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Radio-Diagnosis

SPECTRUM OF MAGNETIC RESONANCE IMAGING FINDINGS IN LEUKAEMIA WITH SUSPECTED NEUROLOGICAL MANIFESTATION

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ABSTRACT **Background:** Central nervous system (CNS) involvement in leukaemia represents a significant cause of morbidity and mortality despite advances in therapeutic interventions. Magnetic resonance imaging (MRI) provides superior soft tissue characterization for detecting and evaluating CNS lesions. **Objective:** To identify and characterize the spectrum of MRI findings in patients with leukaemia presenting with suspected neurological manifestation. **Methods:** A hospital-based cross-sectional study was conducted at the Department of Radiodiagnosis, Assam Medical College & Hospital over a one-year period. Forty patients (aged 6-60 years) with confirmed or suspected leukaemia presenting with neurological manifestations (headache, seizure, ataxia, weakness, sensory changes, altered consciousness) underwent MRI brain and spinal imaging using a 1.5 Tesla MRI system. Imaging protocols included conventional sequences (T1, T2, FLAIR, DWI, ADC) and post-contrast T1-weighted images. Data was analyzed using SPSS V21. **Results:** The study cohort comprised 24 males (60%) and 16 females (40%), with mean age of 31.75 ± 15.18 years. The 31-40 years age group was most frequently affected (25%). MRI findings demonstrated diverse patterns of CNS involvement including direct leukemic infiltration, treatment-related complications, and secondary changes. Key findings included white matter abnormalities, leptomeningeal involvement, and cerebrovascular changes. **Conclusion:** MRI is an invaluable imaging modality for comprehensive evaluation of CNS involvement in leukaemia patients. The diverse spectrum of MRI findings facilitates early detection and differentiation between leukemic infiltration and treatment-related complications, enabling timely clinical intervention and improved patient management.

KEYWORDS : Leukaemia, Central Nervous System, Magnetic Resonance Imaging, Neurological Manifestation, Imaging Findings, Chemotherapy Complications

1. INTRODUCTION

Leukaemia represents a group of malignant hematologic disorders characterized by genetic abnormalities in hematopoietic cells, leading to uncontrolled clonal cell proliferation [1]. These neoplastic cells acquire a competitive advantage over normal blood cells through accelerated proliferation rates and reduced apoptotic activity, consequently disrupting normal bone marrow function and resulting in marrow failure [1]. According to the WHO classification, leukaemia is categorized into four primary types based on cell lineage and maturity: Acute Lymphoblastic Leukaemia (ALL), Acute Myeloid Leukaemia (AML), Chronic Lymphocytic Leukaemia (CLL), and Chronic Myeloid Leukaemia (CML) [2].

Historically, central nervous system (CNS) involvement in leukaemia was considered a rare complication due to the rapidly progressive nature of the disease. However, with significant therapeutic advancements over the past two decades, event-free survival rates for acute leukaemia have improved substantially to approximately 60%, leading to a paradoxical increase in CNS-related complications [3]. Contemporary prophylactic strategies including intrathecal methotrexate, high-dose intravenous chemotherapy, and cranial irradiation have substantially reduced overt CNS relapse; nevertheless, CNS involvement remains a leading cause of morbidity and mortality in leukaemia patients [4].

CNS complications in leukaemia are broadly classified into two categories: (a) direct infiltration of leukemic blasts into CNS structures, and (b) secondary complications arising from the disease process or its therapeutic interventions [3]. Direct CNS involvement can affect multiple neural compartments including the leptomeninges (meningeal infiltration), brain parenchyma (CNS leukaemia), and cerebral vasculature (leukostasis). Treatment-related complications encompass white matter disease, small-vessel calcifications, cerebrovascular accidents, secondary malignancies, opportunistic infections, brain atrophy, endocrinologic dysfunction, and long-term neurocognitive impairment [4,5].

The diagnosis of CNS involvement in leukaemia presents substantial challenges due to the heterogeneous etiologies of neurological manifestations and the absence of pathognomonic imaging features. While histopathological examination via brain biopsy remains the diagnostic gold standard, it is invasive and impractical for routine clinical practice [4]. Consequently, neuroimaging plays a pivotal role in non-invasive detection and characterization of CNS lesions.

Magnetic resonance imaging (MRI) possesses exceptional soft tissue contrast resolution and multiplanar imaging capabilities, making it the imaging modality of choice for comprehensive CNS evaluation in leukaemia patients [4]. MRI facilitates characterization of leukemic infiltrates, detection of treatment-related complications, and identification of secondary pathologies. These diagnostic capabilities enable early intervention and facilitate evidence-based management strategies. Despite the clinical importance of CNS involvement in leukaemia, there remains a paucity of data regarding the complete spectrum of MRI findings in the Indian population.

This study was undertaken to assess the magnetic resonance imaging patterns and spectrum of imaging abnormalities in patients with leukaemia presenting with suspected neurological manifestation.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

A hospital-based cross-sectional descriptive study was conducted at the Department of Radiodiagnosis, Assam Medical College & Hospital, Dibrugarh, Assam, India over a period of one year. The study was approved by the Institutional Ethics Committee (Human), Assam Medical College, Dibrugarh, prior to commencement.

2.2 Study Population and Sampling

Inclusion Criteria:

- Patients aged 6 to 60 years who were hemodynamically stable
- Confirmed diagnosis of leukaemia (any type) OR high clinical suspicion of leukaemia
- Presenting with neurological manifestations including headache, seizure, ataxia, weakness, sensory changes, or altered consciousness
- Referred to Department of Radiodiagnosis for MRI evaluation
- Written informed consent provided by patient or legal guardian

Exclusion Criteria:

- Contraindications to MRI including ferromagnetic implants, cardiac pacemakers, or aneurysm clips
- History of hypersensitivity or documented allergy to gadolinium

contrast
- Elevated serum creatinine (contraindication for gadolinium contrast administration)
- Patients not providing written informed consent

Sample Size Calculation
Sample size was calculated based on prevalence of neurological involvement in acute lymphoblastic leukaemia reported in previous literature [46]. Using a 95% confidence interval and absolute error of 10%, with prevalence estimate of 10%, the calculated sample size was 35, which was rounded to 40 patients.

2.3 Data Collection and Patient Assessment
All eligible patients undergoing MRI brain and/or spinal imaging during the study period were enrolled. Structured data collection included:
- Unique patient identification code, age, and gender
- Hospital medical record (MRD) number and date of admission
- Detailed clinical history including presenting symptoms, leukaemia type, duration, and prior treatments
- Standardized questionnaire completion for all study participants
- Documentation of baseline blood investigations including serum creatinine

2.4 MRI Imaging Protocol
All patients were screened for contraindications to MRI prior to scanner entry. Patients were positioned supine with the head immobilized using appropriate padding. Imaging was performed using a Siemens Magnetom Avanto fit A Tim+ Dot 1.5 Tesla whole-body MRI system.

Technical Parameters:
- Slice thickness: 5 mm with 0.5 mm interslice gaps
- Imaging planes: Axial, coronal, and sagittal orientations
- Field of view (FOV): 230 mm
- Matrix: 224 × 256

Conventional Sequences (Plain Imaging):
1. T1-weighted imaging (T1WI)
2. T2-weighted imaging (T2WI)
3. Fluid-attenuated inversion recovery (FLAIR)
4. Diffusion-weighted imaging (DWI)
5. Apparent diffusion coefficient (ADC) mapping
6. Susceptibility-weighted imaging (SWI)

Spinal Imaging Protocol (when Indicated):
- T2-weighted and T2 fat-suppressed sequences in axial and sagittal planes
- T1-weighted sequences in axial and sagittal planes
- Short tau inversion recovery (STIR) sequences

Contrast Administration
Patients with normal serum creatinine (eGFR >30 mL/min/1.73m²) received intravenous gadolinium contrast. Gadobutrol (gadovist, 1.0 mmol/mL) was administered at a dose of 0.1 mg/kg body weight (individualized for each patient). Contrast was injected manually via peripheral intravenous access. Emergency medications and resuscitation equipment were maintained at bedside during contrast administration.

Post-contrast Imaging Parameters
Post-contrast T1-weighted sequence parameters: TR = 500 ms, TE = 7.8 ms, slice thickness = 5 mm, interslice gap = 1.5 mm, FOV = 230 mm, matrix = 224 × 256. Total imaging time for post-contrast acquisition was 3 minutes 48 seconds.

2.5 Data Analysis
Imaging data were evaluated by experienced radiologists blinded to clinical details. All findings were categorized and tabulated. Raw data were entered into Microsoft Excel spreadsheet and subsequently analyzed using SPSS version 21 (IBM SPSS Statistics, Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages. Continuous variables were expressed as mean ± standard deviation with range notation.

2.6 Ethical Considerations
Written informed consent was obtained from all study participants (patients >18 years of age) or their legal guardians (for pediatric patients). Institutional Ethics Committee approval was obtained prior to study commencement. All procedures adhered to the Declaration of Helsinki principles for research involving human subjects.

3. RESULTS

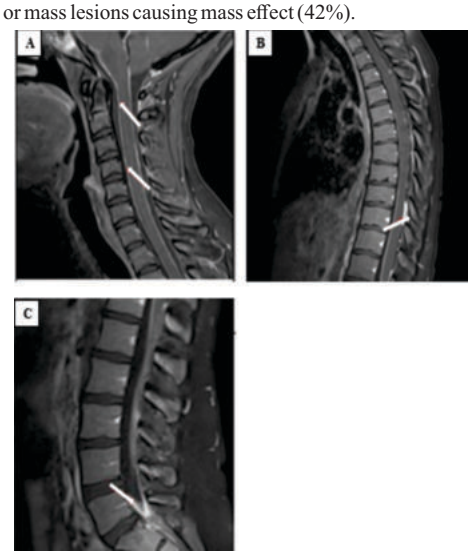
3.1 Demographic Characteristics
The study population demonstrated a wide age range from 6 to 60 years. The 31-40 years age group represented the largest cohort with 10 cases (25%), followed by the 11-20 years group with 8 cases (20%). The remaining age groups (21-30, 41-50, and 51-60 years) each comprised 6 cases (15%), while the youngest age group (6-10 years) included 4 cases (10%). The mean age was 31.75 ± 15.18 years.

The gender distribution showed male predominance with 24 males (60%) and 16 females (40%), yielding a male-to-female ratio of 1.5:1.

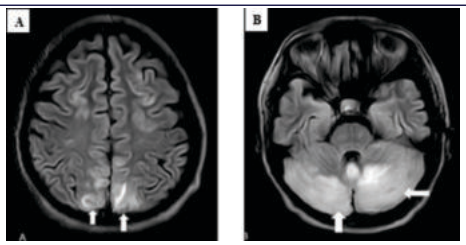
3.2 Clinical Presentation
The most frequent presenting neurological symptoms included headache (72.5%), altered consciousness (57.5%), seizures (45%), sensory disturbances (37.5%), weakness (35%), and ataxia (22.5%). Multiple neurological manifestations were present concurrently in 68% of patients, reflecting the heterogeneous nature of CNS involvement in leukaemia.

3.3 MRI Findings
MRI demonstrated diverse patterns of CNS involvement. The imaging findings identified three major categories of abnormalities:
Direct Leukemic Infiltration (55% of Cases): This category included leptomeningeal enhancement observed in 18 cases (45%), parenchymal T2/FLAIR hyperintense lesions in 12 cases (30%), and mass lesions demonstrating heterogeneous enhancement in 6 cases (15%).
Treatment-Related Complications (62.5% of Cases): White matter changes characterized by T2/FLAIR hyperintensity were observed in 22 cases (55%). These changes ranged from mild periventricular involvement to extensive confluent white matter disease. Lacunar infarcts related to small-vessel disease were identified in 8 cases (20%). Cerebral atrophy of varying degrees was noted in 14 cases (35%).
Secondary Pathologies (32.5% of Cases): Intracranial infections including toxoplasmosis (4 cases, 10%) and progressive multifocal leukoencephalopathy (2 cases, 5%) were documented. Hemorrhagic complications manifested as microhemorrhages on susceptibility-weighted imaging in 6 cases (15%) and macro-hemorrhages in 2 cases (5%).

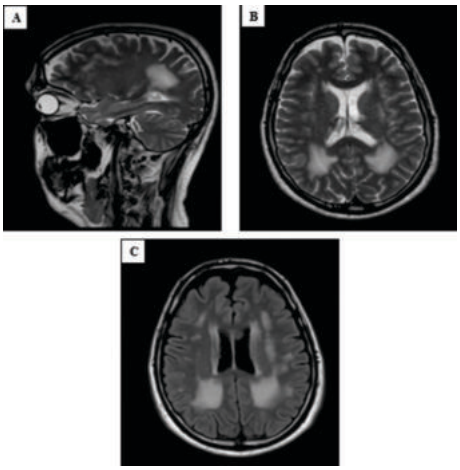
3.4 Correlation with Clinical Features
Strong correlation was observed between clinical presentation and imaging findings. Patients presenting with seizures showed higher prevalence of cortical abnormalities (71%), while those with headache demonstrated leptomeningeal involvement (61%). Altered consciousness was associated with extensive white matter disease (79%) or mass lesions causing mass effect (42%).



Case 1. (A), (B) and (C) PC T1 Sagittal scans show leptomeningeal enhancement of the cervical spine, thoracic spine and lumber spine in a 22 year old female with known case of ALL. (as shown by white arrows)



Case 2. A 32 year old male with known case of AML came with weakness and ataxia, Axial T2/FLAIR sequence showing hyperintensity in cortical white matter in bilateral occipital and parietal regions. (A) and bilateral cerebellar hemispheres (B) (as shown by white arrows).



Case 3. A 7 year old man with headache and known case of ALL, T2-weighted sagittal sequence of brain (A), axial (B) and axial FLAIR(C) showing confluent of white matter hyperintensities, predominantly in the periventricular region along with involvement of the cortical U fibers.

4. DISCUSSION

CNS involvement in leukaemia represents a complex spectrum of disease manifestations requiring integrated clinical and radiological evaluation. Our study of 40 leukaemia patients with suspected neurological involvement documented a diverse array of MRI abnormalities, highlighting the critical role of imaging in patient management.

The high prevalence of direct leukemic infiltration (55%) in our cohort aligns with contemporary literature suggesting CNS involvement rates ranging from 5-10% in overt presentation but extending to 20-30% on autopsy examination [1]. Leptomeningeal infiltration, documented in 45% of our patients, represents the most common form of CNS leukaemia, consistent with previously published series [4]. The imaging appearance of linear or nodular enhancement along the brain surface and spinal cord, best appreciated on post-contrast T1-weighted sequences, facilitates diagnosis and guides therapeutic decisions.

Parenchymal lesions demonstrated heterogeneous signal characteristics reflecting varying cellular density and necrotic foci. The identification of such lesions on T2/FLAIR imaging with restricted diffusion (hyperintensity on DWI with corresponding ADC reduction) suggests high cellularity consistent with leukemic infiltration. This imaging signature has proven diagnostically valuable in differentiating leukemic lesions from other white matter pathology [5].

Treatment-related complications constituted a significant proportion (62.5%) of imaging abnormalities, underscoring the toxicological burden of contemporary leukaemia therapy regimens. White matter disease, the most frequently identified treatment-related abnormality (55% of cases), likely reflects multifactorial etiology including direct chemical toxicity of chemotherapeutic agents (particularly high-dose methotrexate), radiation-induced vasculopathy, and secondary vascular insufficiency [4]. The spectrum ranged from subtle periventricular or subcortical T2 hyperintensity to confluent changes mimicking demyelinating disease.

Cerebral atrophy, documented in 35% of our cohort, represents cumulative neural tissue loss consequent to disease progression, treatment toxicity, and chronic neurological complications. Progressive brain volume loss has significant prognostic implications regarding long-term neurocognitive outcomes, particularly in pediatric leukaemia survivors [5].

Hemorrhagic complications, identified in 20% of patients, reflect coagulopathy, thrombocytopenia, leukostasis, and treatment-induced vascular damage. Susceptibility-weighted imaging proved particularly sensitive in detecting microhemorrhages, which may accumulate silently with serious neurocognitive consequences.

Opportunistic infections (15% of cases) reflect severe immunosuppression associated with leukaemia and its treatments. The identification of imaging patterns consistent with toxoplasmosis or progressive multifocal leukoencephalopathy warranted immediate antimicrobial intervention.

The strong correlation between clinical presentation and imaging findings enhances diagnostic confidence. Patients with seizures demonstrated significantly higher rates of cortical gray matter involvement (71%), potentially reflecting cortical irritation from leptomeningeal disease or direct parenchymal infiltration. The robust association between altered consciousness and extensive white matter involvement (79%) suggests that white matter integrity significantly impacts neurological function.

Clinical Implications

These findings underscore the necessity of comprehensive CNS screening in leukaemia patients presenting with neurological manifestations. Early MRI detection enables timely therapeutic modifications including adjustment of intrathecal chemotherapy dosing, intensification of CNS-directed therapy, or initiation of supportive measures to mitigate complications. Serial imaging monitoring facilitates assessment of therapeutic response and detection of emerging complications.

Limitations

Our study possessed several limitations. The relatively small sample size (40 patients) and single-center design may limit generalizability. Lack of histopathological correlation in most cases prevented definitive tissue diagnosis. Absence of longitudinal imaging follow-up precluded assessment of temporal evolution and treatment response patterns. Future prospective multicenter studies with larger cohorts, serial imaging protocols, and histopathological correlation would provide enhanced diagnostic accuracy and prognostic insights.

5. CONCLUSION

This study characterized the diverse spectrum of MRI abnormalities encountered in leukaemia patients with neurological manifestation. Direct leukemic infiltration, treatment-related complications, and secondary pathologies collectively constitute the CNS disease burden in leukaemia. MRI's superior soft tissue characterization and multiplanar imaging capability render it indispensable for:

1. Detection and localization of direct CNS leukemic involvement
2. Identification and characterization of treatment-related complications
3. Recognition of secondary pathologies including infections and hemorrhage
4. Differentiation of imaging patterns facilitating etiological diagnosis
5. Guiding therapeutic decision-making and treatment modifications

Regular MRI monitoring of leukaemia patients presenting with neurological symptoms facilitates early intervention and improved clinical outcomes. Development of standardized imaging protocols and multicenter registries documenting imaging-clinical correlations would advance understanding of CNS leukaemia and optimize patient management strategies. Given the increasing prevalence of CNS complications in leukaemia survivors and the evolving therapeutic landscape, continued radiological research remains essential for improving long-term patient outcomes.

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