Pineal Parenchymal Tumor with Intermediate Differentiation Treated with Radio-Chemotherapy: First Case Report in Our Institution

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Abstract

Pineal parenchymal tumor with intermediate differentiation (PPTID) is an uncommon lesion of the brain with a controversial management strategy. The aim of this study was to analyse the role of chemo-radiotherapy for a PPTID patient at the institution with one case report treated by multidisciplinary team.

Keywords: pineal parenchymal tumor, pineal parenchymal tumor with intermediate differentiation (PPTID), radiotherapy

Pineal parenchymal tumor with intermediate differentiation (PPTID) is an extremely uncommon tumor in Thailand. A young Thai woman presented at the hospital with visual problems and clinical hydrocephalus. There is no treatment protocol for PPTID as yet. The purpose of this study is to determine specific management guidelines for a multidisciplinary team to follow.

Case Report

A 47-year-old Thai female presented with worsening diplopia and headache, with no improvement with eyeglasses for a couple of months. The patient came to hospital for an investigation, and computed tomography (CT scan) and magnetic resonance imaging (MRI) of the brain was performed, and showed a 5cm mass at the pineal region with obstructive hydrocephalus. The differential diagnosis from brain imaging was a pineal tumor in origin with risk of cerebrospinal fluid (CSF) metastases (Figure 1). This was followed by an MRI of the spine that found multiple enhancing nodules in the thecal sac (Figure 2).

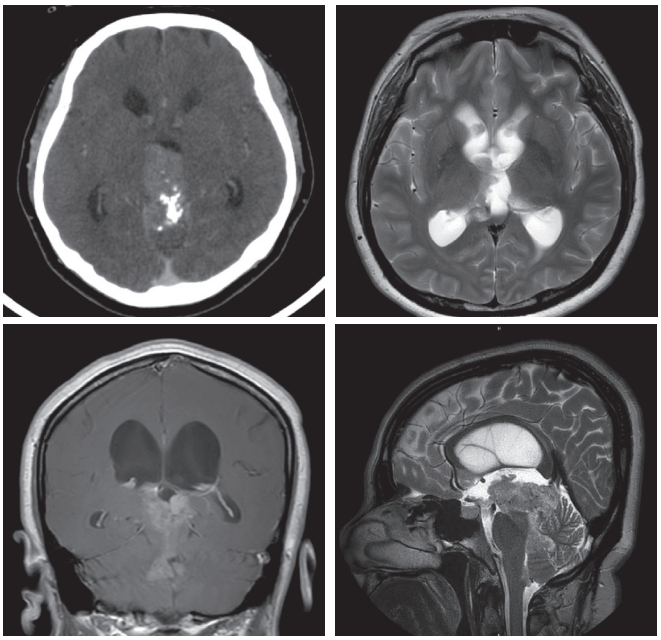


Figure 1: CT Brain, MRI Brain: Inhomogeneous enhancing T2 mass at pineal region 3x4.6x5cm, extending to 3rd and 4th ventricles causing moderate degree of obstructive hydrocephalus with evidence of CSF spreading nodules.

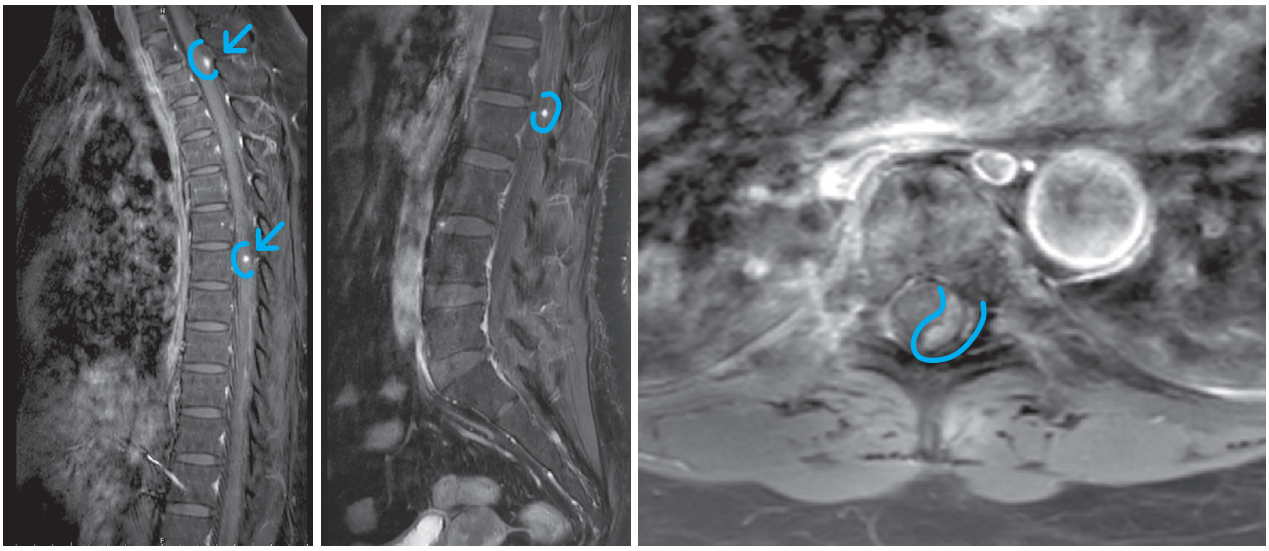


Figure 2: MRI spine: Multiple enhancing nodules in the thecal sac as well as the cauda equine nerve root, drop metastasis is suggested without nerve root compression.

Ventriculoperitoneal shunt (VP shunt) was placed to relieve the hydrocephalus symptoms, and a biopsy was performed simultaneously. Several minute pieces of tissue were obtained for pathological examination. Multiple round cells with vesicular nuclei and scanty cytoplasm were noted (Figure 3A). Nucleoli were seen in some of the cells. Mitotic figures were rarely detected (0-1/10 high-power fields), and this low mitotic count might be due to the limited amount of specimen examined. With immunohistochemical study, the cells strongly expressed synaptophysin (Figure 3B) but only a few of them were reactive with neurofilament protein (Figure 3C). Occasional GFAP-positive reactive glial cells were noted within the lesion. Germ cell markers (AE1/AE3, OCT3/4, and PLAP) were all negative. Ki-67 index was 10% in the most active area (Figure 3D). Combining the clinical and pathologic features, the lesion was consistent with pineal parenchymal tumor of intermediate differentiation (PPTID), defined by the recent WHO 2016 classification of CNS tumors.[1] PPTID corresponds to WHO grade II or III.

The multidisciplinary tumor boards were discussed proper management for this patient whose tumor was uncommon. Anan et al.,[2] reviewed that PPTID is a radiosensitive tumor but the role of the craniospinal irradiation remains controversial even though CSF dissemination is strongly linked to survival outcome.[3] Schild et al.,[4,5] found that a dose of radiation > 50Gy can improve 3-year survival rate. Localized radiation therapy could be an effective treatment strategy for PPTID.[6,7] All findings were presented at the multidisciplinary meeting and it was agreed that the patient would be treated first with radiotherapy to include all the thecal sac (craniospinal irradiation, CSI) with or without adjuvant chemotherapy. The 3600cCGy in 20 fractions of CSI were treated with 3D/IMRT technique with minimally interrupted neutropenia. A planning CT scan doubled up with a post-biopsy MRI scan to delineate tumor volume. Gross Tumor Volume (GTV) was defined as visible tumor on postoperative MRI scan and planning CT scan. Clinical Target Volume (CTV) was created by adding margin of 10 mm to GTV. CTV to Planning Treatment Volume (PTV) margin was 5mm for PTV 46Gy, and 3mm to PTV 50.4Gy respectively as an adaptation to the Glioblastoma radiotherapy recommendation and normal tissue tolerance.[8] The GTV in the thecal sac were given 3mm to create PTV 40.6Gy. A total radiation dose of 5040cGy, 4600cGy & 40.6Gy was administered to the pineal region (GTV) and drop metastases regions in the thecal sac respectively.

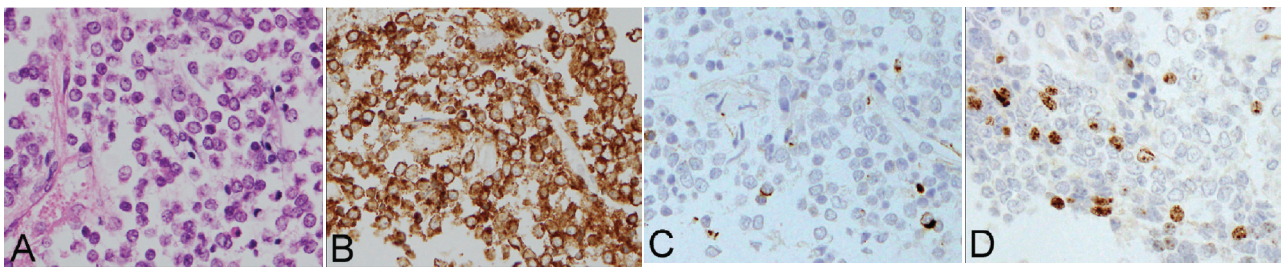


Figure 3: Pathology of pineal parenchymal tumor of intermediate differentiation. Round tumor cells with vesicular chromatin and scanty cytoplasm are shown (A). While most of them express synaptophysin (B), only a few are reactive with neurofilament protein (C). Ki-67 index 10% is observed in the most active region (D). **A:** hematoxylin and eosin, **B:** synaptophysin immunohistochemistry (IHC); **C:** neurofilament protein IHC; **D:** Ki-67 IHC; original magnification of all figures, x400.

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Imaging with MRI (Figure 4) was performed about 6 weeks post complete radiation of a suspected 0.55cm residual enhancing nodule at pineal region while the enhancing nodules in the thecal sac were completely resolved. With a new small enhancing nodule at L1/2 level, arachnoid seeding metastasis was considered, and this still remains a controversial role of chemotherapy.The imaging post radiotherapy reviewed almost complete response in the brain lesion but was controversial in spine lesion. The consensus of the tumor board conference was to opt for chemotherapy.

Given the residual tumor within the irradiated field, she was further adjuvantly treated with chemotherapy of Carboplatin for 6 cycles. MRI scan was repeated 8 weeks post complete chemotherapy with a marked decrease in the size and enhancement of the brain lesion whereas the nodular enhancement of the thecal sac lesion remained unchanged (Figure 5, 6).

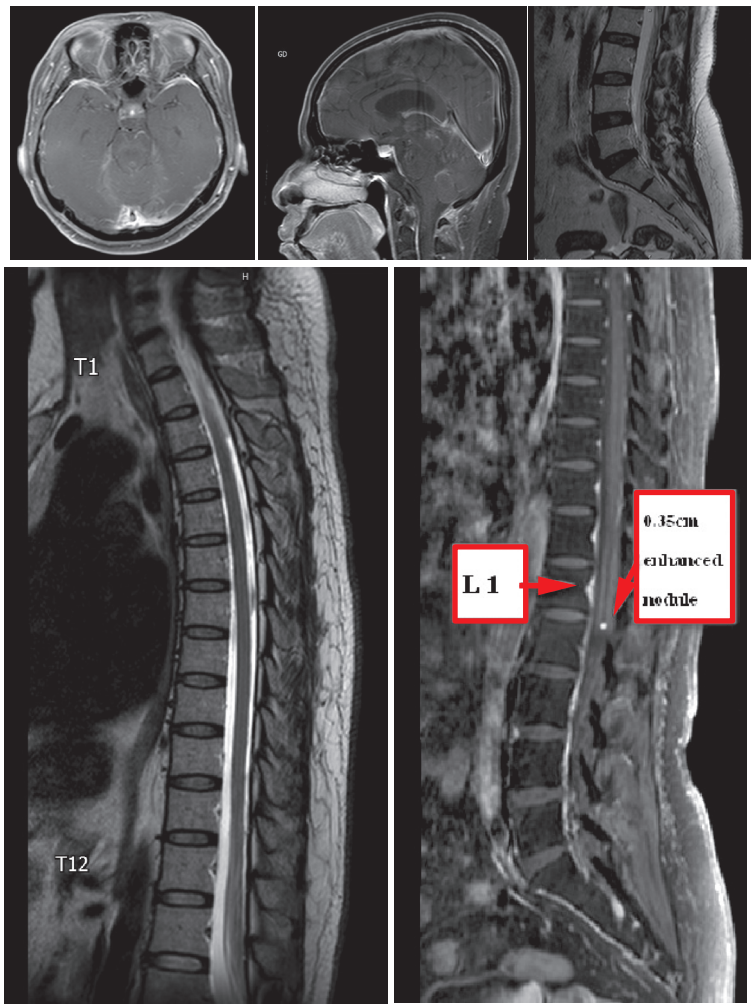


Figure 4: MRI brain and spine 6 weeks post VP shunt and CSI suspected 0.55cm enhancing residual nodule at tumor bed. 0.3cm-enhancing nodule in the thecal sac about L1/2 level was presented.

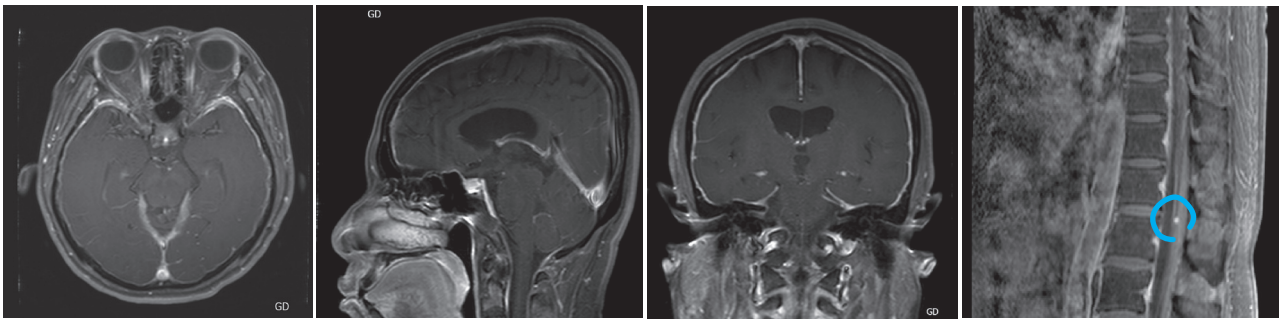


Figure 5: MRI brain and spine 8weeks post chemotherapy: Marked decrease in heterogeneous enhancing lesion in ventricle. Unchanged nodular enhancement in the thecal sac at about L1/2 level.

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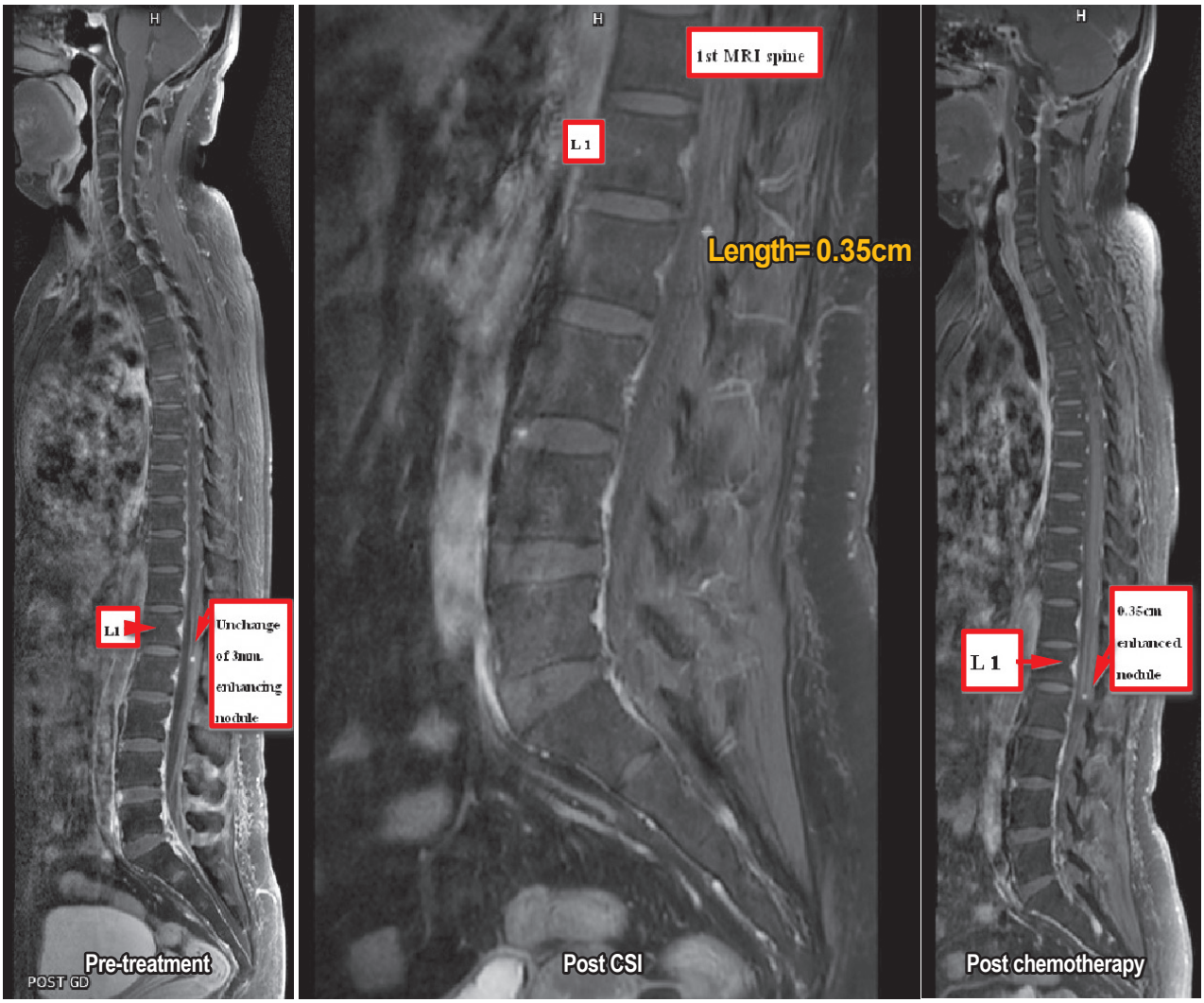


Figure 6: Comparison of MRI spine between first diagnosis, post CSI and post chemotherapy.

In summary, PPTID has a high probability of CSF metastases so there is a role for localized treatment with radiation therapy and the use of chemotherapy as an adjuvant for both localized and metastases lesions should be strongly considered. Long follow up time is needed to demonstrate response, recurrence and future complications.

Discussion

Patients with tumors in the pineal region often present with signs of increasing CSF pressure in the brain or hydrocephalus. Blockage of CSF will cause headache, nausea, vomiting, seizures, memory disturbances and visual changes. Maximal safe resection if possible is the first management of most CNS tumors for diagnosis and planning for proper management. Placement of ventriculoperitoneal (VP) shunt for management of hydrocephalus is acceptable if needed.

Germ cell tumors are by far the commonest neoplasms of the pineal region. Pineal parenchymal tumors (PTTs) and gliomas are rare. Based on the recent WHO classification, PPTs are further subdivided in to pineocytoma (WHO grade I), pineal parenchymal tumor of intermediate differentiation (PPTID) (WHO grade II or III), and pineoblastoma (WHO grade IV).[1] Due to the rarity of these cases, the management of patients with PPTID is controversial, and there is a risk of CSF dissemination.

Prognostic factors were grading of tumor, neuraxis spread, and extent of resection.[7,11] Watanabe et al.,[9] reported on patients with PPTID with cerebrospinal dissemination who received 36Gy of CSI and adjuvant chemotherapy in the management of CSF dissemination. The total radiation dose >50Gy and chemotherapy may be an effective treatment for PPTID with dissemination.[9] The management of CSF metastases with fractionated external beam radiotherapy of 45-54Gy to bulky disease or symptomatic sites is our first local management approach post biopsy. The study of 30 patients of pineal tumors demonstrated a link between radiation dose and survival time.[7]

In this patient, as the first case report of PPTID in our hospital, the total tumor removal was hard to achieve due to the tumor location and invasion toward the surrounding areas. This patient will be monitor with a brain and spine MRI scan for residual lesions and recurrence which will be presented at a multidisciplinary conference.

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Conclusion

PPTID is a rare CNS tumor with risk of CSF dissemination. However, prospective studies conducted at multiple institutes will be needed in order to demonstrate the effectiveness, complications, side effects, and survival rates in patients treated with surgery, chemo-and radiotherapy. This will form the basis for guidelines for institutions.

References

1. Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. Acta Neuropathol 2016;131(6):803-20.
2. Anan M, Ishii M, Nakamura T, et al. Postoperative adjuvant treatment for pineal parenchymal tumour of intermediate differentiation. J Clin Neurosci 2006;13:965-8.
3. Lutterbach J, Fauchon F, Schild SE, et al. Malignant pineal parenchymal tumors in adult patients: patterns of care and prognostic factors. Neurosurgery 2002;51(1):44-55.
4. Schild SE, Scheithauer BW, Schomberg PJ, et al. Pineal parenchymal tumors. Clinical, pathologic, and therapeutic aspects. Cancer 1993;72(3):870-80
5. Schild SE, Scheithauer BW, Haddock MG, et al. Histologically confirmed pineal tumors and other germ cell tumors of the brain. Cancer 1996;15;78(12):2564-71.
6. Mallick S, Benson R, Rath GK. Patterns of care and survival outcomes in patients with pineal parenchymal tumor of intermediate differentiation: An individual patient data analysis. Radiother Oncol 2016;121(2):204-08.
7. Das P, Mckinstry S, Devadass A, et al. Are we over treating pineal parenchymal tumour with intermediate differentiation? Assessing the role of localised radiation therapy and literature review. Springerplus 2016;5:26.
8. Niyazi M, Brada M, Chalmers AJ, et al. ESTRO-ACROP guideline "target delineation of glioblastomas". Radiother Oncol 2016;118(1):35-42.
9. Watanabe T, Mizowaki T, Arakawa Y, et al. Pineal parenchymal tumor of intermediate differentiation: Treatment outcomes of five cases. Mol Clin Oncol 2014;2(2):197-202.
10. Yi J, Kim H, Choi Y, et al. Successful treatment by chemotherapy of pineal parenchymal tumor with intermediate differentiation: a case report. Cancer Res Treat 2013;45(3): 244-9.
11. Raleigh DR, Solomon DA, Lloyd SA, et al. Histopathologic review of pineal parenchymal tumors identifies novel morphologic subtypes and prognostic factors for outcome. Neuro Oncol 2017;19(1): 78-88.