

IMAGING SPECTRUM OF TOXIC AND METABOLIC ENCEPHALOPATHIES: A PATTERN-BASED MRI APPROACH

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Received : 04/09/2026
 Received in revised form : 28/09/2026
 Accepted : 12/10/2026

Keywords:

Toxic encephalopathy; metabolic encephalopathy; magnetic resonance imaging; diffusion-weighted imaging; basal ganglia; hepatic encephalopathy; hypoglycemia.

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DOI: 10.47009/jamp.2026.8.5.154

Source of Support: Nil,
 Conflict of Interest: None declared

Int J Acad Med Pharm
 2026; 8 (5); 976-981



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ABSTRACT

Background: Toxic and metabolic encephalopathies comprise a heterogeneous group of neurological disorders resulting from systemic metabolic abnormalities, organ dysfunction, nutritional deficiencies and exposure to exogenous toxins. The clinical manifestations are frequently nonspecific, while imaging findings may overlap with infectious, inflammatory, vascular and degenerative disorders. Magnetic resonance imaging (MRI), particularly diffusion-weighted imaging, plays an important role in identifying characteristic patterns of brain involvement and narrowing the differential diagnosis. The objective is to evaluate the spectrum of MRI findings in patients with toxic and metabolic encephalopathies and to identify characteristic imaging patterns that may facilitate early diagnosis and clinico-radiological correlation. **Materials and Methods:** A retrospective observational study was conducted in the Department of Radiodiagnosis, Jorhat Medical College and Hospital, Jorhat, Assam, over a period of six months. Thirty patients with clinically suspected and subsequently diagnosed toxic or metabolic encephalopathy who underwent MRI brain during the study period were included. MRI examinations were performed using a 1.5-Tesla MRI system. Axial T1-weighted, T2-weighted, FLAIR and diffusion-weighted images with corresponding ADC maps were obtained in all patients. Additional sequences, including susceptibility-weighted imaging and post-contrast T1-weighted imaging, were performed when clinically indicated. Imaging findings were assessed with respect to signal characteristics, anatomical distribution, symmetry and diffusion restriction and correlated with relevant clinical and biochemical findings. **Result:** Among the 30 patients, the most frequent predominant imaging pattern was T2/FLAIR hyperintensity (12, 40.0%), followed by diffusion restriction (8, 26.7%), T1 hyperintensity (6, 20.0%) and T2/FLAIR hypointensity (4, 13.3%). Characteristic bilateral globus pallidus T1 hyperintensity was observed in chronic hepatic encephalopathy, while unilateral striatal T1 hyperintensity was seen in diabetic striatopathy. T2/FLAIR hyperintensity involving the insular cortex, splenium of the corpus callosum, dentate nuclei and medial thalami was observed in hyperammonemic encephalopathy, cobalamin-related encephalopathy, metronidazole toxicity and Wernicke encephalopathy, respectively. Symmetrical basal ganglia T2/FLAIR hypointensity was observed in hypoparathyroidism-related encephalopathy. Diffusion restriction involving the cerebral cortex and deep grey nuclei was identified in hypoxic-ischaemic and hypoglycemic encephalopathies. **Conclusion:** Toxic and metabolic encephalopathies demonstrate characteristic patterns of MRI signal abnormality and anatomical distribution. A systematic approach based on signal characteristics, lesion distribution, symmetry and diffusion behaviour, combined with clinical and biochemical correlation, can facilitate early diagnosis and help distinguish these potentially reversible disorders from important mimics.

INTRODUCTION

Toxic and metabolic encephalopathies represent a diverse group of disorders resulting from systemic abnormalities that adversely affect the central nervous system. These include hepatic and renal dysfunction, abnormalities of glucose and electrolytes, nutritional deficiencies, endocrine disorders and exposure to drugs or environmental toxins. Although the underlying etiologies differ considerably, several of these disorders demonstrate characteristic patterns of brain involvement on magnetic resonance imaging.^[1-5]

The clinical manifestations are often nonspecific and include altered sensorium, behavioural abnormalities, seizures, movement disorders, headache, gait disturbance and focal neurological deficits. Consequently, imaging plays an important role in establishing an early diagnosis and excluding potentially treatable structural mimics.^[6-10]

MRI is particularly sensitive for demonstrating abnormalities involving the cerebral cortex, basal ganglia, thalami, corpus callosum, cerebellum and brainstem. Conventional T1-, T2- and FLAIR-weighted sequences provide information regarding tissue signal characteristics, while diffusion-weighted imaging (DWI) can demonstrate cytotoxic injury at an early stage.^[11-13]

Several toxic and metabolic disorders show preferential involvement of specific anatomical structures. Bilateral globus pallidus T1 hyperintensity is characteristic of chronic hepatic dysfunction, dentate nucleus involvement is a recognized pattern of metronidazole toxicity, and medial thalamic involvement is commonly encountered in Wernicke encephalopathy. Similarly, cortical and deep grey matter diffusion restriction may occur in hypoxic-ischaemic and hypoglycemic encephalopathy.^[14-16]

de Oliveira et al. described a systematic pattern-based approach to toxic and metabolic brain disorders, emphasizing the predominance of bilateral and symmetrical abnormalities involving deep grey nuclei, cortical grey matter and/or white matter and highlighting the value of recognizing specific imaging signatures.^[17]

MATERIALS AND METHODS

Study Design and Setting: A retrospective observational study was conducted in the Department of Radiodiagnosis, Jorhat Medical College and Hospital, Jorhat, Assam, over a period of six months. A total of 30 patients with clinically

suspected toxic or metabolic encephalopathy who underwent MRI brain during the study period were included.

MRI Protocol: MRI examinations were performed using a 1.5-Tesla MRI system. The routine protocol included axial T1-weighted, axial T2-weighted, axial FLAIR, diffusion-weighted imaging and corresponding apparent diffusion coefficient (ADC) maps. Susceptibility-weighted imaging and post-contrast T1-weighted sequences were obtained in selected patients according to clinical indication.

Image Analysis: MRI examinations were systematically evaluated for predominant signal abnormality, anatomical distribution, symmetry, diffusion restriction, deep grey matter involvement, cortical involvement, white matter involvement, corpus callosum involvement, brainstem and cerebellar involvement, and associated haemorrhage or calcification where applicable. The imaging patterns were categorized into T1 hyperintensity, T2/FLAIR hyperintensity, T2/FLAIR hypointensity and diffusion restriction. Clinical information, including presenting symptoms, relevant systemic illness, biochemical abnormalities and history of drug or toxin exposure, was obtained from medical records. Final diagnoses were established by clinico-radiological and laboratory correlation.

Inclusion Criteria

1. Patients of any age and sex with clinically suspected toxic or metabolic encephalopathy.
2. Patients who underwent MRI brain during the study period.
3. Patients with adequate MRI examinations for interpretation.
4. Patients with a final diagnosis established by clinico-radiological and laboratory correlation.

Exclusion Criteria

1. Patients with primary structural intracranial lesions accounting for the neurological symptoms.
2. Patients with inadequate MRI examinations or significant motion artefacts.
3. Patients with incomplete clinical or laboratory information.
4. Patients in whom a definitive toxic or metabolic etiology could not be established.

RESULTS

A total of 30 patients were included in the study. The age of the patients ranged from 18 to 72 years, with a mean age of approximately 42 years. The study population comprised 18 males (60%) and 12 females (40%).

Table 1: Demographic characteristics of the study population

Variable	Category	Number (n)	Percentage (%)
Age (years)	18-29	5	16.7
	30-39	7	23.3
	40-49	8	26.7
	50-59	5	16.7
	≥60	5	16.7

Total		30	100
Gender	Male	18	60.0
	Female	12	40.0
Total		30	100

Table 2: Distribution of predominant MRI patterns

Predominant MRI pattern	Number (n)	Percentage (%)
T1 hyperintensity	6	20.0
T2/FLAIR hyperintensity	12	40.0
T2/FLAIR hypointensity	4	13.3
Diffusion restriction	8	26.7
Total	30	100

T2/FLAIR hyperintensity was the most frequent predominant imaging pattern, followed by diffusion

restriction, T1 hyperintensity and T2/FLAIR hypointensity.

Table 3: Spectrum of toxic and metabolic encephalopathies

Diagnosis	Number (n)	Percentage (%)
Chronic hepatic encephalopathy	3	10.0
Diabetic striatopathy	2	6.7
Hyperammonemic encephalopathy	3	10.0
Cobalamin-related encephalopathy	2	6.7
Uremic encephalopathy	3	10.0
Carbon monoxide poisoning	2	6.7
Methanol toxicity	1	3.3
Metronidazole toxicity	3	10.0
Wernicke encephalopathy	3	10.0
Hypoparathyroidism-related encephalopathy	3	10.0
Hypoxic-ischaemic encephalopathy	3	10.0
Hypoglycemic encephalopathy	2	6.7
Total	30	100

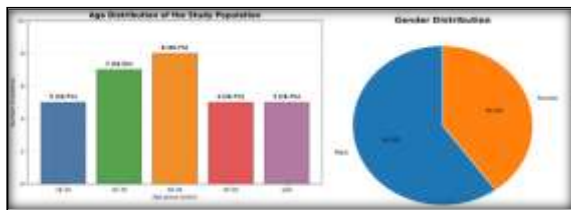


Figure 1: Demographic distribution of study population

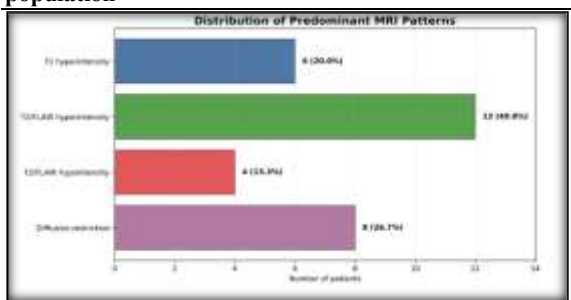


Figure 2: Distribution of predominant MRI patterns

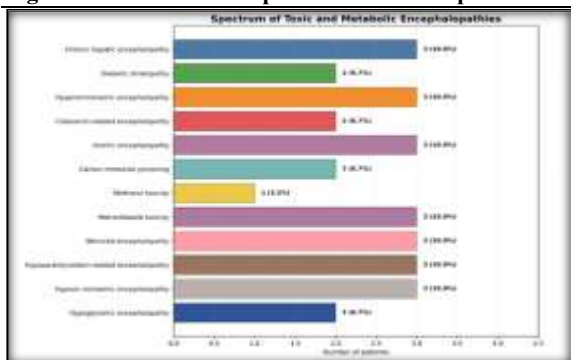


Figure 3: Disease spectrum by percentage distribution

Imaging Findings

T1 Hyperintensity: T1 hyperintensity was identified predominantly in the basal ganglia. In patients with chronic hepatic encephalopathy, symmetrical hyperintensity of the globus pallidus was observed on T1-weighted images. This is a characteristic imaging manifestation of chronic liver dysfunction and is associated with manganese deposition. Diabetic striatopathy demonstrated unilateral striatal T1 hyperintensity involving the caudate nucleus and putamen in patients presenting with abnormal involuntary movements.

T2/FLAIR Hyperintensity: T2/FLAIR hyperintensity was the most frequent predominant imaging pattern. Hyperammonemic encephalopathy demonstrated cortical signal abnormalities, particularly involving the insular region. Cobalamin-related encephalopathy demonstrated T2 hyperintensity involving the corpus callosum, including the splenium. Uremic encephalopathy showed variable involvement of the basal ganglia and cerebral cortex. Carbon monoxide poisoning predominantly involved the globus pallidus, while methanol toxicity was characterized by bilateral putaminal abnormalities.

Wernicke Encephalopathy: Wernicke encephalopathy demonstrated T2/FLAIR hyperintensity involving the bilateral medial thalami. Other characteristic sites include the mammillary bodies, periaqueductal grey matter and tectal plate. In patients with a compatible nutritional or alcohol-related history, this imaging pattern

should prompt immediate clinical consideration of thiamine deficiency.

T2/FLAIR Hypointensity: Symmetrical basal ganglia T2/FLAIR hypointensity was observed in hypoparathyroidism-related encephalopathy. Basal ganglia mineral deposition is a recognized association, and CT can be used when confirmation of calcification is required. Important differential diagnoses include Fahr disease and other disorders associated with basal ganglia mineral or iron deposition.

Diffusion Restriction: DWI demonstrated restricted diffusion in patients with hypoxic-ischaemic and hypoglycemic encephalopathy. Hypoxic-ischaemic injury demonstrated gyriform cortical diffusion restriction, whereas hypoglycemic encephalopathy showed involvement of the deep grey matter and parieto-occipital cortex. The distribution and clinical context are essential because similar patterns can occur with seizures, encephalitis, prion disease and acute vascular injury.

Table 4: Characteristic MRI patterns and differential diagnoses

MRI finding	Important diagnosis	Important differentials
Bilateral globus pallidus T1 hyperintensity	Chronic hepatic encephalopathy	Wilson disease; manganese exposure; TPN-related change
Unilateral striatal T1 hyperintensity	Diabetic striatopathy	Other basal ganglia disorders
Insular/cortical T2/FLAIR hyperintensity	Hyperammonemic encephalopathy	Encephalitis; seizure-related change
Splenic T2 hyperintensity	Cobalamin-related encephalopathy	Toxic/metabolic disorders
Bilateral dentate T2/FLAIR hyperintensity	Metronidazole toxicity	Leigh disease; other toxic disorders
Bilateral medial thalamic hyperintensity	Wernicke encephalopathy	Artery of Percheron infarct; encephalitis
Basal ganglia T2/FLAIR hypointensity	Hypoparathyroidism	Fahr disease; NBIA
Gyriform cortical diffusion restriction	Hypoxic-ischaemic injury	Seizure; CJD; encephalitis
Deep grey matter + cortical diffusion restriction	Hypoglycemic encephalopathy	Hypoxic-ischaemic injury

Representative Cases:

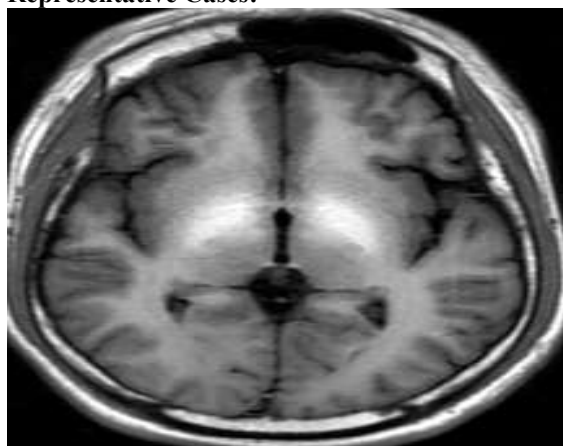


Figure 4: Axial T1-weighted MRI demonstrating bilateral symmetrical hyperintensity of the globus pallidi in chronic hepatic encephalopathy.

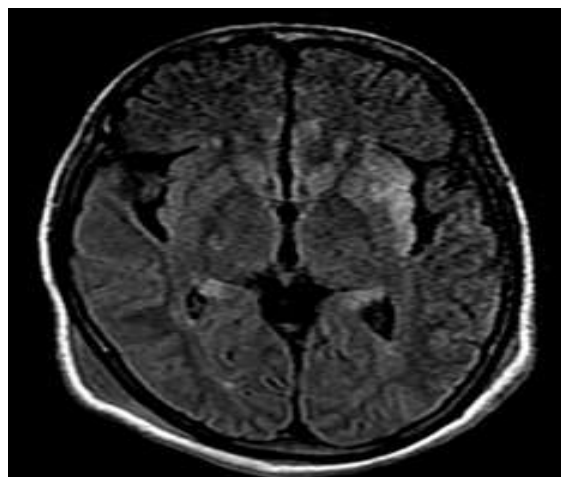


Figure 6: Axial T2/FLAIR MRI demonstrating cortical/insular hyperintensity in hyperammonemic encephalopathy.

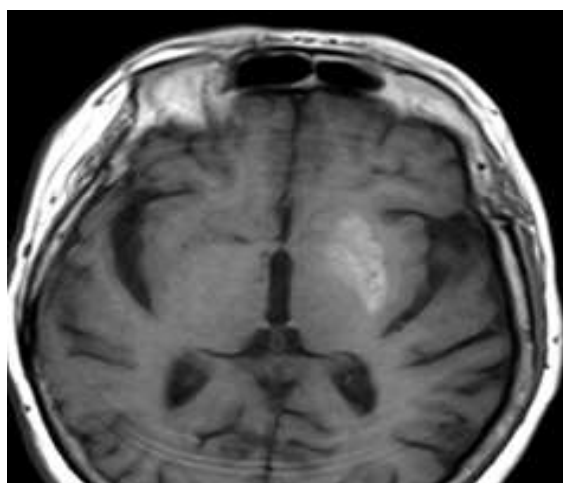


Figure 5: Axial T1-weighted MRI demonstrating unilateral striatal hyperintensity in diabetic striatopathy.

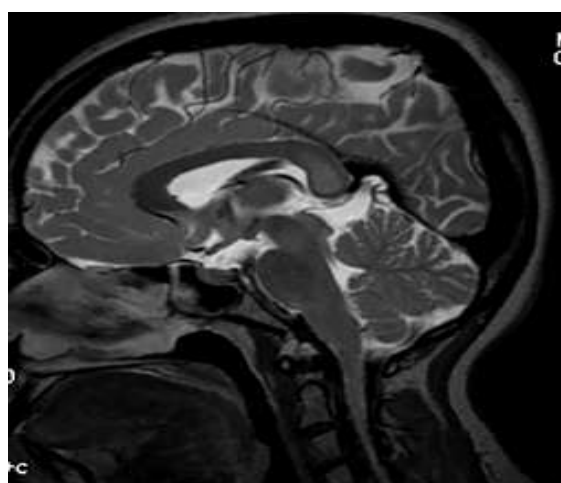


Figure 7: Sagittal T2-weighted MRI demonstrating hyperintensity of the splenium of the corpus callosum in cobalamin-related encephalopathy.

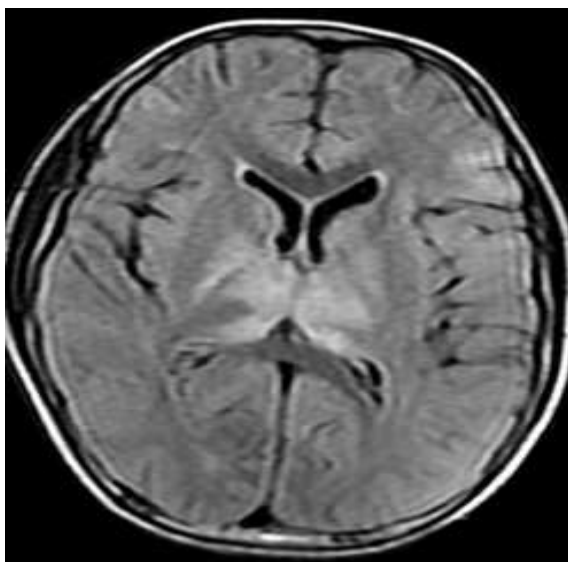


Figure 8: Axial T2/FLAIR MRI demonstrating bilateral medial thalamic hyperintensity in Wernicke encephalopathy.

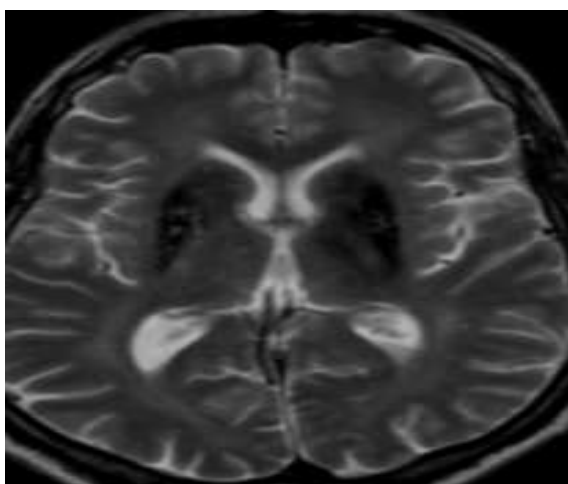


Figure 9: Axial T2/FLAIR MRI demonstrating symmetrical basal ganglia hypointensity in hypoparathyroidism-related encephalopathy.

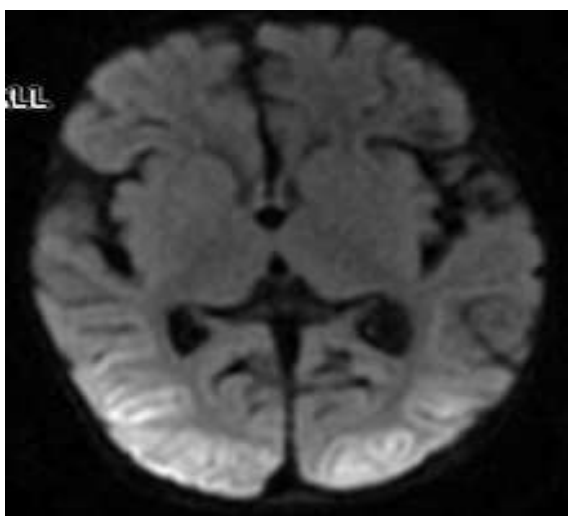


Figure 10: DWI demonstrating gyriform diffusion restriction involving bilateral occipital cortex in hypoxic-ischaemic encephalopathy.

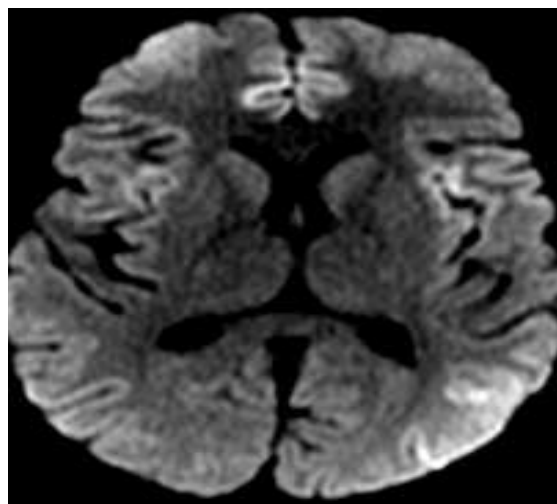


Figure 11: DWI demonstrating diffusion restriction involving deep grey matter and parieto-occipital cortex in hypoglycemic encephalopathy.

DISCUSSION

Toxic and metabolic encephalopathies demonstrate a broad spectrum of MRI appearances, reflecting differences in the underlying pathophysiological mechanisms, duration of insult and selective vulnerability of different brain structures. A pattern-based approach is particularly useful because many disorders demonstrate bilateral and symmetrical involvement of deep grey nuclei, cortical grey matter or white matter.

In the present study, T2/FLAIR hyperintensity constituted the most frequent predominant imaging pattern, followed by diffusion restriction. The anatomical distribution of abnormalities was often more diagnostically useful than signal intensity alone.

The basal ganglia were frequently involved. Bilateral globus pallidus T1 hyperintensity is a well-described feature of chronic hepatic encephalopathy and is associated with manganese deposition. Diabetic striatopathy, in contrast, typically demonstrates unilateral or asymmetric striatal involvement in the setting of severe hyperglycemia and abnormal involuntary movements.

The pattern of T2/FLAIR hyperintensity provides additional diagnostic clues. Dentate nucleus involvement is strongly associated with metronidazole toxicity. A systematic review of metronidazole-induced encephalopathy reported symmetrical dentate nucleus T2/FLAIR hyperintensity in the majority of affected patients, supporting the diagnostic value of this imaging signature.

Wernicke encephalopathy demonstrates a characteristic distribution involving the medial thalami, mammillary bodies, periaqueductal region and tectal plate. MRI is particularly useful when the classical clinical triad is incomplete, and early treatment is important because the neurological manifestations may be reversible.

Diffusion-weighted imaging provides additional information regarding acute cellular injury. Hypoglycemic encephalopathy can demonstrate diffusion restriction in the cerebral cortex, hippocampi, internal capsule and basal ganglia, while hypoxic-ischaemic injury may produce extensive cortical and deep grey matter restriction. Because diffuse cortical diffusion restriction is not specific, imaging must be interpreted together with the clinical history and biochemical data.

The practical value of MRI therefore lies not merely in identifying abnormal signal but in recognizing a combination of signal intensity, anatomical distribution, symmetry and clinical context. A bilateral basal ganglia abnormality, for example, should trigger a different diagnostic pathway from isolated cortical restriction or selective dentate nucleus involvement.

Several disorders are potentially reversible if recognized early. The radiologist can therefore contribute directly to patient management by suggesting the likely systemic or toxic etiology and recommending appropriate clinical or biochemical correlation.

Limitations: The study was a retrospective, single-centre study with a relatively small sample size of 30 patients and a limited study duration of six months. The heterogeneity of the underlying toxic and metabolic disorders limits direct comparison between individual disease entities. The study was primarily descriptive and was not designed to determine the sensitivity or specificity of individual MRI patterns. Larger multicentric studies would be useful for establishing the diagnostic performance and prognostic significance of specific imaging signatures.

CONCLUSION

Toxic and metabolic encephalopathies encompass a wide spectrum of potentially reversible neurological disorders. MRI provides important diagnostic clues by demonstrating characteristic patterns of signal abnormality and anatomical distribution. T1 hyperintensity of the globus pallidus, striatal abnormalities, dentate nucleus involvement, medial thalamic signal alteration, basal ganglia T2/FLAIR hypointensity and characteristic patterns of diffusion restriction should prompt consideration of specific toxic or metabolic etiologies.

A structured approach based on signal characteristics, anatomical distribution, symmetry and diffusion behaviour, followed by appropriate clinical and biochemical correlation, can facilitate

early diagnosis and differentiation from infectious, vascular and inflammatory mimics. Early recognition is particularly important because correction of the underlying systemic abnormality may result in substantial clinical and radiological improvement.

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