Interesting cases NEUROLOGY

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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. Total parenteral nutrition causing Manganese neurotoxicity – A case report
2. A challenging case of Erdheim-Chester disease
3. Rethinking the diagnosis of meningoencephalitis- 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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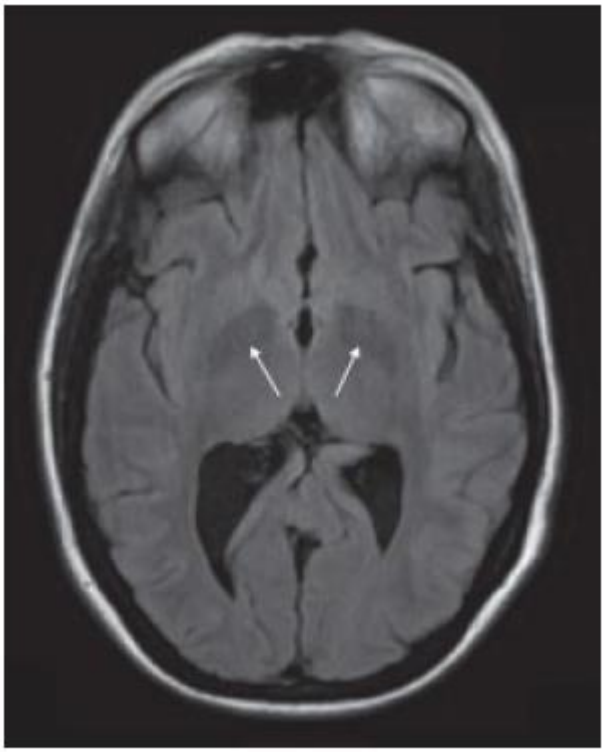
1. Total parenteral nutrition causing Manganese neurotoxicity – A case report

Introduction:

Total parenteral nutrition (TPN) is a adviced for patients who cannot tolerate enteral nutrition. TPN has its own risks, and patients need to be monitored closely while on therapy. A rare complication is manganese toxicity. Manganese being an essential dietary mineral is regulated strictly in human body. Elevated levels of manganese can occur from excessive exposure, through inhalation or parenteral exposure. Manganese exposure to central nervous system results in clinical symptoms of cognitive dysfunction, behavioural changes, and movement disorder resembling Parkinson's disease. Current case study describes such case of Manganese toxicity.

Case Presentation:

36-year-old woman presented with marginal ulcer anastomosis site with subsequent perforation. Patient had underwent Roux-en-Y gastric bypass surgery before 3 years. As patient could not tolerate oral nutrition a PICC line was placed for TPN 2 years back. With TPN use there was recurrent candidemia with blood cultures positive for Candida albicans resistant to fluconazole and voriconazole. Subsequently PICC line was replaced thrice, and treated with micafungin. Patient was admitted several times for altered mental status and unsteady gait. 1 ½ years back patient presented with complaints of tremors, impaired mobility, confusion, gait instability, falls, and lethargy. On admission, she was confused, with horizontal nystagmus and dilated pupils as well as bradypnea. Fundus examination indicated candida retinitis. Patient was lethargic but arousable. Speech was incoherent. History



Manganese toxicity changes

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showed that she had been having tremors, episodes of confusion, and numerous falls for the past several months. At present she had increased irritability and emotional lability during this time. Patient was started on liposomal amphotericin B and flucytosine for a total of 6 weeks. MRI brain showed worsening T1 hyperintensities in the bilateral globus pallidi thought to be due to manganese toxicity from chronic TPN use.

Patient was stopped TPN for 3 months, then MRI performed later showed improvement of the T1 hyperintensities in the bilateral globus pallidi, in substantia nigra. With antifungal treatment and cessation of TPN, patient's mental status and neurological symptoms improved within 3-4 days.

A gastrostomy tube was placed in her remnant stomach. Even though patient presented after seven months of initiation of TPN therapy, Parkinsonian symptoms begun to manifest after three months on TPN. Differential diagnosis includes ischemic or hypoxic encephalopathy, hypoparathyroidism or pseudo hypoparathyroidism, hamartomas of neurofibromatosis type 1, and cerebral haemorrhage due to Japanese encephalitis. Mn toxicity Treatment is dependent on eliminating the source of Mn exposure. Chelation with intravenous EDTA, increase urinary excretion of Mn, may not seem to improve the symptoms of Mn toxicity may still be used to decrease the blood concentration of Mn. Hence in this case, chelation therapy was not attempted. Patient symptoms improved within few days of TPN discontinuation, a cornerstone of treatment.

Discussion:

Mn disrupts the signalling of dopamine, serotonin, and glutamine, evidenced by synchrotron X-ray fluorescent imaging, that provides insight into Mn toxic kinetics and its neural distribution. Manganese levels with increased exposure have been noted to decrease the copper levels in the subventricular and subgranular zones of the brain, responsible for the nonmotor symptoms of Mn-induced Parkinsonism Mn affects primarily globus pallidus and the striatum of the basal ganglia. Mn preferentially deposits in the dopaminergic cells of the basal ganglia, notably the globus pallidus, resulting in extrapyramidal motor disturbances presenting similarly to Parkinson's disease. In fact, Mn has been found to upregulate histone deacetylase (HDAC) and downregulate histone acetyltransferase (HAT) in neuronal cells, which damages dopaminergic neurons.

Mn toxicity can affect internal organs, particularly bones which house 40% of the body's total Mn stores and where Mn has half-life of 8-9 years, serve as a continuous internal source of Mn exposure. As manganese is excreted in bile, it can lead to hepatic encephalopathy in patients with liver dysfunction.

Conclusion:

Manganese toxicity can occur in total parenteral nutrition, that can lead to neurotoxicity affecting cognition and can manifest as Parkinson's disease.

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Reference:
1) Khan A et al. Manganese Neurotoxicity as a Complication of Chronic Total Parenteral Nutrition. 2020; 9484028: 1- 6 pages.

2. A challenging case of Erdheim-Chester disease

Introduction:

A non-Langerhans cell histiocytosis (NLH)type of disease is Erdheim-Chester disease (ECD). It is characterized by infiltration of histiocytes into various organs, producing a heterogeneous clinical picture, ranging from asymptomatic conditions to multisystem, life-threatening forms .ECD usually affects male patients between the 5th - 7th decades and presents with bone pain, diabetes insipidus, constitutional and neurological symptoms. Central nervous system (CNS) involvement (ponto-cerebellar dysfunction, pan-hypopituitarism and seizures) is linked to a worst Diagnosis is based on imaging findings (whole-body CT/MRI/PET), histopathological features and molecular analysis. Mutations of Raf and MEK (mitogen-activated protein kinase kinase), have been associated to ECD and have allowed specific treatment with vemurafenib, a specific BRAF kinase inhibitor , and cobimetinib, a MEK inhibitor. The aim of this case study is to describe a patient affected by ECD, presenting with an uncommon complex cerebellar ataxic syndrome.[1]

Case presentation:

A 50-year-old man presented with an insidious onset of two-year history of slurred speech, dysphagia to liquids and gait disturbance without fall. He had past history of pan-hypopituitarism since the age of 40. Examination of Neurological system revealed lunaris face and bilateral proptosis, cerebellar ataxic gait, bilateral horizontal nystagmus, dysarthria and liquid dysphagia. Deep tendon reflexes were diffusely brisk. Scale for the assessment and rating of ataxia (SARA) showed a score of 14/40. Most frequent causes of cerebellar dysfunction were ruled out by assessing Biochemical workup, serology for vitamin B12, folate, TSH, paraneoplastic markers, anti-GAD antibodies and genetic testing for spino-cerebellar ataxia type 1, 2, 6, 7. MRI Brain revealed a secondary empty sella, with atrophy of the pituitary gland, associated to diffuse multiple FLAIR hyperintensities of the midbrain/pons, atrophy of the superior cerebellar peduncle and cerebellar hemisphere, bilaterally, with enlargement of the 4th ventricle. Axial 3D SWI T2* scans revealed significant reduction of the volume of the dentate nuclei, bilaterally as shown in figure. A presumptive diagnosis of histiocytosis was done. Further diagnostic work up was done by

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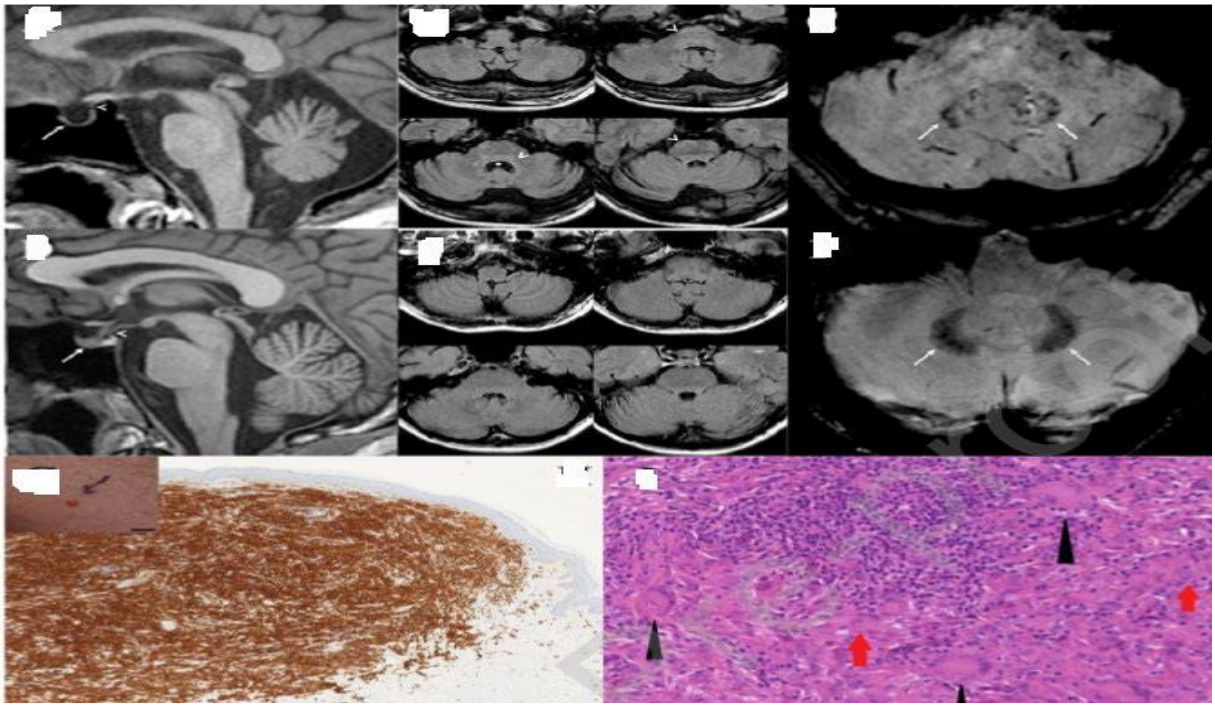
performing a bone RX screening to distinguish between Langerhans cell (LCH) and NLH histiocytosis; skull, proximal bone limbs, pelvis and scapula usually involved in LH, and distal bone limbs in NLH. Rx screening showed widespread sclerosis in the distal femur. A cutaneous translucent papular-nodular lesion was identified in the pectoral region, removed and processed for histopathological analysis, which showed widespread dermal infiltration of foamy histiocytes and Touton's giant cells, intensely positive for CD163, CD68 and fascin but negative for S100 and CD1a (xanthogranuloma), coherent with the diagnosis of ECD. MRI with contrast of whole body revealed: 1) a solid mass (34x55 mm) within the right atrioventricular sulcus ; 2) thickening of the abdominal aorta wall and the retroperitoneal / perirenal region, displacing aorta and inferior caval vein; 3) distal sclerosis of both femurs. Whole-body 18-FDG PET imaging demonstrated a diffuse/inhomogeneous metabolic activity of the retroperitoneal/perirenal tissue and medio-distal spongiosa of the left femur. Patient was started on vemurafenib (up to 240 mg bid-in-day). After 3 months of treatment, the patient developed a bilateral peripheral palsy of the VII cranial nerve, with prompt recovery after 2 weeks with oral methylprednisone (50 mg/day). Currently patient is on vemurafenib for 9 months: at the last clinical evaluation, he showed significant improvement of the ataxia, dysphagia and dysarthria (SARA score: 9/40), and significant relief of bone pain.



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Whole -body MRI showed volume reduction of the cardiac mass (21x34 mm) ,thinning of the aortic and perirenal tissue reduction of distal femur osteosclerosis, with absence of FDG-uptake consistent with the clinical observation,. Despite clinical improvement, brain MRI findings were unchanged at the follow-up.

Conclusion:

Erdheim-Chester disease is a challenging diagnosis, early diagnosis and treatment with the BRAF/ERK inhibitors significantly improves the clinical outcome and the patient's quality of life.

Reference:

1) Todisco A et al. Erdheim-Chester disease: a challenging diagnosis for an effective therapy. Clin Neurol Neurosurg. 2020; 194:105841.

3. Rethinking the diagnosis of meningoencephalitis- A case report.

Fever, vomiting, with CSF pleocytosis usually points towards diagnosis of meningoencephalitis. However another curious disorder can present in a similar way which is Neuromyelitis optica spectrum disorder (NMOSD). It is a rare autoimmune astrocytopathy that leads to demyelination in the central nervous system. It is quite common in females, with presentation in late thirties.Classically presents with optic neuritis and longitudinally extensive transverse myelitis. Area postrema syndrome, a usually less recognized presentation, characterized by intractable

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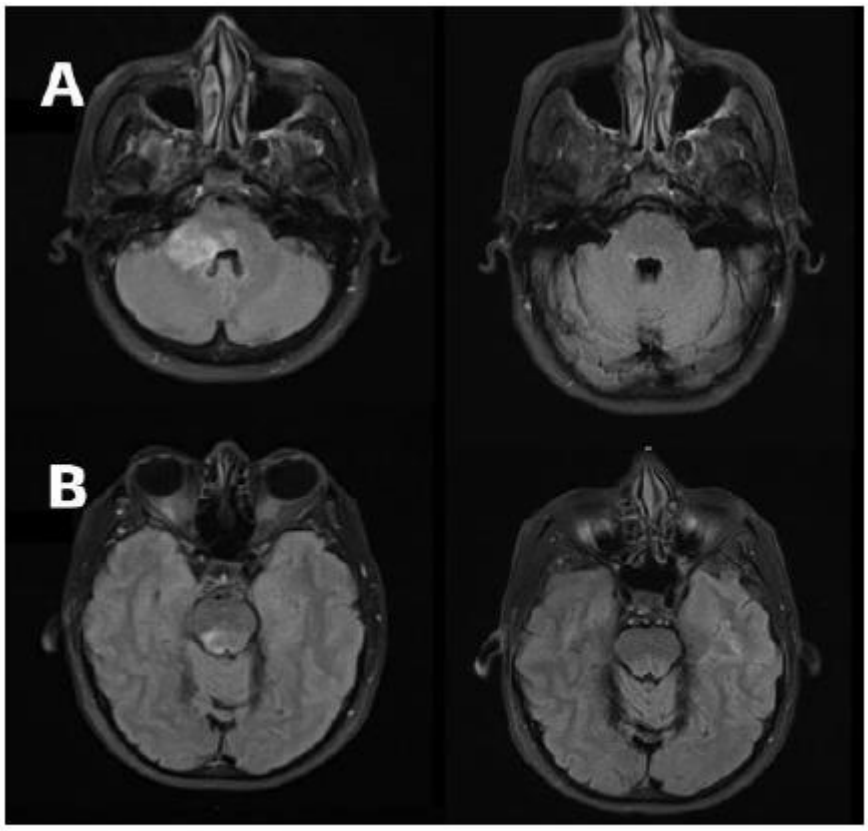
nausea, vomiting and hiccups.1Current is case study of NMOSD with delayed diagnosis due to atypical presentation.

Case presentation:

A 41-year-old female presented with fever and refractory nausea and vomiting for a week; the previous day she had developed neck pain, right hemifacial paresthesia and unsteady gait.On admission she had fever (38.6 °C), right facial hypoesthesia and meningism. Laboratory tests and CT scan were unremarkable, and cerebrospinal fluid (CSF) study revealed 750 cells (75 % polymorphonuclear), high protein levels (0.93 g/L) and normal glucose levels.Probable diagnosis of meningoencephalitis was made and empirical treatment with ceftriaxone and ampicillin was started.Cultures and serology for CMV, EBV, Toxoplasma, Mycobacterium tuberculosis, Mycolplasma pneumoniae, Herpes simplex and varicella zoster were negative.After two days patient developed diplopia on right-side gaze, left horizontal nystagmus, dysphagia, right hemiparesis and hemidysmetria and loss of balance.MRI brain and spinal cord showed a continuous hyperintense lesion on T2 sequences from the right cerebellar hemisphere to the spinal cord (C2 level), with gadolinium enhancement . Visual evoked potentials showed evidence of left optic nerve demyelinating lesion.Aquaporin-4 Immunoglobulin G (AQP4) screening was done. Patient was started on treatment with methylprednisolone IV 1 g for 5 days and then she was started on azathioprine up to 100 mg/day with both clinical and



Axial T2 FLAIR showing hyperintensity in right cerebellar peduncle (A) and area postrema (B

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radiological improvement.AQP4 antibodies were negative and the diagnosis of NMOSD without AQP4 was made. Later, anti-MOG antibodies were screened and were also negative.

Discussion:

Neuromyelitis optica spectrum disorder is one of the auto-immune disorder of the CNS, which causes destruction of astrocytes in the blood-brain barrier. This occurs by development of auto-antibodies against astrocyte's membrane protein aquaporin-4, subsequently causing secondary demyelination.Ig G antibodies to Myelin oligodendrocyte glycoprotein (MOG-IgG) in patients with inflammatory CNS demyelination are known to be present in patients with NMOSD without antibodies against APQ4 in around 50 % of cases.NMOSD most commonly affects optic nerves and spinal cord. Area postrema syndrome can occur in NMO. CSF study in NMOSD during an active phase reveals at least one abnormality (up to 62%) and up to 32% might show pleocytosis.A few cases of NMOSD cases were initially interpreted as CNS infection, due to the clinical presentation with fever, meningism and focal neurological signs and presence of CSF pleocytosis.Suspecting NMOSD as a differential diagnosis of meningoencephalitis is crucial to avoid complications and prevent relapses. 1Axial T2 FLAIR showing hyperintensity in right cerebellar peduncle (A) and area postrema (B

Conclusion:

Neuromyelitis optica spectrum disorder can mimic meningoencephalitis, to be considered as differential diagnosis supported by Brain and spinal MRI, AQ4.

Reference:

1)Rocha AL et al. Fever, nausea and vomiting, and CSF pleocytosis must be meningoencephalitis, right? No, think again!. Clin Neurol Neurosurg. 2020; 194:105813.

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