MICRO LABS SYNAPSE

Interesting cases NEUROLOGY

Vol 1|Issue 4|2020

Dear Doctor,

Greetings from Micro Labs Limited.

We are happy to bring you "Neurology case series", which contains latest and interesting cases in the field of Neurology.

This issue contains

1. A crisis of hyperammonaemia- A case report
2. Epstein Barr associated encephalopathy- A case report
3. Fingolimod-associated immune thrombocytopenic purpura – A case report.

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team,

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1. A crisis of hyperammonaemia- A case report.

Introduction:

Hyperammonemia is caused by either increased production or decreased elimination of ammonia via the liver. Other diagnosis considered were nonhepatic hyperammonemia with increased nitrogen turnover includes infection with urease producing bacteria (eg, Proteus spp, Providencia spp, or Klebsiella spp), increased dietary protein load, steroids, and increased catabolism from trauma or surgery.

Case presentation:

A 50-year-old male with a history of hypertension presented with 2 days of increasing confusion. Patient became progressively more confused, unable to complete simple tasks, and developed decreased appetite, ataxia, and fatigue. On examination, blood pressure was 166/88 mm Hg, heart rate 120 bpm, a temperature of 37.7 Cº, and was saturating, 95% on room air. Patient was awake, with a poor attention span and confusion to place and time. He was perseverating with a flapping hand tremor. No focal weakness was identified. Laboratory findings were unremarkable; however, ammonia level was elevated at 414 mcg/dL. Salicylate and acetaminophen levels were undetectable, and a urine drug screen was negative. Liver-function tests and hepatitis serologies were unremarkable. Infectious work up including urinalysis was negative. Treatment was initiated with Lactulose for hyperammonemia. He had progressive decline of his mental status over the next 24 hours, requiring intubation for airway protection. Then developed eye deviation with rhythmic blinking and facial twitching concerning for seizure activity that resolved after treatment with levetiracetam and propofol. Initial CT and CTA of the head and neck were unremarkable on the day of admission. Head CT repeated after seizure activity developed and showed sulcal effacement and loss of grey white differentiation, suggesting cerebral edema. Brain MRI showed diffusion restriction in the insular, cingulate, frontal, temporal, and parietal cortices. Differential Diagnosis considered was hyperammonemia is liver failure. In the absence of liver failure, nonhepatic causes of hyperammonemia were evaluated. A complete history , his spouse revealed an abnormally high intake of Pacific razor clams at the family's cabin 1 day before symptom onset. There was no history of recent surgery, infection, or prescription drug use associated with hyperammonemia. A high clinical suspicion for high protein intake unmasking a late-onset urea cycle disorder. Additional errors of metabolism such as organic acidemias, fatty acid oxidation defects, and amino acid transport defects were considered less likely because of the absence of acidosis and ketosis.

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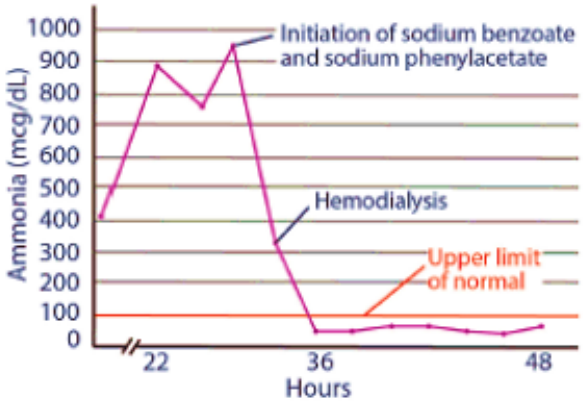
His ammonia levels continued to rise, peaking at 949 mcg/dL, which necessitated treatment with ammonia scavengers sodium phenylacetate/sodium benzoate, hemodialysis, and supplementation with urea cycle intermediates l-arginine and l-carnitine. With treatment Ammonia levels rapidly decreased. Patient was started on a lipid-rich protein-free diet. Protein (0.5 g/kg/day) was gradually reintroduced to his diet. A cerebral pressure monitor was placed because of concern for a intracranial pressure (ICP) crisis and coma. Medical management of ICP was initiated with sedation, seizure prophylaxis, hyperosmolar therapy, and mild hypothermia to 36 Cº for 24 hours. His initial ICP was 16 mm Hg, and he had 2 episodes of ICP crisis (ICP >25 mm Hg for >2 minutes), necessitating midazolam infusion in addition to the ongoing propofol infusion. The ICP crisis resolved with resolution of hyperammonemia. Extubation was done on the sixth day and he began to follow commands on day 8. He had residual severe cognitive slowing with dysarthria. Aggressive physical, occupational, and speech therapy improved his physical strength and verbal communication. He was discharged to rehabilitation on day 19 with orders for a low protein diet, oral sodium benzoate and levocarnitine. After an year, patient remained on low dose sodium benzoate, levocarnitine, and arginine supplementation. He continues adhering to a low protein diet of 1 g/kg/day, has recovered to independent living, and gone back to work. Some occasional word finding difficulties and mild cognitive impairment. Outpatient genetic testing was positive for ornithine transcarbamylase deficiency (OTCD).



Discussion:

Ornithine transcarbamylase deficiency (OTCD) is one of the most common urea cycle disorder. It is characterized by the complete or partial inability to breakdown ammonia in the liver. It is X-linked disorder, OTCD largely affects males, however heterozygotic women may manifest symptoms because of X-inactivation. Normally presents during the newborn period, late-onset presentations can be unmasked by increased nitrogen turnover in the setting of impaired enzyme activity. Late onset presentations often go unrecognized because of their rarity.

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Conclusion:

A case of hyperammonaemia crisis was successfully managed with lactulose, sodium benzoate, levocarnitine and arginine supplementation.

Reference:

Massaro A . Hyperammonemic Crisis . Practical Neurology. 2020; 80-82.

2. Epstein Barr associated encephalopathy- A case report.

Introduction:

Epstein-Barr virus (EBV) infection is accompanied by central nervous system (CNS) symptoms like encephalitis, meningitis, cerebellitis, polyradiculomyelitis, transverse myelitis, cranial and peripheral neuropathies, and psychiatric abnormalities, can occur in 1–18% of patients with EBV infection. EBV-associated encephalopathy/encephalitis often presents with nonspecific symptoms and its diagnosis is based on the detection of EBV antibodies and/or DNA in the cerebrospinal fluid (CSF). Current is case of EBV-associated encephalopathy in immunocompromised patient.

Case presentation:

A 61-year-old man presented with gradually impaired consciousness. He had been diagnosed with acute myeloid leukemia at 59 years of age. Remission of leukemia was achieved after allogeneic hematopoietic stem cell transplantation, and consequently he was treated with prednisolone (2 mg/day) and tacrolimus (0.2 mg/day). About 1 week before admission, he presented with a slight fever and malaise. He became progressively unable to walk and talk. Subsequently, his consciousness level was impaired to 11 points (E3, V3, M5) on the Glasgow Coma Scale (GCS). After admission, his consciousness level further decreased to 9 points (E2, V2, M5) on the GCS. His vital signs (i.e., blood pressure, pulse, and body temperature) were normal. No physical findings of neck stiffness, lymphadenopathy, rash, hepatosplenomegaly, or jaundice. The impaired consciousness was not accompanied by paralysis or convulsions. Blood tests for factors that might cause impaired consciousness, such as inflammation, electrolyte imbalance, hypo/hyperglycemia, and uremia, were normal. Fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) of brain MRI revealed no abnormalities. Magnetic resonance angiography also revealed no abnormalities during hospitalization .

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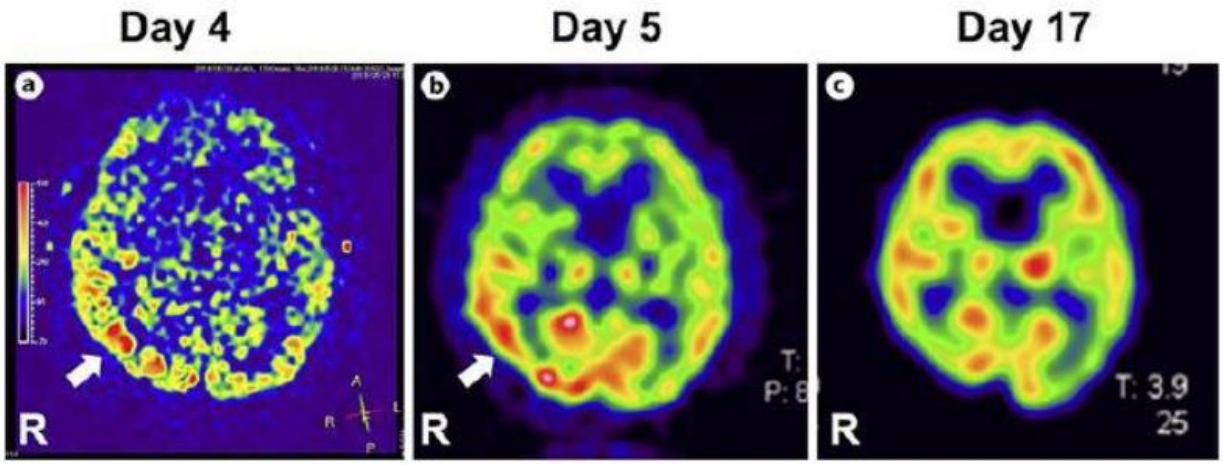
ASL-MRI and brain perfusion SPECT showed cerebral hyperperfusion in the right temporal region. Apart from generalized slower theta or delta frequencies, wakeful electroencephalography revealed no abnormal findings that would indicate epilepsy. Examination of CSF showed slight increases in white blood cell count (14 cells/μL), protein (73.6 mg/dL), and glucose (62.0 mg/dL). CSF cytology found no malignant cells. EBV virus capsid antigen (VCA) immunoglobulin (Ig)M was negative in CSF, yet EBV VCA IgG was positive. Quantitative PCR revealed that EBV DNA in CSF was increased to 720 copies/mL, suggesting EBV reactivation in the CNS. In contrast, DNA of herpes virus type 1 or cytomegalovirus was not detected by PCR. With MRI and EBV DNA in CSF, he was diagnosed with EBV-associated encephalopathy with mild inflammation. Administration of an antiepileptic, levetiracetam (1,000 mg/day) promptly improved his consciousness to 15 points (E4, V5, M6) on the GCS. He regained the ability to stand and walk without any support on the 14th hospital day. SPECT showed disappearance of hyperperfusion in the temporal region on the 17th day. After discharge, the dosage of tacrolimus was decreased from 0.2–0.1 mg/day.



Discussion:

The clinical features of EBV infection in the CNS are heterogeneous and may be dependent upon the degree of cellular dysfunction or destruction, i.e., from encephalopathy to encephalitis. In current case continuous treatment with prednisolone and tacrolimus after stem cell transplantation may have caused latent infection and reactivation of EBV in the CNS. EBV can enter B cells by

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binding to gp350 and complement receptor 2 (CR2), which are highly expressed on the plasma membranes of B cells.

Conclusion:

EBV-associated encephalopathy can lead to epilepsy, particularly in immunosuppressed patients. Case was successfully managed with medications.

Reference:

Ohya Y et al. Epstein-Barr Virus-Associated Encephalopathy Presenting with Nonconvulsive Status Epilepticus in an Immunosuppressive State Case Rep Neurol 2020;12:214–221.

3.Fingolimod-associated immune thrombocytopenic purpura – A case report.

Introduction:

Multiple sclerosis (MS) is a inflammatory demyelinating disease targeting myelin in the central nervous system (CNS). Fingolimod indicated in multiple sclerosis is a sphingosine-1-phospate (S-1-P) modulator that sequesters lymphocytes in lymph nodes leading to fewer available cells entering the CNS and thus preventing myelin destruction and clinical relapses.

Case presentation:

A 31-year-old Caucasian woman with relapsing-remitting multiple sclerosis was started on fingolimod as her initial and only disease-modifying therapy (DMT) since the diagnosis was made in 2012, and she opted not to go on injectables. In 2016, she developed symptoms of left sided paresthesias that resolved following a course of 1g methylprednisolone for 5 days. She maintained clinical and radiological stability while on fingolimod until she developed progressive bruising of her upper extremities and menorrhagia over a period of one week. Platelet count at the time was 5 ×109/L without a prior history of thrombocytopenia. Her previous platelet count over the years were normal and ranged between 200-300 x 109/L. She was admitted and underwent a full serological workup which was unremarkable including a complete blood count (CBC) panel, complete metabolic panel (CMP), prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR), D-dimer level, von Willebrand factor (vWF), vitamin levels, anti-phospholipid antibodies (including lupus anticoagulant, anti-β2-glyocoprotein, and anti-cardiolipin antibodies), infectious panels (such as Human

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Immunodeficiency Virus, Cytomegalovirus, Epstein Barr Virus, Helicobacter pylori, and Hepatitis C Virus), and a blood smear which showed no evidence of any schistocytes. An abdominal ultrasound did not reveal splenomegaly. Patient was treated for presumed immune-thrombocytopenic purpura (ITP) by receiving platelet transfusions, 2g/kg of intravenous immunoglobulin (IVIG) therapy, and 1 g of pulse IV methylprednisolone for 5 days. After 2 weeks, her platelets were 2 ×109/L and additional IVIG was given. Patient received platelet transfusions again, and was started on Eltrombopag, a bone marrow stimulant used for treating ITP. After 2 weeks, her platelet count was zero. She received further multiple medications including dexamethasone, a 3rd course of IVIG, an increased dose of Eltrombopag, Rho (D) immune globulin and Danazol (an androgenic hormone used in refractory ITP). Platelets did not respond to treatment and a bone marrow biopsy was performed which was normal and did not show a lymphoproliferative disease. Cytogenetic analysis for myelodysplastic syndrome was negative. A diagnosis of 'probable drug-induced immune thrombocytopenia' was presumed and fingolimod was discontinued and switched to dimethyl fumarate as an alternative DMT. She subsequently received two infusions of Rituximab 2-weeks apart. One week after discontinuing fingolimod, she experienced a dramatic increase in her platelet counts to 79 $\times 10^9$/L. Currently, after 5 years of follow up, she is without any clinical or radiological evidence of MS exacerbations or thrombocytopenia. Her most recent platelet count was 294 ×109/L.

Discussion:

Immune thrombocytopenia (ITP) is one of the acquired autoimmune hematological and is a diagnosis of exclusion. Drug-induced immune-thrombocytopenia (DITP) is an even more unusual disorder with approximately 1300 case reports in the published literature due to a variety of different medications and may have potentially serious consequences that can be reversed by simply stopping the causative agent.

Conclusion:

A case of Fingolimod induced thrombocytopenia , platelet count improved after stopping the drug.

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Reference:

Mukharesh L et al. Fingolimod-induced immune thrombocytopenic purpura (ITP). Clinical Neurology and Neurosurgery. 2020; 106081.