Tuberous Sclerosis

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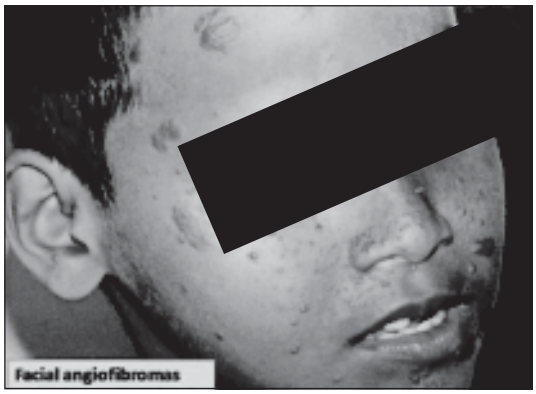
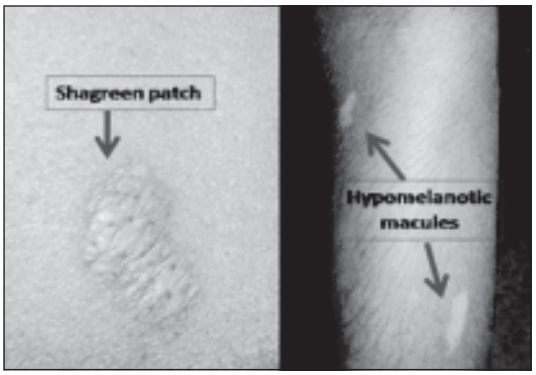
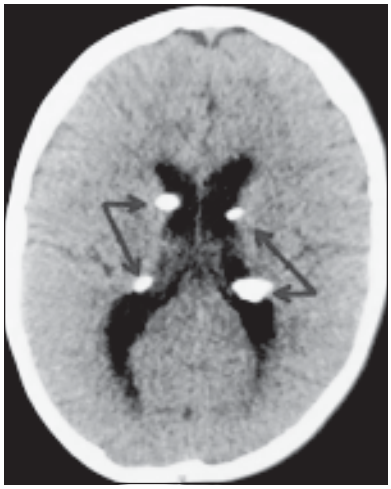
A 12½ years old boy presented with recurrent seizures, which had started since 7 months of age and gradually became more frequent and difficult to control. On examination the boy was found apathetic, non-communicating and severely mentally retarded. He had frequent myoclonic seizures, which involved all 4 limbs lasting for 15-20seconds.On skin survey there were multiple tiny red nodular angio-fibromas over nose and cheeks, 4-5 hypomelanotic macules (ash leaf macule)seen on the back of trunk and thigh. In addition, few*shagreen patches* were also found on back.

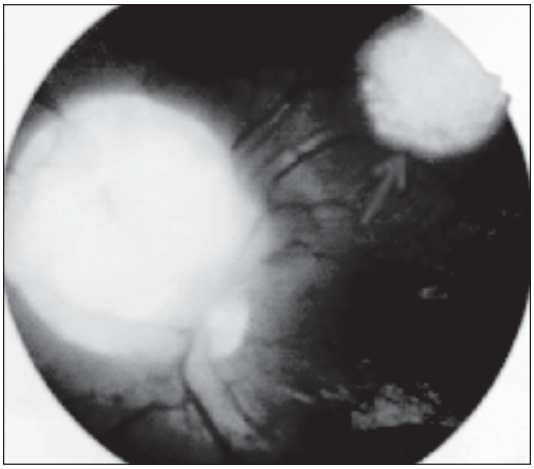




EEG was done which showed hypsarrhythmic pattern. On CT scan of brain there were subependymal noduleswith calcification projecting into the lateral ventricular cavity from the wall with candle-dripping appearance. Fundoscopic examination revealed left sided retinal hamartoma.



Subependymal nodules (calcified)



Left sided retinal hamartoma

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Based on the clinical and investigation finding the boy was diagnosed as a case of Tuberous sclerosis complex (TSC) and vigabatrin was added to control seizure.

TSC is inherited as an autosomal dominant trait with variable expression. Spontaneous genetic mutations occur in 2/3rd of the cases. It is an extremely heterogeneous disease with a wide clinical spectrum ranging from totally asymptomatic to severely affected patients. The diseaseaffects many organ systems mainly skin and brain,also heart, kidney, eyes, lungs, and bone.TSC is diagnosed when at least 2 major or 1 major plus 2 minor features are present as follows-

Major Features	Minor Features
Cortical tuber	Cerebral white matter migration lineMultiple dental pits
Subependymal nodule	Gingival fibromas
Subependymal giant cell astrocytoma	Bone cysts
Facial angiofibroma or forehead plaque	Retinal achromatic patch
Ungual or periungual fibroma (nontraumatic)	Confetti skin lesions
Hypomelanotic macules (>3)	Nonrenalhamartomas
Shagreen patch	Multiple renal cysts
Multiple retinal hamartomas	Hamartomatous rectal polyps
Cardiac rhabdomyoma	
Renal angiomyolipoma	
Pulmonary lymphangioleiomyomatosis	

The hallmark of TSC is the involvement of the CNS that includes cortical tuber and subependymal nodules, which are seen on Brain MRI or CT scan.[3,5] These lesions do not cause any problem; but in 5-10% of cases subependymal nodules can grow into subependymal giant cell astrocytomas (SEGAs) thatwhen blocks CSF circulation, gives rise to hydrocephalus and requires immediate neurosurgical intervention. The common neurologic manifestations of TSC consist of epilepsy, cognitive impairment, and autism spectrum disorders. Many a times, the seizures are difficult to control and, at a later age, they may turn into myoclonic epilepsy. [1,5]

A careful search for the typical skin and retinal lesions should be done in suspected case of TSC presenting with seizure disorder or autism spectrum disorder. [2,3,5] More than 90% of cases hypomelanotic macules (**ash leaf)** are seen on trunk and extremities. Facial angiofibromas develop between 4 and 6 yr of age, which appear as tiny red nodules over the nose and cheeks and are sometimes confused with acne. Later, they enlarge, coalesce, and assume a fleshy appearance. A *shagreen patch* is also characteristic of TSC and consists of a roughened, raised lesion with an orange-peel consistency mostly in the lumbosacral region. During adolescence or later, small fibromas of skin may form around fingernails or toenails in 15-20% of cases.[1,2,3]

Retinal lesions in TSC are of 2 types: hamartomas (elevated mulberry lesions or plaquelike lesions) and white depigmented patches (similar to the hypopigmented skin lesions).[4]

Approximately 50% of children with TSC have cardiac rhabdomyomas, which can cause congestive heart failure and arrhythmias. 75-80% of patients crossing 10 years of age have benign angiomyolipomas tumors in kidneys. Lymphangioleiomyomatosis (LAM) is the classical pulmonary lesion in TSC that affects only women after the age of 20 year.[1,2,3,6]

There is no cure to TSC. Treatment is symptomatic. To optimize quality of life parents need to be educated and counseled properly about the disease. A routine follow-up has to be planned as per recommendation.[4,6]

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Acute Blindness Following Methanol Poisoning

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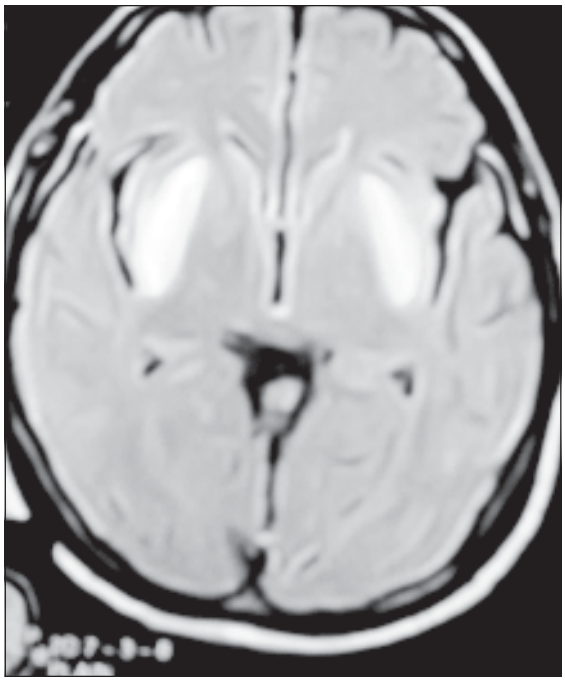
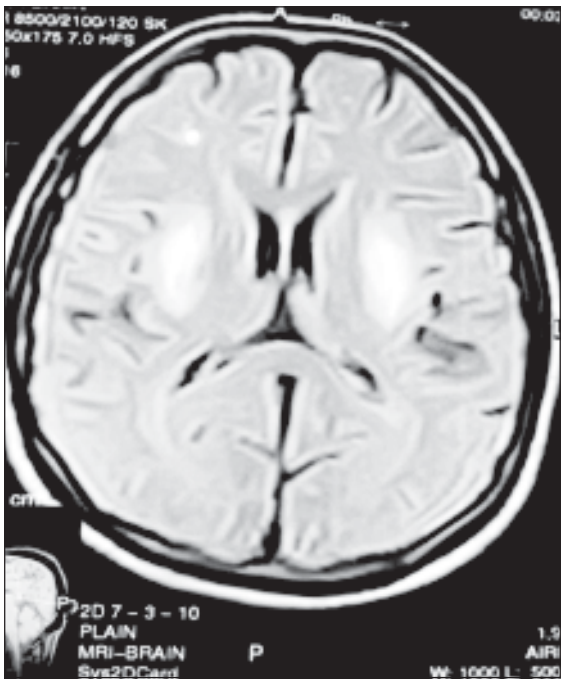
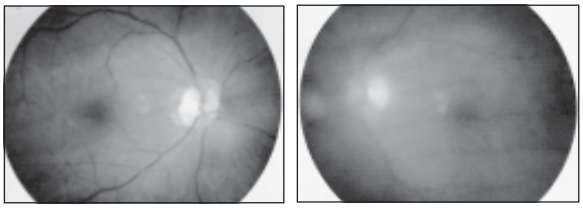


Hyperintensities in both lentiform nucleus.



Hyperintensities in both lentiform nucleus.

A 42 years old, male muslim, married, normotensive, non diabetic, non-smoker was admitted to DMCH with the history of disorientation for 4 days, headache and blurring of vision for 3 days and respiratory distress for 2 days. There is no history of trauma, head injury, fever, cough, vomiting, convulsion, weakness of limbs, bleeding episodes or bowel and bladder incontinence. On query, he confessed that he was taking methanol regularly for last 8 years, but intake was large before the day of admission. Examination revealed patient was mildly anaemic. His pulse was 90/min, BP 90/60 mm Hg, respiratory rate 40 breaths/min, GCS 15/15,



Fundus phorograph: Bilateral Optic atrophy

bilaterally fixed and dilated pupils, absent pupillary light reflex without ptosis and nystagmus. Fundoscopic examination revealed bilateral optic atrophy. Other cranial nerves were intact. He had no signs of meningeal irritation and other systemic examination revealed no abnormalily.

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Investigation findings:

CBC with ESR	Hb-10.7g/dl, WBC-11500/cmm(N-93.5%),Platelet-247000/cmm MCV-96fl,ESR-42 mm in 1st hour
RBS	7.9 mmol/l
S.Creatine	1.22mg/dl
S.Urea	44mg/dl
S.Electrolytes	Na-135 mmol/l ,K-5.8mmol/l, Cl:121 mmol/l, Tco2: 14mmol/L
S. Alcohol	<10mg/dl
Urine R/E	Pus cells-1-4 /HPF, RBC-nil, Albumin-(+)
ECG	Normal
MRI of Brain with contrast	T2 W1 and FLAIR hyperintensities in both lentiform nucleus. No enhancement seen after contrast adminstration. No midline shifting. Ventricles, extraventricular CSF spaces, sellar, suprasellar and parasellar regions appear normal .Normal flow seen in major cerebral blood vessels **Comment: Toxic Encephalopathy**
Arterial blood gas	Metabolic acidosis

Discussion :

Susceptibility to methanol poisoning varies greatly. Methanol poisoning affects the optic nerve and the central nervous system with a predilection for basal ganglia, resulting in symptoms of visual disturbances, blindness, drowsiness, seizures and coma.[1] Methanol intoxication can cause severe metabolic acidosis, visual defects, permanent neurological dysfunction and death.[2] Most patients note visual disturbances ranging from blurred vision to permanent blindness secondary to optic nerve necrosis or demyelination, as one of the first symptoms. Central nervous system symptoms are common and include nausea, vomiting, headache, dizziness, weakness, and malaise. Large amount of methanol ingestion can result in seizures, stupor, coma and sometimes death.[3] The diagnosis is based on the presence of severe metabolic acidosis with high anion and osmolar gap and high serum methanol levels. Neuroradiological findings in methanol poisoning have occasionally been described in the literature. These imaging findings reflect a variety of pathologic processes that can be acute, subacute, or chronic in nature and have concomitantly affected the white matter of the brain. **Multiple sclerosis** (MS) is a common white matter disease process that affects young adults. **Autoimmune/idiopathic diseases -** *Acute disseminated encephalomyelitis (ADEM), Subacute sclerosing panencephalitis (SSPE), Neuromyelitis optica* ,**Infection -** *Lyme neuroborreliosis, Progressive multifocal leukoencephalopathy (PML),* **Vascular -** *Central nervous system vasculitis, CADASIL , Susac's syndrome and* **Acquired conditions-***Radiation necrosis, Osmotic demyelination syndrome, Diffuse axonal injury can cause deep white matter lesion in MRI finding.*[4]

The most characteristic MR findings in methanol toxicity are bilateral putaminal necrosis with or without haemorrhage. On the other hand, putaminal changes may also be seen in Wilson's disease, Leigh's disease, Kearns-Sayre syndrome, carbon mono-oxide inhalation, hypoxic-ischaemic injury, trichloroethane poisoning and acute cyanide intoxication.[5] Cerebral and intraventricular haemorrhage, diffuse cerebral oedema, cerebellar necrosis, and abnormalities of basal ganglia, optic nerve and pontine tegmentum are the other MRI findings of methanol intoxication.[6] Our report illustrates the usual effects of methanol intoxication on the nervous system . CT and MR imaging are able to demonstrate toxic effects of methanol in the CNS. Putaminal necrosis with or without haemorrhage are the most frequent reported findings. Other affected areas that are reported in the literature are subcortical white matter, hippocampus, optic nerve, tegmentum, cerebral gray matter and cerebellum.[3] When a large amount of methanol is ingested, death usually occurs within three days.[7]

Conclusion:

In conclusion when symmetrical lesions are detected in the basal ganglia and white matter along with sudden

visual disturbances, there can be a long list of differential but correct diagnosis could be reached if history of methanol ingestion is available. Since early diagnosis may improve the prognosis in acute phase, methanol intoxication should be considered in the differential diagnosis of such lesions on MRI examinations.

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