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CASE REPORT

Magnetic Resonance Imaging Findings of Acute Hyperammonemic Encephalopathy: Six Case Reports

Akut Hiperamonyemik Ensefalopatinin Manyetik Rezonans Görüntüleme Bulguları: Altı Olgu Sunumu

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Abstract

Acute hyperammonemic encephalopathy is a rare but serious condition that complicates chronic or acute liver diseases as well as nonhepatic causes such as drugs or bacterial infections. High ammonia levels can cause cerebral edema, altered state of consciousness, seizure, coma, or death. Acute hyperammonemic encephalopathy diagnosis frequently depends on the clinical findings. However, magnetic resonance imaging (MRI) findings have gained importance in diagnosis. The insula, diffuse cerebral cortex, cingulate cortex, and thalamus are the most common sites of acute hyperammonemic encephalopathy. In this study, we discuss the MRI findings of six cases with acute hyperammonemic encephalopathy caused by different etiologies in light of the literature.

Keywords: Hyperammonemia; Encephalopathy; Magnetic resonance imaging

Acute hyperammonemic encephalopathy is a rare but serious condition that complicates liver diseases as well as nonhepatic causes such as drugs or bacterial infections. High ammonia levels can cause cerebral edema, altered state of consciousness, seizure, coma, or death.[1] Acute hyperammonemic encephalopathy diagnosis frequently depends on the clinical findings. However, magnetic resonance imaging (MRI) findings have gained importance in diagnosis. The most common involving sites of acute hyperammonemic encephalopathy are the insula, diffuse cerebral cortex, cingulate cortices, and bilateral thalami.[1,2] In addition to these regions, subcortical white matter, basal ganglia, and brainstem are other affected areas. However, these fields are not kept frequently. In MRI, monitoring of these findings in the brain may be stimulating for the diagnosis of acute hyperammonemic encephalopathy.[2,3]

Case Reports

Case 1

A 51-year-old female patient with a known history of gastric malignity was admitted due to a seizure and coma. She had

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Table 1. Summary of the clinical features of the cases

No.	Year	Sex	Clinical signs	Etiology	Serum ammonıa level (µg/dL)	Prognosis	Malignity
1	51	Female	Coma, seizure	Kemoterapathic drug	156	Exitus	Gastric
2	49	Female	Coma	Parenteral nutrition (bariatric surgery)	264	Exitus	–
3	53	Male	Confusion, seizure	Kemoterapathic drug	187	Exitus	Lung
4	76	Female	Coma	Septicemia	159	Exitus	–
5	63	Female	Confusion	Kemoterapathic drug	223	Moderate	Breast
6	36	Male	Confusion	Liver failure	176	Good	–

received chemotherapy treatment (paclitaxel) 1 week ago. Her vital parameters were normal, and she had spontaneous breathing. The patient, who was unresponsive to verbal and painful stimuli, had no prominent lateralizing findings in her neurological examination. Complete blood count, routine biochemical tests, and EEG findings were unremarkable. Her serum ammonia level was 156 µg/dL (normal range: 31–123).

Case 2

A 49-year-old female patient with a known history of bariatric surgery was admitted due to lethargy. She had received parenteral nutrition for a long time. Her vital parameters were normal, and she had spontaneous breathing. The patient, who was minimally responsive to verbal and painful stimuli, had no obvious lateralizing findings in her neurological examination. Complete blood count, routine biochemical tests, and EEG findings were normal. Her serum ammonia level was 264 µg/dL (normal range: 31–123).

Case 3

A 53-year-old male patient with a known history of lung cancer was admitted due to a seizure. He had received chemotherapy (cisplatin + etoposide) 13 days ago. His vital parameters were normal. The patient had no obvious lateralizing findings in his neurological examination. Complete blood count, routine biochemical tests, and EEG findings were unremarkable. His serum ammonia level was 187 µg/dL (normal range: 31–123).

Case 4

A 76-year-old female patient was admitted due to lethargy to the emergency department. She was on antibiotic treatment for a urinary tract infection for 3 days. She had a fever and was hypotensive. She had no hypoxia. The patient, who was minimally responsive to verbal and painful stimuli, had no obvious lateralizing findings in her neurological examination. She had leukocytosis and her C-reactive protein level was 187. EEG showed diffuse slow waves. Her serum ammonia level was 159 µg/dL (normal range: 31–123).

Case 5

A 63-year-old female patient with a known history of breast cancer was admitted due to confusion. She had received chemotherapy treatment (docetaxel + trastuzumab + pertuzumab) 2 weeks ago. Vital parameters were normal. She had spontaneous breathing. The patient was disorientated and uncooperative. The other neurological examination tests were normal. Complete blood count, routine biochemical tests, and EEG findings were unremarkable. Her serum ammonia level was 223 µg/dL (normal range: 31–123).

Case 6

A 36-year-old male patient has been admitted due to confusion. Vital parameters were normal. She had spontaneous breathing. The patient was disorientated and uncooperative. The other neurological examination tests were normal. Complete blood count was normal. In biochemical tests, pathological values were AST 672 IU/L, ALT 885 IU/L, and INR 4.6. EEG had diffuse slow waves. His serum ammonia level was 176 µg/dL (normal range: 31–123).

The clinical features of the reported cases are summarized in Table 1.

Radiological Findings

All cases had similar radiological findings. Extensive diffusion restriction was observed in the cortex, including the insular and cingulate cortices and the thalamus, on diffusion-weighted imaging (DWI) (Fig. 1a–c). Apparent diffusion coefficient (Fig. 1d–f) and fluid-attenuated inversion recovery (Fig. 1g–i) sequences manifested with a less pronounced decrease and increase in signal, respectively.

Discussion

Acute hyperammonemic encephalopathy can be life-threatening if untreated. Ammonia is produced in the gastrointestinal tract as a result of protein digestion and bacterial metabolism. When ammonia production exceeds its metabolic capacity in the liver, it is excreted by the kidneys

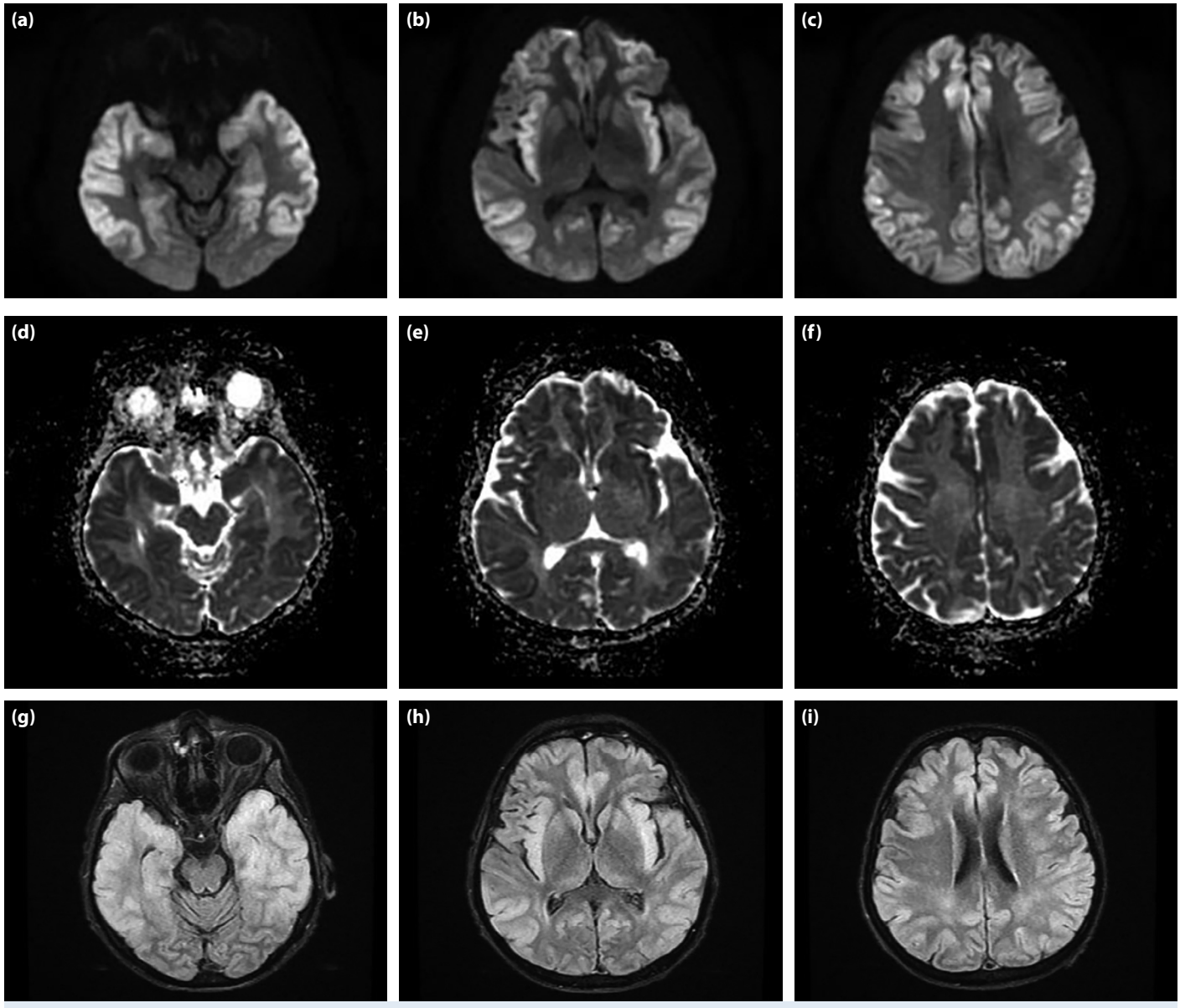

Figure 1. Diffusion-weighted imaging **(a–c)**, with extensive restricted diffusion in cortex, including insular **(b)** and cingulate **(c)** cortices and thalamus. Apparent diffusion coefficient **(d–f)** and fluid-attenuated inversion recovery **(g–i)** sequences with less pronounced decrease and increase in signal, respectively.

and accumulates in the musculoskeletal system and brain. It has been explained by different hypotheses that high ammonia levels are toxic to the brain. Ott and Vilstrup[4] suggested that astrocytic detoxification of ammonia interferes with neurotransmission by leading to the formation of glutamine in concentrations high enough to produce cellular edema. Another hypothesis is described by Desjardin et al.[5] This hypothesis suggests that the increase in the amount of glutamine in astrocytes causes cerebral edema and liver complications with osmotic effects.

Acute liver failure takes the first place among the etiology of hyperammonemic encephalopathy.[6,7] Other etiological causes include drugs (valproic acid, chemotherapy, narcotic, and alcohol), portosystemic shunt surgery, parenteral nutrition, urinary tract infection, bone marrow and solid organ transplantation, and septic shock.[3,8,9] In three of our cases, chemotherapeutic drugs were responsible for the etiology. The other etiologies were malnutrition, septicemia, and acute liver failure.

The radiological findings of acute hyperammonemic encephalopathy have been reported in a few number of reports. However, specific MRI findings of acute hepatic encephalopathy have been reported recently. The most prominent MRI features identified in acute hyper-

ammonemic encephalopathy are bilateral symmetrical cortical signal abnormalities in the insula and cingulate gyrus, often with cytotoxic edema.[10,11] Although the frontal, temporal, and parietal lobes are frequently involved, the occipital and perirolandic cortex are spared.[12] The insula and cingulate cortex are more susceptible to the toxic effects of ammonia.[1] In severe injury, involvement of basal ganglia, brain stem, and subcortical white matter can also be seen.[2] One of our cases was having basal ganglia involvement.

Rosario et al.[1] have reported that thalami and dorsomedial thalami are frequently affected. U-King-Im et al.[2] presented the findings of diffusion restriction in the insula, cingulate, and diffuse cerebral cortex on DWI in four adult patients with acute hyperammonemic encephalopathy. Arnold et al.[12] and Choi et al.[13] reported cases of severe cortical laminal necrosis after hyperammonemic encephalopathy. According to the previous literature on acute hyperammonemic encephalopathy of children, similar adult MRI findings have been reported.[14] Our cases had MRI findings similar to those found in other reports.

Acute hyperammonemia may be misinterpreted as hypoxic-ischemic encephalopathy. Diffuse cerebral cortex and thalamus edema and diffusion restrictions are seen in hypoxic ischemic encephalopathy, similar to acute hyperammonemic encephalopathy. When similar findings are seen in brain MRI, other conditions such as limbic encephalitis, acute hypertension, hyponatremia, or Creutzfeldt-Jakob[15] encephalopathy can be considered in the differential diagnosis. It is very important to mention acute hyperammonemic encephalopathy in the differential diagnosis because it is reversible with early diagnosis and appropriate treatment. However, it can be life-threatening if untreated.

In less severe cases, the data have reported reversal of brain lesions if treatment is started immediately; however, in these patients, despite treatment on follow-up imaging, cortical atrophy has been detected in the affected areas.[16] Four of our cases died, and control imaging has not been performed in two surviving cases yet.

Conclusions

Specific MRI findings observed in acute hyperammonemic encephalopathy facilitate the diagnosis. The four main dominant regions involved are the insula, cingulate cortex, diffuse cerebral cortex (frontal, temporal, and parietal), and thalamus. In the presence of these MRI findings, radiologists should warn of acute hyperammonemic encephalopathy.

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