



Case Report

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Pineoblastoma with Multiple Spinal Metastases: A Rare Case Report

Lt Col V Suhag^a, Brig Vibha Dutta^b, Lt Col Sunita BS^c, Surg Cmde Arti Sarin^d,
Dr AP Dubey^e, Maj Nishant Lohiya^f

^a HOD Radiotherapy, Army Hospital R & R, Delhi, India

^b Consultant and HOD Pathology & Lab Sciences, Army Hospital R & R, Delhi, India

^c Assoc Prof Pathology, Army Hospital (R&R), Delhi, India

^d Consultant Radiodiagnosis & Radiotherapy, Command Hospital (SC), Pune, India

^e Senior resident Medical Oncology, Army Hospital R & R, Delhi, India

^f Resident Radiation Oncology, Army Hospital R & R, Delhi, India

*Corresponding author: virendersuhag@gmail.com

Abstract

Malignant pineal tumors are rare entities comprising less than 1% of primary central nervous system neoplasms. Pineoblastomas represents the most primitive form of all pineal parenchymal tumors corresponding to WHO grade IV tumors. This is a category of an aggressive group of supratentorial primitive neuroectodermal tumors. The standard of care includes maximal surgical resection followed by adjuvant craniospinal radiotherapy and then systemic combination chemotherapy with cisplatin or carboplatin, cyclophosphamide, lomustine and vincristine. We report the case of a 10 year old girl who presented with pineoblastoma with multiple spinal metastases and was managed with surgery, craniospinal irradiation and adjuvant chemotherapy.

Keywords: Pineoblastoma, pineal parenchymal tumours, craniospinal irradiation, spinal metastases.

Introduction

Central nervous system primitive neuroectodermal tumors (CNS-PNET) and pineoblastomas (PB) are rare, highly malignant tumors accounting for 4.8% and 0.6% of childhood brain tumors respectively.^{1,2,3} They are often associated with an unfavorable outcome, and only a few prospective trials have been conducted so far.⁴ However, modern multimodal treatment of pineoblastoma yields a high rate of overall survival, with acceptable short- and long-term toxicity. A greater M-stage at presentation and development of disease recurrence correlate with worse overall survival.⁵ Standard of care includes maximal surgical resection with adjuvant

craniospinal irradiation and systemic chemotherapy, resulting in a median survival of 16 to 25 months and a 5-year over-all survival rate of 10%.³ Radiosurgery is an appealing alternative management strategy for selected patients with biopsy-proven pineal parenchymal tumors and may also be used to boost local tumor dose during multimodality management of malignant pineal parenchymal tumors.^{6,7}

Case-Report

A 10 yr old child with no known co-morbidities presented with history of double vision of

1 month duration. She was first seen by Ophthalmologist and her eye examination was essentially normal. Thereafter she started having headache and difficulty in walking. Neurologically, her power grade was 3/5 in both lower limbs and there was evidence of 6th cranial nerve palsy on left side. Rest of the systemic examination and routine hematological and biochemical profile was normal. Her MRI brain (Figure-1) revealed a 1.9X1.6X1.2 cm sized lobulated mass in pineal region, indenting on the proximal aqueduct with active hydrocephalus. Sagittal sequences showed leptomeningeal enhancement over the dorsal aspect of the

visualized cord. Histopathology of endoscopic biopsy of the pineal region (Figure-2) showed highly cellular tumor composed of small cells with high N:C ratio, round hyperchromatic nuclei and scanty cytoplasm,; arranged in patternless sheets; with areas of necrosis admixed with normal brain parenchyma fragments showing an ependymal lining. On IHC, NSE & synaptophysin were positive; Chromogranin was focal positive; GFAP & NF were Negative and Ki67 was 25%. CSF cytology did not reveal any malignant cells. Based on these HP features, a final diagnosis of pineoblastoma was made.



Figure-1: Contrast enhanced MRI Brain in sagittal view showing mass in pineal gland

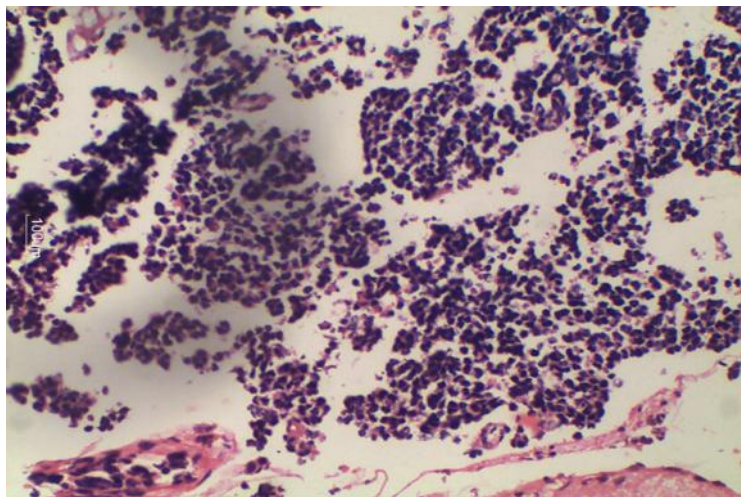


Figure-2: Microphotograph of pineal mass showing Pineoblastoma. Cellular tumor composed of small round cells, hyperchromatic nuclei and scanty cytoplasm,; arranged in patternless sheets.

She was then worked up further for leptomeningeal involvement. Her repeat MRI Brain & screening spine (Figure-3) was suggestive of post endoscopic biopsy status with a tract entering the right frontal horn; along with patchy leptomeningeal deposits along the entire

dorso-lumbar cord especially over its dorsal aspect. Leptomeningeal enhancement was seen even in the sacral spinal canal. A large 2 cm long deposit at level of DV9 was seen to compress the cord without associated cord edema.



Figure-3: MRI Spine showing multiple spinal deposits (marked with arrows)

She underwent laminoplasty of vertebrae DV9-DV10 with excision of dorsal lesion adherent to cord and dura. Histopathology of operative specimen confirmed metastatic deposits from pineoblastoma. Patient was subjected to CSI with post fossa boost and received external beam Radiotherapy on Linear Accelerator to a dose of 45 Gy to spine along with 55.8 Gy to posterior fossa. Post CSI, she was planned for adjuvant Chemotherapy with In Cisplatin, Vincristine and

Cyclophosphamide. Patient tolerated Radiotherapy and chemotherapy well and showed good partial response to planned therapy. However, once her chemotherapy was over, she progressed after 06 months and in view of her deteriorating performance status, was referred to palliative care centre.

Discussion

Pineoblastoma constitute a rare central nervous system neoplasm with a predilection for the pediatric population.¹ Pineoblastomas are a

category of supratentorial primitive neuroectodermal tumors (sPNETs) occurring in the pineal gland; some studies support the impression that patients with pineoblastomas have a worse prognosis than those with other sPNETs.⁸ Among the pineal parenchymal tumors (PPTs), there are 3 major subgroups: pineocytoma (WHO grade I), PPTs of intermediate differentiation (WHO grade II/III), and pineoblastoma (PB, WHO grade IV).⁹ PBs comprise 25% to 50% of PPTs and are most commonly seen in children and adolescents, with an average age at diagnosis of 13 years. These tumors exhibit aggressive clinical behavior with frequent metastases throughout the craniospinal axis.³

Histologic analysis of PBs reveals hypercellularity, high nuclear-to-cytoplasm ratio, and frequent mitoses (17%–40%). Homer-Wright or Flexner-Wintersteiner rosettes may also be present. Immunohistochemical markers characteristic of PB include synaptophysin and neuron-specific enolase, along with variable staining for glial fibrillary acidic protein,

chromogranin A, and neurofilaments.¹ Recent genetic analyses of PB demonstrate several upregulated genes (UBEC2, SOX4, TERT, TEP1, PRAME, CD24, POU4F2, HOXD13) and chromosomal abnormalities (1p rearrangement, 22q loss).³

Patients with PB most commonly present with findings of elevated intracranial pressure (headache, nausea/vomiting, and decreased level of consciousness) as a result of obstructive hydrocephalus from compression of the cerebral aqueduct by the tumor mass. Endoscopic biopsy

with concomitant third ventriculostomy (ETV) is a well-established diagnostic and therapeutic maneuver in patients presenting with non-communicating hydrocephalus resulting from a tumor of the pineal region or posterior third ventricle. Fenestration of the floor of the third ventricle theoretically provides a conduit for the subarachnoid dissemination of an intraventricular tumor.¹⁰ Focal neurologic deficits are present in approximately 25% of patients and are found incidentally in 5%. Initial workup includes a careful neurologic history and physical examination, including a fundoscopic examination. In particular, the presence or absence of focal neurologic deficits, altered level of consciousness, papilledema, and extraocular movement abnormalities are noted. If a significant level of suspicion is present, the next step is intracranial imaging, typically brain and spine magnetic resonance imaging (MRI) with and without contrast, and CSF analysis if clinically indicated.³

Standard treatment options for children older than 3 years with newly diagnosed pineoblastoma include surgery followed by adjuvant radiation therapy and chemotherapy. Total and near-total resection is infrequently obtained in pineoblastomas and the impact of the degree of resection on outcome is unknown. The total dose of radiation therapy to the tumor site is 54 Gy to 55.8 Gy using conventional fractionation. Craniospinal irradiation with doses ranging between 23.4 Gy and 36 Gy is also recommended because of the propensity of this tumor to disseminate throughout the subarachnoid space.¹¹ Children aged 3 years and younger with

pineoblastoma are usually treated initially with chemotherapy in the hope of delaying, if not obviating, the need for radiation therapy.¹² The addition of craniospinal irradiation to chemotherapy-based regimens may successfully treat some children but with anticipated neuro-developmental decline.⁴ High-dose, marrow-ablative chemotherapy with autologous bone marrow rescue or peripheral stem cell rescue has been used with some success in young children. Short intensive induction chemotherapy followed by tandem-HDCT in young children with CNS-PNET/pineoblastomas seems to be superior to the prolonged and less intensive induction regimen.

Our patient presented with spinal metastases at onset of her disease. CNS primitive neuroectodermal tumors (PNETs) and pineoblastomas may be disseminated at the time of diagnosis, although the incidence of dissemination may be somewhat less than that of medulloblastomas, with dissemination at diagnosis being documented in approximately 10% to 20% of patients. Patients with CNS PNETs and pineoblastomas with disseminated disease at the time of diagnosis have a poor overall survival, with reported survival rates at 5 years ranging from 10% to 30%.

Tate M and colleagues¹³ (2012) comprehensively summarized the existing literature of 109 studies on 299 patients with pineoblastoma and identified the variables and treatments that had an impact on outcomes. The analyses demonstrated a markedly worse prognosis for children aged ≤ 5 years compared with older patients (5-year survival rate: 15% for children aged ≤ 5 years vs 57% for children aged > 5 years). In addition, a graded increase in survival was observed with increasing degrees of resection; with 5-year survival rate of 84% for patients who underwent gross total resection vs 53% for patients who underwent subtotal resection vs 29% for patients who underwent debulking; thereby indicating that not achieving gross total resection markedly worsened patient survival.

Gerber NU et al¹⁴ (2014) studied the results of 26 patients between 4 and 21 years of age with

nonmetastatic CNS-PNET or pineoblastoma treated in the prospective GPOH-trial P-HIT 2000-AB4. In this study, after surgery, children received hyperfractionated radiation therapy (36 Gy to the craniospinal axis, 68 Gy to the tumor region, and 72 Gy to any residual tumor, fractionated at 2×1 Gy per day 5 days per week) accompanied by weekly intravenous administration of vincristine and followed by 8 cycles of maintenance chemotherapy (lomustine, cisplatin, and vincristine). 42% of patients showed tumor progression or relapse at a median time of 1.3 years. Five-year progression-free and overall

survival rates were each 58% for the entire cohort; CNS-PNET was 53% and pineoblastoma was 64%. The authors concluded that postoperative hyperfractionated radiation therapy with local dose escalation followed by maintenance chemotherapy was feasible without major acute toxicity.

The prognosis of embryonal tumors and pineoblastomas varies greatly depending on extent of CNS disease at the time of diagnosis, age at diagnosis, amount of residual disease after definitive surgery, tumor histopathology and biological/molecular tumor cell characteristics. Five-year disease-free survival is approximately 50%.¹¹ The HIT-SKK'87 and HIT-SKK'92 trials of the German Society of Pediatric Oncology and Hematology (GPOH) showed 3-year PFS and overall survival (OS) rates of 15% and 17%, respectively. PB has been associated with an unfavorable outcome, compared with CNS-PNET, in young children.² To conclude, pineoblastoma are rare aggressive tumor of the pineal gland and need to be treated multimodally.

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