Cancer Pathogenesis and Therapy 2 (2024) 173–179

Contents lists available at ScienceDirect

Cancer Pathogenesis and Therapy

journal homepage: www.journals.elsevier.com/cancer-pathogenesis-and-therapy

Review article

Diagnosis of choroid plexus papilloma: Current perspectives and future directions

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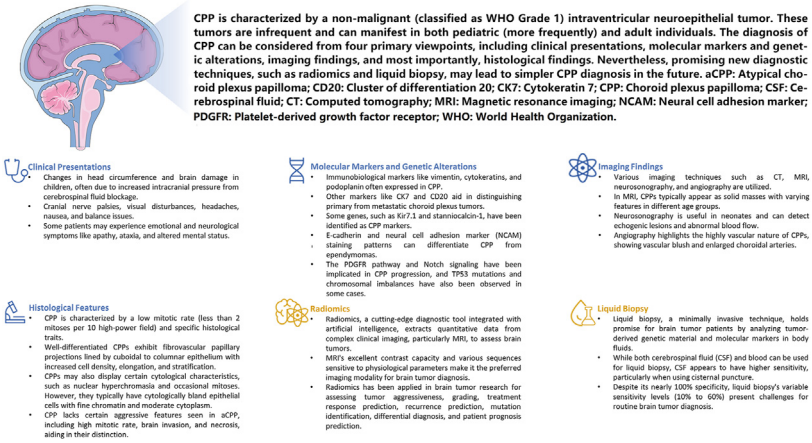
HIGHLIGHTS

- Choroid plexus papilloma (CPP) is a rare tumor that accounts for only 1% of all brain neoplasms. However, the prevalence of CPP reaches 10–20% in children under 1 year of age.
- The diagnosis of CPP primarily relies on clinical, histological, and radiological findings. However, clinical presentation, molecular markers, and genetic alterations provide crucial insights into this disease.
- CPP is distinguished from other choroid plexus tumors by its low mitotic rate (<2 mitoses per 10 high-power fields) and distinctive histological characteristics.
- Promising new diagnostic techniques, such as radiomics and liquid biopsy, may lead to simpler and more accurate CPP diagnoses in the future.

GRAPHICAL ABSTRACT



ARTICLE INFO

Managing Editor: Peng Lyu

Keywords:
Cerebral ventricle neoplasms
Biomarkers
Neuroimaging
Translational research
Histopathological features

ABSTRACT

Choroid plexus papilloma (CPP) is a rare, slow-growing, and typically benign brain tumor that predominantly affects children. CPP is characterized by well-defined circular or lobulated masses in the ventricles, leading to symptoms related to increased intracranial pressure and hydrocephalus. CPP diagnosis relies on a combination of clinical presentation, imaging findings, and histological examination. The World Health Organization (WHO) classification categorizes choroid plexus tumors into CPP (Grade I), atypical CPP (aCPP, Grade II), and choroid plexus carcinoma (CPC, Grade III). This article reviewed current diagnostics modalities and explored the emergence of new diagnostic methods for CPP. Research on molecular markers and genetic alterations associated with CPP is ongoing, and some potential markers have been identified. These results offered insights into potential therapeutic targets and personalized treatment approaches for CPP. Advancements in radiomics and liquid biopsy hold promise for improving diagnostic accuracy and monitoring treatment outcomes for choroid plexus tumors.

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https://doi.org/10.1016/j.cpt.2023.09.005
Received 31 May 2023; Received in revised form 17 September 2023; Accepted 22 September 2023

Radiomics can provide quantitative data from imaging studies, whereas liquid biopsy can analyze tumor-derived genetic material and molecular markers from body fluids, such as cerebrospinal fluid (CSF) and blood. The rapidly evolving fields of molecular and genetic research and novel diagnostic methods require continuous updates and advancements before their application in clinical practice. We hope that these advancements will lead to earlier and more precise diagnoses, better treatment options, and improved outcomes in patients with CPP and other brain tumors.

Introduction

Choroid plexus papilloma (CPP) is typically considered a benign primary brain tumor. According to World Health Organization (WHO), choroid plexus tumors are categorized into three groups based on some histological findings: Grade I or CPP, which is a slow-growing and benign tumor; Grade II or atypical CPP (aCPP), which is a mid-grade tumor with a higher probability of recurrence; and Grade III tumors of choroid plexus carcinoma (CPC) as the malignant neoplasm of choroid plexus.[1] CPP is a rare tumor that accounts for only 1% of all brain neoplasms. Children have a higher risk of developing CPP, and its prevalence reaches 10–20% in children under 1 year of age.[2,3] The location of the lesion also depends on the patient's age[4]; children usually present with increased head circumference or altered mental status, whereas adults present with signs of intracranial hypertension. In CPP, imaging results reveal enhancing intraventricular masses.[3] No noticeable difference is observed in the proportion of male and female patients, although it may occur slightly more frequent in women.[5]

Supratentorial CPPs (in the third and lateral ventricles) are more likely to be observed in children, whereas infratentorial CPPs (in the fourth ventricle) are observed in all age groups.[6,7] Choroid plexus tumors commonly manifest symptoms owing to cerebrospinal fluid (CSF) pathways obstruction, possibly through CSF secretion by tumor cells, leading to fluid accumulation and subsequent development of hydrocephalus. Additionally, the physical presence of the tumor may exert pressure on the surrounding structures, resulting in varying symptoms according to its location. This condition may progress, leading to elevated intracranial pressure.[2] These neoplasms are primarily managed using a surgical resection approach. However, the surgical procedure poses considerable challenges, primarily because of the potential risk of significant intraoperative blood loss. Furthermore, surgical intervention may not completely resolve hydrocephalus in some cases, potentially because of disruptions in CSF reabsorption mechanisms or blockages at other sites within the ventricular system. For cases in which surgery is insufficient, tumor remnants persist after surgery, and tumor recurrence or a shift toward malignancy necessitates supplementary therapeutic interventions.[8]

Previous studies have identified some congenital and genetic factors, autoimmune disorders, and other diseases as the etiology of choroid plexus tumors. Aicardi syndrome, hypomelanosis of Ito, 9p duplication, Li-Fraumeni cancer syndrome, and Bobblehead doll syndrome are among the conditions involved with the etiology of CPP.[3,9] Certain microbial infections, especially those of the Polyomaviridae family of viruses (JC, BK, and SV40 viruses), can also trigger CPP.[10] The investigations demonstrated that mutations such as *TP53*-R337H – R248W and – R72 (less common in CPP, more common in CPC); signaling pathways such as tyrosine kinase, Notch 3, and TWIST1 transcription factor; genes such as Platelet-derived growth factor (*PDGF*), BCL2 Associated Transcription Factor 1 (*BCLAF1*), Transient receptor potential cation channel subfamily M member 3 (*TRPM3*), interleukin-6 signal transducer (*IL6ST*), and Wnt inhibitory factor 1 (*WIF1*); and drugs such as rapamycin are important in CPP.[11–13] This knowledge has facilitated the advancement of targeted therapies, allowing for personalized treatment approaches and improving the precision of diagnostic techniques. Currently, CPP diagnosis primarily relies on histological and radiological findings. Nonetheless, the significance of molecular markers and genetic factors that have the potential to provide more profound insights into CPP cases is gaining recognition. The advent of diagnostic methods based on artificial intelligence (AI) and liquid biopsy offers promising prospects for minimizing side effects and enhancing diagnostic accuracy in CPP cases. However, acknowledging that these methods are still in the early stages of development and yet to be fully implemented in clinical settings for CPP diagnosis is crucial. Accordingly, this article aims to review the current diagnostics modalities and explore the emergence of new diagnostic methods that can be utilized in the future for CPP diagnosis.

Clinical presentation

Depending on the tumor location and size, choroid plexus tumors, particularly CPPs, can present with various clinical symptoms.[14] The difference in symptoms manifested in children compared with that in adults is the change in head circumference size and increased brain damage in the former, which is related to the development of the nervous system at an early age. Most symptoms are caused by increased intracranial pressure because of the blockage of CSF pathways and, less frequently, the mass effect. The patient may experience palsies of cranial nerves III and VI, visual disturbance, headache, nausea, balance problems, and drowsiness.[15,16] Some patients present symptoms such as apathy, dysthymia, dysdiadochokinesis, ataxia, speechlessness, subarachnoid hemorrhage, and altered mental status.[2,3] Although these clinical manifestations may advance to more severe conditions, such as blindness, none have diagnostic significance on their own. To properly manage these symptoms and avoid further difficulties, prompt identification of the paraclinical signs of choroid plexus tumors is crucial.

Imaging findings

Various imaging techniques, including computed tomography (CT), magnetic resonance imaging (MRI), neurosonography (NSG), and angiography, are used to diagnose CPP. However, relying solely on radiological examinations is inadequate to ascertain the presence of CPP. To achieve a precise diagnosis and effective treatment, performing a complete tumor excision and obtaining histologic confirmation is essential.

Computed tomography and magnetic resonance imaging

CT and MRI are the imaging modalities of choice for evaluating CPPs because of their noninvasiveness, wide availability, and excellent contrast resolution. On CT, CPPs manifest as well-defined circular or lobulated solid masses with attenuation levels similar to or higher than those of normal brain tissue on non-enhanced scans. Approximately one-quarter of patients exhibit calcification foci within these tumors, which are distinguishable more readily on CT scans than on MRI. Following the intravenous administration of contrast material, the CPPs display robust enhancement.[17] Children may exhibit heterogeneous characteristics owing to the accumulation of CSF, blood, and blood products in the fronds and papillae. This heterogeneity could serve as an indicator of malignancy. Conversely, most CPPs display heterogeneity in adults owing to cystic and/or calcific degeneration.[18] Additionally, the associated findings often include hydrocephalus, which may affect the lateral, third, and fourth ventricles to varying degrees. The lesions are lobulated with slightly irregular margins and exhibit intense, somewhat diverse contrast enhancement. Angiographic and cross-sectional imaging reveal choroidal artery enlargement. The presence of irregular margins should raise concerns about malignancy. However, differentiating between

benign and malignant tumors using CT is challenging because of limited parenchymal invasion in CPPs.[17]

MRI also characterizes CPPs by depicting their distinct frond-like morphology and associated hydrocephalus. These tumors appear isointense or somewhat hypointense on T1-weighted images (WIs) and isointense to hyperintense on T2-WIs with flow voids.[19] Administration of contrast material results in marked and homogeneous enhancement. Magnetic resonance spectroscopy reveals decreased N-acetyl aspartate (NAA) and increased choline (Cho) levels, offering additional insights into tumor composition. Arterial spin labeling may be able to help differentiate CPPs from CPCs on MRI.[20] The multiplanar imaging capability of MRI plays a crucial role in precisely localizing and assessing the extent of CPP, thereby substantially aiding surgical planning. Moreover, the distinct advantage of MRI lies in eliminating artifacts that occasionally pose challenges to the posterior fossa during CT. MRI also effectively captures any potential local parenchymal invasion, which can be used to distinguish benign tumors from more aggressive or malignant choroid plexus tumors. Thus, MRI is a crucial tool in diagnosing and treating patients with choroid plexus tumors.[21]

Sonography

NSG plays a valuable role in diagnosing CPPs in neonates because their fontanels are not fused. NSG through the anterior fontanels enables the visualization of echogenic lesions within the ventricles. The presence of bidirectional flow throughout the diastole indicates chaotic blood flow through the vessels.[22,23] Sonography is a valuable tool because of its widespread availability, portability, accuracy, cost-effectiveness, noninvasive nature, and elimination of the need for sedation during examinations. Real-time ultrasonography is valuable for detecting hydrocephalus. The tumors present as intraventricular masses with irregular borders and display a heterogeneous and highly echogenic appearance on ultrasonography. Doppler ultrasonographic studies have revealed pulsatile intratumoral vascular channels with biphasic flow, adding to the diagnostic information. Furthermore, intratumoral cysts are sometimes identifiable, appearing as hypoechoic regions, and are presumably indicative of areas undergoing hydropic degeneration.[18]

Angiography

Angiography reveals the highly vascular nature of CPPs; these tumors exhibit an intense vascular blush and may show enlarged choroidal arteries supplying blood to the tumor, along with shunting.[24] Generally, angiographic signs include small spiral arteries, a meningioma-like blush with early tumor circulation, displacement of vessels such as the internal cerebral veins, and evidence of ventricular dilatation.[25]

Histological features

The WHO classification of choroid plexus tumors is based on their histological features. CPP is distinguished from other choroid plexus tumors based on its low mitotic rate (<2 mitoses per 10 high-power fields) and distinctive histological characteristics.[26]

In a well-differentiated CPP, the fibrovascular papillary projections are lined by cuboidal to columnar epithelium, displaying significantly higher cell density, elongation, and stratification than the orderly cobblestone appearance of the normal choroid plexus tissue. Similarly, they often show mildly elevated nuclear-to-cytoplasmic ratios, nuclear hyperchromasia, irregular nuclear profiles, and occasional mitoses. However, the epithelial cells of CPPs are typically cytologically bland and may have fine chromatin and a moderate amount of eosinophilic or clear cytoplasm. Furthermore, CPPs may occasionally demonstrate oncocytic changes, cytoplasmic vacuolization reminiscent of signet ring cells, tubular-glandular architecture, melanization, neuropil-like islands, and focal ependymal differentiation. Identification of CPPs and papillary ependymomas is challenging. The latter exhibit intricate cellular clusters with glial extensions that converge toward a central vascular structure. Additionally, prominent degenerative features may be present in CPP, including hyalinization or calcification, angioma-like increase in blood vessels, formation of metaplastic bone cartilage or adipose tissue, and xanthomatous or mucinous changes. Hypercellularity, brain invasion, papillary architecture loss, noticeable nuclear pleomorphism, and necrosis are absent in CPP but present in aCPP.[22] Therefore, observation of these factors, focal solid growth patterns, anastomosing papillary formations, cribriforming, and most importantly, a mitotic rate >2 per 10 fields can help differentiate CPP from aCPP.[27]

Molecular markers and genetic alterations

Notably, molecular or genetic studies on CPP can be challenging because of the low prevalence and complex nature of its intracellular mechanisms. Therefore, in many studies, the sample size is insufficient to make a definitive conclusion. This is particularly the issue when designing therapeutics and identifying diagnostic markers based on genotype-to-phenotype correlations. Recent studies have shown that despite the existing uncertainties and challenges in diagnosing and differentiating CPP from other choroid plexus tumors, the molecular biology and genetic features of CPP have facilitated considerable attention as potential diagnostic modalities.[10]

Immunohistochemical staining has enabled significant progress in CPP identification and differentiation. Vimentin, cytokeratin, and podoplanin are expressed in almost all CPPs. Although cytokeratins and vimentin are distinctive for CPPs, podoplanin expression is less specific in distinguishing CPP from other types of tumors, especially carcinomas.[28,29] Moreover, laminin, a type of adhesion glycoprotein of the basement membrane, could be more frequently detected in CPPs than in CPC and ependymomas, in which it is rarely detected.[30]

Primary choroid plexus tumors are typically positive for CK7, a type of cytokeratin, and negative for CD20, which differentiates them from metastatic tumors.[31] Excitatory amino acid transporter 1 is believed to stain CP tumors but not metastatic carcinomas. Conversely, human epithelial antigen (HEA)-125 and Ber-EP4 clones, two types of monoclonal antibodies, are stained in metastatic carcinomas but not in CP tumors.[32]

Regarding the investigation of several genes overexpressed in CPP through microarray analysis, Kir7.1, and stanniocalcin-1 were recognized as novel markers of CPP. Kir7.1, an inwardly rectifying K+ channel, has been observed in both the normal choroid plexus and CPPs but not in other brain tumors. Stanniocalcin-1 is involved in calcium homeostasis and confers resistance to hypoxic stress. Thus, they are identified as CPP markers.[33]

Differentiating CPPs from CNS neoplasms ependymomas and subependymomas are important. The staining pattern of E-cadherin and neural cell adhesion markers (NCAMs) in CPP are positive and negative, respectively, whereas that in ependymomas is the opposite.[34] E-cadherin, a junctional molecule, acts as a tumor suppressor, and its low expression may be associated with the epithelial–mesenchymal transition (EMT) and cell migration. However, subependymomas can be easily recognized through histological analysis, thereby reducing the requirement for immunostaining.[35] Moreover, based on an immunohistochemical study, the expression of stratifin (SFN) is increased in CPP and other types of CNS tumors such as glioblastoma.

PDGFR, a receptor tyrosine kinase, contributes to blood cell production and CNS development, resulting in the consideration of these modulators in CPP treatment. Thus, tumor growth and invasion can stem from irregular signaling, which plays a role in the pathogenesis of CPP. Reportedly, the α and β isoforms of PDGFR are expressed in CPPs, leading to an appropriate treatment target.[10] Imatinib, a tyrosine kinase inhibitor, is administered to patients with irregular PDGFR activation. Therefore, this may be a suitable target for treatment.[36]

Regarding recent investigation comparing the expression of genes associated with normal choroid plexus and CPP, several genes have been identified, including *TWIST1*, *IL6ST*, the transmembrane protein Shrew-1

(*AJAP1*), *WIF1*, and *TRPM3*.[37] Expression of TWIST1, a p53 and adenosine diphosphate (ADP) ribosylation inhibitor, is substantially increased in CPP, making it a possible target for CPP treatment by decreasing cell proliferation and the expression of factors such as vascular endothelial growth factor.[10]

Recent findings have indicated the Notch signaling pathway as another factor contributing to the progression of choroid plexus tumors, particularly papillomas. Overexpression of Notch receptor messenger ribonucleic acids (mRNAs) acts as an oncogene in choroid plexus tumor formation.[38] Tumor necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL), a stimulator of apoptotic signaling, has emerged as a cancer treatment strategy. It plays a role in CPP pathogenesis because of the methylation of the genes associated with the TRAIL pathway and the development of cell migration.[39]

According to a previous study, in some cases, some genes, including *RASSF1A*, are methylated in CPP in contrast to the normal cortex, and others, such as *TFRSF10C*,*TFRSF10D*, and *CASP8*, are involved in the TRAIL pathway.[40] *RASSF1A*, the most commonly methylated gene, is a tumor suppressor that contributes to the regulation of mitosis; however, no significant differences in clinical symptoms were observed following methylation.[10,41]

TP53 mutations are present in some CPPs, resulting in a lack of p53 activity, which is linked to genomic instability and poor prognosis.[42] The R248W mutation of the *TP53* gene is the most common type of *TP53* gene variation associated with the lack of its apoptotic role and acquisition of tumorigenic features.[43]

Chromosomal imbalances, such as duplications and deletions, have been recognized in CPPs. Chromosomes 7, 12, 15, 17, and 18 are sometimes duplicated in CPP.[43] However, a comparative genomic hybridization study showed that CPPs are commonly evinced, which in order of abundance included +7q, +5q, +7p, +5p, +9p, and −10q.[10] Furthermore, duplications of chromosomes 8, 12, 14, and 20 are more frequent in the pediatric population than in adults. Chromosomal losses were mainly observed in carcinoma compared with CPP. Summarily, neither the total number of mutations nor the gain or loss of specific chromosomes was observed to affect overall survival in patients with CPP.[40]

Differential diagnosis

Differentiating CPP from other intracranial tumors, disregarding the location involved, is of fundamental importance in the investigation of their clinical and radiographic features, comprising both MRI and CT, which are the main methods in the investigation of choroid plexus tumors, with histological observations to confirm CPP diagnosis.[2] The most essential differential diagnoses for CPP are other choroid plexus tumors. However, differential considerations extend to medulloblastoma, atypical teratoid/rhabdoid tumors (AT/RTs), and ependymomas in the pediatric posterior fossa context, although it is less frequent. In the adult population, differential diagnoses include ependymoma, intraventricular meningioma, subependymoma, central neurocytoma, and exophytic glioma.[15] Additionally, the likelihood of choroid plexus metastasis should be considered. Differentiating these tumors can be achieved through thoughtful and selective application of immunohistological markers coupled with consideration of clinical and imaging features.

In almost all CPP cases, increased intracranial pressure is accompanied by hydrocephalus with transependymal flow resulting from excessive fluid build-up, eventually leading to common symptoms, including headache, dizziness, nausea, anorexia, visual and hearing deterioration, abnormal walking pattern, feeling of agitation, and papilledema.[15,44,45] Less frequent clinical features include subarachnoid hemorrhage, occasionally due to tumor bleeding.[2]

The papillary appearance of CPP helps distinguish it from other neoplasms compared with CPC, which tends to have irregular contours. The CT appearance of CPP shows a lobulated mass with an abnormal frond-like pattern, leading to a cauliflower appearance commonly observed in intraventricular tumors. Additionally, contrast-enhanced imaging shows vascular lesions in CPP, and calcification and attenuation of the surrounding bone can be seen in CT images of some CPP cases.[2]

Most often, T1-WIs indicate gray matter, considering either low intensity or isointensity. However, owing to intratumoral hemorrhage, foci of high signal intensity may be seen on T2-weighted imaging, and highly calcified tumors show high degrees of intensity.[46]

CPPs originate more from the choroid plexus neuroepithelial cells than from the Foramen of Luschka (FL). Differential diagnosis of CPP arising from FL and meningioma can be challenging. In meningioma cases, imaging features, such as elevated density in the adjacent brain, well-demarcated smooth borders, and homogeneous intense contrast, can be helpful for differential diagnosis. Perfusion-weighted imaging (PWI), an advanced MRI technique, can provide information regarding tumor vascularization to compare CPCs and papillomas that sometimes contain cystic features.[47]

In a study comparing aCPP and CPP, in the cerebral hemisphere of patients with aCPPs, giant masses were observed, which were substantially larger than those of CPP.[24,48] Based on MRI analysis, blurred borders, cysts, necrosis, and peritumoral edema are typically observed in aCPP as compared with CPP. Moreover, T1-WI isointense signals were detected in both aCPPs and CPPs, whereas T2-WI slightly low signals were more frequent in CPPs. Additionally, the tumor size of aCPPs was remarkably larger than that of CPPs.[21]

Future directions

Several categories of brain and spinal cord tumors appear comparable under microscopic examination. Despite assessments by skilled pathologists and radiologists, approximately 10% of individuals initially receive an incorrect diagnosis of a brain or spinal cord tumor. The symptoms and some findings of CPP initially overlap with those of common childhood brain tumors and other choroid plexus tumors. Furthermore, the complex diagnostic landscape of CPP increases the probability of delayed diagnosis or misdiagnosis, which rate reaches 80% for extraventricular CPPs.[24] This initial misdiagnosis can potentially affect outcomes.[49] The existing error rates associated with current diagnostic modalities, coupled with the invasive nature of brain sampling, which serves as the gold standard for CPP confirmation, highlight the need to develop more precise, rapid, and safe diagnostic approaches for distinguishing CPP. The landscape of brain tumor diagnosis is experiencing a rapid expansion of innovative and successful techniques. Of these promising diagnostic approaches, radiomics and liquid biopsy are particularly noteworthy and hold promise for the diagnosis of CPP.

Radiomics

Radiomics is a modern computational diagnostic tool based on imaging techniques integrated with AI.[50] Radiomics enables the extraction of a significant amount of quantitative information from intricate clinical imaging arrays and converts them into high-dimensional data that can mined to determine their relevance to the histological characteristics of the tumor. These characteristics reflect the underlying genetic mutations and malignancy, as well as its grade, progression, therapeutic effect, and overall survival. Radiological diagnosis of brain tumors relies heavily on MRI, which is frequently used as the first imaging modality of choice for several reasons. First, MRI effectively detects brain tissue because of its outstanding contrast capacity. Second, various MRI sequences are sensitive to various physiological parameters, such as blood flow and edema in the immediate area, which can be used to determine the tumor microenvironment. Third, MRI can be used noninvasively to monitor the course and effectiveness of treatment.

To date, brain tumor radiomics has been employed for tumor aggression evaluation with the aid of immunohistochemistry labeling,[51] tumor grading,[52] treatment response prediction,[53] recurrence prediction,[54] determination of mutations,[55] differential diagnosis,[56] patient complications, and prognosis prediction.[57] Although radiomics has

accelerated the development of precision medicine and radiological diagnostics for various brain tumors, the lack of substantial data on choroid plexus tumors affects the widespread use of radiomics for effectively diagnosing and characterizing these tumors.

Liquid biopsy

Liquid biopsy is a minimally invasive technique involving analyzing tumor-derived genetic material, molecular markers, and cells in various body fluids. The discovery of circulating brain tumor cells within the bloodstream is a recent and novel revelation, indicating potential clinical benefits for patients with brain tumors.[58] Established detection methods from molecular genetics as diagnostic tools for tissue samples have been successfully applied to liquid biopsy of brain tumors. The initial results were promising, demonstrating the potential of liquid biopsy for brain tumors, and further advancements are encouraged. Currently, CSF is a superior source for liquid biopsy compared with blood-derived samples, serum, or plasma. CSF and blood can be used to identify circulating tumor cells (CTCs), circulating tumor deoxyribonucleic acid (ctDNA), extracellular vesicles, and microRNAs; however, the sensitivity is significantly higher when CSF is used. Notably, when collecting CSF, cisternal puncture shows a slight advantage over lumbar puncture with respect to detection sensitivity.[59] Liquid biopsy exhibits an impressive level of specificity, reaching approximately 100%.[58] However, the individual risks of obtaining CSF must be carefully considered, and measures should be taken to avoid potential brain damage during the process. This advancement in liquid biopsy for brain tumors holds great promise and requires further research and development to improve patient care.

The main obstacle to liquid biopsy implementation in routine diagnostic methods for brain tumors is its limited and variable sensitivity levels, which typically range from approximately 10% to 60%.[58] The conventional method of direct tumor sampling, either through brain tumor removal or stereotactic tumor tissue biopsy, is expected to remain the preferred approach for ensuring a reliable diagnosis, encompassing both histology and genetic profiling. Nevertheless, liquid biopsy is a potential alternative in certain cases in which obtaining direct access to tumor tissue poses risks owing to its location or the presence of comorbidities. Such scenarios should be considered in the near future.[58]

Currently, similar to radiomics, the low incidence of choroid plexus tumors and the lack of proper diagnostic options hinder the application of liquid biopsy in early tumor screening. However, there is potential for its use in patient follow-up. Assessing biomarker levels before and after treatment using liquid biopsy can be instrumental in predicting prognosis, monitoring treatment outcomes, and making therapeutic decisions. Notably, the liquid biopsy approach carries a substantially lower risk than repeat surgical biopsy. With advances in research and technology, the role of liquid biopsy in choroid plexus tumor management is likely to expand, offering additional benefits in certain clinical situations.

Limitations

As this review article is based on information available up to the date of its publication, it is important to recognize that new discoveries and developments may have emerged after the knowledge cutoff date. Moreover, the limited focus of this study compelled us to incorporate older studies. Finally, this review primarily focused on diagnostic perspectives, allowing future research to explore additional aspects of CPP, such as treatment strategies, prognostic factors, and long-term outcomes. We hope that continued research and collaboration among experts in this field will enhance our understanding of CPP and contribute to managing this brain tumor.

Conclusion

CPP diagnosis remains challenging because of its rarity and overlapping clinical and radiological features with other intracranial tumors. Nevertheless, substantial progress has been made in understanding the molecular and genetic aspects of CPP, thereby providing valuable insights into its potential diagnostic markers and therapeutic targets. Imaging techniques, particularly CT, MRI, and NSG, play a pivotal role in the initial evaluation of CPP, allowing for noninvasive visualization of the tumor's location and characteristics. Histological examination remains the gold standard for confirming CPP diagnosis and differentiating it from other choroid plexus tumors and brain neoplasms. Recent studies have also highlighted promising molecular markers and genetic alterations associated with CPP, such as *PDGFR*, *TWIST1*, *IL6ST*, *WIF1*, *TRPM3*, and *TP53* mutations. These markers offer potential targeted therapies and may serve as additional diagnostic tools in the future.

Radiomics and liquid biopsies are promising to improve the diagnostic accuracy and management of CPP. Radiomics, with its ability to extract quantitative data from complex imaging arrays, may aid in differentiating CPP from other tumors and predicting tumor behavior. As a minimally invasive technique, liquid biopsy offers a potential alternative for monitoring treatment response and detecting tumor-derived genetic material in body fluids. Despite these advancements, several challenges remain, including the need for larger and more diverse datasets to validate the diagnostic potential of these approaches. Implementing radiomics and liquid biopsies in routine clinical practice requires further research and validation. Notably, the rapidly evolving fields of molecular and genetic research and novel diagnostic methods require continuous updates and advancements.

Funding

None.

Authors contribution

Conceptualization: Esma'il Akade; methodology: Gholam Abbas Kaydani; validation: Mohammad Bahadoram and Gholam Abbas Kaydani; formal analysis: Esma'il Akade, Fereshteh Aslani, and Kimia Verdi; investigation: Esma'il Akade, Fereshteh Aslani, and Kimia Verdi; resources: not applicable; data curation: not applicable; writing—original draft preparation: Esma'il Akade, Fereshteh Aslani, and Kimia Verdi; writing—review and editing: Mohammad Bahadoram and Gholam Abbas Kaydani; visualization: not applicable; supervision: Mohammad Bahadoram and Gholam Abbas Kaydani; and project administration: Gholam Abbas Kaydani.

Ethics statement

None.

Data availability statement

The datasets used in the current study are available from the corresponding author on reasonable request.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

None.

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