Primary pediatric mid-brain lymphoma: Report of a rare pediatric tumor in a rare location

Rony Benson, Supriya Mallick, Suvendu Purkait, Vaishali Suri, K P Haresh, Subhash Gupta, Dayanand Sharma, Pramod Kumar Julka, Goura Kishore Rath

Rony Benson, K P Haresh, Subhash Gupta, Dayanand Sharma, Pramod Kumar Julka, Goura Kishore Rath, Department of Radiotherapy, All India Institute of Medical Sciences, New Delhi 110029, India

Supriya Mallick, Department of Radiation Oncology, All India Institute of Medical Sciences, New Delhi 110029, India

Suvendu Purkait, Vaishali Suri, Department of Pathology, All India Institute of Medical Sciences, New Delhi 110029, India

Author contributions: All the authors contributed to the paper.

Institutional review board statement: The study was cleared by Institutional Review Board (IRB-AIIMS, New Delhi).

Informed consent statement: Consent was obtained from patient before starting treatment.

Conflict-of-interest statement: None of the authors have any conflict of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Manuscript source: Unsolicited manuscript

Correspondence to: Dr. Supriya Mallick, MD, Senior Research Associate, Department of Radiation Oncology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India. drsupriyamallick@gmail.com
Telephone: +91-98-99448450
Fax: +91-11-26589243

Received: May 15, 2016
Peer-review started: May 17, 2016
First decision: July 11, 2016

Revised: August 16, 2016
Accepted: September 21, 2016
Article in press: September 22, 2016
Published online: December 16, 2016

Abstract
Primary central nervous system lymphoma (PCNSL) is a rare disease in pediatric age group. A thirteen-year-old male child presented with complaints of headache for six months, vomiting and diplopia for three days. Magnetic resonance imaging of the brain showed a single lesion of 1.7 cm × 1.6 cm × 1.6 cm in the mid brain and tectum. He underwent a gross total resection of the tumor. The histopathological evaluation revealed B cell high grade non Hodgkin lymphoma. The patient was treated with High dose methotrexate and cranio spinal radiation. The patient was alive without disease 12 mo after completion of treatment. This case highlights importance of keeping PCNSL as differential in brain stem lesions of pediatric patients also. Radiation and chemotherapy remains the most important treatment for such patients.

Key words: Primary; Midbrain; Lymphoma; Paediatric

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Primary central nervous system lymphoma (PCNSL) in pediatric population is an uncommon disease. In addition location in the brainstem is far less common. We are reporting a rare case of PCNSL in the brain stem location in a 13-year-old patient. Brain stem lesions are not generally considered for lymphoma. This case highlights importance of keeping brainstem lymphoma as a differential.
Benson R et al. Primary pediatric mid-brain lymphoma

Benson R, Mallick S, Purkait S, Suri V, Haresh KP, Gupta S, Sharma D, Julka PK, Rath GK. Primary pediatric mid-brain lymphoma: Report of a rare pediatric tumor in a rare location. World J Clin Cases 2016; 4(12): 419-422. Available from: URL: http://www.wjgnet.com/2307-8960/full/v4/i12/419.htm DOI: http://dx.doi.org/10.12998/wjcc.v4.i12.419

INTRODUCTION

Primary central nervous system lymphoma (PCNSL) most commonly occurs in the age group of 50-70 years and is rare in pediatric age group[1,2]. Tectum (midbrain) is a very rare site of PCNSL. Here we report a case of primary midbrain lymphoma in a 13-year-old child.

CASE REPORT

A 13-year-old male child was evaluated with complaints of headache for six months, vomiting and diplopia for three days. The child was evaluated with a contrast enhanced magnetic resonance imaging (MRI) of the brain which showed a single lesion 1.7 cm × 1.6 cm × 1.6 cm in the mid brain and tectum with intense contrast enhancement and hydrocephalus. The lesion was mildly hypo-intense in T1 and heterogeneously hyper-intense on T2W image with few hypo-intense areas. There was edema extending to mid part of pons (Figure 1). With a diagnosis of focal midbrain glioma, the patient underwent a ventriculo-peritoneal shunt (Figure 1). With a diagnosis of focal midbrain glioma, the patient underwent a ventriculo-peritoneal shunt (Figure 1). With a diagnosis of focal midbrain glioma, the patient underwent a ventriculo-peritoneal shunt (Figure 1). With a diagnosis of focal midbrain glioma, the patient underwent a ventriculo-peritoneal shunt (Figure 1). With a diagnosis of focal midbrain glioma, the patient underwent a ventriculo-peritoneal shunt (Figure 1).

Postoperative MRI revealed no residual mass. MRI screening of the spine did not reveal any drop metastasis or lesion. Cerebro spinal fluid (CSF) cytology was done and showed lymphoma cells. The bone marrow biopsy showed normal hematopoiesis cell. Ophthalmic evaluation did not reveal any vitreous lesions and serology for HIV 1 and 2 was negative. Whole body positron emission tomography (PET-CT) showed no abnormal fluoro-deoxy glucose avid areas except inflammatory lymph node in mesentery.

Patient was planned for adjuvant chemotherapy with high dose methotrexate. Methotrexate was given at a dose of 3.5 g/m² with adequate hydration and Leucovorin rescue. The patient received 6 cycles of chemotherapy with high dose methotrexate and craniospinal irradiation. The dose of craniospinal irradiation planned was 36 Gray in 18 fractions over 3.5 wk followed by boost to the whole cranium for 9 Gray in 5 fractions over 1 wk. The patient is surviving without disease 1 year after treatment.

DISCUSSION

PCNSL is a very rare tumor in children. Pediatric cases account for about 1.5% of cases of primary CNS lymphoma reported to the brain tumor registry of Japan (1969-1990)[3,4]. Patients with human immune deficiency virus infection are at a higher risk for development of primary CNS lymphoma[5].

Pediatric PCNSL are different from adult group in that they are more frequently occurring in the posterior fossa (33.5% vs 9%) and have higher incidence of meningeal metastasis[6].

The majority of the patients of PCNSL have histology of diffuse large B-cell lymphoma (DLBCL). About 10% of the patients may have other histologies like Burkitts Lymphoma, indolent B-cell lymphomas and T cell lymphoma[7]. EBV may be seen associated with DLBCL of the CNS and may be more commonly associated in non-immune compromised patients[8]. Contrast enhanced MRI of the brain, spine screening MRI, CSF cytology, ophthalmic evaluation whole body CT/PET CT, viral markers are the important investigations in management of PCNSL.

It has been reported that adult PCNSL occurs in supra tentorial location in majority of patients with posterior fossa as a location of tumor only in 7% of the cases[9]. Only 3% cases have been reported to have a brainstem involvement and majority of such lesions are of T-cell lineage. Contrast enhanced MRI is the preferred imaging modality in these cases of PCNSL. Approximately 90% of these cases present with contrast enhancing lesions[10]. Ring like enhancement is rarely observed in immune competent patients, but commonly found in immune compromised patients[11]. The lesions may be multiple especially in immune compromised patients.

PCNSL is a highly radiosensitive and chemosensitive infiltrative tumor. Steroids may be deferred till the diagnosis of PCNSL is confirmed. Surgery is helpful in confirming the diagnosis. A median survival of 4.6 mo has been reported for patients treated with surgical excision alone. Whole brain radiotherapy has conferred a median survival of 14.5-18 mo and a 5-year survival of 35%. However, patients treated with radiation alone experience early local failure. This finding paved for the combined modality therapy of chemotherapy and radiation therapy in sequential manner. Presently, high dose methotrexate forms the back bone of therapy in PCNSL with low dose whole brain radiation having important role in long term disease control[12]. Cytosine arabinoside has been added to high dose methotrexate to improve survival in this group of patients[13]. In another series 5-year event free survival was reported to be 70% in patients treated with combination chemotherapy of high dose methotrexate and Cytosine arabinoside without radiotherapy[14]. A radiation dose
of 40-45 Gray to the whole cranium is recommended. Cranio spinal irradiation and intra thecal methotrexate is useful in patients with spinal drop metastasis or CSF dissemination. But this aggressive treatment approach is associated with significant toxicity. Neuro cognitive effects, hormonal imbalances, growth abnormalities and

Figure 1  Axial and sagittal section of contrast enhanced magnetic resonance imaging. It shows a lesion 1.7 cm × 1.6 cm × 1.6 cm in the mid brain and tectum with intense contrast enhancement. The lesion was mildly hypo-intense in T1 and heterogeneously hyper-intense on T2W image with few hypo-intense areas. There edema was extending to mid part of pons.

Figure 2  The histopathological evaluation revealed B cell high grade non Hodgkin lymphoma. A, B: Photomicrograph showing infiltration of large atypical lymphoid cell with interspersed lymphocytes; C: The tumor cells were immunopositive for LCA; D: CD20; E: While negative for CD3; F: Synaptophysin.
secondary malignancies are very important when we treat a pediatric case with such aggressive approach\textsuperscript{[2]}. In conclusion, lymphoma in mid brain in pediatric age group is extremely rare. Chemotherapy forms the most important part of therapy for such cases. Low dose whole brain radiotherapy may be considered for improving long term disease control.

**COMMENTS**

**Clinical diagnosis**
Focal midbrain glioma.

**Differential diagnosis**
Tectal glioma, primitive neuroectodermal tumor.

**Laboratory diagnosis**
B cell lymphoma (DLBCL).

**Imaging diagnosis**
Focal midbrain glioma.

**Pathological diagnosis**
DLBCL.

**Treatment**
Gross total excision, high dose methotrexate based 6 cycles of chemotherapy, cranio spinal irradiation.

**Peer-review**
This is a very rare location of a lymphoma in a teenager. The case presentation is interesting.

**REFERENCES**

1. Korfel A, Schlegel U. Diagnosis and treatment of primary CNS lymphoma. *Nat Rev Neurol* 2013; 9: 317-327 [PMID: 23670107 DOI: 10.1038/nrneurol.2013.83]

2. Abla O, Weitzman S, Blay JY, O’Neill BP, Abrey LE, Neuwelt E, Doolittle ND, Baehring J, Pradhan K, Martin SE, Guerraera M, Shah S, Ghesquieres H, Silver M, Botensky RA, Batchelor T. Primary CNS lymphoma in children and adolescents: a descriptive analysis from the International Primary CNS Lymphoma Collaborative Group (IPCG). *Clin Cancer Res* 2011; 17: 346-352 [PMID: 21224370 DOI: 10.1158/1078-0432.CCR-10-1161]

3. Rodriguez MM, Delgado PI, Petito CK. Epstein-Barr virus-associated primary central nervous system lymphoma in a child with the acquired immunodeficiency syndrome. A case report and review of the literature. *Arch Pathol Lab Med* 1997; 121: 1287-1291 [PMID: 9431321]

4. Kai Y, Kuratsu J, Ushio Y. Primary malignant lymphoma of the brain in childhood. *Neurol Med Chir* (Tokyo) 1998; 38: 232-237 [PMID: 9631639 DOI: 10.2176/nmc.38.232]

5. Preusser M, Woehrer A, Koperek O, Rottenfusser A, Dieckmann K, Gatterbauer B, Roessler K, Slave I, Jaeger U, Streubel B, Hainfellner JA, Chott A. Primary central nervous system lymphoma: a clinicopathological study of 75 cases. *Pathology* 2010; 42: 547-552 [PMID: 20854073 DOI: 10.1002/path.2450.2010.50876]

6. Sutherland T, Yap K, Liew E, Tartaglia C, Pang M, Trost N. Primary central nervous system lymphoma in immunocompetent patients: a retrospective review of MRI features. *J Med Imaging Radiat Oncol* 2012; 56: 295-301 [PMID: 22697326 DOI: 10.1111/j.1754-9485.2012.02366.x]

7. Johnson BA, Fram EK, Johnson PC, Jacobowitz R. The variable MR appearance of primary lymphoma of the central nervous system: comparison with histopathologic features. *AJNR Am J Neuroradiol* 1997; 18: 563-572 [PMID: 9090424]

8. Milgrom SA, Yahalom J. The role of radiation therapy in the management of primary central nervous system lymphoma. *Leuk Lymphoma* 2015; 56: 1197-1204 [PMID: 25219590 DOI: 10.3109/10428194.2014.961014]

9. DeAngelis LM, Yahalom J, Heinemann MH, Cirrincione C, Thaler HT, Krol G. Primary CNS lymphoma: combined treatment with chemotherapy and radiotherapy. *Neurology* 1990; 40: 80-86 [PMID: 2296388 DOI: 10.1212/WNL.40.1.80]

10. Abla O, Sandlund JT, Sung L, Brock P, Corbett R, Kiror I, Griffin TC, Blaser S, Weitzman S. A case series of pediatric primary central nervous system lymphoma: favorable outcome without cranial irradiation. *Pediatr Blood Cancer* 2006; 47: 880-885 [PMID: 16365864 DOI: 10.1002/pbc.20736]

**P-Reviewer:** Alshehabi Z, Delwail V, Kupeli S, Mihaila RG  
**S-Editor:** Qiu S  
**L-Editor:** A  
**E-Editor:** Wu HL
