Neurodegeneration with Brain Iron Accumulation – Late Onset Slowly Progressive Variant

Priya V Patil*, Gajendra Manakshe**, Dinesh P Mahajan+, Dattatray B Solanke++, Tejas Sakale+++ 

Introduction

Hallervorden spatz disease is a rare degenerative disorder of the basal ganglia, now renamed as “Neurodegeneration with brain iron accumulation” (NBIA). The classical variety is characterized by progressive extrapyramidal degeneration presenting as a spectrum of dystonias, tremor, retinal degeneration, dementia in the first decade of life. In the atypical variety of the disease, onset of symptoms is later and progression is slower and more variable.

Case Report

A 23 year old male born of non consanguineous marriage was brought by relatives with history of difficulty in speech since 8 years, which initially started in the form of stammering at speech, and his speech difficulty gradually progressed and patient had no verbal speech since the last 2 years. Patient also developed dystonic movements in the form of extension of neck, along with sudden opening of the jaw since 8 years (Fig. 1). The dystonic posturing was absent during sleep. Patient had history of seizures since 10 years of his age for which he was not on any medication. None of the patient’s family members had similar complaints. Patient had no history of jaundice in the past.

On general examination patient was moderately built and nourished. His intellect was normal and patient obeyed oral commands and could communicate by writing on paper. Patient’s vision and extraocular movements were normal. Patient had wasting of his muscles of hand and feet with pes cavus (Figs. 2, 3). Reflexes were normal. Patient had severe dystonic movements in the form of sudden extension of neck along with sudden opening of the jaw, associated with trick movements in the form of placing his palm below the right temperomandibular joint to relieve himself of the discomfort.

Patient’s liver function test were normal. His serum ceruloplasmin levels were normal [23mg/dl]. Serum ferritin levels were normal [277ng/ml], USG abdomen was normal. Patient’s slit lamp examination for KF ring was negative. Patient’s fundus examination was normal. Patient’s MRI brain was suggestive of central hyperintensities surrounded by hypointensities in the globus pallidus on T2W sequence, suggestive of “eye-of-the-tiger” appearance. A diagnosis of NBIA was made based on the basis of progressive nature of the patients complaints, characteristic MRI findings, and exclusion

Abstract

Neurodegeneration with Brain Iron Accumulation (NBIA) is a rare type of neuroaxonal dystrophy that can be familial or sporadic, characterized by progressive extrapyramidal degeneration. We report a case of 23 year old male who presented with cervical dystonia, dysarthria and MRI brain suggestive of characteristic “eye-of-the-tiger” appearance in the globus pallidus.

Fig. 1: Dystonic spasm

Fig. 2: Atropy of musles of hand

Fig. 3: Atropy of musles of lower limb
of other close clinical entities. Patient could not be subjected to any genetic analysis as facilities for the same were not available.

Patient was started on symptomatic treatment for his dystonias in the form of trihexiphenydyl and levodopa/carbidopa, which did not cause significant improvement in the patient’s symptoms.

Discussion

Neurodegeneration with brain iron accumulation (NBIA) is a rare disorder characterized by progressive extrapyramidal dysfunction and dementia. Onset is most commonly in late childhood or early adolescence, but cases with adult onset have been described. The disease can be familial or sporadic. When familial, it is inherited recessively and has been linked to chromosome 20. Recently, a mutation in the pantothenate kinase (PANK2) gene on band 20p13 has been described in patients with typical NBIA, coding for pantothenate kinase 2 which is required for the phosphorylation of pantothenic acid, in the formation of coenzyme A. Due to the defective phosphorylation of pantothenic acid there is underutilization of cysteine which in excess causes chelation of iron leading to free toxic radical production. The preferential involvement of the basal ganglia is attributed to excess of pantothenate kinase receptors. Thus the term pantothenate kinase 2 associated neurodegeneration (PKAN) may be preferable instead of Hallervorden–Spatz disease.

Recently, neurodegenerative disease of brain with accumulation of iron (NBIA) have been classified according to the age of onset and gene defect into different groups (Table 1).

The characteristic MRI finding of the “eye-of-the-tiger sign” corresponds to the pathological findings (Fig. 4). The hypodensity on T2 weighted image is because of iron deposition and central hyperintensities is secondary to gliosis and spongiosis. The other condition in which high signal intensity, like NBIA can be observed are metabolic disorders, like organic acidurias, early onset levodopa responsive Parkinsonism and cortico-basal ganglionic degeneration. The other disorder affecting the basal ganglia such as Leigh’s disease, mitochondrial encephalopathies, infantile bilateral necrosis and Wilson’s disease more frequently involve the putamen rather than the globus pallidus.

The other differential of iron deposition in the basal ganglia and “eye-of-the-tiger” sign include aceruloplasminemia and neuroferritinopathy. These are distinct condition of abnormal iron metabolism but unlike NBIA present in adult or late life (6). Neuroferritinopathy is characterized by onset at 40-45 yrs of age and defect is localized to the gene encoding ferritin light chain polypeptide at 19q 13.3. Aceruloplasminemia is associated with diabetes mellitus and there is complete deficiency of ceruloplasmin protein. The gene is localized to chromosome 3q 13.3.

Symptoms in NBIA are predominantly extrapyramidal including dystonia (cranial and limb musculature), gait difficulty, slowness of movement, choreoathetosis and tremor. Significant speech disturbance in the form of dysarthria and palilalia can occur. Dysphagia is common and due to rigidity and corticobulbar involvement. Visual impairment due to retinal degeneration and optic atrophy can rarely be the presenting feature of the disease. Seizures have been described. Psychiatric symptoms including personality changes with impulsivity and violent outbursts, depression and emotional lability is also seen. Based on the common clinical features the following criteria have been proposed (Table 2).

Table 1: Showing classification of neurodegenerative disorders with iron accumulation in brain

<table>
<thead>
<tr>
<th>NBIA</th>
<th>EARLY ONSET, RAPIDLY PROGRESSIVE NBIA</th>
<th>LATE ONSET SLOWLY PROGRESSIVE NBIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PKAN</td>
<td>OTHER</td>
<td>PKAN</td>
</tr>
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Table 2: All the obligate findings and at least two of the corroborative findings should be present. None of the exclusionary factors should be present (8).

Obligate features
- Onset during the first 2 decades of life.
- Progression of signs and symptoms
- Evidence of extrapyramidal dysfunction including one or more of the following: dystonia, rigidity, choreathetosis

Corroborative features
- Corticospinal tract involvement
- Progressive intellectual impairment
- Retinitis pigmentosa and/or optic atrophy
- Seizures
- Positive family history consistent with autosomal recessive inheritance
- Hypointense areas on the MRI involving the basal ganglia
- Abnormal cytosomes in the circulating lymphocytes and/or sea-blue histiocytes in the bone marrow

Exclusionary features
- Abnormal ceruloplasmin levels and/or abnormalities in copper metabolism.
- Presence of overt neuronal ceroid lipofuscinosis
- Predominant epileptic symptoms
- Severe retinal degeneration or visual symptoms preceding other symptoms.
- Presence of family history of Huntington chorea or other Autosomal dominant inherited movement disorders.
- Presence of caudate atrophy on imaging studies
- Deficiency of hexosaminidase A
- Deficiency of GM 1 gangliosidase
- Nonprogressive course
- Absence of extrapyramidal symptoms

Hayflick et al studied 123 cases from 98 families and classified
Two Cases of a Rare Treatable Limb Girdle Muscle Disease

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Abstract

We report two cases of limb girdle pattern of muscle weakness caused by hyperparathyroidism due to parathyroid adenoma. It can be easily missed as early symptoms are non specific but once diagnosed it is easily treatable and complete recovery occurs over a period of time.

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disease. Always an attempt should be made to look for treatable cause. Other evidences of endocrine dysfunction, joints, skin and other system involvement, rapid progression, significant pain, constitutional symptoms and well elicited reflexes point to possible secondary cause. It is always important to look for such clues clinically as even laboratory data can be misleading unless they are directed specifically at suspected diagnosis. Here we report two cases of muscle weakness associated with hyperparathyroidism.

Case 1

Thirty two year old female presented with the following history, during July 2005 at Medical College Thiruvananthapuram. Her illness started nine years ago as recurrent dislocation of the patella. This was followed by fatigue, difficulty in climbing up, getting up from sitting posture and frequent buckling. She experienced disabling pain in the infrascapular, sub costal region and low back. This was followed by difficulty in lifting objects and drooping of shoulders (Fig. 1).

She was evaluated at several places with MRI spine, electrophysiological studies and muscle biopsy. Electrophysiology showed mixed picture in the form of positive sharp waves in the resting muscle and motor unit action potentials were showing myopathic picture. Muscle biopsy showed group atrophy (Fig. 2). There were no inflammatory cells. Hence, she was diagnosed as suffering from degenerative muscle disease. However as her symptom was progressive she was brought to Medical College Hospital, Thiruvananthapuram. Examination showed pallor, hyper extensible joints and mild hypertension 150/100mm Hg.

Neurological evaluation showed normal cranial nerves. Her power was grade four proximally and normal distally in the upper limbs and grade three proximally and grade four distally in the lower limbs. There was no wasting, hypertrophy, pseudo hypertrophy or fascication. Deep tendon reflexes were grade three in all groups. Superficial reflexes, organic reflexes, primitive reflexes and sensations were normal. This finding of exaggerated reflexes in the setting of a muscle disease prompted us to examine her thyroid gland. There was a palpable circumscribed swelling about one cm in size seen at the right inferior pole of thyroid gland. She had no goitre.

Her investigations showed normal urine examination, Hb: 9.1gm%, TC: 5600 cells/ cu.mm, Neutrophil 49%, Lymphocyte: 50%, Eosinophil :1%, ESR 40mm/hr. Platelet count 3.2lac/cu mm.

Peripheral smear showed normocytic normochromic anemia, random blood sugar 95mg/dl, urea 30mg, creatinine 1mg, CPK 35 u/lit (25 to 1950),LDH 657 u/l (163-518),alkaline phosphatase 1038 u/lit (15- 1450), serum calcium 1.1mg/dl on admission and when repeated six days later showed 12mg/dl, phosphorus 2mg/dl (2.5 to 4.5). Magnesium levels were not done. Parathormone level was 100 pg/ml (10 to 60). Anti nuclear antibody, Rheumatoid factor, LE cell, Anti double stranded DNA antibody and thyroid functions were normal. ECG and echocardiogram were normal. EMG repeated in our institution showed myopathic pattern in the following sampled muscles, right quadriceps femoris, right biceps, right abductor pollicis brevis and deltoid. Muscle biopsy was not repeated in our department. Muscle biopsy is an invasive procedure and it was not considered necessary in this case, for the following reason. Denervation changes are common in chronically disused muscles. The fast twitch fibres when not put in use undergo atrophy irrespective of the cause of the patients problem, especially type 2 fibres become angular and appear to group themselves. This picture should not be interpreted as anterior horn cell disease without correlating with other phenotypic characters.

Ultrasound scan of thyroid showed 22 x18 mm hypo echoic lesion in relation to posterior and inferior part of right lobe of
thyroid gland and 8 x 6.7 mm lesion with tiny calcification in the left inferior lobe. Ultrasound scan of abdomen showed tiny calcifications involving medullary region and calyces of both kidneys. Para thyroid scintigraphy using 99 MTC- methoxy isobutyle isonitrile showed bilateral inferior parathyroid adenoma; right larger than the left (Fig. 3). X-ray skull lateral view showed classical pepper salt skull (Fig. 4). X-ray pelvis and chest showed diffuse osteopenia involving all bones. There was
narrowing of pubic symphysis (Figs. 5, 6). X ray of both hands showed sub-periosteal bone resorption (Fig. 7).

Patient underwent para-thyroidectomy of both inferior and left superior gland and subtotal thyroidectomy (Fig. 8). Post operatively patient’s serum calcium rose to 13.6 mg/dl and remained at 11 mg /dl until the fourth post operative day. This was treated with 0.9 % Sodium chloride intravenously at 20 ml/kg in the first one hour followed by slow continuous infusion along with 20 mg of Frusemide fourth hourly to facilitate renal excretion of calcium. Reassessment of calcium on the sixth day showed 8.5 mg/dl and patient clinically developed features of hypocalcaemia in the form of muscle cramps. This was treated with 1.5 gms of oral calcium /day. By the end of six months her hypocalcaemia was completely reverted to normal (Fig. 9). Her hypertension was treated with 1.5 gms of oral calcium /day. By the end of six months her phenotypic characters including myopathy completely reverted to normal (Fig. 9). Her hypertension was treated with beta blockers which could be withdrawn after few months completely.

Case 2

Twenty year old female was treated with plaster of paris cast for a fracture which she sustained in the lower end of right femur following a fall in the year 1999. Two months later when she started bearing weight it was found that she could not get up from sitting posture and was buckling while standing. She had a collapsing chest cage with limb girdle pattern of weakness. Her deep tendon jerks were exaggerated and superficial reflexes were normal. She had no cranial nerve palsy or sensory symptoms. She had normal thyroid gland with a palpable nodule about one centimeter in size in the left inferior pole. Ultra sound scan abdomen showed bilateral stag horn calculi. Skeletal survey showed diffused osteopenia. Her serum calcium was 11.6 mg per and phosphorus 2.1 mg/dl, parathormone level 110 pg/dl. She opted to undergo surgery at her native state. However it was reported that in the postoperative period she went in stupor and could not be saved. No pictures with reference to this patient is available. In view of the unfortunate eventuality which happened to this patient.

Discussion

The most common manifestation of primary hyperparathyroidism is asymptomatic hypercalcemia accidentally detected. Severe bone and stone disease is seen in places where hypovitaminosis D exists. The symptoms and signs are due to the combined effect of increased parathormone secretion and hypercalcemia. Non specific symptoms like fatigue, anorexia, depression are common² Five percent of patients present with bone disease and 15 to 20% with nephrolithiasis.³

The neuromuscular syndrome associated with hyperparathyroidism is extremely rare. Clinically exaggerated reflexes and histopathologically type II fibre atrophy can be seen.⁴ Neuropsychiatric manifestations in the form of lethargy, depressed mood, and cognitive decline can occur. However improvement after surgery is variable. Fractures are common at distal forearm, pelvic and vertebra. Bone thinning due to endosteal bone resorption appears to be the cause.

Hypertension is a common association with hyperparathyroidism.⁵ Left ventricular hypertrophy and diastolic dysfunction are also known. However, evidence for improvement of these features after surgery is lacking. Rheumatological complications in the form of pseudo gout with pyrophosphate crystals in the joints hyper uricemia, gout and calcifications of articular cartilage are common.

Severe classical hyperparathyroidism is associated with increased mortality due to cardiovascular disease. There is a small increase in the risk of death from cancer Parathyroid crisis is severe hypercalcemia with serum calcium more than 15 mg/dl and central nervous system dysfunction in the form of coma and confusion.⁶ This can be precipitated by associated inter current infection and dehydration.⁷

The pathogenesis of neuro-muscular complications have been described. Serum phosphate concentration decreases because parathormone inhibits proximal tubular reabsorption of phosphate leading to increased phosphate excretion. This is due to decreased activity of sodium phosphate co-transporter in the luminal membrane. So entry of filtered phosphate into tubular cells and its return to systemic circulation is reduced. Hypophosphatemia limits the phosphorylation reaction and synthesis of ATP in muscles and this leads to weakness.⁷ Hypocalcaemia is expected due to reuptake of calcium in to the hungry bones once parathormone level comes down.

Limb gridle pattern of muscle weakness occurs in a vast majority of conditions. Painless non selective wasting, weakness, areflexia, fasciculations, and tremors with normal muscle enzymes, denervation pattern in EMG and biopsy suggest spinal muscular atrophy. Painless muscle weakness with selectivity pseudo hypertrophy, retained ankle jerk, abnormal muscle enzymes, myopathic pattern in EMG and biopsy suggest dystrophic muscle disease. Painfull muscle weakness with brisk reflexes, mild to moderate enzyme changes, inconclusive electrophysiology and histology with evidence for other system involvement should alert the physician regarding treatable muscle disease.

Lessons Learnt

Primary hyperparathyroidism is a condition to be remembered in patients with muscle weakness and exaggerated reflexes. As the symptoms and signs can be evasive, diagnosis can be easily missed. If not treated on time multisystem involvement occurs and can result in mortality. Denervation pattern in EMG can be seen in less used muscle and does not always indicate anterior horn cell disease. Immediate post operative hypercalcemia and later hypocalcemia are expected complications and should be managed adequately.

Conclusion

Whatever may be the duration of the illness when unusual features complicate common illnesses, it’s always worthwhile to look for less common and treatable factors. Primary Hyper parathyroid myopathy is a relatively less common limb girdle muscle disease which presents with exaggerated muscle weakness and is completely reversible with surgery of parathyroid adenoma.

References

SC Chaudhary*, SK Sonkar*, Vivek Kumar*, Abhinav Gupta**

Abstract
Falciparum malaria is a common disease in tropical countries associated with myriad of complications that can be life-threatening. We hereby report an 85 year old male who was suffering from falciparum malaria and presented with subdural hematoma, an unusual complication of central nervous system secondary to severe thrombocytopenia.

Introduction
Malaria is common health problem in India and contributes about 80% of the total cases in South East Asia. Falciparum malaria is known for its various complications including cerebral malaria, severe anemia, thrombocytopenia, acute renal failure, acute lung injury, jaundice, hypoglycemia, and circulatory collapse. Hemorrhagic central nervous system complication secondary to thrombocytopenia is unusual.

Case Report
An 85 year old male presented with complaints of high grade fever associated with chills and rigor for seven days and altered sensorium for one day. He was known hypertensive for last 3 years for which patient was on irregular treatment. There was no history of trauma or any addiction. On examination patient was altered (GCS E4M5V2), moving all four limbs on deep painful stimuli, planter reflexes were non elicitable bilaterally and there was no any apparent neurological deficit. His blood pressure was 150/80 mmHg, pulse rate 80/min, other general and systemic physical examination were normal. Investigation revealed hemoglobin 6.9gm%, total leukocyte count 8900/mm³ (Neutrophil – 93%, lymphocyte – 4%, eosinophil- 3%), platelet count 10000/mm³, blood urea 145.3mg/dl and serum creatinine 2.88mg/dl. Liver function test, prothrombin time, bleeding time, coagulation time, random blood sugar, and serum electrolyte were normal. IgM antibody for dengue fever was negative and ELISA for malaria parasite was positive for Plasmodium falciparum. Contrast enhanced computed tomography head showed crescentic shaped subdural mass on right side suggestive of subdural hematoma with compression of sulci, gyri and lateral ventricle (Fig. 1). Patient was diagnosed as a case of complicated malaria, started on injection artesunate along with other conservative measures and four units of platelets and two units of whole blood were transfused. Despite all these patient had not shown any improvement, platelet count was decreased to 1000/mm³ and subsequently patient expired on third day of hospitalization.

Discussion
Malaria is one of the most common diseases in tropical countries. It has a myriad of presentations and complications with cerebral malaria being one its most devastating and lethal sequelae. Cerebral malaria usually manifests as diffuse symmetric encephalopathy but can lead to a variety of complications including hemiplegia, convulsions, delirium and death. Hematological alterations are frequent in patients with malaria and thrombocytopenia is the commonest one. The exact mechanism of thrombocytopenia is not known but there are certain speculations including immune mechanisms, oxidative stress, alterations in splenic functions and a direct interaction between plasmodium and platelets.1 Hematological alterations rarely manifest clinically. We are presenting a rare case of spontaneous subdural hematoma in a case of falciparum malaria.

The occurrence of intracerebral hemorrhage or spontaneous subdural hematoma is a rare complication in malaria. It is likely that subdural hematoma in our patient was contributed by the thrombocytopenia as there was no history of trauma. On extensive search we have find only few cases of falciparum malaria associated with haemorrhagic complications including subarachnoid haemorrhage,2,3 cerebral haemorrhage,4 subdural empyema5 and bilateral subdural hematoma.6
Conclusion

Despite several strategies for malaria prevention and control, malaria continues to pose several public health challenges in the developing world. This case has been reported to illustrate the occurrence of rare and alarming complications in our patient. An open and inquisitive approach to the multiple symptoms of patients presenting with malaria would enable the prompt recognition of these complications and a successful outcome.

References


Atypical Central Nervous System Involvement in Acute Organophosphorous Poisoning

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Abstract

Extrapyramidal syndrome is an uncommon sequelae of acute organophosphorous (OP) poisoning. It is a manifestation of the intermediate syndrome described in OP poisoning. It may or may not be associated with neuroimaging changes in the striatum. We present a case of acute OP poisoning with interesting positive CT scan findings.

Introduction

Three distinct phases of neurological illness following OP poisoning have been described. Type I is described as an acute paralysis secondary to continued depolarization at the neuromuscular junction. Type II (intermediate syndrome) was described in 1974; it is reported to develop 24-96 hours after resolution of the initial phase. It is characterized by weakness of proximal muscles, cranial nerve palsies and may require mechanical ventilation. Extrapyramidal symptoms, a part of intermediate syndrome, are characterized by dystonia, cogwheel rigidity and parkinsonian features. Type III or organophosphate-induced delayed polyneuropathy (OPIDP) occurs 2-3 weeks after exposure. Chronic organophosphate-induced neuropsychiatric disorders (COPIND) have also been reported though the mechanism is not known.

Case Report

A 28 year old female patient presented in the emergency with deliberate ingestion of pesticide containing Dimethoate, an organophosphorous compound. She was unconscious with frothing from mouth, and had fasciculations over both upper and lower limbs. Clinical examination revealed bilateral constricted pupils, bronchorrhoea, blood pressure of 110/80, pulse 68/min, regular, equally palpable in all extremities. Respiratory rate was 20/min with bilateral vesicular breath sounds on chest auscultation. Heart sounds were normal with non responsive plantar response bilaterally.

She was administered atropine and pralidoxime, and shifted to the intensive treatment unit. She regained consciousness on the 2nd day and was never required to be put on the ventilator. The patient was restless and developed psychotic symptoms on the 3rd day of admission. Considering atropine toxicity the drug was tapered with relief of the symptoms. From the 5th day onwards she started having behavioral abnormalities characterized by non-cooperation, slight disorientation and less interaction with others and surroundings. It was associated with dystonia of both the upper limbs. Neurological examination was unremarkable except for cogwheel rigidity of all four limbs. Plantar reflex was flexor on both sides. Kayser-Fleisher ring was absent. She had no past history of psychiatric disorders, convulsions, toxin
exposure, jaundice, fever, arthralgia, rashes, cardiac disorders or drug exposure (metoclopramide, neuroleptics).

Laboratory investigations were unremarkable with mild anemia, leukocyte count of 12,500/mm³, platelet count of 1.80 lac/mm³; blood sugar, serum urea and creatinine along with liver function tests were within normal limits. Antiinflammatory factor was found to be negative. Chest radiography, echocardiography, carotid Doppler, abdominal ultrasound were normal. Plain CT scan of brain showed bilateral symmetrical caudate nuclei and putaminal infarcts (Fig. 1), which was most likely to be due to OP poisoning in the present perspective. She was prescribed amantadine and trihexyphenidyl. Subsequently MRI was advised but the patient was lost to follow up.

Discussion

Extrapyramidal symptoms in the form of parkinsonism with or without involvement of the basal ganglia have been reported. It was first reported by Bhatt et al in 1999. Bilateral symmetrical involvement of the basal ganglia owing to OP poisoning is rare. A research on 30 healthy cats following OP poisoning was done in China showing symmetrical bilateral involvement of the basal ganglia.

In the above case the patient had behavioral changes along with extrapyramidal symptoms following OP poisoning. A plain CT scan showed bilateral symmetrical caudate nuclei and putaminal infarcts. Basal ganglia infarcts are rare as an entity and are much more so as an effect of OP poisoning. Symmetrical basal ganglia involvement may occur due to metabolic disorders like Wilson’s disease, Hallervorden–Spatz, methylmalonic acidemia, hypoxic insults, emboli or toxins like methanol, cyanide, carbon monoxide and toluene. Moreover, studies using ⁹⁹mTc- hexamethylpropylene amine oxime (Hm PAO) brain single photon emission computed tomography have evaluated the changes in acute phase SPECT findings with the neuropsychological sequelae in OP and carbon monoxide poisoning, SPECT findings demonstrated the involvement of the frontal and temporal lobe in patients displaying disorientation, fronto-parietal changes in patients manifesting confusion. Parkinsonian features were found in patients having changes in parieto-occipital, parietal and frontal lobe. In our patient there was involvement of bilateral basal ganglia. SPECT study was not possible in our setup.

In the present case, there was no episode of hypotension, features of vasculitis or any source of emboli to account for the CT scan findings. Our patient was also not exposed to any of the toxins mentioned above. The authors think that the most likely etiology of the bilateral symmetrical caudate nuclei and putaminal infarcts in this case was due to OP poisoning and intense literature search did not reveal documentation of this type of case presentation in the past.

Conclusion

In the setting of extrapyramidal manifestations following OP poisoning the authors recommend that neuroimaging studies be performed to rule out basal ganglia infarct.

References


Sturge Weber Syndrome

SC Chaudhary*, SK Sonkar*, Vivek Kumar*, Sandeep Golchha**

Abstract

Sturge Weber Syndrome also called as encephalotrigeminal angiomatosis is a sporadically occurring neurocutaneous syndrome, characterized by vascular malformation with capillary venous angiomas that involve face, choroid of eye and leptomeninges with resulting neurological and orbital manifestations. We hereby report a young unmarried girl who diagnosed as a case of SWS on the basis of Port wine stain since birth, past history of seizures since the age of four years and at this time presented with status epilepticus, mental retardation (I.Q - 30 to 35), EEG abnormality and characteristic imaging findings. This may be a common condition for paediatrician and neurologist but as a physician we usually do not see it that often.

Introduction

The Sturge-Weber syndrome (SWS), also called encephalotrigeminal angiomatosis, is a neurocutaneous disorder with angiomas involving the leptomeninges and skin of the face, typically in the ophthalmic (V1) and maxillary (V2) distributions of the trigeminal nerve. Neurological manifestations include seizures (partial /generalized), focal deficits,developmental disorders, including developmental delay, learning disorders, and mental retardation with involvement of ipsilateral eye leading to buphthalmos and glaucoma. The diagnosis of SWS is considered in a child with facial naevus flammeus and seizure but in the absence of cutaneous manifestations the diagnosis remains elusive. Radiological investigations are most useful in such circumstances.
and ocular abnormalities. Its exact incidence is not known and 

outcomes. Once the diagnosis is made early and effective 
imaging (MRI) playing a pivotal role in demonstrating the 
cerebral changes. Once the diagnosis is made early and effective 
seizure control is mandatory for an improved prognostic 
outcome.

Case Report

We hereby report a 16 year old female who had history of 
generalized tonic clonic seizures since 4 years of age presented 
presented to our department in status epilepticus. There was no 
history of fever, headache or vomiting and patient attendant also 
denied from any history of tuberculosis. On examination she had 
Port Wine Stain on right side of face involving V1, V2 and V3 
divisions of trigeminal nerve (Fig. 1). She was deeply comatose, 
maintaining her vitals and signs of meningeal irritation were 
absent. Rest of the general and systemic examinations were 
normal. Based on the above clinical findings we kept the 
possibility of Sturge Weber Syndrome and she was managed 
on the lines of status epilepticus with phenytoin. Subsequent 
investigations revealed normal haemoglobin including platelet 
counts, normal liver and kidney function tests, random blood 
sugar and normal serum electrolytes including calcium level. 
Chest radiograph and ultrasound abdomen were also normal 
and ELISA for HIV was non-reactive. Ophthalmic examination 
revealed dilated episcleral vessels in right eye but on gonioscopy 
examination angle was normal with normal intra-ocular 
pressure. CT head showed gyriform calcification in right parieto- 
temporal region with surrounding atrophy & thickening 
of calvarium. MRI showed Atrophy of right cerebral hemisphere 
with hypertrophy of ipsilateral skull, hypertrophy of choroid plexus 
in right lateral ventricle and calcified angioma in right parieto-
temporal convexity.

Discussion

SWS is a phakomatosis characterized by a port wine stain 
(PWS) over the trigeminal area, leptomeningeal angiomatosis 
and ocular abnormalities. Its exact incidence is not known and 

has no racial or sex predilection. Typically patient presents at 
birth with facial angiomas, however the reverse is not always 
true. Facial naevus flammeus (Portwine stain) is a congenital 
macular lesions which may be initially light pink turning dark 
purple and thicker later on. PWS involves the area of distribution 
of trigeminal nerve. Those with involvement of entire first 
division of trigeminal nerve have highest risk of associated SWS. 
Neurological outcome in children with SWS is highly variable, 
ranging from minimal or no neurological signs to a devastating 
impairment with uncontrolled seizures, hemiparesis, visual 
field defect and progressive mental retardation. Seizures is a 
very common feature, often occurs during the first year of life
and result from cortical irritability caused by angioma through 
the mechanism of hypoxia, ischaemia and gliosis. About 80% of 
affected persons have focal seizures involving the contralateral 
side of the portwine stain. The hypoperfusion of cortical tissue is 
then further accelerated by seizures, thereby worsening the prognosis. Developmental delay and mental retardation are almost always 
associated with seizures. The main ocular manifestations 
buphthalmos and glaucoma occur due to secondary increase 
in intraocular tension due to increased secretion of aqueous 
humor by choroidal haemangioma. Glaucoma and buphthalmos 
typically occur when portwine stain involves eyelids. It can 
develop at any age, is usually unilateral and ipsilateral to 
portwine stain. Other features include visual loss, macrocephaly 
and hemiatrophy.

Neuroimaging studies help to establish the diagnosis, assess 
severity and follow the progression of brain involvement in SWS, 
although CSF analysis may reveal elevated protein due to micro 
aemorrhages. Skull films may reveal tram track calcification 
caused by calcification in apposing gyri, ipsilateral calvarial 
thickening and enlargement of the paranasal sinuses and mastoid. 
Cranial CT demonstrates abnormal contrast enhancement of 
angioma, enlarged choroid plexus ipsilateral to the angioma and 
aves. Cortical atrophy underlying the angioma with gyriform “tram track” 
calcification is the characteristic imaging feature. Calcification 
however is unusual before 2 years of age and most commonly 
involves the parietal and occipital lobes. MRI is the current 
“gold standard” for diagnosis of disease which is reliable even 
in very young infants. MRI demonstrates thickened cortex,
decreased convolutions, abnormal white matter and gadolinium enhancement of leptomeningeal angiomma. Sinovenous occlusion can be seen on MR Venography. Angiography reveals lack of superficial cortical veins and nonfilling of dural venous sinuses with abnormal tortuous vessels that course towards the vein of Galen. Other vascular abnormalities demonstrated on angiography include thrombotic lesions and arteriovenous malformations. MRI abnormalities are correlated, to a certain extent, with the severity of neurological symptoms. However, they are not reliable predictors of neurological deficit in the early stage of the disease. Functional cerebral studies using PET and SPECT have shown abnormalities of metabolism and perfusion in SWS. A study of cerebral blood flow using SPECT in very young infants with SWS revealed a specific functional pattern before the onset of seizures and they suggested that seizures are responsible for decreased flow of blood to underlying cerebral cortex and thus epilepsy acts as an additional worsening factor in SWS.

Medical management of Sturge Weber Syndrome includes treatment for seizures, treatment for glaucoma with carbonic anhydrase inhibitors, β- antagonists to prevent optic nerve atrophy and use of aspirin for headache and to prevent vascular disease. Portwine stain requires treatment with pulsed tunable dye laser which should be started as soon as possible. Patients with rapidly progressive convulsive disorders that are recalcitrant to treatment should be considered for surgical extirpation of the affected lobe or hemispherectomy. Early surgery has been advocated for better seizure control, to improve outcome and prevent developmental delay.

**Conclusion**

To conclude, the diagnosis and management of patients with Sturge Weber syndrome requires the combined skills of a physician, radiologist and a psychologist. Seizures play a major role in failure of mental development and deterioration of mental function, hence effective seizure control is mandatory.

**References**


A Pandeya, SK Das, P Kumar, M Kumar, D Meena, V Garg

**Milwaukee Shoulder Syndrome**

**Abstract**

Milwaukee shoulder syndrome or rapid destructive arthritis of the shoulder; is a particular form of arthritis which affects mainly elderly patients, predominantly women, with limited pain and sometimes neuropathic joints, rotator cuff tear, joint instability, mildly inflammatory or noninflammatory, blood-stained effusion, calcium apatite crystals, and marked joint and bone destruction. This is very uncommon condition and very sparsely reported and so far, there is no case report from India, hence, we report a case of Milwaukee shoulder syndrome from India.

**Introduction**

Milwaukee shoulder is a rapid destructive arthritis of the shoulder, although uncommon, has received much attention in the recent medical literature. It has been described by several authors under varied names: hemorrhagic shoulder of the elderly, Milwaukee shoulder syndrome, rapid destructive arthritis of the shoulder, apatite-associated destructive arthritis and idiopathic destructive arthritis of the shoulder.

**Case**

A 65-year-old woman presented with painless right shoulder swelling which was painful to start with, extending up to the arm and chest wall (Fig. 1). Active range of motion was severely restricted. Radiographs of the shoulder showed a destructive lesion in the greater tuberosity with displacement of the humeral head. Laboratory investigations revealed elevated erythrocyte sedimentation rate and C-reactive protein. A biopsy of the shoulderjoint showed findings consistent with Milwaukee shoulder syndrome. The patient was treated with intravenous antibiotics and physical therapy. The shoulder improved significantly after the treatment.

![Figure 1](image_url)
limited and passive mobility largely unrestricted. She had had no history of recent trauma to the shoulder area, diabetes and syphilis. Arthrocentesis yielded a hemorrhagic noninflammatory fluid; intra and extracellular non-birefringent globules or aggregates of calcium apatite crystals that stain bright red with alizarin red S were seen on polarized microscopy. All cultures were negative, and cytological analysis did not reveal any malignant cells. Radiography of the right shoulder was suggestive of degenerative arthritis and lateral distention of the sub acromial bursa (Fig. 2). MRI (Right shoulder joint) revealed effusion, debris and loose bodies within right shoulder joint with disarticulation, resorption of right humeral head and erosion at acromioclavicular joint with atrophy of surrounding muscles (Fig 3). VDRL was negative and MRI (spine) was normal.

Discussion

Milwaukee shoulder syndrome occurs in the elderly patients in the age group of (60-90 years). There is female preponderance in the ratio of 4:1, but this might be due in part to their greater longevity. Unilateral shoulder joint involvement is more common & seen on dominant side but in bilateral involvement, disease process is almost uniformly more advanced on the dominant side. Long history of painful shoulder with restricted movements is present. Radiographic changes include degenerative changes in glenohumeral joint with rupture of the rotator cuff. Synovial fluid aspirated is typically bloody, noninflammatory and positive for calcium apatite crystals. Damage to rotator cuff precedes crystal deposition and shedding of crystals is responsible for sudden, acute episodes of inflammation. Unique feature in

References