.8 months, during which, three patients died, and one showed recurrence at 16 months. Four patients were alive by the end of the study period with no progression in disease. Based on their experience and review of literature, they suggested a treatment protocol dependent upon the location and size of the tumour, the number of lesions, the overall state of systemic disease and symptoms of patients at the time of diagnosis. For patients with a single primary intracranial malignant melanoma lesion greater than 3 cm in diameter that presented with significant mass effects or CSF obstruction, microsurgical excision was recommended first, followed by local radiation therapy (such as SRS) or whole brain radiation therapy (WBRT). However, in patients with a lesion less than 3 cm in diameter, or located deep in the brain, local radiation therapy (SRS or Gamma-knife) or auxiliary WBRT were recommended.[4]

In a retrospective cohort of 24 patients Byun et al., compared the management of PIMM with metastatic intracranial malignant melanoma and concluded that maximal safe resection plus adjuvant radiation and chemotherapy for intracranial malignant melanomas as first line treatment options, improved prognosis and prevented disease relapse.[2] The overall survival rates of PIMM, independent of treatment modalities applied, were 100% at 6 months, reducing to 25% at 18 months of follow up. The progression free survival rate of PIMM at 3 months was 66.7%, going down to 16.7% at 12 months.[2]

Arai et al., reviewed 49 patients from the literature and concluded gross total surgical resection to be the most promising intervention for longer survival.[10] In their study, 42 patients underwent surgical resection, with the mean overall survival for gross total resection being better than that of surgeries leaving behind residual tumour (>22 months vs. 12 months). Nine patients received adjuvant chemotherapy; 6 patients with temozolomide and 3 patients with a variety of regimens. Eighteen patients underwent post-operative radiation therapy, with two patients from different studies showing prolonged overall survival. However, they found no significant difference in overall survival, with or without adjuvant therapy.[10]

In the most recent, and perhaps the most exhaustive study on the topic, involving 115 patients with PIMM, 15 from the author's own center and a 100 from the literature, Li et al., reported an overall survival rate of 62.8% at 6 months, falling to 17.2% at 5 years, with an estimated median survival time (EMST) of 12 months.[3] The EMST was better in patients with a solitary-type lesion (13 months) as compared to those with a diffuse type lesion (5 months). In their review of all patients, those receiving gross total resection with adjuvant radiation therapy and/or chemotherapy, had significantly higher 1-year and 5-year overall survival rates (73.0% and 40.1%, respectively) and a longer EMST (53 months) than patients who underwent gross total resection alone (20.5 months) or radiation and/or chemotherapy without resection (13.0 months). They also suggested adding targeted therapy to the treatment protocol, given its efficacy in metastatic intracranial melanomas.[3]

Conclusion

We conclude that for PIMM, whenever feasible, gross total resection of lesion remains the strategy of choice. Adjuvant radiation and chemotherapy have also been shown to prevent disease progression and relapse. Immunotherapy and targeted therapies may have prospects for future management of the disease.

References

1. Balakrishnan R, Porag R, Asif DS, Satter AM, Taufiq M, Gaddam SS. Primary intracranial melanoma with early leptomeningeal spread: A case report and treatment options available. Case reports in oncological medicine. 2015;293802.
2. Byun J, Park ES, Hong SH, Cho YH, Kim YH, Kim CJ, et al. Clinical outcomes of primary intracranial malignant melanoma and metastatic intracranial malignant melanoma. Clin Neurol Neurosurg 2018;164:32-8.
3. Li CB, Song LR, Li D, Weng JC, Zhang LW, Zhang JT, et al. Primary intracranial malignant melanoma: proposed treatment protocol and overall survival in a single-institution series of 15 cases combined with 100 cases from the literature. J. Neurosurg.. 2019:1-12.
4. Wang J, Guo ZZ, Wang YJ, Zhang SG, Xing DG. Microsurgery for the treatment of primary malignant intracranial melanoma: a surgical series and literature review. Eur J Surg Oncol : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 2014;40:1062-71.
5. Gibney GT, Forsyth PA, Sondak VK. Melanoma in the brain: biology and therapeutic options. Melanoma Res.. 2012;22:177-83.
6. Paul MJ, Summers Y, Calvert AH, Rustin G, Brampton MH, Thatcher N, et al. Effect of temozolomide on central nervous system relapse in patients with advanced melanoma. Melanoma Res>. 2002;12:175-8.
7. Nakagawa H, Hayakawa T, Niiyama K, Nii Y, Yoshimine T, Mori S. Long-term survival after removal of primary intracranial malignant melanoma. Case report. Acta neurochirurgica. 1989;101:84-8.
8. Önal C, Ozy G, Akyürek S, Selek U, Ozyar E, Atahan L. Primary intracranial solitary melanoma: A rare case with long survival. Turk J Cancer. 2006;36:185-7.
9. Martin-Blondel G, Rousseau A, Boch AL, Cacoub P, Sene D. Primary pineal melanoma with leptomeningeal spreading: case report and review of the literature. Clin Neuropathol. 2009;28:387-94.
10. Arai N, Kagami H, Mine Y, Ishii T, Inaba M. Primary Solitary Intracranial Malignant Melanoma: A Systematic Review of Literature. World Neurosurg 2018;117:386-93.