Posterior fossa Hodgkin’s lymphoma radiographically mimicking an arteriovenous malformation: illustrative case

Joshua D. McBriar, ScM,1 Kyriakos Papadimitriou, MD,2 Danielle Golub, MD, MSCI,2 Hayley Donaldson, MBS,3 Jian Y. Li, MD, PhD,4 Pallavi Khatkar, MD,4 Samuel Singer, MD,5 Karen S. Black, MD,6 and Thomas W. Link, MD2

© 2024 The authors, CC BY-NC-ND 4.0 (http://creativecommons.org/licenses/by-nc-nd/4.0/)

BACKGROUND Intracranial Hodgkin's lymphoma (HL) is an exceedingly rare condition that is at an increased risk of misdiagnosis and mismanagement, especially when initial radiographic evidence points to an alternative pathology.

OBSERVATIONS The authors describe the case of a 75-year-old female who presented with a posterior fossa lesion initially concerning for a vascular malformation on computed tomography imaging due to perilesional hypervascularity. Subsequent angiography revealed a developmental venous anomaly (DVA) but no arteriovenous shunting. The patient's clinical history combined with magnetic resonance imaging findings prompted a tissue biopsy, which demonstrated a rare case of central nervous system (CNS) HL. The neoangiogenesis of this CNS HL with an adjacent DVA contributed to the original radiographic misdiagnosis of an arteriovenous malformation. HL’s angiogenic potential, coupled with the proangiogenic environment induced around DVAs, may have contributed to this rare CNS HL metastasis to the cerebellum. The potential misdiagnosis of posterior fossa CNS HL has also been seen in several prior cases reviewed herein.

LESSONS Hypervascular tumors, especially when associated with an adjacent DVA, should also be considered when first evaluating suspected intracranial vascular lesions. Although rare, CNS HL should be included in the differential diagnosis for patients with a prior history of HL.

https://thejns.org/doi/abs/10.3171/CASE24238

KEYWORDS intracranial Hodgkin’s lymphoma; developmental venous anomaly; central nervous system Hodgkin’s lymphoma; posterior fossa lymphoma metastasis; neuroradiology

Hodgkin’s lymphoma (HL) is a hematological malignancy arising from B lymphocytes, in which central nervous system (CNS) involvement is extremely rare, seen in only 0.02%–0.5% of cases.1,2 CNS HL typically presents as a supratentorial parenchymal lesion associated with various focal neurological deficits, seizures, and mass effect symptoms similar to those in other intracranial space-occupying lesions.3 Histopathological diagnosis requires a tissue sample demonstrating the classic Reed-Sternberg cells expressing CD15 and CD30.1,2 The literature regarding the treatment of CNS HL is limited due to the disease’s rarity; however, case reports and series generally describe resection followed by a combination of radiation therapy (RT) and chemotherapy, such as doxorubicin, bleomycin, vinblastine, and dacarbazine.2,4 Rare neoplasms, such as CNS HL, are often low on the differential diagnosis of intracranial lesions and naturally carry an increased risk for misidentification and potentially delayed diagnosis and treatment.5,9 This risk can be compounded by various imaging features that mimic more common intracranial lesions. For instance, the presence of a dural attachment has been reported in several cases of histopathologically confirmed CNS HL, which the authors had originally thought were meningiomas.7,9 Furthermore, significantly vascularized tumors can sometimes be mistaken for vascular malformations, potentially confounding the initial diagnostic workup.10-13 A few cases of hypervascular anaplastic oligodendrogliomas have been reported in which the original radiographic diagnosis was arteriovenous malformation (AVM) based on magnetic resonance imaging (MRI).10,11 Similarly, cases of
hypervascular glioblastomas (GBMs) and hemangioblastomas have been initially mistaken for AVMs based on significant flow voids on MRI and arteriovenous shunting on angiography. In all of these cases, the patients underwent conventional catheter angiography to evaluate each lesion’s angioarchitecture before obtaining a final tissue diagnosis due to significant tumor neovascularization.

The neovascularization potential of CNS HL has yet to be explored in the literature. However, non-CNS HL has been associated with significant angiogenesis promoted by its tumor microenvironment and the expression of various endothelial growth factors. When compared to healthy individuals, patients with HL have been shown to have a significantly higher number of endothelial progenitor cells as well as increased concentrations of vascular endothelial growth factor (VEGF) A in the bloodstream. This angiogenic potential likely contributes to tumor growth and metastasis, which may factor into its presentation in the CNS. We describe the case of an older female who presented with a posterior fossa lesion initially suspected to be a vascular malformation but later revealed by angiography and tissue diagnosis to be a rare case of CNS HL. We used the CARE case report guidelines and checklist when writing this report.

Illustrative Case

A 75-year-old female had a history of metastatic HL diagnosed 1 year prior to presentation that was treated with brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine (AAVD regimen) with complete remission on positron emission tomography (PET) scanning 6 months prior to presentation. She presented to the emergency department with a 1-week history of intermittent headaches and vertigo. Neurological examination revealed no focal deficits. Head computed tomography (CT) demonstrated a 2.3 × 2.2-cm right cerebellar hyperdensity with surrounding edema and significant compression of the fourth ventricle with moderate hydrocephalus (Fig. 1A and B), suspected to be a subacute hemorrhage. CT angiography (CTA) showed conspicuous vascularity circumferentially with a larger, more prominent vessel extending from the lesion along the lateral right cerebellum (Fig. 1C and D). Given the hypervascularity of the lesion on initial imaging, she was initially suspected to have a ruptured AVM and was admitted to the neurosurgical intensive care unit on a nicardipine drip for strict blood pressure control.

Cerebral angiography was performed the following day to assess the nature of the suspected vascular lesion. While no nidus or arteriovenous shunting was observed, a right cerebellar developmental venous anomaly (DVA) was seen draining into the torcula (Fig. 1E and F), corresponding to the prominent vessel initially observed on CTA. MRI of the brain on hospital day 3 subsequently confirmed the presence of a homogeneously enhancing and diffusion-restricting lesion with a large flow void, again observed posterolateral to the lesion (consistent with the newly characterized DVA; Fig. 2A–F). Magnetic resonance spectroscopy (MRS) was also performed to further characterize the lesion. It showed an elevated choline/creatinine ratio, a decreased N-acetylaspartate peak, and an elevated lipid peak, altogether most concerning for a malignant neoplasm (Fig. 2G).

Given her history of prior lymphoma, the homogeneous enhancement on MRI, and the lipid peak observed on MRS, a diagnosis of CNS HL was suspected. Stereotactic needle biopsy of the mass was performed on hospital day 9, and final histopathology was consistent with CNS HL (Fig. 3). CT of the chest, abdomen, and pelvis demonstrated no evidence of systemic metastatic disease. Subsequent whole spine MRI, however, revealed some areas of enhancement in several cervical, thoracic, lumbar, and sacral vertebral bodies consistent with likely lymphoma metastasis. She was discharged home with a final diagnosis of CNS HL with resolution of her headaches and in stable neurological condition on postoperative day 7 (hospital day 18). Outpatient follow-up for a PET scan and possible bone marrow biopsy were recommended by the neuro-oncology and medical oncology teams.

Patient Informed Consent

The necessary patient informed consent was obtained in this study.
Observations

In this case, the hypervascularity and adjacent DVA mimicking an AVM, combined with the rarity of CNS HL, largely contributed to the delay in diagnosis. CNS lymphomas are typically hyperdense on noncontrast CT because of their high cellular density and high nuclear/cytoplasmic ratio. A large AVM nidus can often appear as a hyperdensity on noncontrast CT, especially when associated with an acute or subacute hemorrhage, which accounted for the initial concern in this case. After angiography revealed no nidus or arteriovenous shunting and the presence of the DVA, MRI was performed and demonstrated features highly suggestive of lymphoma. On conventional MRI without contrast, the hypercellularity of CNS lymphoma gives it an isodense appearance relative to gray matter. Hemorrhage and necrosis are more common in immunodeficiency-related CNS lymphomas, and our patient’s immunocompetent status is consistent with the lack of these features. Homogeneous contrast enhancement on MRI is generally seen in immunocompetent patients, with ring-enhancing lesions being more common in immunocompromised patients due to the higher rate of necrosis. It is important to note that steroids were not given to our patient prior to her imaging studies, as steroids have been shown to decrease contrast enhancement in CNS lymphoma likely due to normalization of the blood-brain barrier. As seen in our patient, lymphomas demonstrate restricted water diffusion on diffusion-weighted imaging with corresponding low apparent diffusion coefficient (ADC) values consistent with high cell density. As another tool in the arsenal of diagnostic imaging, MRS utilizes nuclear magnetic resonance, which can distinguish specific compounds based on their resonant frequency and how they vary with their surrounding chemical environment. The combined evidence of MRI and MRS findings, along with the patient’s history and lack of arteriovenous shunting on catheter angiography, ultimately prompted our decision to biopsy this lesion.

As previously mentioned, the extreme rarity of CNS HL was another contributing factor to this patient’s delay in diagnosis and initial suspicion of a more common vascular lesion. A recent review by Lee et al. identified 47 cases of intracranial HL between 1980 and 2023. The average age at diagnosis of CNS HL was 53.3 years, and only 16 lesions were found in the posterior fossa, as seen in Table 1. Each of these lesions enhanced with contrast on CT or MRI, with 44% having dural attachments, but none were associated with a longitudinal vascular lesion or noted hypervascularity. When imaging was performed, the most common initial suspected lesion solely based on imaging was meningioma, largely based on the presence of a dural attachment and homogeneous enhancement. Angiography was performed in only 1 of these lesions showing an “avascular mass” (the reason for this imaging was not reported, but it was likely utilized for surgical planning).

FIG. 2. Coronal (A) and axial (B) postcontrast T1-weighted MRI at the level of the medulla and the pons (C) showing a homogeneously enhancing right paramedian cerebellar lesion with irregular borders and the previously noted large venous anomaly superolateral to the lesion. Axial T2 fluid-attenuated inversion recovery MRI (D) at the level of the pons demonstrating significant edema surrounding the lesion and extending to the right brachium pontis and medial left cerebellar hemisphere. A flow void is notable at the area of the venous anomaly. Axial diffusion-weighted MRI (E) and ADC map (F) showing moderate diffusion restriction throughout the right cerebellar lesion. MRS (G) of the right cerebellar mass demonstrating an elevated choline/creatine ratio and elevated lipid peaks suggestive of a malignant neoplasm, especially concerning for lymphoma.
were resected, 6 were treated with chemotherapy, 13 were treated with RT, and 1 was additionally treated with immunotherapy.

In addition to the general rarity of CNS HL (especially in the posterior fossa), the initial imaging findings in this case, including perilesional hypervascularity with a large draining vein—later determined to be a DVA—confounded the initial differential diagnosis as a presumptive vascular malformation. DVAs are vascular lesions comprising radially oriented medullary veins, or “caput medusa,” draining normal brain parenchyma coalescing to form a single dilated venous structure, with a prevalence of about 3% in the general population.35 DVAs are mostly asymptomatic unless compression of adjacent intracranial structures by the DVA or thrombosis of the vein occurs.36,37 Observation is the typical management for these generally incidental and benign lesions, as their obliteration risks venous infarct.35,36 While there remains no consensus on the precise etiology of DVAs, most theories revolve around alterations in fetal cerebral hemodynamics that lead to compensatory DVA formation.35,36,38 The hemodynamics of DVAs are thought to play a role in the pathogenesis of associated cavernous malformations (cavernomas).35,37 Specifically, the chronic pressure elevation at the confluence of the caput medusae medullary veins with the main draining vein results in repeated microhemorrhages inducing cavernoma formation by activating VEGF and other angiogenic growth factors.36,38

The proposed pathogenesis of DVA-induced cavernoma formation raises the question of whether other lesions, mainly neoplasms, can also take advantage of the proangiogenic environment surrounding DVAs. The metastatic spread of neoplasms to the CNS relies on several features of the individual cancer, with tumor angiogenesis and a proangiogenic environment playing crucial roles.39 Specifically, the colonization and proliferation of a metastatic lesion in the CNS depend on neoangiogenesis, largely driven by VEGF expression, which has been observed in colon carcinoma and melanoma, among other cancers.39-41 While the specific association between DVAs and CNS HL has not been previously examined, HL is also associated with increased levels of proangiogenic factors in the bloodstream, including VEGF.35 Hypervascular HL may be more likely to develop at the site of a DVA rather than an alternative CNS site due to the proangiogenic environment induced by the DVA. Additionally, DVAs have previously been observed in conjunction with pediatric gliomas,42 adult diffuse gliomas,43 and rare thalamic gliomas.44 In most of these studies regarding primary CNS neoplasms, however, the location of the DVA does not seem to impact the location of tumor development, as many DVAs are found distant from the associated lesion. The colocalization of DVAs with either primary or metastatic intracranial neoplasms has yet to be explored in the literature, although a recent case report identified a DVA inside of a large GBM.45 Further exploration of adjacent venous anomalies coinciding with CNS tumors may be of interest in potentially revealing novel aspects of neoplastic pathogenesis and metastatic potential.

In our patient, a diagnosis of HL was suspected after angiography showed no evidence of arteriovenous shunting and MRI demonstrated...
### TABLE 1. Posterior fossa histopathologically confirmed CNS HL in the literature from 1980 to 2023

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Location</th>
<th>Imaging Findings*</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doorly et al., 1987</td>
<td>51</td>
<td>M</td>
<td>Cerebellar hemisphere</td>
<td>CT w/ contrast: “uniformly enhancing, surrounding edema, 4th ventricular compression”</td>
<td>Chemo, Rx, RT</td>
<td>NED at 1 yr</td>
</tr>
<tr>
<td>Clark et al., 1992</td>
<td>53</td>
<td>F</td>
<td>Paravermian</td>
<td>MRI w/ contrast: enhancing mass w/ area of hypointensity posteriorly, mild hydrocephalus</td>
<td>Rx, RT</td>
<td>NED at 6 mos</td>
</tr>
<tr>
<td>Johnson et al., 2000</td>
<td>55</td>
<td>F</td>
<td>Cerebellar hemisphere/ tentorial</td>
<td>MRI w/ contrast: homogeneously enhancing, dural tail, mild hydrocephalus</td>
<td>Rx, RT</td>
<td>NED at 8 mos</td>
</tr>
<tr>
<td>Figueroa et al., 2004</td>
<td>23</td>
<td>F</td>
<td>Cerebellar hemisphere</td>
<td>MRI w/ contrast: homogeneously enhancing, dural attachment</td>
<td>Chemo, Rx</td>
<td>NR</td>
</tr>
<tr>
<td>de Castro et al., 2007</td>
<td>63</td>
<td>M</td>
<td>Cerebellar hemisphere</td>
<td>MRI w/ contrast: ring enhancing, no significant surrounding edema</td>
<td>RT</td>
<td>NR</td>
</tr>
<tr>
<td>Hwang et al., 2007</td>
<td>64</td>
<td>F</td>
<td>Cerebellar hemisphere</td>
<td>MRI w/ contrast: nodular enhancing mass, surrounding edema</td>
<td>Rx, RT</td>
<td>NED at 16 mos</td>
</tr>
<tr>
<td>Gessi et al., 2013</td>
<td>77</td>
<td>M</td>
<td>Cerebellar hemisphere</td>
<td>MRI w/ contrast: homogeneously enhancing, dural attachment</td>
<td>Rx, RT</td>
<td>NED at 6 mos, died at 8 mos due to myocardial infarction</td>
</tr>
<tr>
<td>Gessi et al., 2013</td>
<td>59</td>
<td>M</td>
<td>Medulla</td>
<td>MRI w/ contrast: homogeneously enhancing</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Kresak et al., 2013</td>
<td>70</td>
<td>M</td>
<td>Cerebellar hemisphere/ tentorial</td>
<td>MRI w/ contrast: “enhancing mass w/ edema &amp; mass effect,” “dural attachment”</td>
<td>Rx, RT</td>
<td>NED at 10 yrs</td>
</tr>
<tr>
<td>Kresak et al., 2013</td>
<td>72</td>
<td>M</td>
<td>Cerebellar hemisphere/ tentorial</td>
<td>MRI w/ contrast: homogeneously enhancing, dural attachment, surrounding edema, 4th ventricular compression</td>
<td>Rx, RT</td>
<td>NED at 6 mos</td>
</tr>
<tr>
<td>Henkenberens et al., 2014</td>
<td>47</td>
<td>M</td>
<td>Multifocal: vermian, cerebellar hemisphere, tentorial</td>
<td>MRI w/ contrast: nodular enhancing, dural attachment, surrounding edema, 4th ventricular compression, mild hydrocephalus</td>
<td>Chemo, Rx, RT</td>
<td>NED at 9 mos</td>
</tr>
<tr>
<td>Sharaf et al., 2014</td>
<td>77</td>
<td>M</td>
<td>Cerebellar hemisphere</td>
<td>MRI w/ contrast: heterogeneously enhancing, dural attachment, surrounding edema</td>
<td>Rx, RT</td>
<td>NED at 7 mos</td>
</tr>
<tr>
<td>Martinez et al., 2014</td>
<td>74</td>
<td>F</td>
<td>Pontomedullary</td>
<td>MRI w/ contrast: homogeneously enhancing, 4th ventricular compression, mild hydrocephalus</td>
<td>RT</td>
<td>NED at 6 mos</td>
</tr>
<tr>
<td>Alfaseh et al., 2019</td>
<td>38</td>
<td>M</td>
<td>Vermian</td>
<td>MRI w/ contrast: homogeneously enhancing, surrounding edema, 4th ventricular compression, mild hydrocephalus</td>
<td>Chemo, Rx, RT</td>
<td>NED at 7 yrs</td>
</tr>
<tr>
<td>Szczepanek et al., 2020</td>
<td>33</td>
<td>F</td>
<td>Vermian/intraventricular</td>
<td>MRI w/ contrast: homogeneously enhancing</td>
<td>Chemo, Rx, RT</td>
<td>NR</td>
</tr>
<tr>
<td>Fu et al., 2021</td>
<td>60</td>
<td>M</td>
<td>Cerebellar hemisphere</td>
<td>MRI w/ contrast: nodular enhancing mass, surrounding edema, 4th ventricular compression, moderate hydrocephalus</td>
<td>Chemo, Rx, Ix</td>
<td>NED at 5 yrs</td>
</tr>
</tbody>
</table>

*x = immunotherapy; NED = no evidence of disease; NR = not reported; Rx = resection.*

*Findings are reported when imaging was provided in the study; otherwise, findings inside quotation marks appear when no images were provided.
features concerning for lymphoma. After tissue diagnosis, the decision was made to pursue a primarily chemotherapy-based treatment paradigm rather than attempt resection, given the patient’s previously robust response to chemotherapy after her initial systemic diagnosis. Additionally, the surgical risk of injuring the adjacent large DVA, which likely contributed to a significant portion of this patient’s cerebellar venous drainage, was believed to be significant.

Lessons
We report a case of histopathologically confirmed CNS HL, which, in combination with likely opportunistic neoangiogenesis and adjacent DVA, radiographically mimicked an AVM on initial CTA. Conventional catheter angiography was crucial in ruling out an AVM before proceeding with the tissue biopsy that yielded a definitive diagnosis of CNS HL. The limitations of this case revolve around its nature as a single retrospective case report and the inability to draw comparisons among patients, treatments, and outcomes. Additionally, this report is limited by the scarce literature regarding CNS HL and DVA-associated lesions other than cavernomas.

This unique case demonstrates the need to maintain a broad differential when evaluating intracranial lesions and the thorough utilization of diagnostic imaging to eventually confirm a diagnosis. DVAs and other anatomical lesion characteristics may complicate diagnosis, especially when a rare neoplasm is involved, such as CNS HL. It is also possible that DVAs can provide a localizing proangiogenic environment for the growth of hypervascular neoplasms, such as HL. As seen in this case, cerebral angiography is an invaluable tool for evaluating suspected vascular lesions on conventional brain imaging and avoiding the pitfalls associated with misdiagnosing intracranial neoplasms as vascular malformations, which can result in a delay in treatment. Although rare, CNS HL should be kept on the differential of intracranial space-occupying lesions, especially in a patient with a prior history of HL.

Acknowledgments
We would like to thank Dr. Michael Schulder for his program leadership and unwavering support of the residents and students who worked on this project.

References


Disclosures

Dr. Ngwenya reported grants from Abbott and grants from Biogen outside the submitted work.

Author Contributions

Conception and design: Papadimitriou, Singer, Link. Acquisition of data: McBriar, Papadimitriou, Golub, Singer, Black, Link. Analysis and interpretation of data: Papadimitriou, Golub, Donaldson, Li, Link. Drafting the article: McBriar, Papadimitriou, Golub, Donaldson, Li, Link. Reviewing the article: McBriar, Papadimitriou, Golub, Donaldson, Li, Link. Reviewed submitted version of manuscript: McBriar, Papadimitriou, Golub, Li, Link. Approved the final version of the manuscript on behalf of all authors: McBriar. Administrative/technical/material support: Golub. Study supervision: Singer, Link. Final diagnosis and interpretation on histological examination: Khattar.

Correspondence

Joshua D. McBriar: Donald and Barbara Zucker School of Medicine at Hofstra/Northwell Health, Hempstead, NY. jmcбриar@northwell.edu.