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Occasional autoptic finding of Choroid Plexus Papilloma in the cerebellopontine angle in infant: a case report and brief review

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Case Report

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Abstract

Choroid Plexus Papilloma (CPP) is a rare benign tumor of neuroectodermal origin that occurs more commonly in infants who suffer from genetic syndromes. Although the most frequent site in children is the lateral ventricle, we describe the autopsy case of a premature infant with occasional findings of CPP in the cerebellopontine angle. The infant was affected by notable dysmorphic features, including microcephaly and retro-micrognathia, as well as bronchopulmonary dysplasia, coloboma, generalized hypotonia, digestive disorders, and a microdeletion in the 2p21p16.2 region. No other autopsy cases of neonates with choroid plexus papilloma have been reported in literature.

Introduction

Choroid plexus papilloma (CPP) is a rare benign tumor of the central nervous system that arises from the epithelium of the choroid plexus. In the pediatric population, CPP is the third most frequent congenital brain tumor and accounts for 0.4–0.6% of all intracranial neoplasms, with an average age of 3.5 years [1, 2, 3]. Males are more affected than females at a ratio of 1.2:1 [4].

Pathologically, CPP is associated with simian virus (SV) 450 [5] and, according to other studies, with BK and John Cunningham (JC) viruses [6]. Furthermore, one of the most frequent mutations is that of the TP53 gene [7] responsible for Li-Fraumeni Syndrome [8], abnormalities of the X chromosome responsible for Aicardi Syndrome [9], hypomelanosis of Ito, and 9p duplication [2].

CPP presents locations and clinical manifestations that vary depending on the age group.

In newborns and children the most frequent site is supratentorial within the lateral ventricles [10]; in adults the most common site is the fourth ventricle [11]. It is rarely located at the cerebellopontine angle and in the third ventricle [12, 13]. In particular, it is reported in the literature that CPPs resulting from the cerebellopontine angle occur almost exclusively in adults and are rarely found in children [11, 14].

Clinical manifestations are predominantly caused by hydrocephalus [15]. In particular, in newborns and children CPP manifests itself with increased head circumference, altered mental status, poor nutrition, associated with paralysis of upward gaze, reduced activity and alteration of consciousness [2]. Instead, in adults CPP presents with signs of increased intracranial tension, such as vomiting, headache, paralysis of lateral gaze, visual field defects of the same name and alteration of mental status [2].

According to the current World Health Organization Classification [16], these choroid plexus tumors are classified into choroid plexus papilloma (CPP) when < 2 mitotic figures per 10 high-power fields (grade 1), atypical choroid plexus papilloma (aCPP) when they have 2–5 mitotic figures per 10 high-power fields (grade 2) and choroid plexus carcinoma (CPC) when they have > 5 mitotic figures per 10 high-power fields (grade 3).

Furthermore, choroid plexus tumors are classified into 3 epigenetic subgroups [17] based on the DNA methylation profile critical for prognosis, such as low-risk supratentorial pediatric choroid plexus tumors

including CPP and aCPP, infratentorial choroid plexus tumors low-risk adult which includes CPP and aCPP, high-risk pediatric supratentorial choroid plexus tumors which includes CPP, aCPP and CPC.

Macroscopically, CPP appears as well-circumscribed friable cauliflower-like masses, sometimes cysts, hemorrhages, and calcifications are present [18].

Microscopically, CPP is characterized by papillary architecture similar to normal choroid plexus, single layer of monomorphic cuboidal to columnar cells, mild nuclear pleomorphism, and mitotic activity < 2/10 high-power fields with no necrosis [19]

On immunohistochemistry, tumors are positive for cytokeratin, vimentin, podoplanin, S-100, and glial fibrillary acidic protein (GFAP) is positive in 20% of CPP [20].

In the case here presented judicial autopsy was requested by prosecutor as the Although there is extensive literature on the histopathological findings of Choroid Plexus Papilloma (CPP), to the best of our knowledge, no previous reports of autopsy findings in neonates with CPP exist. Autopsy evidence is crucial for understanding the pathogenesis of this rare tumor. We present the first documented autopsy case of a premature infant with incidental findings of CPP in the cerebellopontine angle. This case highlights the importance of autopsy in elucidating both the pathogenesis of CPP and the underlying cause of death. In this case, a forensic autopsy was requested as the infant's parents alleged poor management of the respiratory insufficiency that led to the death.

Case report

A 29 weeks gestation infant was born weighing significantly below the average for his gestational age, indicative of intrauterine growth restriction. At birth, he had initial severe cardiorespiratory distress that necessitated intensive care support.

Throughout his early life, he faced multiple complications associated with his prematurity including bronchopulmonary dysplasia (BPD) and a disease of the hyaline membranes (stage 2–3), further complicating his respiratory status.

He also developed acute parainfectious anemia and acute renal failure associated with a septic condition.

Genetic testing revealed de novo deletion of the 2p21p16.2 region, providing a potential genetic underpinning for some of his clinical manifestations, including developmental and morphological anomalies such as microcephaly and retro-micrognathia. Notably, this specific deletion and associated syndrome have not been described in the literature, highlighting the rarity and uniqueness of his condition.

His ongoing care involved monitoring for growth and development, addressing the common post-premature birth issues such as feeding difficulties and potential reflux, for which he was treated with

magnesium alginate as advised by the pediatrician. Despite these interventions, the vulnerability to infections and other complications remained high. Indeed, he underwent some episodes of apnea possibly triggered by medication side effects, transient episodes of pallor, and an overall failure to thrive as indicated by sporadic refusal to feed and hyporeactivity.

His repeated hospital admissions underscored the complexity of his condition, with each episode presenting a challenge in balancing the immediate clinical needs with long-term developmental outcomes. The final admission to the hospital was prompted by symptoms of respiratory distress, where despite aggressive treatment measures, he experienced a rapid decline, culminating in death. Given the sudden and unexpected deterioration in his condition, coupled with the complex medical history and the presence of multiple underlying health issues, the exact cause of death was not immediately apparent. An autopsy was required, which identified the cause of death as respiratory failure due to bronchopulmonary dysplasia. Lung sections examined showed a marked inflammatory infiltrate with areas of fibroatelectatic and emphysematous parenchyma, consistent with the diagnosis of bronchopulmonary dysplasia [21, 22]. Further microbiological tests revealed the presence of Rhinovirus and Bocavirus in the material collected through oropharyngeal and nasopharyngeal swabs. Bocavirus, along with Rhinovirus, is a leading cause of severe respiratory infections in preterm infants, surpassed only by Respiratory Syncytial Virus [23, 24].

With regard to the finding of the CPP on macroscopic examination, a well-demarcated cauliflower-shaped mass was found in the cerebellopontine angle site [Figure 1 – A and B].

On histological examination, the mass was characterized by papillary architecture with a single layer of cuboidal to columnar monomorphic cells and mild nuclear pleomorphism with rare mitotic activity < 2/10 high-power fields [figure 2 – A and B].

Macroscopic and microscopic examination were conclusive for the diagnosis of Choroid Plexus Papilloma, WHO grade 1.

Discussion

The occurrence of Choroid Plexus Papilloma (CPP) in this premature infant, who also presented with a microdeletion syndrome, underscores the complexity of diagnosing and managing co-existing genetic and neoplastic conditions in a neonatal intensive care setting. CPPs, while benign, pose significant risks due to their capacity for causing hydrocephalus, a life-threatening condition if not promptly addressed [25]. The capacity of CPPs to induce hydrocephalus through CSF overproduction or obstruction highlights the need for vigilant surveillance for hydrocephalus in infants with brain tumors, regardless of the benign nature of the lesion [26].

In infants with complex medical histories, such as the patient discussed, the overlapping symptomatology between their genetic condition and the sequelae of a CPP can obscure the presence of the latter. As seen in this case, despite rigorous monitoring, the CPP was only identified post-mortem.

This indicates a potential diagnostic blind spot in current pediatric surveillance protocols and imaging techniques, which may require revaluation to improve early detection rates, especially in high-risk infants.

Moreover, the interplay between the patient's microdeletion syndrome and CPP could have compounded his vulnerability to developing hydrocephalus. The vulnerable state of a premature infant with such a syndrome may amplify the effects of CPP, underlining the importance of a tailored approach to neonatal care that factors in the presence of such genetic anomalies.

The unexpected post-mortem discovery of the CPP also calls attention to the limitations of current non-invasive imaging modalities in detecting small or atypically presenting neoplasms in the neonatal brain, especially considering that two cranial ultrasounds were performed approximately 4 and 7 months after birth, which did not reveal the presence of the CPP. There may be a need for heightened awareness and potentially more advanced or targeted imaging strategies in neonates with complex medical backgrounds.

It is essential to consider also some neuroethical implications also arise from decision-making in the context of uncertain prognosis and the balancing act between aggressive treatment for one condition in the light of compromised health due to another.

The unfortunate outcome of this case also highlights the need for comprehensive, multi-disciplinary approaches in the management of neonates with complex conditions. The cooperation among geneticists, neurologists, and neurosurgeons in the care team could facilitate the early detection and appropriate management of similar cases in the future [28].

Conclusions

This case illustrates the challenges in diagnosing and managing CPP in premature infants, particularly those with concurrent genetic disorders. The results underscore the imperative for refining diagnostic protocols and adopting an interdisciplinary care framework paying particular attention to ethical issues linked to these patients. Such an approach is essential for ensuring comprehensive and respectful treatment modalities. Lastly, this study reaffirms the importance of performing hospital autopsy examinations in all individuals who have died during the neonatal period.

Declarations

Author Contribution

Vito Maria Goffredo, Davide Ferorelli, Alessandro Dell'Erba, Federica Mele, and Biagio Solarino were responsible for the autopsy and forensic investigations. Andrea Marzullo and Cecilia Salzillo contributed to the histological examination.The abstract, introduction, and discussion were written by Vito Maria Goffredo with the collaboration of Cecilia Salzillo. The discussion was developed by Vito Maria Goffredo,

Cecilia Salzillo, and Federica Mele regarding the general structure. Other sections of the manuscript were written by all authors, and the final manuscript is the result of contributions from all authors.

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Informed Consent Statement

Informed consent for publication was obtained from the parents of the patient.

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Conflicts of Interest

The authors declare no conflict of interest.

References

1. Bahar M et al (2017) Choroid plexus tumors in adult and pediatric populations: the Cleveland Clinic and University Hospitals experience. J neuro-oncology vol 132(3):427–432
2. Joseph JJ, Joe M, Das Choroid Plexus Papilloma StatPearls StatPearls Publishing, 5 June 2022.
3. Singh SK et al (2023) Extracerebral choroid plexus papilloma in a newborn: a rare presentation. BMJ case reports vol. 16,11 e256794. 23 Nov
4. Cannon, Donald M et al Choroid plexus tumor epidemiology and outcomes: implications for surgical and radiotherapeutic management. J Neurooncol 121,1 (2015): 151–157
5. Okamoto H, Mineta T, Ueda S, Nakahara Y, Shiraishi T, Tamiya T, Tabuchi K (2005) aprile Rilevamento delle sequenze di DNA del virus JC nei tumori cerebrali nei pazienti pediatrici. J Neurochirurgia. ; 102(3 Suppl):294-8
6. Zhen HN, Zhang X, Bu XY, Zhang ZW, Huang WJ, Zhang P, Liang JW, Wang XL (1999) Espressione dell'antigene tumorale di grandi dimensioni del virus delle scimmie 40 (Tag) e formazione dei complessi Tag-p53 e Tag-pRb nei tumori cerebrali umani. Cancro 15 novembre 86(10):2124–2132
7. Yankelevich M, Finlay JL, Gorsi H, Kupsky W, Boue DR, Koschmann CJ, Kumar-Sinha C, Mody R (2021) febbraio Approfondimenti molecolari sulla progressione maligna del papilloma atipico del plesso coroideo. Cold Spring Harb Mol Case Stud. ; 7(1)
8. Tabori U et al (2010) TP53 alterations determine clinical subgroups and survival of patients with choroid plexus tumors. J Clin oncology: official J Am Soc Clin Oncol vol 28(12):1995–2001
9. Aicardi J (2005) Aicardi syndrome. Brain Dev vol 27(3):164–171

10. Dash C, Moorthy S, Garg K, Singh PK, Kumar A, Gurjar H, Chandra PS, Kale SS (2019) gennaio Gestione dei tumori del plesso coroideo nei neonati e nei bambini piccoli fino a 4 anni di età: un'esperienza istituzionale. Mondo Neurochirurgico. ; 121:E237-E245
11. Prasad GL, Mahapatra AK (2015) Serie di casi di papilloma del plesso coroideo in bambini in sedi non comuni e revisione della letteratura. Surg Neurol Int 6:151
12. Chen Y et al (2021) Pediatric atypical choroid plexus papilloma: Clinical features and diagnosis. Clin Neurol Neurosurg 200:106345
13. Kabashi A, Ahmetgjekaj I Choroid Plexus Papilloma - Case Presentation. Curr Health Sci J 2021 Apr-Jun ;47(2):310–313
14. Gaddi MJS et al (2021) Pediatric choroid plexus papilloma arising from the cerebellopontine angle: systematic review with illustrative case. Child's Nerv system: ChNS : official J Int Soc Pediatr Neurosurg vol 37(3):799–807
15. Zhou WJ, Wang X, Peng JY, Ma SC, Zhang DN, Guan XD, Diao JF, Niu JX, Li CD, Jia W (2018) Clinical Features and Prognostic Risk Factors of Choroid Plexus Tumors in Children. Chin Med J (Engl) 131(24):2938–2946
16. Louis DN et al The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 131,6 (2016): 803–820
17. Thomas C et al (2020) Epigenetics impacts upon prognosis and clinical management of choroid plexus tumors. J neuro-oncology vol 148(1):39–45
18. Jaiswal S, Vij M, Mehrotra A, Kumar B, Nair A, Jaiswal AK, Behari S, Jain VK (2013) Choroid plexus tumors: A clinico-pathological and neuro-radiological study of 23 cases. Asian J Neurosurg 8(1):29–35. 10.4103/1793-5482.110277PMID: 23741260; PMCID: PMC3667458
19. Safaee M, Oh MC, Bloch O, Sun MZ, Kaur G, Auguste KI, Tihan T, Parsa AT (2013) Choroid plexus papillomas: advances in molecular biology and understanding of tumorigenesis. Neuro Oncol 15(3):255–267. 10.1093/neuonc/nos289Epub 2012 Nov 21. PMID: 23172371; PMCID: PMC3578480
20. Prendergast N, Goldstein JD, Beier AD (2018) Choroid plexus adenoma in a child: expanding the clinical and pathological spectrum. J Neurosurg Pediatr 21(4):428–433
21. Wang T, Liu Y, Guo Y et al (2024) Retrospective evaluation of neonates with fatal congenital lung malformation: A single center 15-year forensic autopsy experience. Forensic Sci Med Pathol. https://doi.org/10.1007/s12024-024-00853-0
22. Dettmeyer RB (2014) The role of histopathology in forensic practice: an overview. Forensic Sci Med Pathol 10:401–412. https://doi.org/10.1007/s12024-014-9536-9
23. van Piggelen RO, van Loon AM, Krediet TG, Verboon-Maciolek MA (2010) Human rhinovirus causes severe infection in preterm infants. Pediatr Infect Dis J. ;29(4):364-5. 10.1097/INF.0b013e3181c6e60f. PMID: 19935443
24. García-Garcia ML, González-Carrasco E, Quevedo S, Muñoz C, Sánchez-Escudero V, Pozo F, Casas I, Calvo C (2015) Clinical and Virological Characteristics of Early and Moderate Preterm Infants

Readmitted With Viral Respiratory Infections. Pediatr Infect Dis J. ;34(7):693-9. 10.1097/INF.0000000000000718. PMID: 25923427

25. Squier MV (1997) Pathological approach to the diagnosis of hydrocephalus. J Clin Pathol 50(3):181–186. 10.1136/jcp.50.3.181PMID: 9155665; PMCID: PMC499809
26. Ceddia A, Di Rocco C, Carlucci A (1993) Idrocefalo congenito con iperproduzione liquorale da ipertrofia villosa del plesso corioideo associata a papilloma controlaterale [Hypersecretive congenital hydrocephalus due to choroid plexus villous hypertrophy associated with controlateral papilloma]. Minerva Pediatr 45(9):363–367 Italian. PMID: 8302232
27. Wilkinson D (2016) Ethical Dilemmas in Postnatal Treatment of Severe Congenital Hydrocephalus. Camb Q Healthc Ethics 25(1):84–92. 10.1017/S0963180115000316
28. Manuel C-G (2018) David Dacruz Álvarez, Laura Pérez Gay. Some Therapeutic Aspects in Pediatric Hydrocephalus. Acad J Ped Neonatol 6(4):555748. 10.19080/AJPN.2018.06.555748

Figures



Figure 1

Macroscopy CPP. A) Sections of the brain with absence of papilloma. B) Section of the pontocerebellar angle with well-demarcated cauliflower-shaped mass (green arrow).

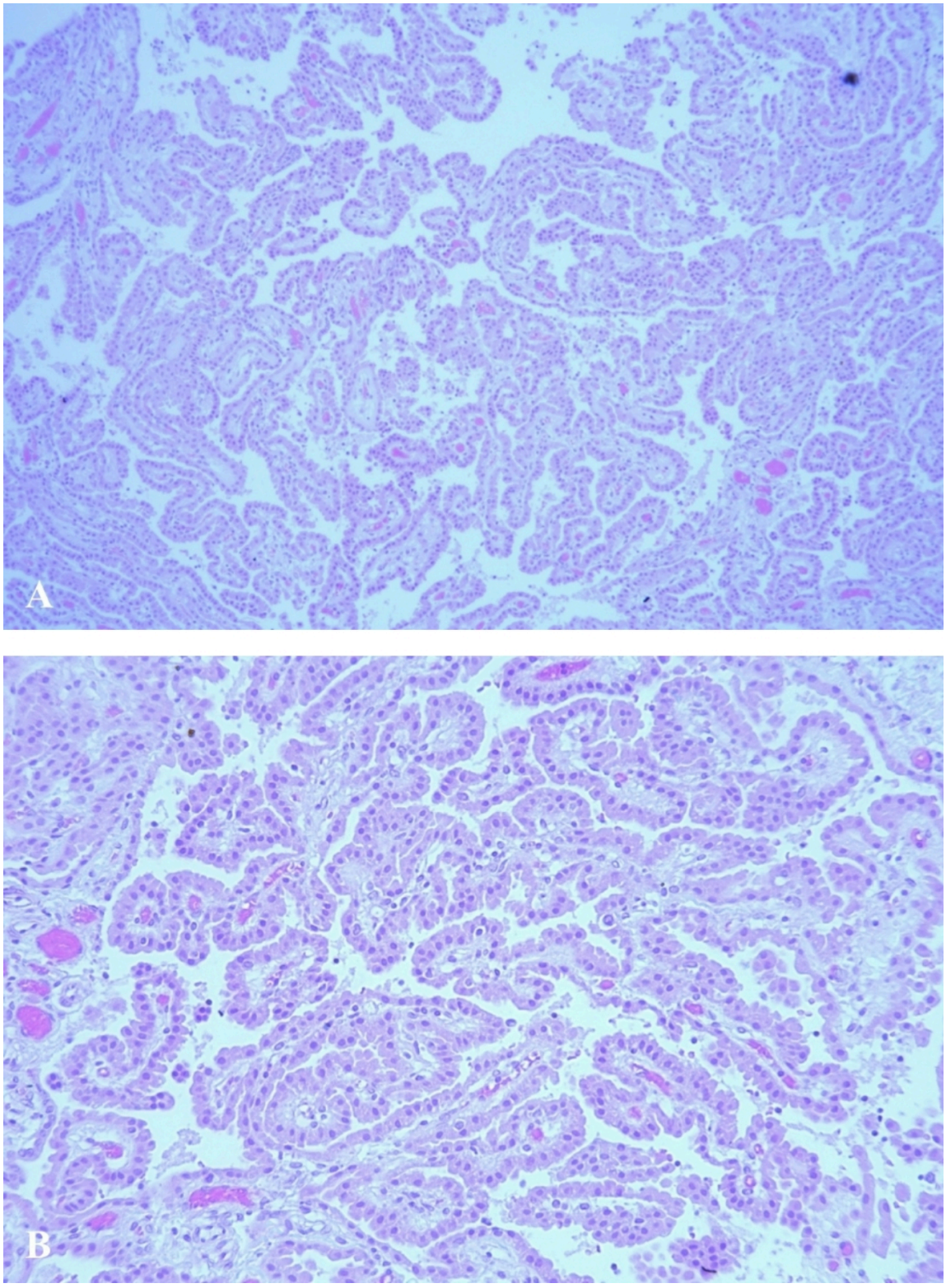


Figure 2

Microscopic CPP. A) B)