Primary Solitary Intracranial Malignant Melanoma: A Systematic Review of Literature

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Key words
- Anti-PD1 receptor
- BRAF 600E mutation
- Melanoma
- Pembrolizumab
- Primary solitary cerebral malignant melanoma
- Primary solitary intracranial malignant melanoma

Abbreviations and Acronyms
CT: Computed tomography
GTR: Gross total removal
IQR: Interquartile range
MMM: Metastatic malignant melanoma
MRI: Magnetic resonance imaging
PET: Positron emission tomography
PF: Posterior fossa
PIMM: Primary intracranial malignant melanoma
PR: Partial removal
TMZ: Temozolomide
STR: Subtotal removal
WBRT: Whole brain radiotherapy

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INTRODUCTION: **Primary solitary intracranial malignant melanoma (PIMM) is extremely rare. In 1992, an extensive review of 81 patients with PIMM was undertaken. Imaging studies, microsurgery, and adjuvant therapy have developed considerably over the last 25 years, and targeted therapy recently has been proven successful for metastatic melanoma. These factors could influence current and future clinical PIMM results.**

METHODS: **We undertook a literature search of PIMM patients since 1992.**

RESULTS: **We reviewed 49 cases of PIMM. The mean age was 45.8 years. No significant sex difference was found. Intracranial hypertension and focal neurologic deficits were commonly observed around 70% and 40%, respectively. There were no significant differences of survival period according to tumor sites. Surgeries were performed in 42 of 49 patients with PIMM reviewed (92%). The mean survival of the gross total removal group was significantly longer than that of surgical results (>22 months vs. 12 months (interquartile range: 5—22 months; $P = 0.026$). For adjuvant therapy, 9 patients underwent chemotherapy and 18 patients underwent radiotherapy postoperatively There was no significant difference in survival period between with and without adjuvant therapies. Leptomeningeal enhancement diagnosed in the initial MRI, was the worst prognostic factor.**

CONCLUSIONS: **Gross total removal of the PIMM was the most promising treatment. Currently adjuvant therapy has not been associated with the survival period. To improve clinical outcome, immunotherapy and targeted therapies are likely to become more important.**

INTRODUCTION

Malignant melanoma commonly originates from cutaneous sites, whereas primary malignant melanoma originating in the brain, gastrointestinal tract, or the lung is uncommon. Malignant intracranial melanomas are divided into primary and secondary subtypes. Secondary malignant melanoma, which is metastatic, is known for its aggressive and progressive malignant features and comprises the third largest group of metastatic adult intracranial tumors. On the contrary, solitary primary intracranial malignant melanoma (PIMM) is an extremely rare entity. To the best of our knowledge, approximately 250 primary intracranial melanomas have been reported in the literature[1] since Ogle[2] first reported PIMM. These forms of melanoma comprise only 0.07% of all intracranial tumors.[3]

In 1992, Rodriguez y Baena et al.[4] extensively summarized 81 patients with PIMM. Imaging studies such as magnetic resonance imaging (MRI) and positron emission tomography (PET)—computed tomography (CT), microsurgery, radiotherapy, and antitumor drugs have developed considerably over the last 25 years. These advances in technology are likely to have influenced the prognosis of PIMM. Furthermore, targeted therapy for BRAF 600E and MEK mutations has been shown to be successful for metastatic malignant melanoma (MMM).[5] Although effective targeted therapy for PIMM has not yet been confirmed, the prognosis for PIMM is expected to improve in the near future. Therefore, current data regarding the prognosis of PIMM within contemporary medicine and not involving targeted therapy should be reviewed now. A literature search revealed 49 reports of PIMM[6-43] since 1992 (Table 1). In this article, the clinical and imaging characteristics, treatment options, and prognosis are discussed.

METHODS

According to Preferred Reporting Items for Systematic Reviews and Meta-Analyses criteria, a scrutinized PubMed- and Medline-based search for all relevant case reports, case series, and studies published during the years 1993—2017

Table 1. Review of 49 Cases Reported Previously Between 1993 and 2017

No.	Study	Age, years	Sex	Site	Symptom	Surgery	Chemotherapy	Radiation	Lepto-	Outcome
1	Yamane et al., 1994[6]	53	Female	Pineal	Headache	Bx	Dacarbazine, ACNU, vincristine, IFN	No	No	>48 months
2	Mitchell et al., 1998[7]	49	Male	Pineal	Vomiting, weight loss	Bx	No	No	No	NR
3	Farnsworth, 1998[8]	79	Male	Occipital	Memory loss, homonymous hemianopia	GTR	No	No	No	>12 months
4	Miyazaki et al., 1998[9]	32	Male	Frontal	Hemiparesis	NR	NR	NR	NR	NR
5	Suzuki et al., 2001[10]	50	Female	Pineal	Poor memory	PR	No	Yes	No	22 months
6	Desai et al., 2001[11]	17	Female	CPA	Headache, vomiting, diplopia	GTR	No	6000cg/14	NR	>12 months
7	Tosaka et al., 2001[12]	20	Male	No	Headache, vomiting	Autopsy	No	No	Yes	5 months
8	Greco Crasto et al., 2001[13]	74	Male	Temporal	Aphasia	GTR	No	No	No	>24 months
9	Sagiuchi et al., 2002[14]	24	Male	Frontal	Headache, vomiting	Bx	Dacarbazine, nimustin, hydrochloride, vincristine	No	Yes	5 months
10	Kashiwagi et al., 2002[15]	54	Male	Temporal	Aphasia	GTR	No	No	Yes	4 months
11	Son et al., 2003[16]	12	Male	Parietal-falx	Headache	GTR	No	Whole brain 3500	Yes	2.5 months
12	Lee et al., 2004[17]	66	Male	Frontoparietal	Headache, hemiparesis	GTR	No	No	Yes	6 months
13	Bookland et al., 2007[18]	20	Female	Pineal	Headache, cervical pain	Bx	TMZ75	Whole brain, gamma knife	No	9 months
14	Önal et al., 2006[19]	38	Male	Posterior fossa	Headache, vomiting, ataxia	GTR	Yes	Yes	No	>204 months
15	Barron et al., 2007[20]	73	Female	Pineal	Headache, gait disturbance, diplopia	Autopsy	No	No	No	18 months
16	Mekni et al., 2007[21]	30	Female	Intraventricular	Headache, gait disturbance, diplopia	Autopsy	No	Yes	No	18 months
17	Mekni et al., 2007[21]	54	Male	Parietal	Headache, vomiting	GTR	No	No	No	>24 months
18	Mekni et al., 2007[21]	29	Female	Parietal	Headache, blurred vision, gait disturbance	GTR	No	No	No	>1 month
19	Mekni et al., 2007[21]	28	Female	Parietal	Headache, blurred vision, vomiting	GTR	No	No	No	>3 months
20	Mekni et al., 2007[21]	44	Male	Pineal	Headache, blurred vision, vomiting	GTR	No	No	No	>21 months
21	Martin-Blondel et al., 2009[22]	44	Male	Pineal	Epileptic seizure	Bx	TMZ75	Whole brain	Yes	3 months
22	Azar et al., 2010[23]	22	Male	Parietal	Headache, hemiparesis	GTR	TMZ75	Whole brain	No	>12 months
23	Arantes et al., 2011[24]	54	Female	Pineal	Gait disturbance, memory loss	Bx	TMZ75	Whole brain + local	No	>20 months
24	Bhandari et al., 2012[25]	29	Male	CPA	Headache, vertigo	STR	No	Yes	No	12 months
25	Gempt et al., 2011[26]	71	Male	Fontal	Dysarthria	GTR	No	No	No	>18 months
26	Cedeño Diaz et al., 2011[27]	70	Male	Pineal	Headache, gait disturbance	PR	No	Yes	NR	10 months
27	Gu et al., 2012[28]	45	Male	Frontal	Headache, vomiting	STR	No	56 Gy	NR	5 months
28	Shinsato et al., 2012[29]	49	Female	Pineal	Tinnitus, hearing loss	STR	No	Whole brain	NR	>12 months
29	Azimi et al., 2012[30]	22	Female	Pineal	Headache, gait disturbance	GTR	No	No	NR	3 months
30	Shah et al., 2013[31]	28	Female	Temporal	Headache, numbness, diplopia	GTR	No	No	No	>48 months
31	Xie et al., 2014[32]	57	Female	Frontal	Myoclonic seizure	GTR	No	5500	No	>19 months