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Original Research Article

Imaging Spectrum of Toxic and Metabolic Encephalopathies

Nath A[1], Pegu BJ[2], Kutum T[3], Islam MI[4]

[1]Post Graduate Trainee, Department of Radiology, Silchar Medical College and Hospital, Assam
[2,3]Assistant Professor, Department of Radiology, Silchar Medical College and Hospital, Assam
[4]Registrar, Department of Radiology, Silchar Medical College and Hospital, Assam

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Corresponding author: Dr. Ankita Nath
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Abstract:
The basal ganglia and thalami are paired deep grey matter structures with extensive metabolic activity that renders them susceptible to injury by various diseases. Most pathological processes lead to bilateral lesions, which may be symmetric or asymmetric, frequently showing characteristic patterns on imaging studies. Toxic and metabolic brain disorders manifest secondary to derangements of a well-balanced environment encompassing metabolic substrates, neurotransmitters, electrolytes, physiologic pH levels, and blood flow, either by endogenous malfunctions or exogenous toxic effects. Patients with these disorders often present to the emergency department and are diagnosed with global cerebral dysfunction presenting as acute confusional state and delirium. Imaging plays a key role in these cases, as imaging findings can be used to diagnose the condition or narrow the differential diagnosis.

Keywords: Basal ganglia, Thalamus, Bilateral lesions, Symmetric lesions, MRI, CT.

Introduction

Often referred to as the "central grey matter," the paired grey matter structures known as the basal ganglia and thalami are situated deep within the brain hemispheres. Because they have a role in the control of limbic, motor, sensory, autonomic, and endocrine processes, they have a higher metabolic requirement during resting states than the cerebral cortex. Movement problems are commonly associated with abnormalities of the basal ganglia, but these neurons also have a role in memory, emotion, and other cognitive processes outside of the extrapyramidal system.

Subcortical sensory and motor input is received by the thalamus, a complex hub that projects to the striatum and cortex. Chronic pain, sensory loss, forgetfulness, dystonia, and other illnesses can be brought on by thalamic injuries. [1] The manifestation of toxic and metabolic brain illnesses results from imbalances of an environment that is normally maintained by blood flow, neurotransmitters, electrolytes, pH levels in physiology, and metabolic substrates. These imbalances can be caused by endogenous malfunctions or exogenous toxic effects. Individuals suffering from these conditions frequently arrive at the emergency room where they are diagnosed with global cerebral dysfunction, which manifests as acute confusion and delirium.

In these situations, imaging is crucial because the results can be utilized to narrow down the differential diagnosis or pinpoint the ailment. [2]

This case series illustrates nine cases of toxic and metabolic Encephalopathies. The findings at MRI are presented.

Case Series-

Case 1: CO poisoning

A 70 years old female who cooks on coal chulha and uses it to keep her room warm at night. One day she was found unconscious in her room. MRI shows symmetrical areas of hypointensity in the bilateral globus pallidi on T1WI and hyperintensity on T2WI. ADC map shows decreased ADC values in the involved region (a, b, c).

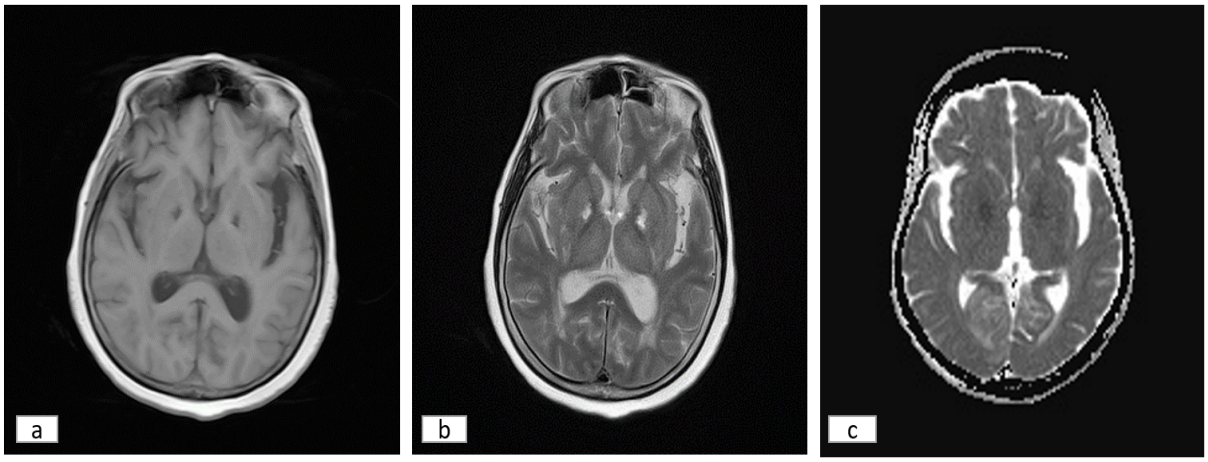

Figure 1: MRI shows a) bilateral symmetrical T1 hypointensity b) T2 hyperintensity c) ADC map shows decreased ADC values.

Case 2: Wilson's Disease

A 13 years old male came with complaints of chorea along with increased urinary copper. On MR evaluation, there were symmetrical and bilateral hyperintensities in the T2 and FLAIR images in bilateral caudate nuclei, putamina and ventrolateral thalami. ADC map shows increased ADC values in the involved region (d, e, f, g).

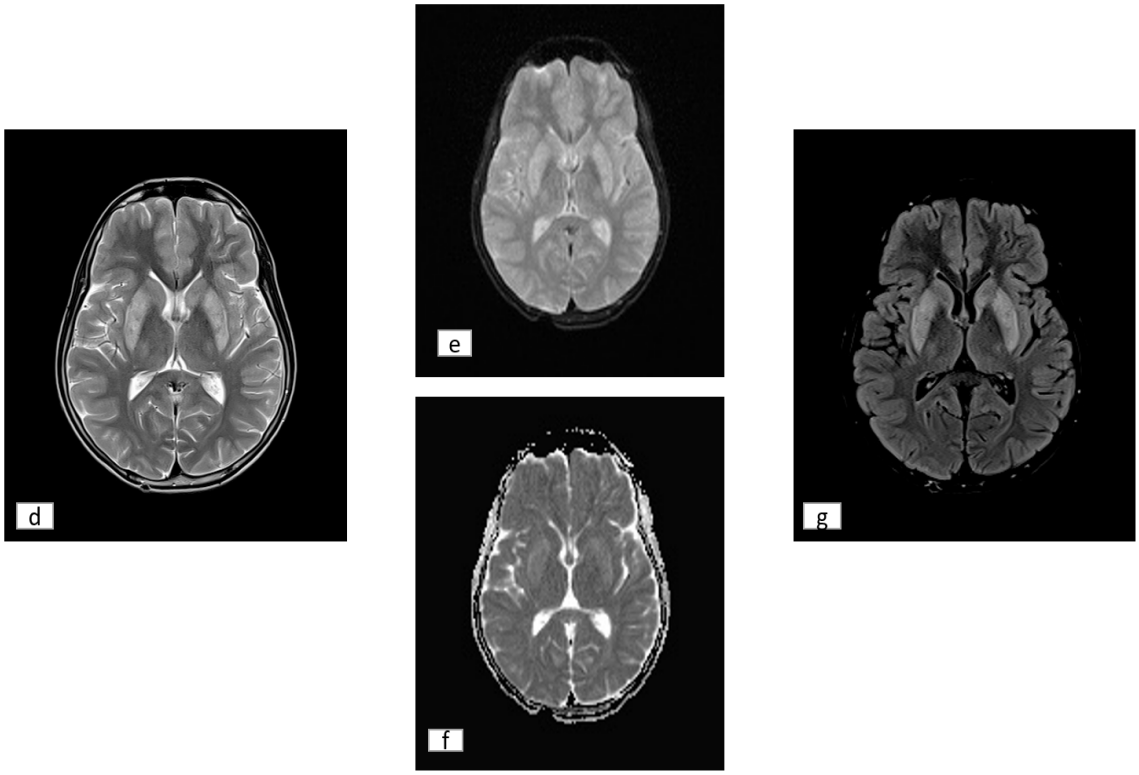

Figure 2: MRI shows d) &e) symmetrical and bilateral hyperintensities in the T2 and g) FLAIR images in bilateral caudate nuclei, putamina and ventrolateral thalami. f) ADC map shows increased ADC values

Case 3: Chronic hepatic encephalopathy

A 42 years female with a long history of cirrhosis accompanied by portal hypertension. On MR evaluation, there were symmetrical and bilateral hyperintensities involving globus pallidi and substantia nigrae on T1W images.

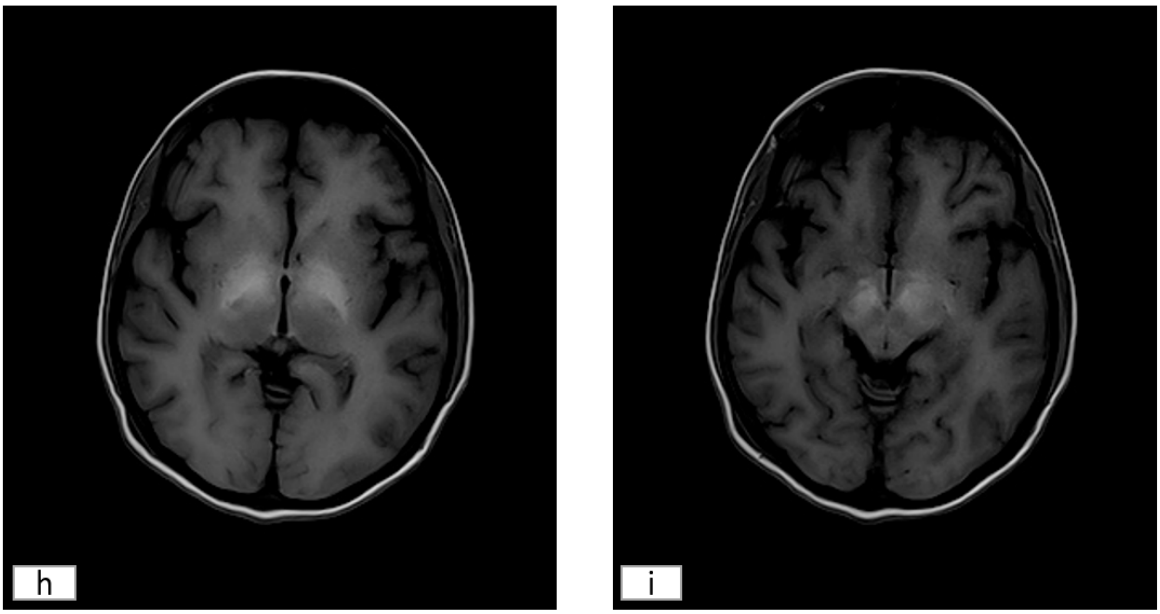

Figure 3: MRI shows h) & i) symmetrical and bilateral hyperintensities on T1W images in bilateral globus pallidi and substantia nigrae.

CASE 4- Wernicke's encephalopathy

A 55 years male with frequent alcohol intake came with confusion and ataxia. The findings include- symmetrical FLAIR hyperintensities involving bilateral dorsomedial thalamus, around the third ventricle and periaqueductal area. ADC map shows decreased ADC values in the involved region (j, k, l, m).

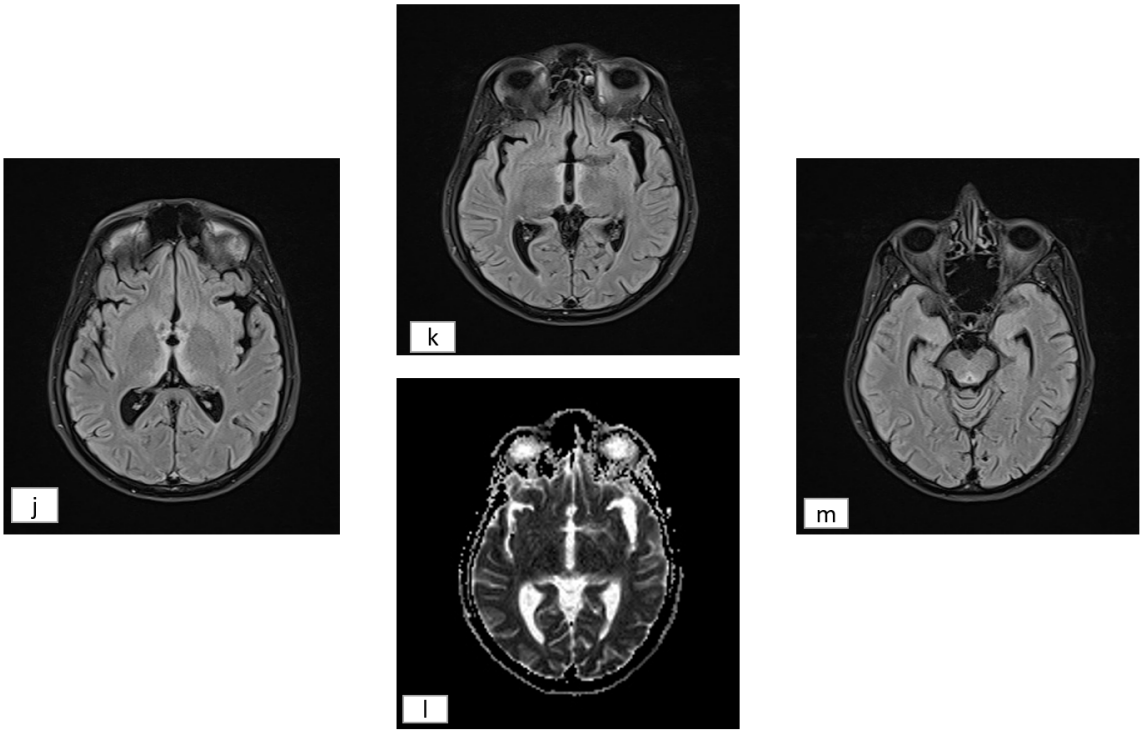

Figure 4: MRI shows j) k) & m) symmetrical and bilateral FLAIR hyperintensities involving dorsomedial thalamus, around the third ventricle and periaqueductal area. f) ADC map shows increased ADC values

Case 5: Metronidazole-induced encephalopathy

A 10 years male who had a long-term history of hospital admission and parenteral metronidazole therapy, recently developed altered sensorium and seizures. On MR evaluation, symmetrical T2 and FLAIR hyperintensities noted

involving bilateral dentate nucleus and dorsal pons. ADC map shows increased ADC values in the involved region (n, o, p).

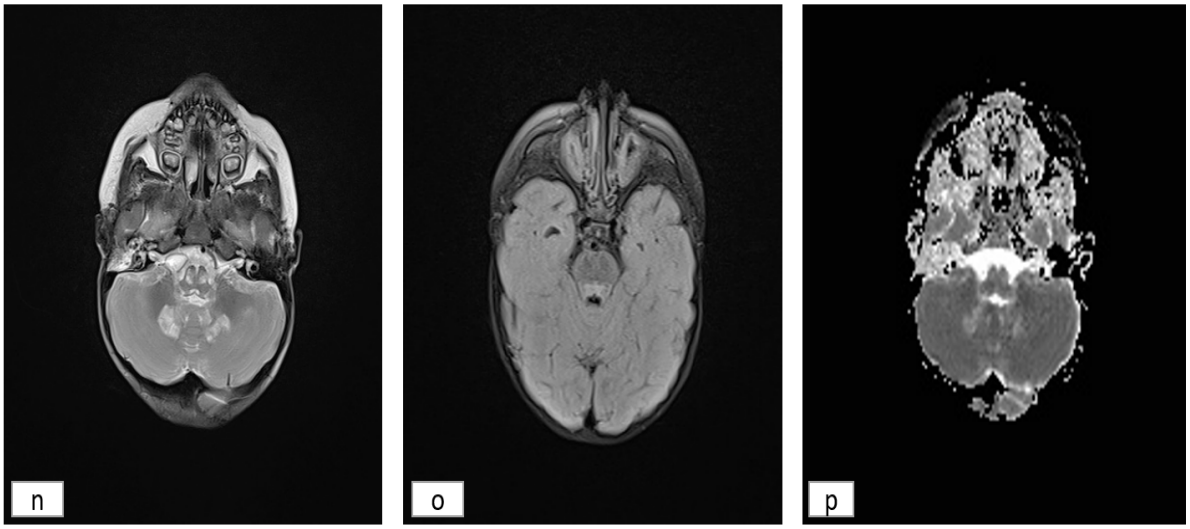

Figure 5: MRI shows n) symmetrical T2 hyperintensity involving bilateral dentate nucleus and o) FLAIR hyperintensities noted involving bilateral dorsal pons. p) ADC map shows increased ADC values

Case 6: Diabetic Striatopathy

A 67 years old male with Type II diabetes mellitus presented to emergency department with altered sensorium and involuntary non-patterned movements (hemichorea and hemiballismus). At presentation the mean glycemic level was 431 mg/dl. On MR evaluation, unilateral hyperintensity noted involving the striatum on T1WI. ADC map shows increased ADC values in the involved region (q, r, s).

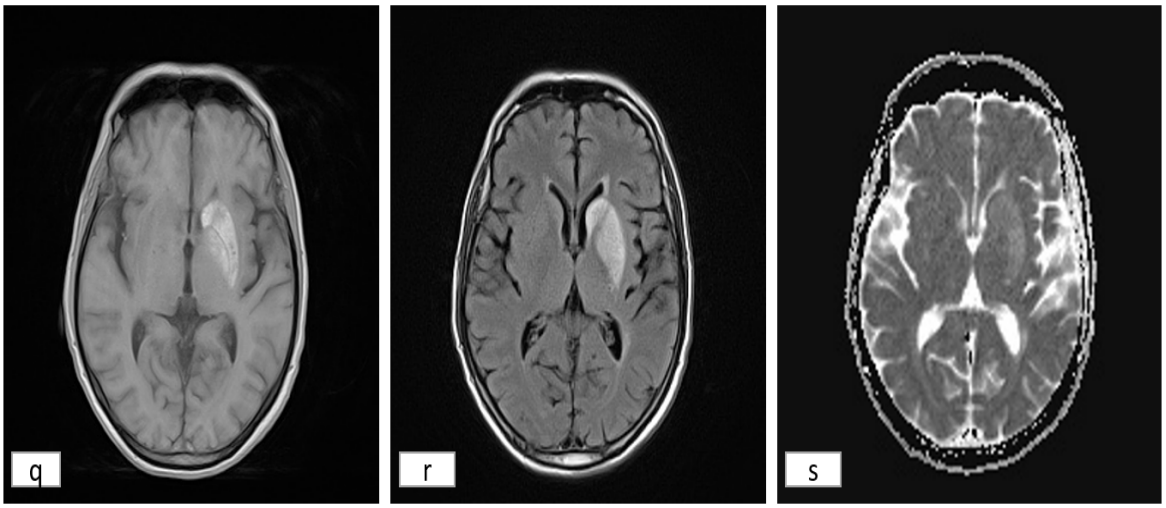

Figure 6: MRI shows q) unilateral T1 hyperintensity involving left striatum and r) unilateral FLAIR hyperintensity involving left striatum. s) ADC map shows increased ADC values.

Case 7: Adult Hypoglycemic Encephalopathy

A 58 years old male with cirrhosis who presented in a comatose state with a glucose level of 20 mg/dl. T2/FLAIR hyperintensity noted involving bilateral insular cortex, bilateral hippocampus, anterior temporal lobe and bilateral basal ganglia, showing strong diffusion restriction (t, u, v, x, y). Affected grey matter are swollen and appears hypointense on T1 (w).

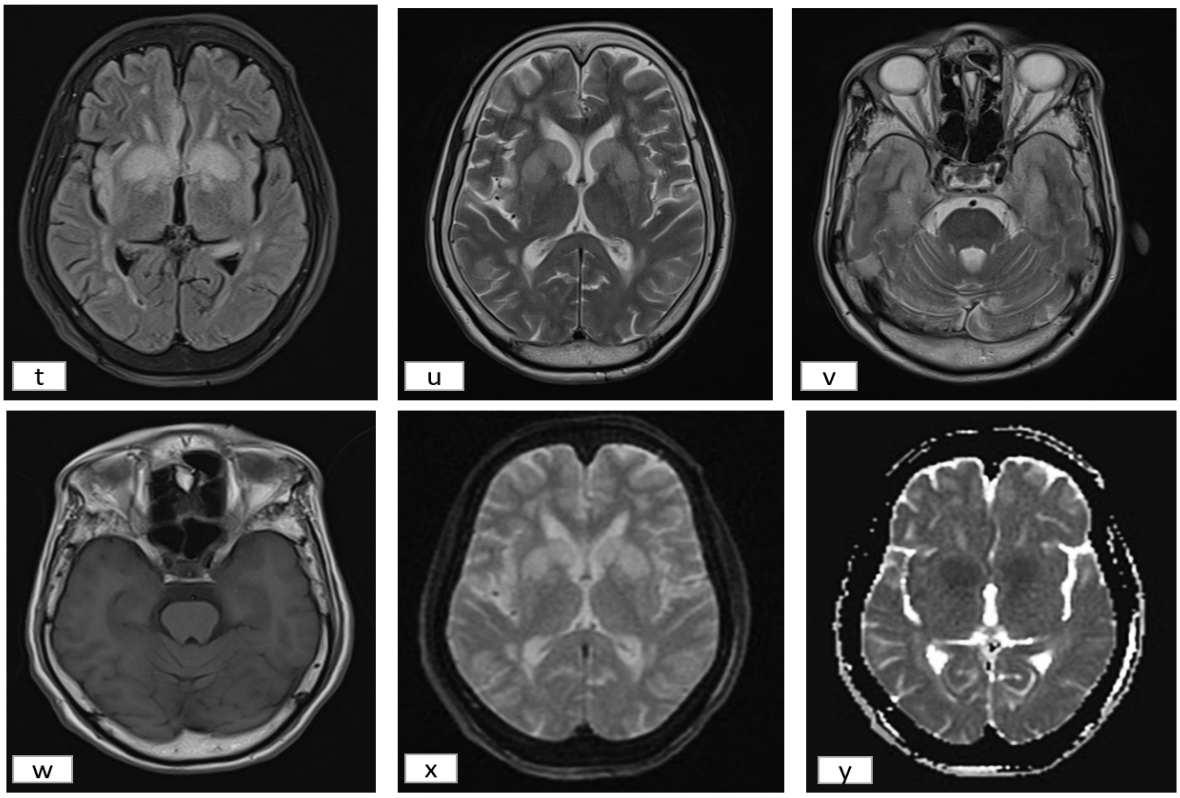

Figure 7: MRI shows t), u) &v) T2/FLAIR hyperintensity noted involving bilateral insular cortex, bilateral hippocampus, anterior temporal lobe and bilateral basal ganglia. w) Affected grey matter are swollen and appears hypointense on T1 x) & y) shows strong diffusion restriction.

Case 8: Marchiafava-Bignami Disease (MBD)

A 55 years old male, chronic ethanolic presented with altered sensorium and seizures. On MR evaluation, thinning of genu of corpus callosum noted with linear T1 hyperintensity (Sandwich sign), showing no restriction on DWI/ADC sequences (i, ii, iii, iv).

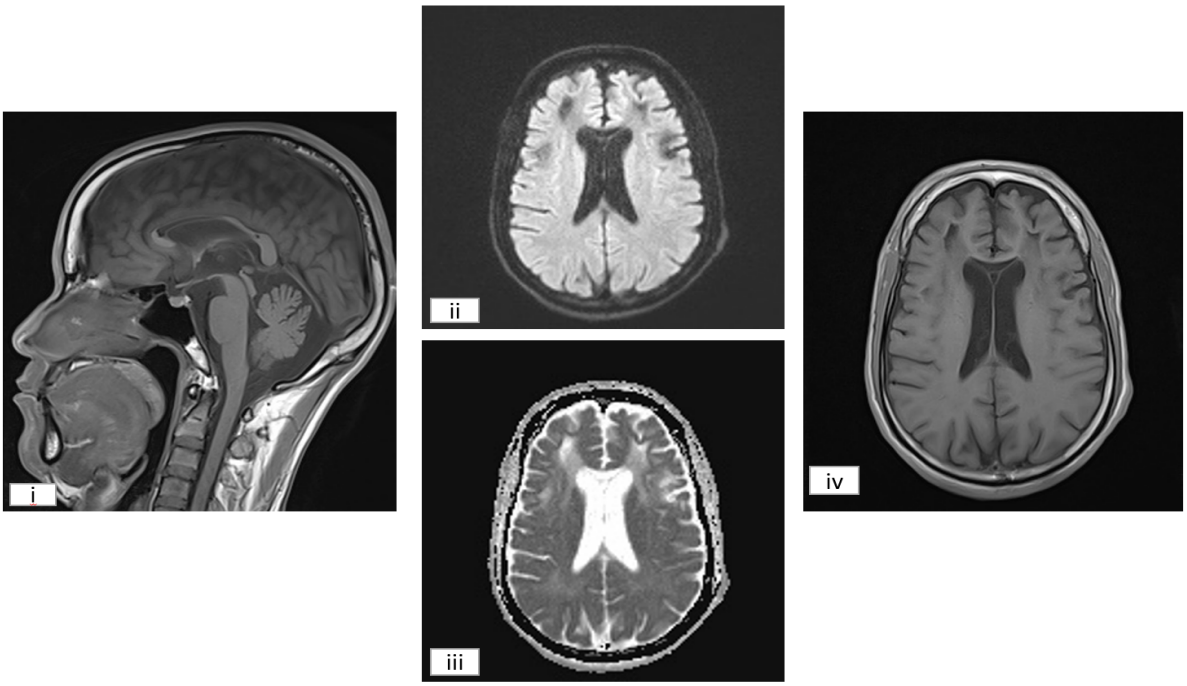

Figure 8: MRI shows i) & iv) thinning of genu of corpus callosum noted with linear T1 hyperintensity (Sandwich sign) ii) & iii) shows no restriction on DWI/ADC sequences.

Case 9: Uremic Encephalopathy

A 51 years female with end-stage kidney disease presented to the emergency room with seizure like activity. On MR evaluation, bilateral symmetric T2/FLAIR hyperintensities noted involving white matter surrounding bilateral lentiform nucleus and thalamus (Lentiform Fork sign), showing no restriction on DWI/ADC sequences (v, vi, vii, viii).

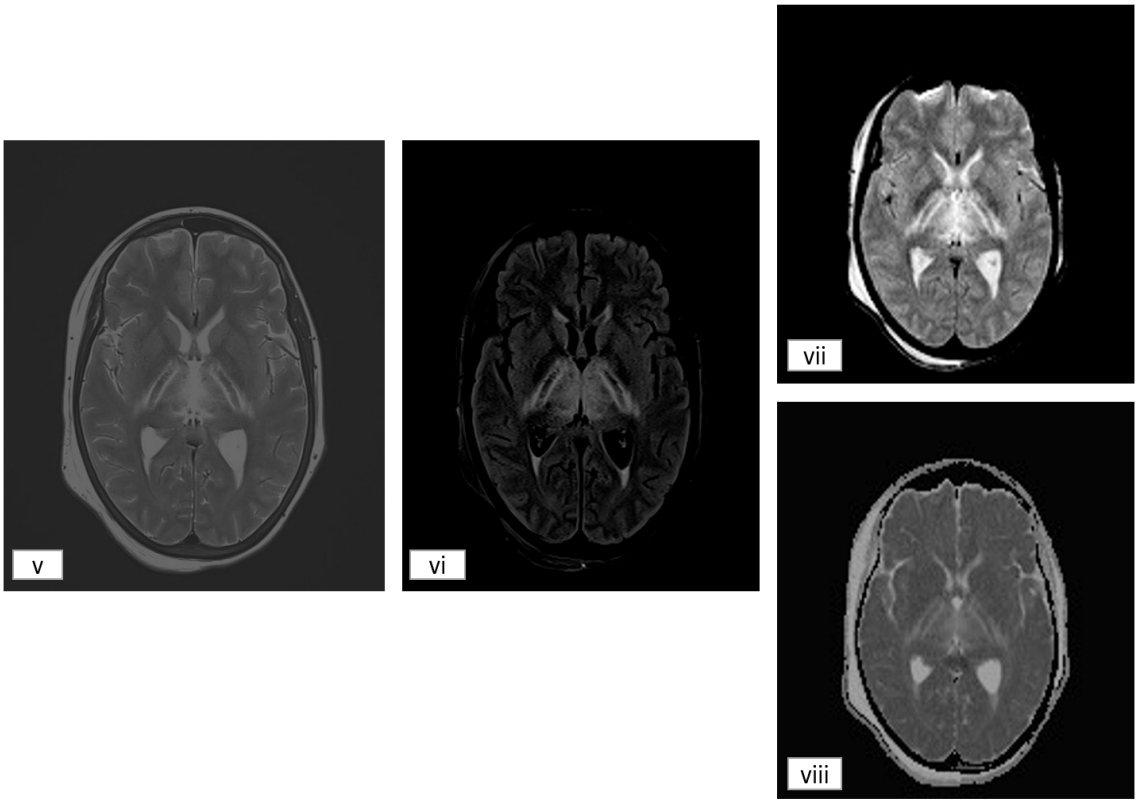

Figure 9: MRI shows v & vi) bilateral symmetric T2/FLAIR hyperintensities noted involving white matter surrounding bilateral lentiform nucleus and thalamus (Lentiform Fork sign) vii) & viii) showing no restriction on DWI/ADC sequences.

Discussion

Excitotoxic brain injury is intimately associated with toxic and metabolic illnesses because they frequently cause high glutamate release.

While the brain has many receptors linked to excitotoxic damage, certain classic CNS sites—such as the corpus callosum, periventricular white matter, cortical gray matter, and basal ganglia and thalami—are more vulnerable to this process than others. This differential susceptibility is significant because it suggests certain distinctive imaging patterns that may prompt the diagnosing process to take metabolic and toxicological factors into account. [3-5]

It is important to recognize that the images of toxic and metabolic disorders affecting the central nervous system typically follow certain patterns of involvement that are closely related to the pathophysiologic mechanism of damage. Each pattern can suggest a likely diagnosis and even provide a prognosis. For a given set of diseases, each pattern denotes the areas that are most frequently affected; nevertheless, a disease may exhibit multiple patterns and impact different structures.

The following are the key patterns:

1. Basal ganglia and/or thalami involvement. The periventricular white matter and the cortical gray matter may be also involved. This pattern is usually related to cytotoxic brain edema, poor outcomes, and irreversibility.
2. Dentate nuclei involvement.
3. Prominent cortical gray matter involvement. Although cortical lesions can coexist with basal ganglia- and white matter–associated involvement, they are the most distinguishing feature.
4. Symmetric periventricular white matter involvement with gray matter sparing. This is a pattern that includes ATL causes and is more related to intra-myelinic edema and higher possibilities of reversibility and better outcomes.

5. Corticospinal tract region involvement.
6. Corpus callosum involvement.
7. Asymmetric white matter involvement in a demyelinating disease pattern.
8. Parieto-occipital subcortical vasogenic edema.
9. Central pons involvement.

Carbon monoxide poisoning can result from unintentional inhalation when fuels burn incompletely. Since carbon monoxide has a 200-fold higher affinity than oxygen for combining with hemoglobin, the harmful mechanism is secondary to impeded oxygen transfer. [6,7,8] Carbon monoxide poisoning is characterized by bilateral symmetric necrotic involvement in the globus pallidus, which is sensitive to hypoxia. In acute poisoning, T2 prolongation in the basal ganglia is common, frequently accompanied by restricted diffusion on diffusion-weighted MR images. T1 shortening in the globus pallidus and delayed leukoencephalopathy are possible outcomes of carbon monoxide poisoning.

Wilson disease, also known as hepatolenticular degeneration, is an autosomal recessive disorder brought on by mutations in the ATP7B gene, which lead to defects in the transport of copper, which accumulate in the liver and deposit in other areas of the body, including the brain. Low levels of ceruloplasmin and the Kayser Fleischer ring surrounding the iris are usually indicative of the diagnosis, which is further corroborated by genetic testing and elevated urine copper. Extrapyramidal and behavioral symptoms usually appear in the second or third decade of life, although they can also appear in early childhood and in elderly individuals. [9–11] T2 prolongation in the putamen, globus pallidus, caudate nuclei, and thalamus are common MR imaging findings. Usually, only the ventrolateral side of the thalamus is affected. (12) The cortical and subcortical regions, mesencephalon, pons, vermis, and dentate nuclei may also be involved. Diffusion restriction is often seen in the early stages of the disease. [13, 14]

Chronic hepatic encephalopathy occurs in the setting of persistently severe liver failure that may be curable. The majority of patients have had portosystemic shunting or portal hypertension along with their cirrhosis for a long time. [6, 15, 16] Manganese is the material most closely associated with changes. Neurotoxic chemicals build up within brain tissue. Bilateral and symmetric T1 hyperintensity involving the globi pallidi and substantiae nigrae is a distinctive imaging feature that is observed in 80% to 90% of individuals with chronic liver failure. This hyperintensity is most likely caused by manganese buildup. Wernicke encephalopathy usually arises from a deficiency of vitamin B1 (thiamine), which is secondary to malnourishment brought on by long-term parenteral therapy without vitamin supplementation, gastrointestinal or hematologic neoplasms, chronic dialysis, bowel obstruction, or hyperemesis gravidarum. The symptoms can be confounding and may not necessarily manifest at the time of clinical onset with altered consciousness, visual dysfunction, and ataxia—the typical clinical trial. [17] Symmetric T2 prolongation in the tectal plate, mamillary bodies, periaqueductal region, and medial thalamus are typical MR imaging findings.

It was recently found that metronidazole, an antibiotic used to treat a wide range of bacterial and protozoal infections, hardly ever causes CNS harmful effects. All patients are susceptible to these toxic consequences, which often manifest after prolonged treatment—typically more than 25 days of usage (average duration, 54 days). However, it's crucial to note that shorter treatments—as short as 7 days—have also been linked to similar toxic effects. [18,19] Cerebellar dysfunction symptoms include confusion (33%), seizures (13%) and dysmetria, ataxia, and dysarthria (75% of cases) in patients [18]. MR scans of metronidazole-induced brain toxicity reveal bilateral symmetric lesions in the cerebellum, especially implicating the dentate nuclei, in nearly all cases (up to 93%) of the poisoning. A majority of cases (86%) show a characteristic pattern of bilateral symmetric involvement of the dentate nuclei, vestibular nuclei, tegmenta, and superior olivary nuclei.

Diabetic striatopathy is also known as hyperglycemia-induced hemichoreahemiballismus, exhibit distinctive non-patterned, involuntary movements. This nonketotic delayed hyperglycemia consequence may occasionally result in a type 2 diabetes diagnosis. The average age and glycemia level at presentation are 71 years old and 431 mg/dL, respectively. [6, 20, 21] The diagnosis is almost entirely based on imaging results, which typically include unilateral T1 hyperintensity including the striatum and hyperattenuation in the same location on CT scans. In 73% percent of cases, diabetic striatopathy is fully curable.

Adult hypoglycemic encephalopathy or hypoglycemic brain injury is caused by an imbalance between supply and consumption of glucose by cerebral cells, leading to brain injury. (22) In individuals with diabetes (usually those on insulin replacement therapy), the clinical manifestation is marked by seizures, a decreased state of consciousness, and even coma. [6,22] The most typical imaging findings include symmetric hyperintensities on T2-weighted and FLAIR images and strong restricted diffusion affecting the gyri in the parieto-occipital and temporal regions on diffusion-weighted images. Early symptoms are better seen as sulcal effacement on T1-weighted images due to gyral enlargement, and hypoattenuation can be seen on CT images. Marchiafava-Bignami Disease or MBD, is an

uncommon condition marked by osmotic demyelination and eventual corpus callosum destruction. Chronic ethanol use and vitamin B complex deficiency are the main causes of this disease. [6, 23, 24] There are two clinical types of MBD. The first is type A (acute), which typically results in death within a few days and manifests in patients as seizures, coma, or involvement of the entire corpus callosum. The second kind, known as type B (chronic), is characterized by isolated lesions in the corpus callosum (usually in the genu) and mild encephalopathy in individuals. [23,24]

The involvement of the corpus callosum is the basis for the imaging diagnosis of MBD. One particularly revealing result of MBD is the selective involvement of the middle layers of the corpus callosum in the setting of chronic ethanol use. Sagittal FLAIR images are the most useful for visualizing the early alterations linked to acute MBD. The term "sandwich sign" refers to central callosal involvement that spares the periphery. On T1-weighted images, chronic MBD manifests as corpus callosum thinning with central linear hypointensities.

A metabolic disease known as uremic encephalopathy can develop in people with acute or chronic renal failure. It is a consequence of endogenous uremic toxins present in patients with severe renal failure. (25, 27) The most typical finding is symmetric bilateral basal ganglia involvement with varying cortical-associated involvement and white matter involvement. [25,26] Patients with uremic encephalopathy may have a characteristic "lentiform fork" sign, which is suggestive of underlying metabolic acidosis coexisting with uremia—a commonly observed relationship. On T2-weighted and FLAIR images, the hyperintensity of the white matter surrounding the lentiform nuclei (the medullary laminae and internal and exterior capsules) defines the lateral and medial limits of both putamina. [25,28]

Conclusion

Toxic and metabolic brain illnesses are a diverse set of diseases that are still difficult to diagnose. Certain imaging findings can be very specific for a few illnesses, despite the fact that many imaging manifestations are nonspecific. However, imaging examinations can provide some prognostic information, either by pointing to a significant involvement of cerebral structures or by showing a reversible subjacent etiology. When brain scans reveal lesions of the central grey matter, a methodical strategy integrating imaging, clinical, and demographic data is required. By pinpointing the precise location of the anomalies and recognizing the distinctive results on many MR sequences, as well as occasionally on CT, one can reduce the number of possible diagnoses and, in certain situations, even determine the final diagnosis.

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Data Availability: The authors confirm that the data supporting the findings of this research are available within the article.

Disclaimer: The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

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