

Neuroimaging Spectrum of Leukemia in Children: Focus on Magnetic Resonance Imaging Findings

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ABSTRACT

Background: Leukemia is the most common childhood malignancy and a major contributor to cancer-related morbidity and mortality in pediatric populations. Central nervous system (CNS) involvement is a well-recognized complication, either from direct leukemic infiltration, secondary hematological disturbances, opportunistic infections, or treatment-related neurotoxicity. Magnetic resonance imaging (MRI) has become the cornerstone modality for the evaluation of CNS manifestations in pediatric leukemia, offering unparalleled tissue contrast, multiplanar capability, and functional insights without ionizing radiation. A wide imaging spectrum is encountered, ranging from meningeal enhancement and parenchymal infiltration to cerebrovascular insults, opportunistic infections, and late effects of chemotherapy and cranial irradiation. These manifestations are often clinically nonspecific, making MRI indispensable in early diagnosis, therapeutic monitoring, and prognostication. The aim of this review is to comprehensively evaluate the neuroimaging spectrum of pediatric leukemia with a particular focus on MRI findings. By integrating anatomical and vascular principles relevant to interpretation, we highlight the typical and atypical manifestations of CNS involvement. Direct leukemic manifestations, including meningeal infiltration, granulocytic sarcoma, and marrow involvement, are discussed alongside secondary cerebrovascular complications such as hemorrhage, dural sinus thrombosis, and ischemic infarctions. Equally important are infectious sequelae in immunocompromised children, with MRI offering critical diagnostic clues for fungal, bacterial, viral, and parasitic CNS infections. Furthermore, treatment-related changes—including methotrexate-induced leukoencephalopathy, posterior reversible encephalopathy syndrome, arachnoiditis, and delayed radiation necrosis—are detailed, underscoring the dual role of imaging in monitoring both disease and therapy-related injury. Recent advances in functional and quantitative MRI techniques have further enhanced diagnostic accuracy. Diffusion-weighted imaging, perfusion sequences, spectroscopy, and diffusion tensor imaging provide valuable biomarkers of leukemic burden, therapeutic response, and neurocognitive prognosis. Emerging techniques such as chemical exchange saturation transfer and radiomics promise earlier detection of subclinical disease and more precise risk stratification. In conclusion, MRI remains the imaging modality of choice in the evaluation of pediatric leukemia with CNS involvement. A structured understanding of its diverse manifestations, combined with advanced imaging insights, ensures accurate diagnosis and guides optimal management. Future integration of multiparametric MRI with molecular profiling and artificial intelligence-driven tools may transform neuroimaging into a cornerstone of personalized care in pediatric leukemia.

Keywords: Neuroimaging, Leukemia, Children, Magnetic Resonance Imaging

INTRODUCTION

Leukemia accounts for nearly one-third of all childhood cancers, with acute lymphoblastic leukemia (ALL) being the most common subtype, followed by acute myeloid leukemia (AML) [1]. Despite advances in systemic therapy and supportive care, the central nervous system (CNS) remains a critical site of disease involvement due to its status as a sanctuary protected by the blood–brain barrier. CNS relapse contributes substantially to morbidity, neurological deficits, and treatment failure, making early detection and monitoring of CNS disease pivotal [2].

Magnetic resonance imaging (MRI) has emerged as the imaging modality of choice for evaluating CNS manifestations in pediatric leukemia. Its ability to provide superior soft tissue contrast, assess meningeal and parenchymal involvement, and characterize vascular or infectious complications without ionizing radiation renders it indispensable in this vulnerable population [3]. Beyond structural assessment, advanced MRI techniques including diffusion-weighted imaging (DWI), perfusion imaging, and MR spectroscopy (MRS) have expanded diagnostic capability, enabling detection of subtle leukemic infiltration and therapy-related neurotoxicity even before clinical symptoms emerge [4].

The existing literature on CNS involvement in pediatric leukemia is scattered, with many studies focusing on either hematologic aspects or isolated neuroimaging findings. While some reports describe meningeal disease or treatment-related leukoencephalopathy, few reviews provide an integrative synthesis of the full MRI spectrum—from direct leukemic infiltration to cerebrovascular, infectious, and therapy-induced complications [5]. This gap in comprehensive radiological perspective hampers early recognition and standardization of imaging-based follow-up strategies.

The aim of this review is therefore to provide a consolidated overview of the neuroimaging spectrum of pediatric leukemia, with emphasis on MRI findings. We outline the relevant anatomical and vascular background for interpretation, review direct and indirect CNS manifestations, and highlight advanced imaging approaches that refine diagnosis and prognostication. By doing so, we aim to strengthen the role of MRI as a cornerstone in both clinical care and research for pediatric leukemia patients with CNS involvement [6].

Normal Brain Anatomy and Vascular Supply

Accurate interpretation of MRI findings in pediatric leukemia requires a baseline understanding of neuroanatomy as visualized radiologically. Grey and white matter differentiation, ventricular configuration, and meningeal coverings provide the framework for detecting subtle pathological alterations. Leukemic infiltration often targets the leptomeninges, appearing as abnormal contrast enhancement or thickening, while therapy-induced changes preferentially involve the white matter, leading to diffuse or patchy T2 hyperintensity [7]. Recognition of these normal structures ensures that pathological deviations are not overlooked.

The vascular anatomy of the brain is of particular radiodiagnostic relevance, given the high incidence of cerebrovascular complications in leukemic patients. Infarctions are typically localized to arterial territories of the anterior, middle, or posterior cerebral arteries, and their distribution on diffusion-weighted imaging provides critical clues to etiology [8]. Venous anatomy, especially the superior sagittal sinus and transverse sinuses, must be carefully evaluated on MR venography, as dural venous sinus thrombosis is a recognized sequela of chemotherapy, asparaginase therapy, or the hypercoagulable state induced by leukemia itself [9].

Understanding venous collateral pathways and cortical venous drainage is equally essential, since cortical vein thrombosis may mimic infectious meningitis or leukemic infiltration on conventional MRI. Susceptibility-weighted imaging (SWI) adds sensitivity for detecting small hemorrhages and venous clots in these cases [10]. Thus, familiarity with neurovascular anatomy in MRI interpretation not only aids in identifying CNS leukemia but also assists in differentiating its complications from therapy-induced or infectious mimics.

Leukemia in Children – Overview

Leukemia is the most prevalent pediatric malignancy, with acute lymphoblastic leukemia (ALL) accounting for approximately 75% of cases, followed by acute myeloid leukemia (AML). Chronic forms such as CML and CLL are rare in children [11]. From a radiological standpoint, MRI plays a limited role in the primary diagnosis of leukemia but is indispensable in detecting central nervous system (CNS) complications and in monitoring therapy-related changes [12].

CNS involvement in leukemia arises both from direct leukemic infiltration and as a consequence of treatment strategies. Prophylactic intrathecal chemotherapy and cranial irradiation, historically used to reduce CNS relapse, frequently leave distinctive imaging footprints. These include diffuse white matter hyperintensity, cortical atrophy, and delayed leukoencephalopathy on MRI, underscoring the dual role of imaging in assessing both disease progression and iatrogenic injury [13].

Importantly, neuroimaging does not replace cerebrospinal fluid cytology, which remains the gold standard for CNS leukemia detection. However, MRI provides a non-invasive means to detect subtle meningeal disease, parenchymal lesions, and vascular complications, often identifying abnormalities before clinical deterioration becomes evident [14]. This complementary role makes MRI essential in comprehensive management of pediatric leukemia, especially in long-term surveillance where radiation-free modalities are preferred.

Central Nervous System Leukemia

CNS leukemia arises when malignant cells infiltrate the meninges, perivascular spaces, or brain parenchyma, bypassing the protective blood–brain barrier. In children, it represents a major cause of relapse and treatment resistance, with the leptomeninges being the most frequent site of involvement [15]. On MRI, meningeal disease typically manifests as diffuse or nodular enhancement along sulci, cisterns, or spinal roots, often subtle in early stages. Such findings, though nonspecific, are highly relevant when correlated with clinical suspicion or cerebrospinal fluid results [16].

Parenchymal involvement is less common but radiologically significant. It may appear as focal masses resembling granulocytic sarcoma or as diffuse infiltrative changes with T2/FLAIR hyperintensity. These can mimic infectious or inflammatory disorders, highlighting the importance of multiparametric MRI to differentiate pathology. Diffusion-weighted imaging is particularly useful in detecting high cellularity lesions typical of leukemic deposits [17].

Beyond direct infiltration, CNS leukemia predisposes patients to a spectrum of secondary complications. Disruption of vascular integrity leads to hemorrhage or ischemia, while immunosuppression promotes opportunistic infections that may mimic disease recurrence. In all these scenarios, MRI serves as the most sensitive tool for detection and monitoring, guiding timely therapeutic intervention [18].

Thus, understanding the radiological patterns of CNS leukemia is critical for accurate diagnosis and for distinguishing true disease relapse from treatment- or infection-related mimics. This forms the basis for the subsequent discussion on the detailed MRI spectrum of pediatric leukemia.

MRI Spectrum of CNS Findings in Pediatric Leukemia

Direct CNS Manifestations of Leukemia

Leukemic Meningitis

Leptomeningeal infiltration is the most common form of CNS involvement in pediatric leukemia. MRI demonstrates diffuse or nodular meningeal enhancement on post-contrast T1-weighted imaging, often accentuated along sulci and basal cisterns. In early stages, enhancement may be subtle and easily overlooked without high-quality contrast studies. Fluid-attenuated inversion recovery (FLAIR) sequences with contrast are especially sensitive for detecting superficial leptomeningeal disease [19]. These findings, though nonspecific, raise strong suspicion in the context of hematologic malignancy and require confirmation with cerebrospinal fluid cytology [20].

Spinal Leptomeningeal Involvement

The spinal meninges may also harbor leukemic cells, producing diffuse or focal enhancement along nerve roots and cauda equina. MRI of the spine with gadolinium is particularly important in children presenting with back pain, radiculopathy, or unexplained neurologic deficits. High-resolution contrast-enhanced T1-weighted imaging in sagittal and axial planes remains the diagnostic standard [21].

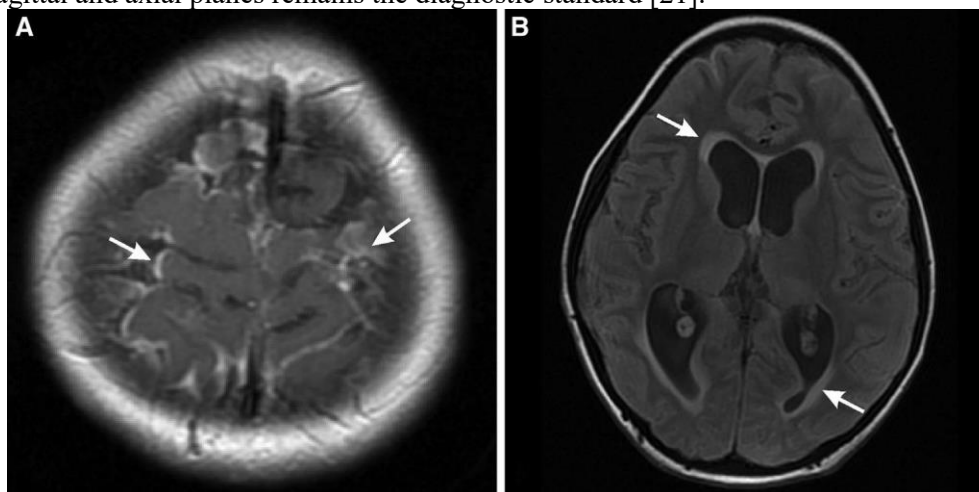


Figure (1): A 9-year-old child with attacks of headache and seizures who had received treatment developed leptomeningeal carcinomatosis with subsequent hydrocephalus. Abnormal leptomeningeal contrast improvements (arrows) are visible in the axial contrast-enhanced T1-weighted magnetic resonance imaging (A). Axial FLAIR MR image (B) shows periventricular interstitial oedema (arrows) and secondary hydrocephalic changes [21].

Granulocytic Sarcoma (Chloroma)

A rarer but radiologically distinctive manifestation is granulocytic sarcoma, or chloroma, more often seen in AML. On MRI, these appear as extra-axial or parenchymal masses, isointense to grey matter on T1, slightly hyperintense on T2, and enhancing homogeneously after contrast. Their imaging appearance can mimic lymphoma or meningioma, but diffusion restriction and clinical context usually aid differentiation [22]

Bone Marrow Infiltration

Calvarial and skull base marrow infiltration can also be detected on MRI, often manifesting as T1 hypointensity with variable T2 signal. These abnormalities may extend into adjacent dura, mimicking meningeal disease. MRI is particularly useful in differentiating marrow infiltration from red marrow reconversion in younger patients, which may otherwise confound interpretation [23].

Optic Nerve and Ocular Involvement

Leukemic cells may infiltrate the optic nerves, chiasm, or orbital structures. MRI findings include optic nerve thickening, abnormal enhancement, and occasionally intraocular masses. Dedicated orbital MRI with fat-suppressed contrast-enhanced sequences is essential when visual symptoms are present, as early detection can guide timely therapy and potentially preserve vision [24].

Hematologic and Cerebrovascular Complications

Intracranial Hemorrhage

Hemorrhagic complications are relatively common in leukemic children, arising from thrombocytopenia, disseminated intravascular coagulation, or treatment-induced vascular fragility. On MRI, acute hemorrhage demonstrates susceptibility artifacts on SWI and variable signal intensities on T1 and T2 depending on the stage of blood degradation. In pediatric leukemia, microbleeds may remain clinically silent yet are readily detected on high-resolution susceptibility imaging, providing critical prognostic information [25].

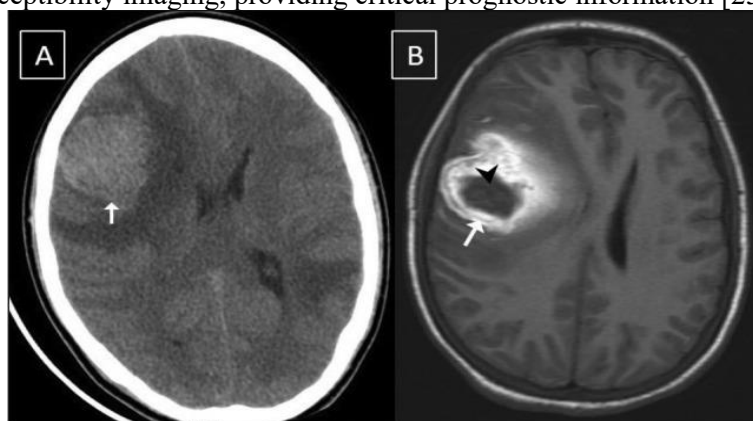


Figure (2): A 16-year-old boy developed altered sensorium followed by loss of consciousness. Plain CT scan (A) shows a hyperdense lesion (arrow) in the right frontoparietal region, with surrounding white matter edema and mass effect. Axial plain T1W MRI (B) at the corresponding level shows a hyperintense periphery (arrow) due to the presence of intracellular methemoglobin and central hypointensity (arrowhead) due to deoxyhemoglobin [25].

Dural Venous Sinus Thrombosis (DVST)

DVST is a recognized complication, often linked to L-asparaginase therapy or the hypercoagulable state of leukemia itself. MRI combined with MR venography is the modality of choice, showing absence of normal flow voids, intraluminal filling defects, and parenchymal venous infarcts. T2/FLAIR hyperintensity in adjacent brain tissue may suggest venous congestion, while susceptibility-weighted imaging aids in confirming intraluminal thrombus [26].

Arterial Infarctions

Leukemic children are predisposed to arterial ischemic events due to leukostasis, hyperviscosity, or chemotherapy-induced vascular injury. MRI demonstrates restricted diffusion in affected arterial territories on DWI, with ADC reduction confirming cytotoxic edema. Stroke in this context often involves the middle cerebral artery territory and may present with multifocal lesions rather than a single large infarct, complicating differentiation from infectious vasculitis [27].

Cortical Vein Thrombosis

Although less common than DVST, cortical vein thrombosis carries significant morbidity. On MRI, cortical vein thrombosis may appear as linear susceptibility signal on SWI or as focal cortical edema with venous infarction. Contrast-enhanced MR venography can demonstrate abrupt cut-off or non-opacification of cortical veins. Radiological recognition is crucial, as clinical presentation often mimics meningitis or relapse of leukemic infiltration [28].

Cerebrovascular complications thus represent a major component of CNS morbidity in pediatric leukemia. Multiparametric MRI, particularly with advanced vascular sequences, plays a central role in early detection, differentiation from relapse, and in guiding anticoagulant or supportive management.

Infectious Complications

Children with leukemia are profoundly immunocompromised due to both the underlying disease and intensive chemotherapy, predisposing them to a wide spectrum of opportunistic CNS infections. MRI plays a pivotal role in early diagnosis, as clinical features are often nonspecific and CSF studies may be inconclusive in severely ill patients [29].

Fungal Infections

Fungal pathogens, especially *Aspergillus* and *Candida*, are among the most feared opportunistic infections in this group. On MRI, fungal abscesses often appear as ring-enhancing lesions with low signal on T2-weighted imaging due to the presence of fungal elements and hemorrhagic byproducts. Susceptibility-weighted imaging further highlights microhemorrhages within the lesions, while diffusion restriction at the core can help distinguish fungal abscesses from leukemic infiltration [30].

Bacterial Infections

Bacterial meningitis and abscesses are also frequent. MRI findings include leptomeningeal enhancement, subdural empyema, or parenchymal abscess formation with central diffusion restriction. In leukemic children, bacterial abscesses often present with atypical imaging features, including multilocularity or poor capsule formation, complicating differentiation from choroma or necrotic tumor [31].

Viral Infections

Neurotropic viruses such as herpes simplex virus (HSV), cytomegalovirus (CMV), and JC virus may cause devastating encephalitides in immunocompromised hosts. MRI typically reveals bilateral asymmetric T2/FLAIR hyperintensity in the temporal lobes in HSV, periventricular white matter lesions in CMV, and multifocal demyelination in progressive multifocal leukoencephalopathy (PML). The non-enhancing, patchy white matter lesions of PML with restricted diffusion are particularly important to differentiate from treatment-induced leukoencephalopathy [32].

Parasitic Infections

Parasitic CNS infections, though less common, can occur in endemic regions. Toxoplasmosis may present as multiple ring-enhancing lesions with surrounding edema, showing eccentric target signs on contrast imaging. Recognition of these features is crucial in children where clinical suspicion may be low [33].

MRI thus provides invaluable clues in differentiating infectious complications from relapse or treatment-related changes. Early radiological diagnosis can guide antimicrobial therapy and prevent catastrophic neurological sequelae in this vulnerable population.

Therapy-Related Complications

Therapeutic regimens for pediatric leukemia, while lifesaving, are frequently associated with acute and chronic CNS toxicities. Neuroimaging, particularly MRI, is critical for early identification of these complications, which may mimic relapse or infection [34].

Chemotherapy-Induced Neurotoxicity

Methotrexate (MTX) Toxicity:

High-dose or intrathecal MTX can cause leukoencephalopathy. On MRI, this appears as bilateral, symmetric T2/FLAIR hyperintensities in the periventricular white matter, often sparing U-fibers. Diffusion-weighted imaging (DWI) may show restricted diffusion in the acute stage (“panda eye sign” in the centrum semiovale). Subacute cases demonstrate reversible diffusion restriction, helping to distinguish MTX toxicity from ischemic infarction [35].

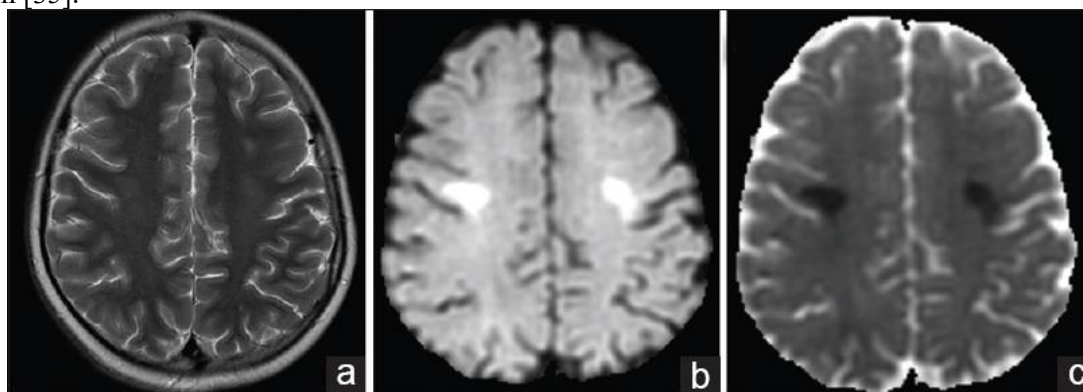


Figure (3): A 16-year-old boy with leukemia. Ten days after the 2nd high-dose methotrexate dose, the patient developed dysarthria and dysphagia. The patient had complete resolution of symptoms spontaneously within 24 hours. His computed tomography and magnetic

resonance imaging of the brain were normal. T1, T2 (a), T2-fluid-attenuated inversion recovery, and postcontrast magnetic resonance imaging did not reveal any significant abnormality. The diffusion-weighted imaging showed bilateral restriction in diffusion (b and c) in the centrum semiovale [35].

Cytarabine and Other Agents:

Cytarabine may induce cerebellar dysfunction and diffuse leukoencephalopathy. MRI findings include hyperintense lesions on T2/FLAIR involving the deep white matter and cerebellum. Vincristine-related neurotoxicity typically affects peripheral nerves, but CNS involvement may mimic demyelination [36].

Posterior Reversible Encephalopathy Syndrome (PRES):

Commonly linked to corticosteroids, cyclosporine, and asparaginase. MRI reveals vasogenic edema predominantly in the parieto-occipital lobes, hyperintense on T2/FLAIR. DWI helps differentiate PRES (increased ADC) from ischemia. The condition is potentially reversible with prompt management [37].

Radiotherapy-Related Changes

Early Effects:

Early delayed injury manifests within months as transient diffuse T2/FLAIR hyperintensity in the periventricular white matter, often clinically silent.

Late Effects:

Chronic radiation injury may result in cerebral atrophy, leukoencephalopathy, mineralizing microangiopathy (seen as basal ganglia calcifications on CT and corresponding hypointensity on susceptibility MRI), and secondary vascular malformations. Secondary tumors (e.g., meningioma, glioma) can appear years later as enhancing space-occupying lesions with mass effect [38].

Radiation Necrosis:

Presents as focal T2/FLAIR hyperintensity with heterogeneous enhancement and mass effect. MR perfusion and spectroscopy aid differentiation from tumor recurrence—necrosis shows low perfusion and elevated lipid-lactate peaks [39].

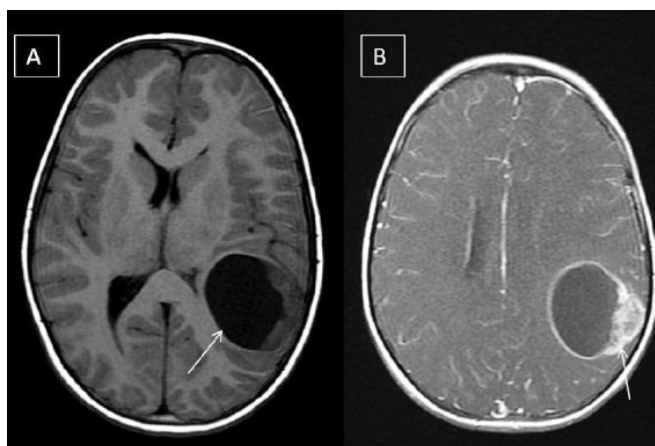


Figure (4): Axial T1W (A) and contrast-enhanced T1W (B) MRI images in a 9-year-old boy who was treated for ALL 4 years back and now presented with seizures, reveal a predominantly cystic space-occupying lesion with an enhancing solid component along its lateral wall (arrow). The imaging features are suggestive of a low-grade brain tumor; however turned out to be a primitive neuroectodermal tumor [39].

Hematopoietic Stem Cell Transplantation (HSCT)-Related Complications

Neurotoxicity in HSCT arises from conditioning regimens, immunosuppressants, and infections. PRES is particularly frequent post-transplant due to calcineurin inhibitors. Opportunistic CNS infections (fungal, viral, parasitic) are also more common in this population [40]. MRI is essential to distinguish these from leukemic relapse.

Vascular Complications

Asparaginase therapy predisposes to cerebral venous sinus thrombosis due to acquired prothrombotic states. On MRI/MRV, thrombosed sinuses appear hyperintense on T1/T2 with absence of flow void; the “empty delta sign” on post-contrast CT/MR confirms the diagnosis. Arterial ischemic strokes, both lacunar and territorial, may also occur, with restricted diffusion on DWI [41].

MRI thus provides a comprehensive toolset for identifying therapy-induced CNS changes, allowing clinicians to distinguish reversible conditions (e.g., PRES, MTX toxicity) from progressive injuries (e.g., radiation necrosis, secondary tumors). Radiologists play a pivotal role in guiding clinical decisions, balancing disease control with prevention of long-term neurotoxicity.

Advanced MRI Techniques in CNS Leukemia

Conventional MRI sequences (T1, T2, FLAIR, GRE) remain the cornerstone in assessing CNS involvement in pediatric leukemia. However, advanced MRI techniques provide additional insights into microstructural, metabolic, perfusional, and functional changes that improve diagnostic accuracy, therapeutic monitoring, and prognostic evaluation [42].

Diffusion-Weighted Imaging (DWI) and Diffusion Tensor Imaging (DTI)

DWI is highly sensitive in detecting early ischemic changes and therapy-induced complications such as methotrexate leukoencephalopathy. Restricted diffusion with reduced ADC values suggests cytotoxic edema, whereas increased ADC reflects vasogenic edema, typical of PRES [43]. DTI offers tractography-based visualization of white matter integrity, useful in evaluating treatment-related leukoencephalopathy and long-term neurocognitive sequelae. Fractional anisotropy maps can detect subtle microstructural changes even before conventional MRI becomes abnormal [44].

Magnetic Resonance Spectroscopy (MRS)

MRS provides metabolic fingerprints of CNS involvement. Elevated choline (Cho) and reduced N-acetyl aspartate (NAA) suggest cellular proliferation and neuronal injury. Lactate and lipid peaks indicate anaerobic metabolism or necrosis, often seen in leukemic infiltration or radiation necrosis [45]. In drug-induced toxicity, such as methotrexate injury, MRS may show decreased NAA and increased Cho with variable lactate, reflecting reversible neuronal dysfunction rather than true tissue loss [46].

Perfusion-Weighted Imaging (PWI)

Perfusion imaging, using DSC or DCE techniques, measures cerebral blood volume (CBV) and permeability. Leukemic infiltrates often demonstrate increased perfusion compared to normal white matter. Conversely, radiation necrosis and demyelination show hypoperfusion [47]. Arterial spin labeling (ASL) offers a non-contrast alternative, particularly useful in children and patients requiring repeated follow-up scans [48].

Susceptibility-Weighted Imaging (SWI)

SWI enhances detection of microhemorrhages, calcifications, and venous thrombosis, all of which are frequent in leukemia due to coagulopathy or therapy-related vascular injury. It is superior to conventional GRE in identifying small hemorrhagic foci in the basal ganglia and cortex [49].

Functional MRI (fMRI) and Resting-State fMRI

fMRI evaluates blood oxygenation level-dependent (BOLD) signals, allowing assessment of cortical function. In pediatric leukemia survivors, fMRI can detect altered activation in attention and memory networks, correlating with neurocognitive deficits from chemotherapy and radiation [50].

Chemical Exchange Saturation Transfer (CEST) Imaging

CEST, particularly amide proton transfer (APT) imaging, provides contrast based on endogenous proteins and peptides. Early studies suggest its potential in differentiating leukemic infiltration from post-treatment changes, as leukemic tissue exhibits higher mobile protein content [51].

Multiparametric and Hybrid Imaging Approaches

The integration of DWI, MRS, PWI, and SWI into multiparametric MRI protocols increases diagnostic specificity. Hybrid PET/MRI systems allow combined metabolic and structural evaluation, helping distinguish relapse from therapy-induced necrosis or infection [52].

Conclusion

Central nervous system involvement in pediatric leukemia represents one of the most challenging aspects of disease management, both in terms of early detection and long-term monitoring. Magnetic resonance imaging has established itself as the modality of choice, owing to its excellent soft tissue contrast, multiplanar capability, and ability to detect subtle changes across the meninges, parenchyma, vasculature, and spinal axis. The imaging spectrum is broad, encompassing direct leukemic infiltration, secondary hematologic and vascular insults, opportunistic infections, and a wide array of therapy-related complications. Recognizing these diverse manifestations is crucial for timely intervention and for distinguishing disease relapse from treatment-induced or infectious mimics.

Beyond conventional sequences, advanced MRI techniques now play a vital role in refining diagnostic accuracy. Diffusion, perfusion, spectroscopy, and susceptibility imaging provide biomarkers of cellularity, vascularity, metabolism, and microvascular injury. More recently, functional MRI, diffusion tensor imaging, and emerging tools such as chemical exchange saturation transfer have opened new avenues for detecting subtle neurotoxicity and for predicting neurocognitive outcomes in survivors. Together, these tools not only enhance immediate diagnostic confidence but also support longitudinal follow-up in an era where survival rates for childhood leukemia are steadily improving.

Looking ahead, the integration of multiparametric MRI with molecular biology, artificial intelligence, and hybrid imaging platforms promises to transform neuroimaging into a cornerstone of personalized pediatric oncology. Automated image analysis and radiomics have the potential to uncover imaging biomarkers predictive of relapse, treatment response, and long-term outcomes. Such innovations will allow radiologists and clinicians to move beyond descriptive imaging toward predictive and prognostic frameworks tailored to individual patients.

In summary, MRI provides a comprehensive lens through which the complex neurological landscape of pediatric leukemia can be understood. By recognizing its full spectrum of manifestations, harnessing advanced imaging tools, and integrating with emerging technologies, MRI will continue to play a pivotal role in improving outcomes and quality of life for children affected by this disease.

REFERENCES

1. Ward E, DeSantis C, Robbins A, Kohler B, Jemal A. Childhood and adolescent cancer statistics, 2014. *CA Cancer J Clin.* 2014;64(2):83-103.
2. Pui CH, Howard SC. Current management and challenges of malignant disease in the CNS in pediatric leukemia. *Lancet Oncol.* 2008;9(3):257-268.
3. Moritani T, Ekholm S, Westesson PL. *Diffusion-weighted MR Imaging of the Brain.* Springer; 2005.
4. Castillo M. Imaging manifestations of complications of cancer therapy. *Radiology.* 2006;240(3):629-642.
5. O'Connor J, Micallef I, Kumar AJ, et al. CNS manifestations of leukemia and lymphoma. *Clin Radiol.* 2002;57(8):533-540.
6. Yousem DM, Grossman RI. *Neuroradiology: The Requisites.* 4th ed. Philadelphia, PA: Elsevier; 2016.
7. Osborn AG, Salzman KL, Thurnher MM, Rees JH, Castillo M. *Diagnostic Imaging: Brain.* 3rd ed. Elsevier; 2015.
8. Wintermark M, Albers GW, Alexandrov AV, et al. Acute stroke imaging research roadmap II. *Stroke.* 2013;44(9):2628-2639.
9. Sébire G, Tabarki B, Saunders DE, et al. Cerebral venous sinus thrombosis in children: risk factors, presentation, diagnosis and outcome. *Brain.* 2005;128(Pt 3):477-489.
10. Mittal S, Wu Z, Neelavalli J, Haacke EM. Susceptibility-weighted imaging: technical aspects and clinical applications, part 2. *AJNR Am J Neuroradiol.* 2009;30(2):232-252.
11. Hunger SP, Mullighan CG. Acute lymphoblastic leukemia in children. *N Engl J Med.* 2015;373(16):1541-1552.
12. Cheng SC, Rau RE, Mullighan CG. Advances in the genetics of acute lymphoblastic leukemia in children. *Br J Haematol.* 2020;190(6):843-862.
13. Buizer AI, de Sonnevile LM, Veerman AJ. Effects of chemotherapy on neurocognitive function in children with acute lymphoblastic leukemia: a critical review of the literature. *Pediatr Blood Cancer.* 2009;52(4):447-454.
14. Frishman-Levy L, Izraeli S. Advances in understanding the pathogenesis of CNS acute lymphoblastic leukaemia and potential for therapy. *Br J Haematol.* 2017;176(2):157-167.
15. Gökbüget N, Stanze D, Beck J, et al. Outcome of relapsed adult acute lymphoblastic leukemia depends on response to salvage chemotherapy, prognostic factors, and performance of stem cell transplantation. *Blood.* 2012;120(10):2032-2041.
16. Ahn JH, Lee JH, Lee KH, et al. MRI findings of CNS involvement in leukemia. *J Comput Assist Tomogr.* 2002;26(6):1006-1011.
17. Kizilkilic O, Tali ET, Guzel A, et al. Central nervous system involvement in leukemia: magnetic resonance imaging findings. *Eur Radiol.* 2004;14(6):1169-1176.
18. Poretti A, Meoded A, Huisman TA. Neuroimaging of children with acute lymphoblastic leukemia: pictorial essay. *Neuroradiology.* 2014;56(5):387-400.
19. Kato Y, Matsuo K, Takahashi H, et al. Contrast-enhanced FLAIR MR imaging in the diagnosis of leptomeningeal metastasis: comparison with contrast-enhanced T1-weighted imaging. *AJNR Am J Neuroradiol.* 2010;31(6):1040-1046.
20. Chamberlain MC. Leptomeningeal metastasis. *Curr Opin Oncol.* 2010;22(6):627-635.
21. Hyare H, Jaunmuktane Z, Brandner S, Jäger HR. Leptomeningeal disease: diagnosis and imaging. *Semin Ultrasound CT MR.* 2017;38(5):462-473.
22. Yamauchi K, Yasuda M. Comparison in treatments of nonleukemic granulocytic sarcoma: report of two cases and review of 72 cases in the literature. *Cancer.* 2002;94(6):1739-1746.
23. Vande Voorde K, Dhooge C, Laureys G, et al. MR imaging of bone marrow in hematologic malignancies of childhood. *Eur J Radiol.* 2010;74(1):50-56.
24. Sharma T, Grewal J, Gupta S, Murray PI. Ophthalmic manifestations of acute leukaemias: the ophthalmologist's role. *Eye (Lond).* 2004;18(7):663-672.

25. Barnes PD, Vezina G. Neuroimaging of acute complications of leukemia in children. *AJNR Am J Neuroradiol.* 2000;21(4):682-688.
26. Nowak-Göttl U, Kenet G, Mitchell LG. Thrombosis in childhood acute lymphoblastic leukaemia: epidemiology, aetiology, diagnosis, prevention and treatment. *Best Pract Res Clin Haematol.* 2009;22(1):103-114.
27. deVeber G, Roach ES, Riela AR, Wiznitzer M. Stroke in children: recognition, treatment, and future directions. *Semin Pediatr Neurol.* 2000;7(4):309-317.
28. Crassard I, Bousser MG. Cerebral venous thrombosis. *J Neuroophthalmol.* 2004;24(2):156-163.
29. Rubin LG, Levin MJ, Ljungman P, et al. Infectious diseases in immunocompromised children: guidelines. *Clin Infect Dis.* 2014;58(4):e1-e38.
30. Kamezaki T, Arakawa H, Morikawa M, et al. Fungal infections in immunocompromised hosts: MR imaging findings. *Radiographics.* 2010;30(4):1043-1059.
31. Oguz KK, Anlar B, Senbil N, et al. MR imaging of the brain in children with acute bacterial meningitis. *Neuroradiology.* 2004;46(9):735-741.
32. Whitley RJ, Kimberlin DW, Roizman B. Herpes simplex viruses. *Clin Infect Dis.* 1998;26(3):541-553.
33. Luft BJ, Remington JS. Toxoplasmic encephalitis in AIDS. *Clin Infect Dis.* 1992;15(2):211-222.
34. Reddick WE, Glass JO, Helton KJ, et al. Atypical white matter volume development in children following craniospinal irradiation. *Neuro Oncol.* 2005;7(1):12-19.
35. Rollins N, Winick N, Bash R, Booth T. Acute methotrexate neurotoxicity: findings on diffusion-weighted imaging and correlation with clinical outcome. *AJNR Am J Neuroradiol.* 2004;25(10):1688-1695.
36. Inaba H, Pui CH. Glucocorticoid use in acute lymphoblastic leukaemia. *Lancet Oncol.* 2010;11(11):1096-1106.
37. Bartynski WS. Posterior reversible encephalopathy syndrome, part 1: fundamental imaging and clinical features. *AJNR Am J Neuroradiol.* 2008;29(6):1036-1042.
38. Armstrong GT, Liu Q, Yasui Y, et al. Long-term outcomes among adult survivors of childhood central nervous system malignancies. *J Natl Cancer Inst.* 2009;101(13):946-958.
39. Sundgren PC, Cao Y. Brain irradiation: effects on normal brain parenchyma and radiation injury. *Neuroimaging Clin N Am.* 2009;19(4):657-668.
40. Poretti A, Meoded A, Huisman TA. Neuroimaging of children after hematopoietic stem cell transplantation: state of the art and review of literature. *Neuroradiology.* 2013;55(6):647-661.
41. Grace RF, Dahlberg SE, Neuberg D, et al. The frequency and management of asparaginase-related thrombosis in pediatric and adult patients with acute lymphoblastic leukemia. *Leukemia.* 2011;25(4):590-596.
42. Pui MH. Diffusion-weighted imaging of the brain: beyond stroke. *Hong Kong J Radiol.* 2010;13(1):14-24.
43. Shuper A, Stark B, Kornreich L, Cohen IJ, Avrahami G, Yaniv I. Methotrexate-related neurotoxicity in the treatment of childhood acute lymphoblastic leukemia. *Cancer.* 2000;88(8):1849-1858.
44. Khong PL, Leung LH, Fung AS, et al. White matter anisotropy in post-treatment childhood cancer survivors: preliminary evidence of association with neurocognitive function. *J Clin Oncol.* 2006;24(6):884-890.
45. Panigrahy A, Nelson MD Jr, Blüml S. Magnetic resonance spectroscopy in pediatric neuroradiology: clinical and research applications. *Pediatr Radiol.* 2010;40(1):3-30.
46. Leung LH, Kwan CM, Yuen HL, et al. MR spectroscopy of methotrexate-induced neurotoxicity in childhood leukemia. *Neuroradiology.* 2004;46(9):758-762.
47. Law M, Young RJ, Babb JS, et al. Gliomas: predicting time to progression or survival with cerebral blood volume measurements at dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging. *Radiology.* 2008;247(2):490-498.
48. Warmuth C, Günther M, Zimmer C. Quantification of blood flow in brain tumors: comparison of arterial spin labeling and dynamic susceptibility-weighted contrast-enhanced MR imaging. *Radiology.* 2003;228(2):523-532.
49. Tong KA, Ashwal S, Holshouser BA, et al. Hemorrhagic shearing lesions in children and adolescents with posttraumatic diffuse axonal injury: improved detection and initial results. *Radiology.* 2003;227(2):332-339.
50. Kesler SR, Gugel M, Huston-Warren E, Watson C. Altered resting state functional connectivity in young survivors of acute lymphoblastic leukemia treated with chemotherapy. *Brain Imaging Behav.* 2014;8(4):611-620.
51. Zhou J, Payen JF, Wilson DA, Traystman RJ, van Zijl PC. Using the amide proton signals of intracellular proteins and peptides to detect pH effects in MRI. *Nat Med.* 2003;9(8):1085-1090.
52. Verger A, Guedj E. PET and MRI in oncology: review of integrated imaging in clinical practice. *Cancer Imaging.* 2018;18(1):5.