Case Report

DOI: 10.21276/APALM.2948

Choroid Plexus Carcinoma of Third Ventricle: A Rare Case Report

Shivali Awasthi*, Prateek Kinra and Nisha Verma

Dept of Pathology, AFMC Pune, Maharashtra, India

ABSTRACT

Choroid plexus tumors are very rare tumors accounting for 0.5% of all brain tumors. They most commonly occur in childhood and present with features of raised intra-cranial pressure. World Health Organization (WHO) classifies them into 3 broad categories namely papilloma (grade 1), atypical papilloma (grade 2) and carcinoma (grade 3). These tumors are most commonly seen in the supratentorial compartment with lateral ventricle followed by third ventricle, being the most common site. Rarely, they may present in infratentorial region in adults. Dissemination through cerebrospinal fluid space is the inevitable natural course of the disease. Treatment requires total surgical resection with adjuvant chemoradiotherapy being controversial. In this study, we present a case of 7-year-old child who visited to the out-patient department of our center with progressive quadriparesis and altered sensorium and on imaging was found to have a well-defined, lobulated mass lesion with intense post contrast enhancement in posterior part of third ventricle with resultant obstructive hydrocephalus. The patient underwent craniotomy and on immuno-histopathological examination was diagnosed as a case of choroid plexus carcinoma. However, the patient succumbed to his illness a month after his surgery. The aim of this report is to highlight a rare entity, its diagnostic challenge and effect of early management in the form of surgery and chemo-radiotherapy.

Keywords: *Childhood, Choroid plexus carcinoma, third ventricle, SMARCB1, SMARCA4, P53*

Introduction

Choroid plexus tumors are extremely rare tumors and account for approximately 2% of all intracranial glioma and 0.5% of brain tumors [1]. Average annual incidence of this tumor is approximately 0.3 per 1,000,000.[2] They comprise 0.77% of all brain tumors and 14% of them occur in less than 1 year of age. Approximately 80% of choroid plexus carcinoma (CPC) occur in children.[3]

Choroid plexus tumors range from well-differentiated papilloma (WHO Grade I) to very aggressive choroid plexus carcinoma (WHO Grade III) with an intermediate form named atypical choroid plexus papilloma (WHO Grade II).[1]

These tumors arise in ventricles, most commonly in lateral and fourth ventricle; lateral ventricle being the commonest site in children and fourth ventricle being in adults. Other sites include infratentorial region and cerebellopontine angle.[4]

Case Report

We present to you a case of 7-year-old male who came to our center with history of progressive quadriparesis with gait ataxia and altered sensorium for 2 weeks along with up gaze palsy. On examination, there was eye opening to painful stimuli, no verbal response, anisocoria, bilateral papilledema (Grade II) and abnormal flexion response. On imaging, Contrast Enhanced MRI (CE-MRI) Brain showed a 4.9x4x4.5 cm well defined, lobulated mass lesion with intense post contrast enhancement in posterior part of third ventricle with resultant expansion of the ventricles and obstructive hydrocephalus (Fig 1a and 1b)

Further, NCCT Head revealed pneumocephalus in left frontal region with a large 3rd ventricular space-occupying lesion (SOL) (Fig 1c and 1d). The patient was planned for surgery and underwent right parasagittal craniotomy with anterior interhemispheric transcallosal approach and excision of SOL.

We received multiple reddish-grey fragmented bits during frozen section and the case was reported as High-Grade Carcinoma. On further histopathological examination, we saw a highly cellular tumor, predominantly arranged in sheets with focal papillae formation. Individual tumor cells showed high N:C ratio, inconspicuous nucleoli and scant cytoplasm. Tumor was seen to invade brain parenchyma focally.

On immunohistochemistry, these tumor cells were found to be positive for cytokeratin (CK), Glial Fibrillary Acidic Protein (GFAP) and P53 and were negative for S100, synaptophysin, Epithelial Membrane Antigen (EMA) and vimentin. INI-1(Integrase Interactor-1) was retained by the tumor cells (Figure 3). Based on immuno-histological findings a final diagnosis of Choroid Plexus Carcinoma (WHO Grade III) was given.

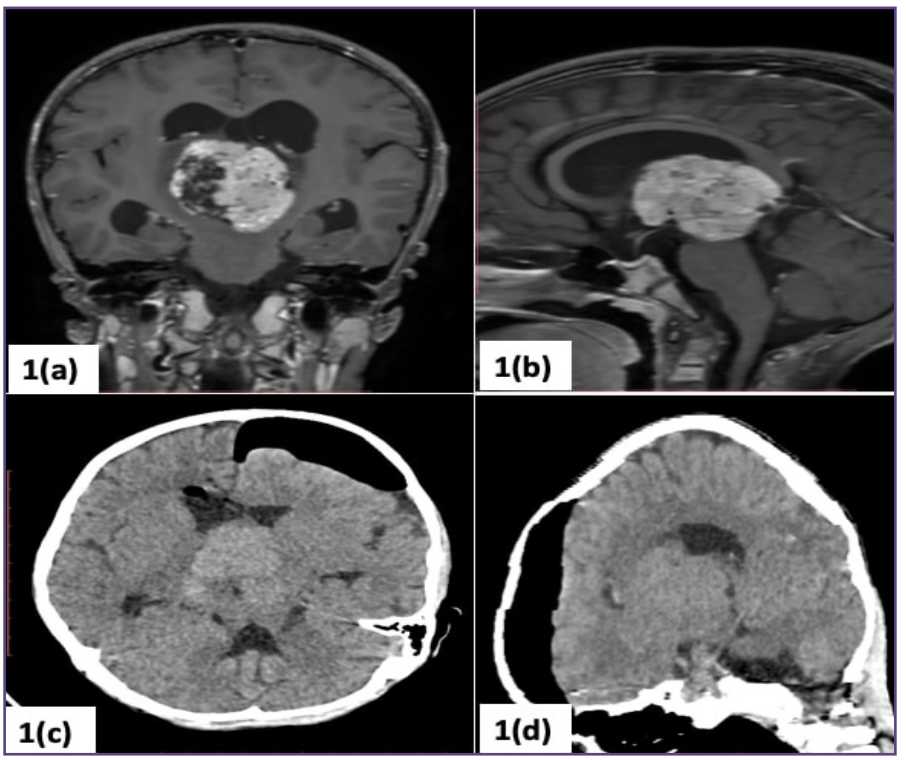

Fig. 1 (a) &1(b): CEMRI Brain showed a 4.9x4x4.5 cm well defined, lobulated mass lesion with intense post contrast enhancement in posterior part of third ventricle with resultant expansion of the ventricles and obstructive hydrocephalus; Figure 1(c) &1(d): NCCT Head revealed pneumocephalus in left frontal region with a large 3rd Ventricular SOL.

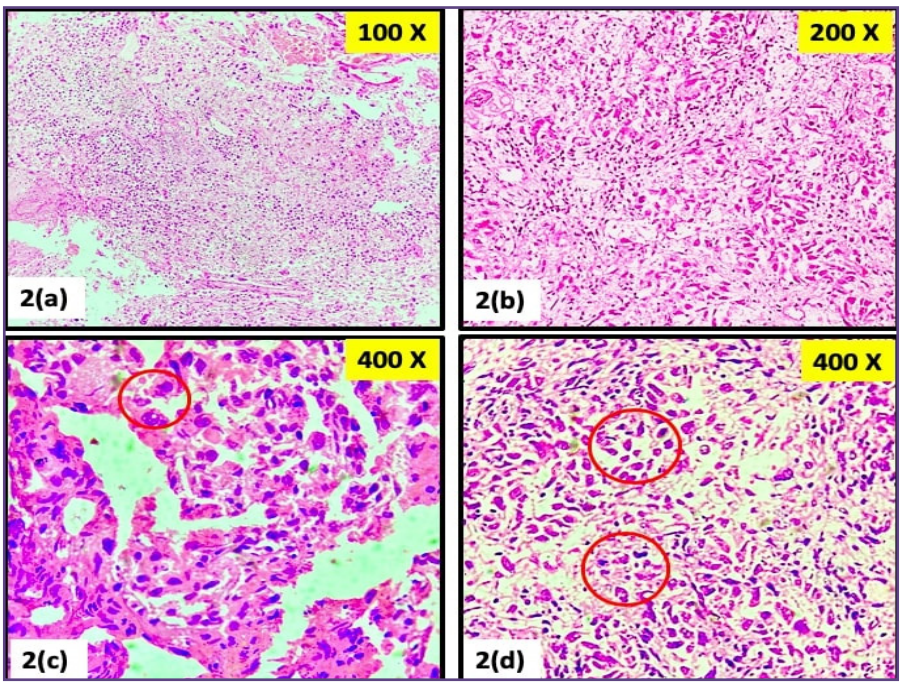

Fig. 2(a): On low magnification, an infiltrative tumor arranged in sheets with blunting of papillary pattern is noted. Large areas of necrosis and hemorrhage present; Figure 2(b): 200X. Highly cellular tumor with marked cellular pleomorphism; Figure 2(c) &2(d): On high power(40X), individual tumor cells show marked pleomorphism with high N:C ratio, hyperchromatic nuclei, inconspicuous nucleoli and scant eosinophilic cytoplasm. Mitosis(inset) is brisk.

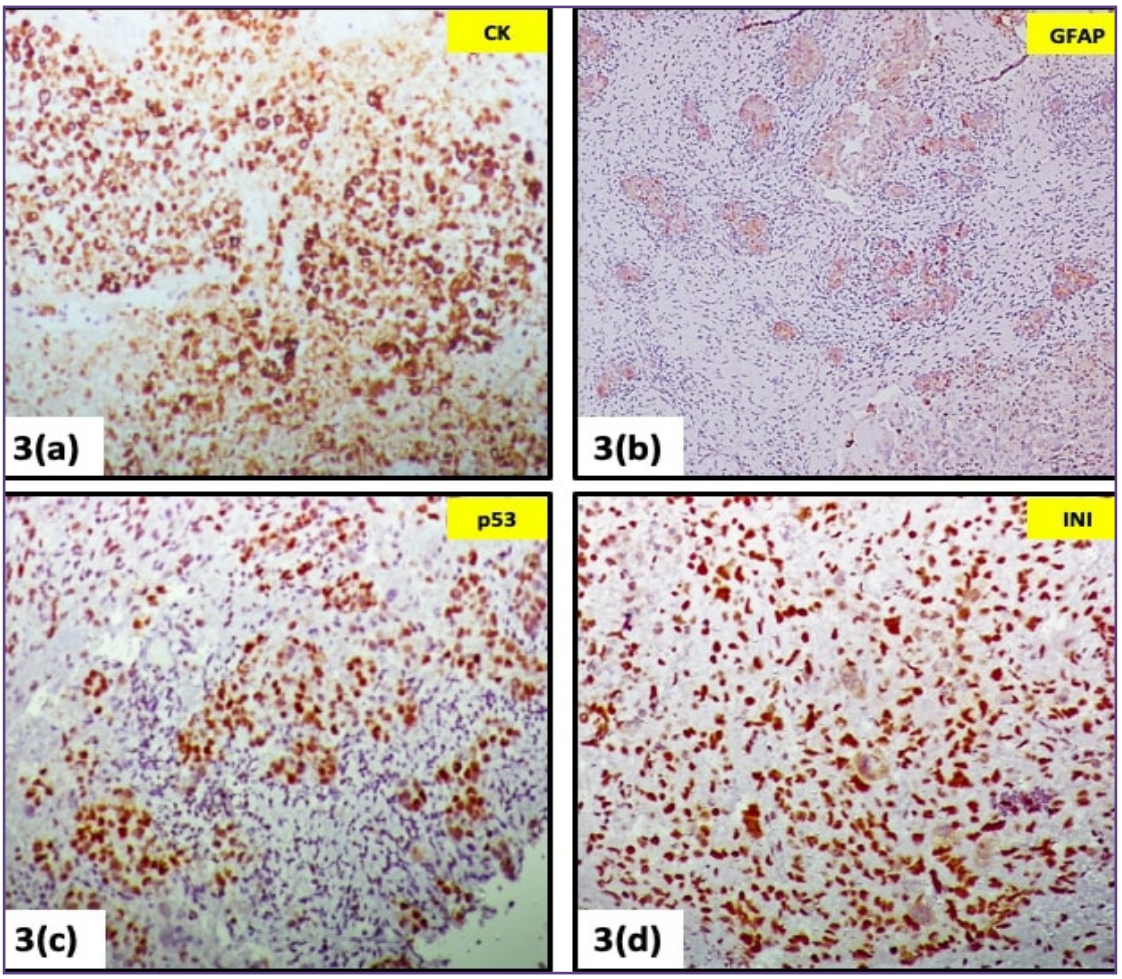

Fig. 3(a-c): Tumor cells show positivity for cytokeratin, GFAP and p53; Figure 3(d): INI-1 was retained by tumor cells.

Discussion

Choroid plexus carcinomas (CPCs) are frankly malignant epithelial neoplasm most commonly occurring in the lateral ventricles of children, showing at least 4 out of 5 histological features: increased mitoses(>5/10hpf), increased cellular density, nuclear pleomorphism, blurring of papillary pattern with poorly structured sheets of tumor cells, and necrotic areas.[5]

Most occur sporadically, but may occur in association with hereditary syndromes like Aicardi syndrome or Li-Fraumeni syndrome.[6]

Radiologically, these tumors typically present as large intraventricular lesions with irregular enhancing margins, a heterogenous signal on T2-weighted and T1-weighted images, oedema in adjacent brain, hydrocephalus, and disseminated tumor.[7] As seen in the current case, the tumor was well-defined and lobulated with intense post-contrast enhancement characteristic of this tumor.

As seen in the reported case, grossly, these tumors are well-circumscribed, solid, may shows areas of necrosis, highly vascular, tendency to bleed and invade into the surrounding brain parenchyma. On microscopy, they show frank signs of malignancy as discussed above. Diffuse brain invasion is common.[8]

In this case, the tumor appeared frankly malignant with high cellularity and tumor arranged in diffuse sheets and occasional papillae. Individual tumor cells showed high N:C ratio, inconspicuous nucleoli and scant cytoplasm. Invasion into parenchyma was focal and evident. No ependymal rosettes or pseudo rosettes were seen, thereby ruling out ependymoma. The tumor was positive for CK and p53 while was negative for S100. Papillary meningioma closely mimics CPC, however is negative for CK. INI-1 was also was retained by the tumor cells, thereby ruling out atypical teratoid/rhabdoid tumor (ATRT) which is a malignant childhood tumor and must always be excluded in such cases.

As per WHO, CPCs like their benign counterparts (Choroid Plexus Papilloma), are positive for cytokeratin, but are less commonly positive for S100 and transthyretin.[9] They may show p53 positivity in cases with associated TP53 mutation. Ki67 proliferation index is higher than other choroid plexus tumors. 20% cases may show positivity for GFAP. Almost all cases retain nuclear positivity for SMARB1and SMARCA4. This helps to differentiate them from atypical rhabdoid tumor which account for 1-2 % of pediatric brain tumors. There is usually no membranous positivity for EMA.[10]

The various differential diagnosis includes atypical rhabdoid tumor, ependymoma- papillary variant, papillary meningioma, cerebellar medulloblastoma and astrocytoma. These can be differentiated by various subtle morphological and immunohistochemical features. The atypical cells in papillary variant of ependymoma characteristically have stippled nuclear chromatin and micronucleoli. Ependymal rosettes and perivascular pseudo-rosettes with cell processes oriented towards the blood vessel are commonly seen. These cells are positive for GFAP on immunohistochemistry. Papillary meningioma (WHO grade III) can both occur in pediatric age group as well as can arise in choroid plexus but are negative for cytokeratin on immunohistochemistry. In our case, the tumor cells were strongly positive for cytokeratin on immunohistochemistry. Another differential diagnosis can be astrocytoma, but they are positive for S100 and negative for CK while in our case the tumor cells were S100 negative and CK positive**.** Tumor cells in cerebellar medulloblastoma are arranged in sheet like pattern with individual cells showing hyperchromatic nuclei in a fibrillary background. Homer-Wright Rosettes are also commonly seen. Here the tumor cells are positive for neuronal markers like NFP, Neu-N and synaptophysin and are negative for S-100 and Cytokeratin.[11]

About 50% of these tumors, harbor TP53 mutation. Classic cytogenetic and genome-wide array-based approaches have shown hyper- or hypodiploidy in choroid plexus carcinomas.

Gross total resection forms the mainstay of treatment and is associated with improved overall survival, though often may be associated with increased morbidity. The use of adjuvant therapies is yet to be standardized, although studies suggest a combination of chemotherapy and radiotherapy may be beneficial in patients with incompletely resected CPCs. Use of radiation therapy is limited in younger children (<3 years) and is not recommended.[12]

With appropriate treatment, 3-year and 5-year progression free survival rates of choroid plexus carcinoma have been reported as 58% and 38% respectively and overall survival rates as 83% and 62%. One study demonstrated that CPCs with loss of chromosome arm 12q were associated with a significantly shorter survival rates than tumors without this alteration.[13]

Conclusion

Choroid plexus carcinoma is an aggressive tumor and should be kept in mind in differentials when dealing with a childhood CNS malignancy. Site of involvement along with clinic-radiological features are soft indicators of this tumor. Appropriate and timely diagnosis of this malignancy can considerably affect the survival and prognosis of the patient. The aim of this report is to highlight the approach to CNS malignancy in childhood especially in the setting of overlapping histopathological features of this tumor with other tumors and rarity of this entity.

Acknowledgements

Nil

Funding

Nil

Competing Interests

Nil

Reference

1. Paulus W, Brandner S. Choroid plexus tumours. In: Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, editors. WHO Classification of Tumours of the Central Nervous System. Lyon, France: IARC Press; 2007. pp. 81–5
2. Hasselblatt M, Bohm C, Tatenhorst L, Dinh V, Newrzella D, Keyvani K, et al. Identification of novel diagnostic markers for choroid plexus tumors, a microarray-based approach. Am J Surg Pathol. 2006; 30:66–74
3. Kim T, Park MR, Hong EK, et al. Choroid Plexus Carcinoma in Adults: Two Case Reports. Brain Tumor Res Treat, 2019; 7(1): 48-52
4. Rickert CH, Paulus W. Tumors of the choroid plexus. Microsc Res Tech. 2001;52:104.
5. Newbould MJ, Kelsey AM, Arango JC, Ironside JW. The choroids plexus carcinomas of childhood: Histopathology, immunocytochemistry and clinicopathological correlations. Histopathology 1995; 26:137-43
6. Krutilkova, V., Trkova, M., Fleitz, J., Gregor, V., Novotna, K., Krepelova, A.,Sedlacek, Z. Identification of five new families strengthens the link between childhood choroid plexus carcinoma and germline TP53 mutations. European Journal of Cancer, 2005;41(11): 1597-1603
7. Meyers, S. P., Khademian, Z. P., Chuang, S. H., Pollack, I. F., Korones, D. N., & Zimmerman, R. A. Choroid plexus carcinomas in children: MRI features and patient outcomes. Neuroradiology. 2004;46(9): 770–780.

8. Crea, A., Bianco, A., Cossandi, C., Forgnone, S., Fornaro, R., Crobeddu, E., Panzarasa, G. Choroid plexus carcinoma in adults: literature review and first report of a location into the third ventricle. World Neurosurgery. 2019

9. Louis D et al. WHO Classification of Tumours of the Central nervous System. 5th edition. 2021.

10. Pawel, B. R. SMARCB1-deficient Tumors of Childhood: A Practical Guide. Pediatric and Developmental Pathology,2017;21(1), 6–28.

11. Singh A, Vermani S, Sharma S, Chand K. Papillary meningioma: a rare but distinct variant of malignant meningioma. Diagn Pathol. 2007;2:3

12. Sun, M. Z, Oh, M. C, Ivan, M. E, Kaur, G, Safaee, M, Kim, J. M,Parsa, A. T. Current management of choroid plexus carcinomas. Neurosurgical Review. 2013; 37(2): 179–192.

13. Zaky, W., Dhall, G., Khatua, S., Brown, R. J., Ginn, K. F., Gardner, S. L., Finlay, J. L. Choroid plexus carcinoma in children: The Head Start experience. Pediatric Blood & Cancer. 2015; 62(5): 784–789.

***Corresponding author:**
Dr. Shivali Awasthi, 1713, Clover Highlands, NIBM-Undri Road, Kondhwa, Pune- 411048
Phone: +91 9442437116
Email: shivaliawasthi3@gmail.com

Financial or other Competing Interests: None.

Date of Submission : 15/10/2020
Date of Final Revision : 14/02/2021
Date of Acceptance : 22/02/2021
Date of Publication : 30/03/2021