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National Immunization Program in India

It is well established that immunization program is one of the most effective public health interventions. Widespread immunization is the mainstay in reduction of morbidity and mortality due to various vaccine preventable diseases world over. Globally, vaccination programs prevent more than 2.5 million child deaths each year. Vaccination programs are the most cost effective health investment. The success of global smallpox eradication in 1980s and subsequent eradication of polio from most part of the world are testimony of the positive impact of immunization programs across all countries. Unvaccinated and incompletely vaccinated children are most susceptible to childhood diseases and disability; they have three to six times higher risk of death as compared to fully immunized children.

Introduction of a new vaccine in the National Immunization Program is associated with a lot of programmatic implication, particularly in a huge and geographically diverse country like India. It is essential to ensure safe and effective vaccines. Certain criteria should be considered before introduction of new vaccines in UIP:

i) Disease burden

ii) Safety and efficacy of the vaccine

iii) Program capacity to introduce a new antigen including cold chain capacity

iv) Affordability and financial sustainability of vaccination program

v) Availability of domestic or overseas vaccine supply

vi) Cost effectiveness of vaccination program

NTAGI is a group of experts of vaccination and immunization related fields in India. The NTAGI was constituted in 2001 and it was reconstituted in 2010. Following analysis of the entire perspective NTAGI advises the National Government regarding the technical issues related to the vaccination and immunization appropriate for India. Primarily the guidelines of international bodies like World Health Organization Strategic Advisory Group of Experts (WHO - SAGE) are considered for vaccine introduction. The technical decision of NTAGI is considered by Immunization division, Ministry of Health and Family Welfare (MOHFW), Govt. of India for any vaccine introduction.

The chronology of immunization program in India is shown in table 1.

Table 1. Immunization program in India

1978	Expanded Program on Immunization (EPI): BCG, DPT, OPV, Typhoid-Paratyphoid Vaccines (in urban areas) for children up to 5 years
1983	TT Vaccine for pregnant women
1985	Universal Immunization Program (UIP) – Measles added, typhoid-paratyphoid vaccine removed

Cont...

1995	Polio: National Immunization Days (NIDs) or Pulse Polio Immunization (PPI)
1997	VVM introduced on vaccines in UIP
2002	Hepatitis B vaccine introduced in UIP in selected areas
2005	• National Rural Health Mission launched • Auto Disable (AD) syringes introduced in UIP
2006	JE vaccine introduced after campaigns in endemic districts
2007-08	Hepatitis B vaccine expanded to all districts in 10 states and schedule revised to 4 doses from 3 doses
2010	Measles 2nd dose introduced in RI and Measles Catch-up Mass Campaigns (14 states)
2011	• Hepatitis B universalized to all states • *Haemophilus influenzae* type-b vaccine introduced as Pentavalent vaccine in 2 states • Open Vial Policy introduced for vaccines in UIP
2013	• Pentavalent vaccine expanded to 9 states • Second dose of JE vaccine introduced
2014	India and South East Asian region certified as polio free
2015	• India validated for Maternal and Neonatal Tetanus elimination (MNTE) • Pentavalent expanded to all states • IPV introduced • New vaccines introduction announced – Rotavirus, Pneumococcal Conjugate Vaccine (PCV) and Measles-Rubella (MR)
2016	• Rotavirus vaccine introduced in 4 states in Phase I • National Switch Day: 25 April 2016 (tOPV to bOPV) • 2 doses of fractional IPV (intradermal route) introduced in selected states (16 states / UT)
2016	• PCV13 introduced in phase manner in various states

The Expanded Program on Immunization (EPI) was launched in India in 1978. It included BCG, OPV, DPT and Typhoid-paratyphoid vaccine. Subsequently, Typhoid-paratyphoid vaccine was removed from the schedule in 1981.

The program was renamed as Universal Immunization Program (UIP) in 1985. Measles vaccine was introduced in the schedule. The main aim of UIP was to achieve 100% coverage of pregnant women with 2 doses of tetanus toxoid (or a booster dose) and at least 85% coverage of infants with 3 doses each of DPT, OPV, one dose of BCG and one dose of measles vaccine by the year 1990. The main focus was to achieve reduction in mortality and morbidity due to six vaccine preventable diseases in the country.

In 1992 Child Survival and Safe Motherhood (CSSM) program was formed by merger of UIP and the Safe Motherhood program. In 1997 the program was renamed as the Reproductive and Child Health (RCH) Program. In 2005 UIP became a part of the National Rural Health Mission (NRHM).

No vaccine was added in the national immunization program for 16 years since UIP. Hepatitis B vaccine was introduced on pilot basis during the year 2002-03. Subsequently Japanese Encephalitis (JE) vaccine was introduced on priority basis in JE endemic districts in 2006.

Second dose measles vaccination in the UIP schedule was introduced in India in 2010 following the

recommendation of National Technical Advisory Group on Immunization (NTAGI).

Haemophilus influenzae type B (Hib) vaccine was introduced in December 2011 in phased manner as Pentavalent vaccine (DPT, Hepatitis B, Hib) and it was gradually implemented in all states by the end of 2015.

WHO-SAGE recommended withdrawal of Polio virus type 2 vaccine from the Oral Polio Vaccine (OPV) used all over the world. Global decision was to switch over from trivalent OPV (tOPV) to bivalent OPV (bOPV) containing type 1 and type 3 vaccine viruses. WHO issued guidelines to all the 156 OPV countries to switch from tOPV to bOPV and to finalize the National Switch day. India decided 25 April 2016 as National Switch day. Prior to the National Switch day, at least one dose of IPV in addition to OPV was recommended to all exclusive OPV using countries as risk mitigation against type 2 virus. But this could not be achieved in practice. Subsequently IPV was introduced in the National Immunization Program mainly as fractional dose of IPV (fIPV) through intradermal route administered over right deltoid region.

Rotavirus vaccine was administered as three dose schedule at 6, 10 and 14 weeks along with Pentavalent, bOPV. IPV was initially introduced in 4 states, Andhra Pradesh, Odisha, Himachal Pradesh and Haryana in February 2016. Subsequently it was introduced throughout India.

Measles Rubella (MR) vaccine replacing both doses of the Measles Containing Vaccine (MCV) at 9 months and 16-24 months was introduced. The main aim was to account for any potential paradoxical increase in cases of Congenital Rubella Syndrome (CRS). MR vaccine campaigns targeting all individuals from 9 months up to 15 years of age in the country were conducted.

National Technical Advisory Group on Immunization (NTAGI) recommended phased introduction of Pneumococcal Conjugate Vaccines (PCVs) at 6 weeks, 14 weeks and 9 months of age. PCV13 vaccine was preferred based on prevalent serotypes in India.

National Immunization Schedule

Age	**Vaccine**
At birth	BCG, OPV-0, Hep B-birth dose
6 weeks	OPV1, Penta1, fIPV1, Rota 1, PCV13
10 weeks	OPV2, Penta2, Rota 2
14 weeks	OPV3, Penta3, fIPV2 / IPV, Rota 3, PCV13
9-12 months	MR 1, PCV13 booster, JE1 (where applicable)
16–24 months	MR 2, DPT first booster, OPV booster, JE2 (where applicable)
5-6 years	DPT second booster
10 years	Td
16 years	Td

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Raised Intracranial Pressure and Management

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Introduction

Increased intracranial pressure (ICP) is a Life threating situation. It can be seen in emergency with both traumatic and non-traumatic neurological illnesses. After the primary insult, secondary injury by brain shift and cerebral ischemia leads to poor outcomes. Management of raised ICP is the cornerstone of neuro-critical care. It accounts for about 20% of all admissions to PICU of Indian setting.

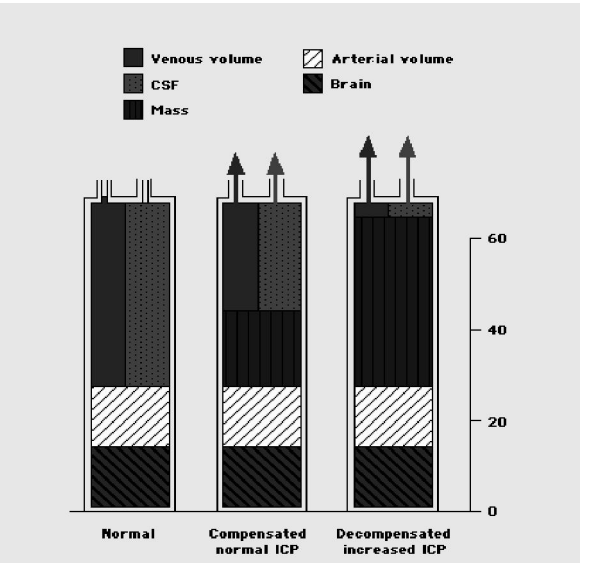
Intracranial physiology

According to Monro-Kellie doctrine, the total volume within the skull remains constant and is determined by the sum of the brain tissue compartments (≈80%), blood (≈10%) and cerebrospinal fluid (≈10%). The volume of these intracranial compartments is tightly regulated, and cerebral blood flow (CBF) is kept constant by vasoconstriction and/or vasodilatation cascades of the cerebral vessels despite fluctuations in systemic blood pressure called as autoregulation. When additional volume is added to the compartment, one or more of the other components must decrease to keep ICP constant .

Cerebral Blood Flow (CBF) and cerebral autoregulation

The brain receives between 15% and 25% of the cardiac output. In adults CBF is 50-70 ml/100g/min, whereas it is 40 ml/100g/min in neonates and as high as 108 ml/100g/min in children[7]. The critical threshold for ischemia is 5 – 10 ml/100g/min in the infant and children.

The process whereby the cerebral arteries (specifically arterioles) maintain a constant blood flow (CBF) in the face of changing cerebral perfusion pressure (CPP) is referred to as cerebral pressure autoregulation. As shown in figure 2, between CPP pressures of 50–150mm Hg CBF is relatively



Intracranial compensation for an expanding mass lesion
Data from Pathophysiology and management of the intracranial vault. In: Textbook of Pediatric Intensive Care, 3rd ed, Rogers, MC (Ed), Williams and Wilkins 1996. p. 646; figure 18.1.

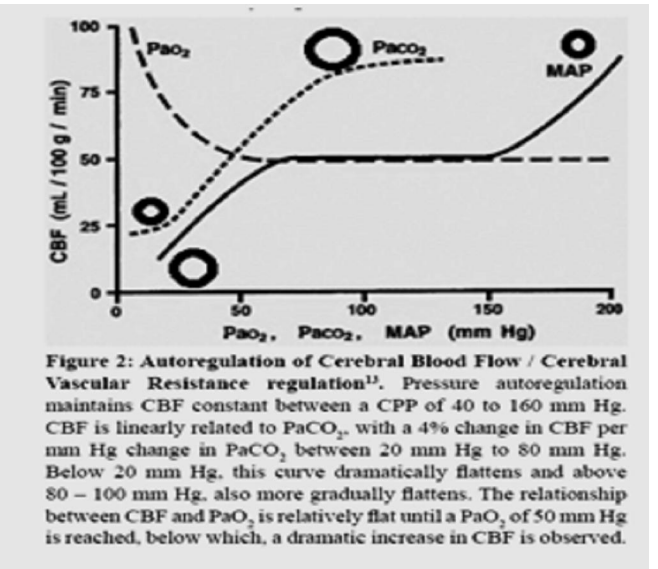


Figure 2: Autoregulation of Cerebral Blood Flow / Cerebral Vascular Resistance regulation[13]. Pressure autoregulation maintains CBF constant between a CPP of 40 to 160 mm Hg. CBF is linearly related to $PaCO_2$, with a 4% change in CBF per mm Hg change in $PaCO_2$ between 20 mm Hg to 80 mm Hg. Below 20 mm Hg, this curve dramatically flattens and above 80 – 100 mm Hg, also more gradually flattens. The relationship between CBF and PaO_2 is relatively flat until a PaO_2 of 50 mm Hg is reached, below which, a dramatic increase in CBF is observed.

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Table 1. Intracranial pressure (ICP) Values

Normal	Abnormal
• Infant : < 5 mm • Children : 5- 8 • Older children : 8 -12	• > 20 for > 5 min is seriously high • Sustained ICP >40mm Hg Life threating If symptoms and signs of raised ICP are present, consider that ICP is more than 20 mmHg and treat accordingly. CPP = 50 – 70 mm Hg

Table 2. Common causes of raised ICP

A. Increase in Brain Volume	Cerebral edema: Primary CNS illness	Encephalitis, meningitis, Head injury, Reye's syndrome
	Cerebral edema: Secondary to systemic illness:	Hypoxic ischemic injury, ischemic stroke/ infarct, metabolic encephalopathy– hyperpyrexia, hepatic failure, lead intoxication
	Space-occupying lesions:	Hematomas, tumors, abscesses
B. **Increase in Blood Volume**	Venous obstruction- Cerebral venous sinus thrombosis Hemorrhage Vasodilatation: Due to hypoxia, drugs orhypercapnia Status epilepticus.	
C. **Increases in CSF Volume**	Obstructive hydrocephalus, Communicating hydrocephalus . Impaired reabsorption: Subarachnoid hemorrhage. Increased production: Tumors	

constant; above and below these values, however, CBF varies markedly with CPP.Cerebral autoregulation is primarily determined by PaCO2, MAP, and to a lesser extent, by PaO2, adenosine, pH, etc. Figure 2. CBF fluctuate by 4% for each mmHg change of CO2. However, when the upper or lower limits of these autoregulatory mechanisms are exceeded, CBF becomes absolutely dependent on MAP. ICP values and common causes of raised ICP are shown in Table 1 and 2.

Approach and management

All patients with an modified Glagow Coma Score (m-GCS) =8 (Table 3) are likely candidates for raised ICP. Urgent neuro-imaging may be needed, after stabilization of airway, breathing and circulation and reversing potential or clinically manifest herniation, to rule out surgically correctable causes of raised ICP.

Clinical features

Irritability, headache, vomiting, confusion and decreased alertness, and neck retraction. These are neither sufficiently sensitive nor specific. Tense fontanel on palpation and papilledema, are reliable signs of raised ICP, but the later is usually absent in acute conditions.

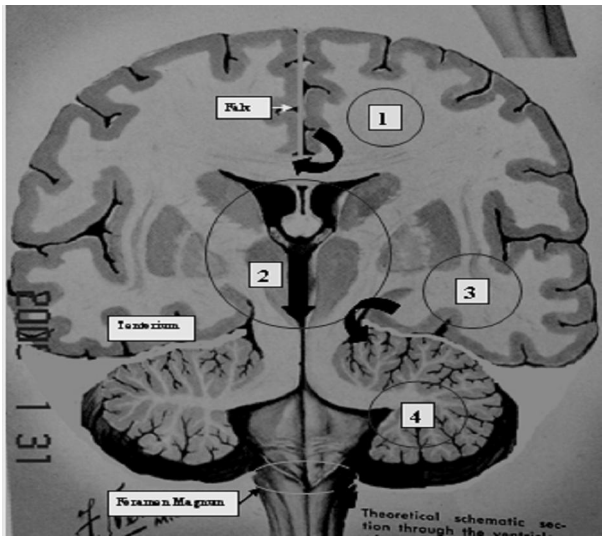
Table 3. Modified Glasgow Coma Scale

Modified Glasgow Coma Scale for Infants and Children

	Child	Infant	Score
Eye opening	Spontaneous To speech To pain only No response	Spontaneous To speech To pain only No response	4 3 2 1
Best verbal response	Oriented, appropriate Confused Inappropriate words Incomprehensible sounds No response	Coos and babbles Irritable cries Cries to pain Moans to pain No response	5 4 3 2 1
Best motor response*	Obeys commands Localizes painful stimulus Withdraws in response to pain Flexion in response to pain Extension in response to pain No response	Moves spontaneously and purposefully Withdraws to touch Withdraws to response in pain Abnormal flexion posture to pain Abnormal extension posture to pain No response	6 5 4 3 2 1

*If patient is intubated, unconscious, or preverbal, the most important part of this scale is motor response. Motor response should be carefully evaluated.

Overt Sign of Raised ICP- The Herniation Syndromes (fig 3).



1.Subfalcine –	Small Reactive Pupil. Headache.Contra lateral Leg Paralysis
2. Central herniation	Early coma, Cushing triad, Mid dilated fixed pupil, Decorticate posturing., Cheyen – stroke respiration
3. Uncal herniation	Variable consciousness, Ipsilateral pupil dilation, Ext ophthalmoplegia Contralateral hemiphresis , Decerebrate posturing'.
4 Trans foraminal	**Cushing triad, Coma, Respiratory arrest .**

Fig 3. Overt sign of raised ICP - the herniation syndromes

Neuroimaging

Head CT on admission, after stabilization.

Repeat imaging within the first 24 hours, or more emergently if new symptoms or signs appear.

CT scan signs (fig 4)

CT scan may be normal even in the presence of documented raised ICP (> 20 mm Hg) in 25% of patients.

1. Loss of sulci, slit-like ventricle,
2. Loss of gray-white distinction
3. Obliteration of suprasellar and quadrigeminal cistern.
4. Hematoma, mass, midline shift

Targets of management

Intracranial pressure monitoring (fig 5):

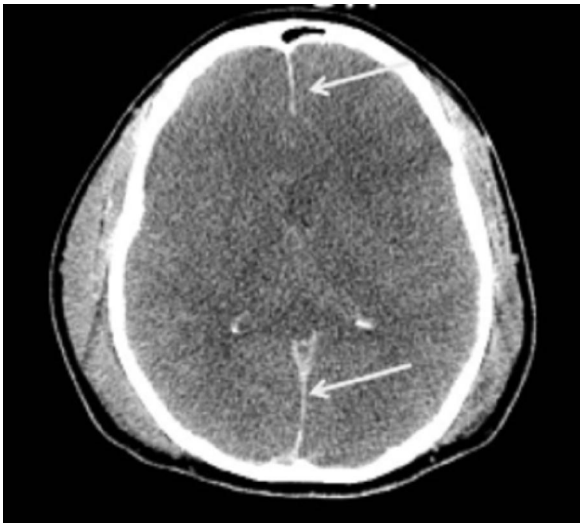


Fig 4. CT scan - Loss of sulci, slit-like ventricle, hematoma with midline shift

- Clear goals of therapy
- Monitor CPP
- Early identification of refractory cases for more aggressive interventions.
- Most of the literatures are on traumatic brain injury.
- Not available in most of the centers in our country.

Indications of ICP monitoring

Traumatic brain injury :

- Moderate to severe head injury who can't be serially neurologically assessed
- Severe head injury (GCS < 8) + abnormal CT scan

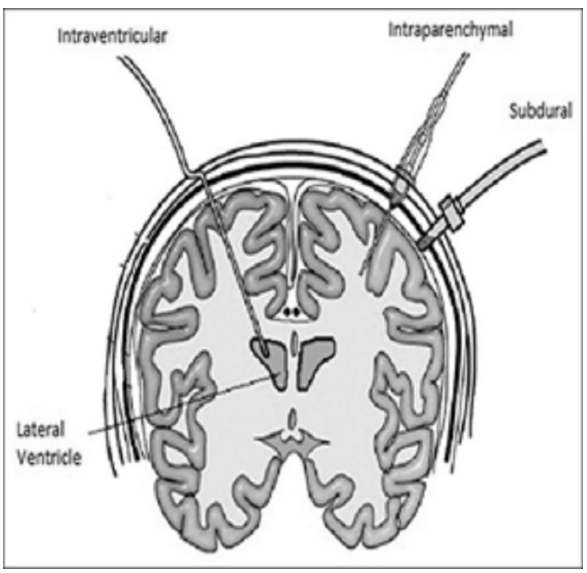


Fig 5. Intracranial pressure monitoring

- Severe head injury + normal CT if 2 of the following are present:
- Age > 40 yrs

  BP < 90mmHg

  Abnormal motor posturing.

Non traumatic brain injury :

- Acute CNS infection
- Hepatic encephalopathy grade III or IV.
- Ischemia > 50% MCA territory.
- Hemorrhage with mass effect.
- Metabolic/toxin encephalopathy

Target Cerebral Perfusion Pressure (CPP)

CPP = MAP – ICP

MAP = Mean arterial pressure

Target CPP in children – 50-70 mmHg

Assume ICP at least 20 if you cannot measure it.

So target MAP should be 70 mmHg

Goals and principles of therapy

The immediate goal :

- Prevent progression to herniation
- Reverse the herniation if present, CPP >60 mmHg and ICP <20 mmHg.
- Maintain Airway, Breathing and Circulation.

Indications for endotracheal intubation :

- Modified Glasgow coma score (m-GCS)=8
- Patients with signs of respiratory distress
- Declining O_2 saturation
- Signs of inadequate ventilation
- Refractory convulsion.

Preparation for intubation

- Hyperventilate before intubation
- Give volume if necessary
- Administer Lidocaine -1 mg/kg/dose .
- Give Proper Sedation and Analgesia –
- Thiopentone/propofol/ketamine
- Neuromuscular blocked – Atracuronium.
- Should be done by trained person.

General measures and first tier therapy

Head in neutral position, 30° elevation

1. Ensure oxygenation – Normoxia (PaO_2>60 mmHg, SpO_2>94%)
2. Mild short-term hyperventilation – Impending herniation. Manual ventilation double the normal breathing rate for given age for 10 min duration. Target a $PaCO_2$ 30–32 mmHg. In general ventilate to achieve $PaCO_2$ 35 -40mmHg.
3. Ensure adequate circulating volume Normovolumia, maintain normal BP, MABP >70 by fluid and vasoactive agent.
4. Pain – Adequate sedation–analgesia, midazolam 1–3 µg/kg/min, Morphine 0.1 mg/kg/ dose. Achieve deep sedation - Ramsay sedation scale score of 3–4. Avoid loud noise, invasive stimuli
5. Glucose control – Keep random blood sugar (RBS) around 150 mg/dl. Hypogycemia (<60 mg/dl) and hyperglycemia (>180 mg/dl) should be avoided.
6. Seizure prophylaxis – Severe head injury, focal symptoms and signs and CNS infections Phenytoin 20 mg/kg IV loading, followed by 5 mg/kg/d for the first 7 d only.
7. Comatose children should also be considered for EEG monitoring.
8. Use Lidocaine – 1 mg/kg/dose 5 min before endotracheal suctioning and procedure (IV and ET). Do not repeat within 2 h.
9. Anemia – Maintain Hb concentration around 10 g/dl.

Osmotherapy

First osmotic agent of choice is hypertonic saline

Hypertonic (3%) saline	Mannitol
• Hypertonic (3%) saline infusion: 2-5 ml/kg bolus, followed by 0.1 ml?1.0 ml/kg h infusion. • Favorable effect on systemic hemodynamics , ease of use, and proven efficacy. • Augmenting the CPP, Diminish inflammation, induce glutamate re-uptake. • Sodium goal set at 145 –155 mEq/ L and is intensified up to 160 mEq/L	• Mannitol 0.25–0.50 /kg i.v. over 20 min,repeat S.O.S • Monitor the urine output , serum osmolality <320 mOsm and take care of hypovolemia . • Mannitol is contraindicated in shock, oliguria , anuria and heart failure.

Approach to increased ICP in neurologically injured children shown in fig 6

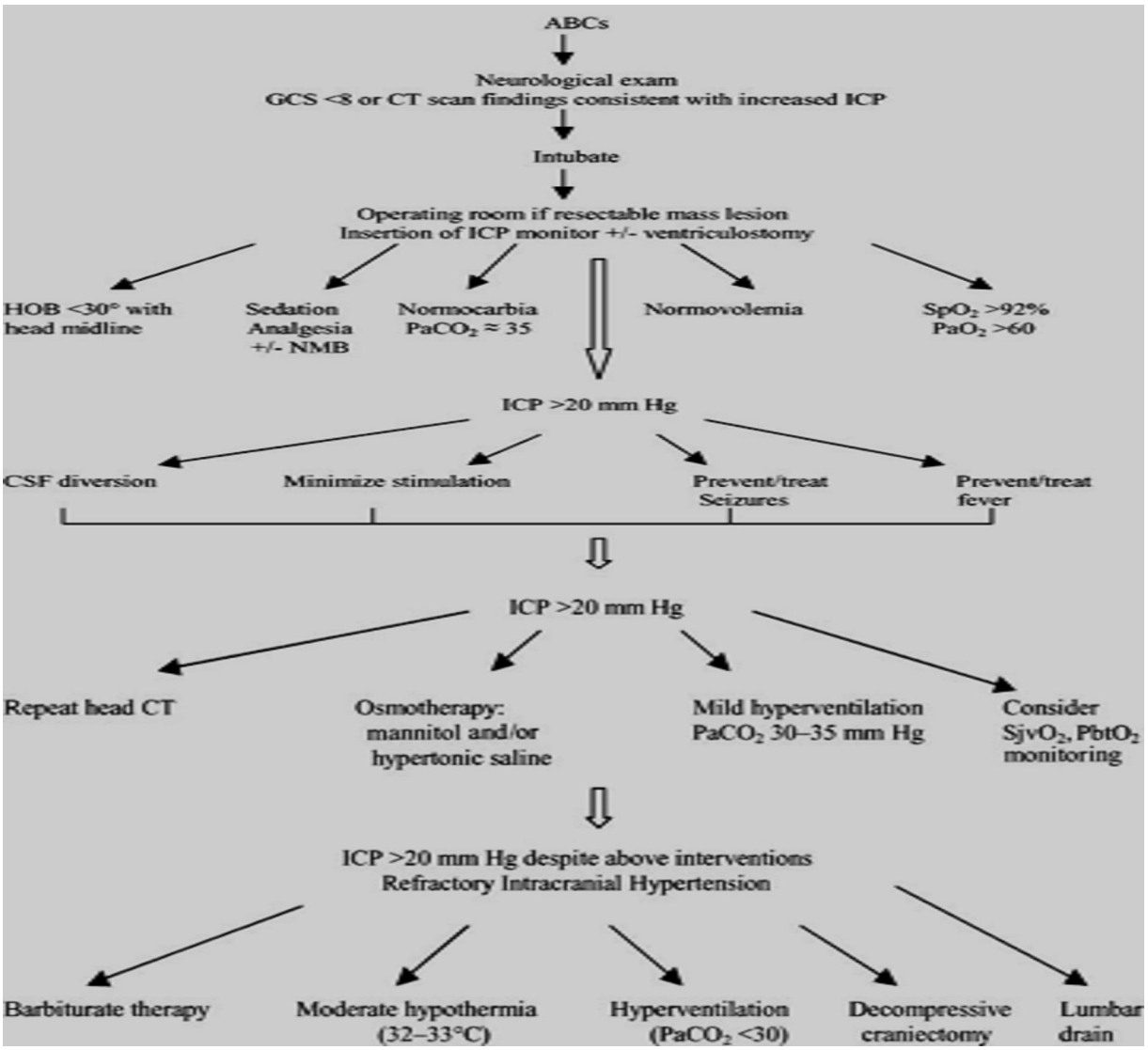


Fig 6. Approach to increased ICP in neurologically injured children

Suggested reading

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Immune Thrombocytopenia Following Scrub Typhus Infection: A Rare Entity

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Abstract

There has been resurgence of scrub typhus infection in the different area of Indian subcontinent. It presents with different manifestations .Howevere,immune thrombocytopenia is its rare complication.Here we are reporting a case of immune thrombocytopenia following scrub typhus infection.

Introduction

Scrub typhus infection is an acute illness caused by *Orientia tsutsugamushi*. It is an important cause of acute febrile illness mainly confined in south east Asia. It is mainly transmitted via larval stage of Trombiculidae family. Humans are the accidental hosts in this zoonotic disease. During the second world war scrub typhus was the most dreaded disease among the soldiers of far east. In India, the scrub typhus illness broke out in epidemic form in Assam and West Bengal during second world war. It is endemic to a part of world extending from northern Japan, Russia to south east Asia: known as Tsutsugamushi triangle. Recently, there has been a resurgence of this disease, reported from almost all geographical region of India with variety of clinical manifestations extending from acute febrile illness to severe multiorgan dysfunction syndrome, disseminated intravascular coagulopathy, shock, meningoencephalitis. Although thrombocytopenia has been reported in one third of patients with scrub typhus infection, but immune thrombocytopenia following scrub typhus infection is a rare entity. Hence, we are reporting this case because of two causes :

1. It is a rare entity. It may be the second reported case on india.
2. Early diagnosis, thorough physicians' examination may be helpful regarding favorable outcome.

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Case report

A 4 year male child was admitted with history of high-grade fever since last 4days with myalgia without any other relevant complaint. On admission, the child was conscious and oriented. There was no evidence of respiratory distress, any circulatory insufficiency, neurological deficit, bleeding manifestation, hepatosplenomegaly. On head to toe examination, there was an eschar in the right foot (fig 1).

Among the preliminary investigations, there was leukocytosis with thrombocytopenia (Hb 11.8gm/dl,

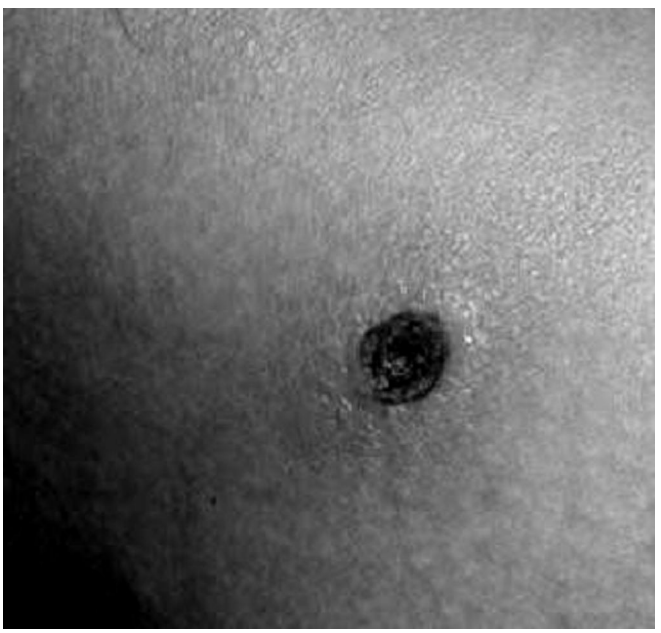

Fig 1. Eschar in the right foot

WBC 15430, platelet count 18000). The parameters regarding renal and liver function tests were within normal limit. As the scrub typhus is a re-emerging disease now-a-days and based on clinical suspicion, injection doxycycline was started. The subsequent investigation revealed this case to be a scrub typhus infection and the other reports regarding dengue NS1,widal,IgM for Leptospira were negative. The patient improved clinically, but there was persistent thrombocytopenia.

On day 7, the patient had petechial spots all over the body while the platelet count was 10,000. Bone marrow examination revealed normal erythroid and myeloid ratio with megakaryocytic hyperplasia-provisionally diagnosed to be a case of immune thrombocytopenia. The markers for viral hepatitis and SLE were negative. Intravenous immunoglobulin was given followed by oral steroid. The patient recovered within 5days (Platelet count 1.4lakh) and discharged successfully on 14th day of admission.

Discussion

Scrub typhus infection is an endemic and re-emerging infection in India. The manifestation is different as far the cases were reported. It can affect cardiovascular system, central nervous system, gastrointestinal system. The severity of the disease depends on the strain of the organism involved and also on the host. It invades endothelial cells to produce disseminated vasculitis and perivascular inflammatory lesions, causing vascular leakage and end organ injury. The organism downregulates the host defense mechanism by downregulating the GP-96 on the macrophages and the endothelial cells, which play a prime role in antigen presentation, antibody production and cross priming of the immune system. Though, the pathogenesis of thrombocytopenia here is poorly understood. It is hypothesized that it may be due to following mechanisms : (1)widespread endothelial damage,(2) disseminated intravascular coagulation, (3)hypersplenism, (4)decreased marrow production,(5) immune mediated platelet destruction.

This case was diagnosed to be a case of immune thrombocytopenia following scrub typhus infection as IgM for scrub typhus infection was reactive in blood and other causes of ITP were ruled out.

As it is a rare but dreaded complication following scrub typhus infection, it warrants the physicians for thorough physical examination and investigations for favorable outcome.

Conclusion

Immune thrombocytopenia is a rare manifestation of scrub typhus infection. So the clinicians should be concerned about this and further studies should be carried out regarding molecular mechanism of immune thrombocytopenia and scrub typhus infection.

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Coronary Artery Aneurysms : An Unusual Manifestation of Scrub Typhus

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Abstract

Scrub typhus is a zoonotic disease caused by Orientia tsutsugamushi. This case report reviews one of the uncommon presentations of the disease. A 5 year old female child presented in emergency with fever and acute congestive cardiac failure. Echocardiography revealed coronary artery dilatation and aneurysms. Patient was tested positive for Scrub Typhus IgM, and responded dramatically to doxycycline.

Introduction

Scrub typhus is a zoonotic disease caused by *Orientia tsutsugamushi*. The vector is the chigger form of the trombiculid mite (Leptotrombidium). People usually get bitten by the mite when they visit grasslands, especially freshly cut ones, or come in contact with an animal that bears these mites. Scrub typhus can present with a myriad of signs and symptoms, ranging from fever to myocarditis or meningoencephalitis. Eschar, the necrotic skin lesion suggesting the point of entry of the organism, though highly suggestive, can be absent in many cases.

Case report

A 5 year old female patient presented in OPD with generalized edema and fever for last 15 days. Fever was high grade, associated with chills and rigor, headache, irritability and myalgia. Edema was initially present in abdominal region but later involved face and extremities. Patient also complained of respiratory distress on and off for the last 5 days. There was an associated history of decreased urination over the last few days.

Examination showed a sick looking child, who was very irritable, with marked respiratory distress, with tachycardia(HR 130/min), tachypnea(RR 42/min), BP 110/60. SpO_2 was 100% in room air. There was bilateral equal air entry on chest auscultation, with no crepitations or rhonchi. A gallop rhythm was heard on precordial auscultation. On abdominal palpation we found a tender hepatomegaly and ascites, but no splenomegaly. A provisional diagnosis of acute congestive cardiac failure was made, and antifailure management was initiated with frusemide.

General examination revealed no pallor, icterus, cyanosis, clubbing. Edema was marked, especially pitting pedal edema. Multiple small cervical lymph nodes were present bilaterally.

Blood reports showed normal CBC (Hb 13gm%, TLC 4000 with 74% lymphocytes, platelet 2.8 lakhs) raised CRP(10.6), hypoalbuminemia (2.5), and normal electrolytes (Na 135, K 4.3). Urine examination showed no evidence of proteinuria, and liver function test was within normal limits. The patient also tested negative for malaria, dengue and typhoid.

The patient was started on Azithromycin initially, but continued to have high grade fever (103°F) associated with chills and rigor, occurring 2-3 times each day. Suspecting a scrub typhus induced myocarditis to be the cause of the failure, next day onwards the patient was treated empirically with doxycycline (2.2 mg/kg BD). However repeated examination failed to reveal any eschar. Fever subsided following the very first dose of doxycycline,

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by 2-3 days of doxycycline therapy, all signs of irritability also vanished. Enalapril was added next, and after 2 days of combined therapy, the features of failure finally receded.

After initial failure management we sent the patient for an echocardiography to rule out any structural heart disease. 2D echo revealed dilated LAD(Z score +4.33), dilated RCA(Z score +3.45) along with small LAD and RCA aneurysms (fig 1). There were other features including loss of tapering and perivascular brightness. There was also trivial mitral

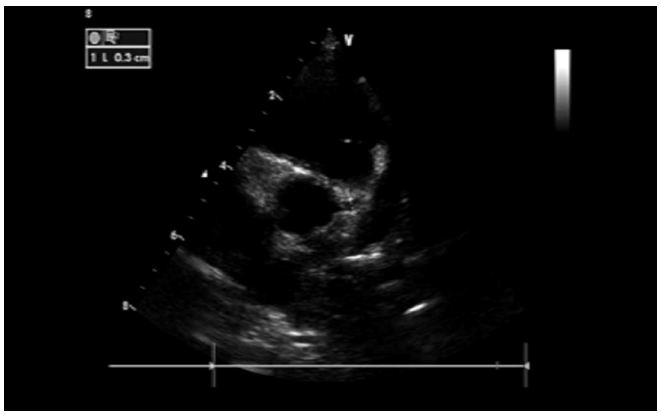

Fig 1. Echocardiography Showing Coronary Artery Dilatation With Aneurysm

regurgitation, and mild pericardial effusion seen all around the heart. Echocardiology report was thus suggestive of Kawasaki disease. But other than mild limb edema, no other clinical features specific to Kawasaki disease were present in this patient. ECG tracing was also within normal limits. Also there was no history of prolonged fever in the past suggestive of a previous episode of KD.

The patient was started on prophylactic aspirin therapy following this discovery.

In the meantime the report for Scrub typhus IgM came positive, and doxycycline was continued for a total of 5 days, following which the patient was discharged in afebrile condition.

The patient came for follow up about 1month later. Echocardiography was repeated, which revealed complete resolution of the coronary artery aneurysms and dilatation.

Discussion

Scrub typhus is a disease that can manifest in many ways, and cardiac affection is one of them. Hence there are instances of scrub typhus being misdiagnosed as Kawasaki disease[1,2].

The most well known cardiac manifestation of scrub typhus is myocarditis[3]. Other findings like pericarditis, infective endocarditis, circulatory shock can also occur. This case however presented with coronary artery dilatation and aneurysms, findings classical to Kawasaki disease. The major evidence pointing towards scrub typhus before the IgM was tested positive, other than the obvious clinical suspicion, was perhaps the dramatic response to doxycycline. Fever subsided the same day, and heart failure was controlled over the next two days. There have been instances of scrub typhus associated with coronary artery dilatation before, though they are quite rare[4].

By studying this patient, we can come to either of the two following conclusions. Either coronary artery aneurysms are manifestations of scrub typhus itself, or *Orientia tsutsugamushi* is one of the organisms leading to Kawasaki disease, though incomplete in this case. There is no controversy as to the diagnosis of scrub typhus, both from the IgM positivity, and the miraculous response to doxycycline.

The exact etiopathogenesis of Kawasaki disease is hitherto unknown. There have been speculations as to an infective origin, though the causative organisms have not been isolated as yet. Suspected pathogens have included Parvovirus, Adenovirus, CMV, EBV, Rotavirus, Meningococcus, Klebsiella, Rickettsia etc. A study done in 2009 seems to be the first case report of complete Kawasaki Disease following an episode of Rocky Mountain Spotted Fever[5]. Hence the speculation that this coronary artery affection was a sign of Kawasaki disease, seems to have some validation. But since Kawasaki is essentially a clinical diagnosis, and no other clinical features were present in the child, this hypothesis cannot be proven.

And lastly, scrub typhus itself known to be associated with coronary artery dilatation, as shown in a study in Kerala[4]. However, we failed to find any reference of the disease being associated with coronary artery aneurysms.

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WBAP CLINICAL MEETING 2020

30th January	:	Chittaranjan Sishu Sadan
27h February	:	Apollo Gleneagles Hospital
26th March	:	Institute of Child Health, Kolkata
30th April	:	Ramakrishna Mission Seva Pratisthan & Command Hosp.
28th May	:	Dr B C Roy PGIPS, Kolkata
25th June	:	Calcutta National Medical College
30th July	:	R G Kar Medical College
27th August	:	NRS Medical College
24th September	:	Medical College
15th October	:	CMRI
26th November	:	SSKM Hospital
24th December	:	B R Singh & NH, Andul

(a) All the usual days and weeks related to child health will be observed as per standard guidelines of CIAP. Details will be informed at appropriate time.

(b) WBAP monthly classes for PG students will be held in the office premises on 1st Saturday of every month from 2 pm

(c) WBAP monthly meet of EB members will be held at office premises on the 3rd Saturday of every month from 1 pm

This schedule may change in some unavoidable exigent situations with appropriate prior information.

Acute Disseminated Encephalomyelitis Presented As Squint Following Pneumonia

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Abstract

Acute disseminated encephalomyelitis (ADEM) is a rare disease of central nervous system of early childhood presents with polyfocal neurologic deficit.ADEM is caused by immune-mediated inflammatory demyelination, often associated with immunization or viral illness. Here we present a case of 2 year 8 month old hindu male child who presented to us with fever, refusal to feed and vomiting with consolidation of middle lobe of right lung, developed squint of left eye suddenly on day four of admission. Neuroimaging showed focal demyelination involving posterior periventricular region, and pons and upper part of medulla. We have treated the child with oral prednisolone for 2 week then tapered over 2 week, patient responded and is doing well currently.

Keywords

Acute disseminated encephalomyelitis, central nervous system, neuroimaging. multiphasic disseminated encephalomyelitis

Introduction

Acute disseminated encephalomyelitis (ADEM) is an autoimmune inflammatory disorder of the central nervous system (CNS). Etiopathogenesis is thought to be immune mediated, because in up to three-fourths of the cases; it follows an antecedent infection or immunization[1]. Magnetic resonance imaging (MRI) is the imaging modality of choice to diagnose ADEM, which shows lesions in white matter of the brain. No specific biomarkers are available currently to diagnose ADEM.

Case report

A 2 year 8month old hindu boy presented with fever for 4days, refusal to feed for 2days, vomiting 2 to 3 episodes for 1 day. There is history of cough and cold 10 days back with watery nasal discharge and sneezing, developed fever after 6 days of cough and cold, initially low grade became high grade in 2 days, with no chills and rigor.Fever from day two was associated with refusal of feed and from day three with vomiting. Antenatal, natal, and postnatal histories were uneventful. Developmental history was normal.There was no history of contact of tuberculosis. All immunization received up to the age according to national immunisation schedule.

His general examination revealed pulse rate 130/min, respiratory rate 46/min, temperature 38.5^{O}C. Pallor, cyanosis, icterus and edema were absent. On systemic examination, chest auscultation revealed crepts at middle and lower part of right lung and reduced vesicular breath sound (VBS).On CNS examination, child was found to be conscious, oriented to time, place, and person. Higher functions were intact. All cranial nerves were functioning normally. Tone, power, reflexes were within normal limit.

On investigations, complete blood count showed neutrophilic leucocytosis, serum electrolytes, and kidney and liver function test results were found to be normal. Chest x-ray revealed consolidation on middle lobe of right lung. It was diagnosed that patient was having pneumonia. We started the patient on IV antibiotics. Fever subsided within 48 hour but irritability persisted, on day four of admission patient became more lethargic, developed squint of left eye which was esotropic and concomitant in nature.

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Blood culture report was normal. Result of cerebrospinal fluid (CSF) examination was normal. Gene-Xpert for TB PCR in CSF was negative.MRI of the brain revealed hyperintensity at posterior periventricular region, and pons and upper part of medulla,suggestive of focal demyelination (fig.1,2). As the child presented withacute onset neurologic deficit (squint of left eye) accompanied by encephalopathy (abnormal behaviour, lethargy, more sleepiness) and changes compatible with demyelination on brain MRI, so squint was due to acute disseminated encephalomyelitis, though there was no signs of myelitis. We put the patient on oral prednisolone for 2 week then tapered over 2 week.Child responded to the treatment and squint disappeared in 4 week. We followed up the patient and done MRI brain after 3 months which showed disappearance of those focal demyelination, so this was a case of monophasic ADEM (fig. 3,4). MOG Ab in serum was negative in our patient.

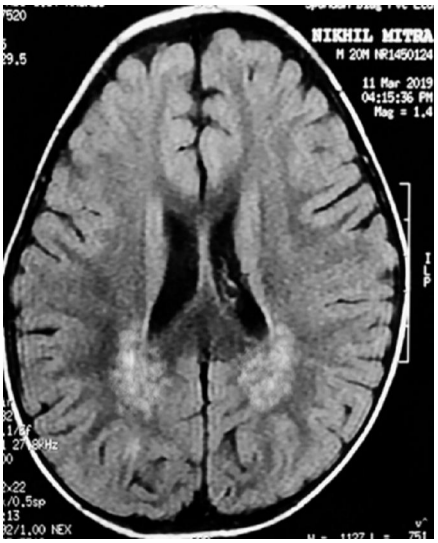

Fig 1: FLAIR MRI of brain show hyperintensity at posterior periventricular region

Discussion

The annual incidence of ADEM is reported to be 0.4–0.8 per 100,000 and the disease mostly affects children and young adults in winter/spring. Most of the case are reported post-exanthematous infection or vaccination[2-6]. There seems to be no gender predominance.The mean age at presentation is 6–8 years[7]. ADEM is usually monophasic. Recurrence may occur,if the recurrence is 3 month or longer then its called multiphasic disseminated encephalomyelitis(MDEM).50% ADEM are associated with MOG Ab positivity,almost all cases

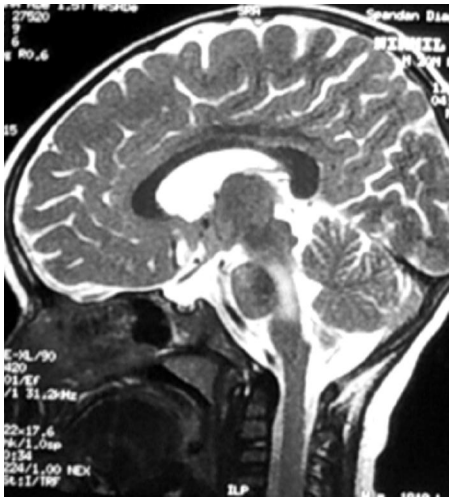

Fig2:T2W image of brain show hyperintensity at pons and upper part of medulla

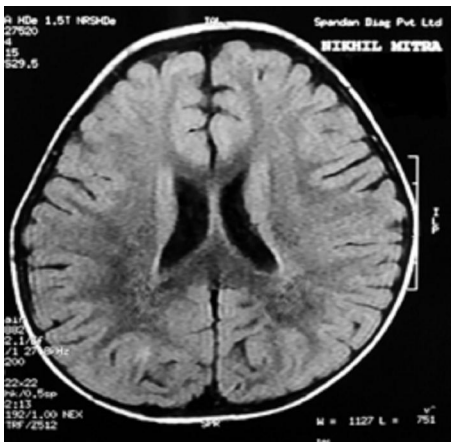

Fig 3: FLAIR image of brain after 3 month show no demyelination of posterior periventricular region

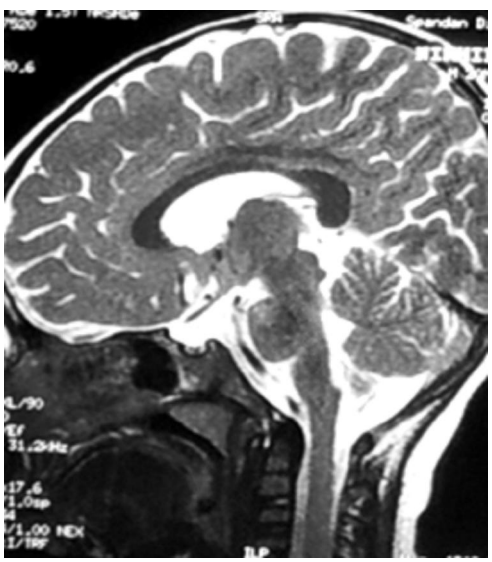

Fig 4: T2W image of brain after 3 month show no demyelination of pons and upper part of medulla

of MDEM are MOG Ab positive.In our case serum MOG Ab was negative. Characteristic clinical features include sudden onset multifocal neurologic disturbances such as visual field defects, aphasia, motor and sensory deficits, ataxia, movement disorders, a depressed level of consciousness, focal or generalized seizures, and psychosis. As in our case child presented with pneumonia but suddenly developed squint of left eye, became more lethargic.CSF is usually normal, but sometimes mild elevation of protein with lymphocytic pleocytosis can be found. Markers such as oligoclonal immunological bands, IgG or myelin basic protein (MBP) are sometimes detectable, but not diagnostic[8]. In our case CSFstudies were normal.With the wider use of MRI, ADEM is now diagnosed more frequently. MRI T2 enhancing images shows disseminated multifocal lesions in the white matter,basal ganglia, thalamus, and brainstem consistent with edema, inflammation, and demyelination[8].Spontaneous improvement may occur, though the recovery is incomplete in patients with ADEM not receiving any form of immunomodulatory treatment.There is no controlled trial on its treatment. Most of the literature is in consensus with the use of high-dose intravenous methyl prednisolone, intravenous immunoglobulin (IVIg), and plasmapheresis as various modality of treatment. Intravenous methyl prednisolone is the first-line drug (10–30 mg/kg/day, up to a maximum of 1 g/day) for 3–5 days followed by oral corticosteroid treatment continued with gradual tapering over 6 weeks to reduce the risk of relapses.Intravenous immunoglobulin (IVIg) (0.4 gm/kg/day for 5 days) is another option. Either plasma exchange or IVIg, could be the second-line treatment, when corticosteroids fail[9]. In our case we used oral prednisolone,patient responded well.Due to lack of any pathognomonic clinical feature or specific biomarker few differential diagnoses must be excluded before diagnosing ADEM. First priority should be to rule out infective causes of meningoencephalitis after ruling out infective causes demyelinating inflammatory process should be looked for.The outcome of ADEM is generally good, with 57–89% of children making a full recovery[10]. Follow up should be done as it may be the first attack of other demyelinating event.We have done a follow up MRI of brain after 3 month.A new lesion may produce suspicion of multiphasic episode.

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Incomplete Kawasaki : A Diagnostic Conundrum

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Abstract

Incomplete Kawasaki Disease (KD), unlike the complete variant, often presents in the form of a diagnostic dilemma in infants. A rare and occasionally fatal complication of this entity is Macrophage Activation Syndrome (MAS).Thus, a great deal of suspicion is required for timely diagnosis, management and prevention of mortality/morbidity.Here we present the story of a one-year old girl, who presented with prolonged fever with desquamating rash and was eventually diagnosed as a case of Incomplete Kawasaki disease, which was further complicated by MAS.

Keywords

Kawasaki, Macrophage activation syndrome, desquamating rash,prolonged fever.

Case report

A one-year old girl, hailing from Malda presented with a history of fever for 25 days that was high grade, intermittent,not subsided on taking paracetamol (oral and iv). This was accompanied by a generalised maculopapular rash which was first seen on day four of fever, and eventually started desquamating from day 10 of fever. She was initially treated in the local district hospital for 10 days with IV antibiotics and IV fluids,before referral. On admission, child was hemodynamically stable,but extremely sick looking, with poor oral intake. There was also mild pallor, edema of hands, feet with erythema of palms, soles, erythema of lips along with moderate splenomegaly. We started a new course of broad- spectrum antibiotics (Ceftriaxone, Vancomycin, Doxycycline). Initial total leukocyte count was 4400 with lymphocytic predominance, hemoglobin was 6.5 gm/dl, platelet count was 1.9 Lacs/cmm. However, fever spikes did not reduce in frequency or intensity,even after 72 hours post admission. Blood culture was sterileandScrub typhus Ig M was negative. This led us to the possibility of some immune mediated disorder, especially Incomplete Kawasaki Disease, as 2 out of 5 clinical criteria were present in this child (erythema of lips, skin peeling and edema of hands, feet,erythema of palms, soles). Lab investigations revealed elevated CRP (30mg/dl) and ESR(47 mm/hour), deranged liver enzymes, hypoalbuminemia and anemia (Hb 6.5gm/dl),further confirming our provisional diagnosis.We started IV Ig at 2gm/kg immediately which was infused over 12 hours. High dose aspirin was added at80mg/kg/day.Urgent echocardiography did not reveal any coronary artery aneurysm.Despite the above interventions,child was still febrile and was deteriorating clinically.Based on previous experiences and case reports,we began suspecting MAS which was confirmed by hyperferritinemia (>16,500 ng/ml), hypertriglyceridemia (278 mg/dl), hyponatremia (Na 127 mEq/L). So, we started IV methylprednisolone at 30 mg/kg/day which was continued for five days.The child became afebrile after three days of starting steroids with clinical improvement.After child became afebrile for forty-eight hours, oral aspirin was tapered to 5mg/kg/day.Repeat echocardiography was also normal without any features of coronary artery aneurysm. CRP and ESR levels decreased.The child was discharged with oral aspirin(for 6 weeks) and prednisolone(tapered over 2 weeks).

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Discussion

Kawasaki disease, also known as mucocutaneous lymph node syndrome is an acute febrile illness in childrenhas the highest incidence in Asia[1]. The American Heart Association in 2017 proposed a diagnostic and treatment guideline for KD based on more than 5 days of fever and ≥ 4 main clinical characteristics. If a child has fever for ≥ 5 days and meets 2 or 3 main clinical characteristics with or without coronary artery dilatation, the child can also be diagnosed with incomplete KD[2].

MAS is a type of hemophagocytic lymphohistiocytosis (HLH) that occurs under the circumstance of rheumatic diseases and is a life-threatening immune activation syndrome[3]. The inflammatory status of the patient is a major contributor of MAS.Genetics also play an important role particularly to macrophages hyper-responsiveness.MAS is typically characterized by high fever,lymphadenopathy,signs of liver,central nervous,system,renal involvement and may lead to multiple organ failure[4]. MAS is a rare entity compared to other complications in a patient with KD, with an occurrence rate less than 2%[5,6]. Mortality rate in MAS varies from 8-22%[7,8]. Early diagnosis and management is required for better prognosis.Early diagnosis of KD complicated with MAS is difficult as both of these entities have many overlapping manifestations and laboratory findings like persistent fever, rash, anaemia, deranged liver enzymes, hypertriglyceridemia[9]. Splenomegaly is rarely seen in KD,but it occurs in 69% cases of KD complicated with MAS.KD patients should be considered for the possibility of MAS if there is persistent fever with splenomegaly[10]. A high level of suspicion for MAS is very helpful for early diagnosis in cases of persistent fever for more than ten days or IV Ig non responsive Kawasaki disease patients[11].

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CLOVES Syndrome: A Rare Disorder of Overgrowth Syndrome

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Abstract

CLOVES syndrome characterized by Congenital Lipomatous Overgrowth, Vascular malformations,Epidermal nevi, and Skeletal anomalies is a recently described sporadic syndrome from postzygotic activating mutations in PIK3CA. This 9 year old boy presenting with features of overgrowth of body parts mainly extremities with cutaneous naevi and lipomatous deposition over back since childhood. Examination revealed wide large extremities with large fingers, scoliosis, epidermal naevi. The parents did not give consent for genetic studies because of financial constraints. The CLOVES syndrome has emerged as an uncommon yet distinct clinical entity with some phenotypic variations. Its diagnosis is usually from cutaneous, truncal, spinal, and foot anomalies in clinical and radioimaging studies. Proteus syndrome remains the major differential.

Keywords

Congenital asymmetric overgrowth of extremities, cutaneous naevi, Congenital lipomatous deposition, CLOVES syndrome, PIK3CA related gene, Proteus syndrome

Case report

A 9 year old boy presented in the OPD with disproportionate and asymmetric growth of body parts, hands, feet and fingers since birth and hyperpigmented lesions over fore arms since birth. No history of photophobia,visual,hearing problems. No history of respiratory distress or pain or swelling of abdomen. But the boy had skeletal anomaly like scoliosis. He was born out of non consanguineous marriage. Single child and perinatal history was uneventful. Fully immunized as per age. Family history was nothing significant. No delay in developmental milestones IQ was normal.

Height was 135 cm, weight 45kg, asymmetric overgrowth of extremities with abnormally large wide hands and feet, large fingers and toes were noted. Limb length discrepancy was present (fig 1). Skin examination revealed cutaneous nevi over upper limb (fig 2). There was deposition of fatty tissue over scapular region (fig 3). Characteristic finding of foot is the presence of wide sandal gap biletrally.

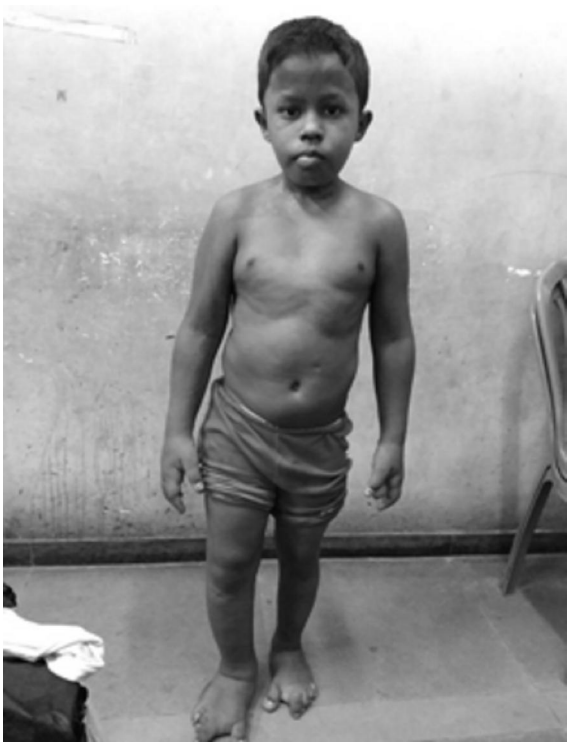

Fig 1. Limb length discrepancy

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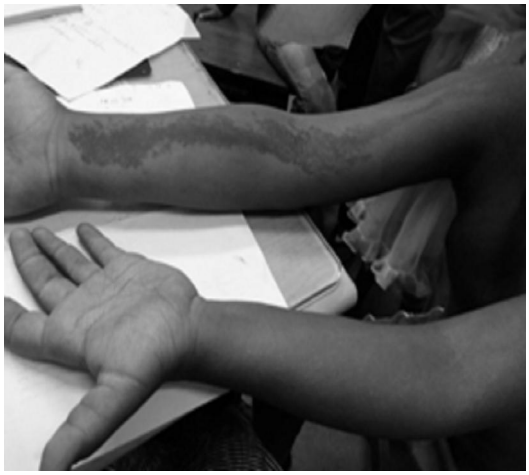

Fig 2. Epidermal naevi

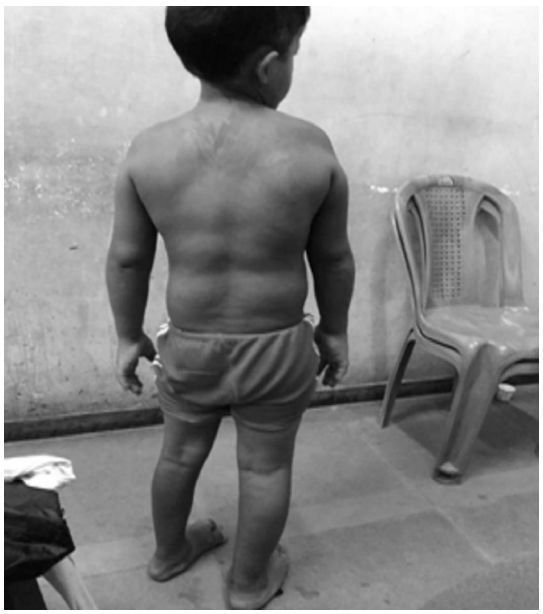

Fig 3. Lipomatous overgrowth

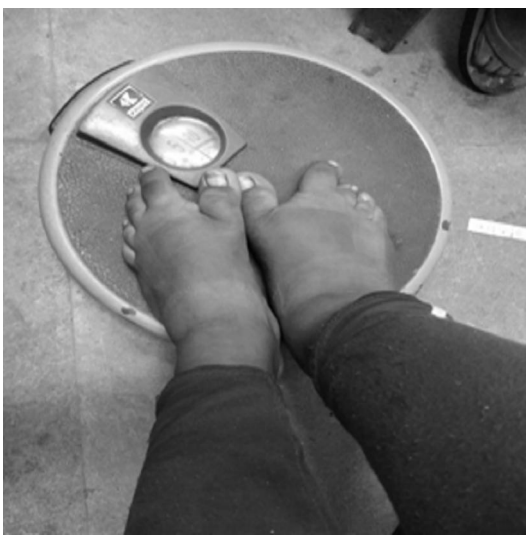

Fig 4. Wide sandal gap

Examination of spine revealed presence of scoliosis.

(i) Large wide hands and feet

(ii) Large Fingers or toes

(iii) Wide sandal gap (fig 4)

Clinically the features were suggestive of CLOVES syndrome.

C : Congenital – Present since birth

L : Lipomatous – Benign soft fatty tissue tumor presents since birth usually visible over back

O : Overgrowth – Abnormal increase in size in body parts. Asymmetric overgrowth of extremities arms and legs with large wide fingers toes, wide gap between fingers of toes

V : Vascular malformations

E : Epidermal naevi

S : Spine / skeletal; anomalies like scoliosis

Investigations

Spinal MRI was done to evaluate spinal dysraphism. Right upper quadrant USG was done to exclude Wilms tumor. Echocardiography was done to rule out heart disease and Doppler study was done for AV malformations. Genetic study could not be done as parents did not give consent due to financial constraints.

Discussion

This 9 year old boy presenting with asymmetric overgrowth of body parts mainly extremities since birth. Wide large hand, foot with large fingers and toes . Characteristics wide sandal gap in feet. Boy also had fatty tissue deposition over back and nevus like lesions over upper limb with scoliosis. There was no spinal dysraphism and renal tumor and vascular malformations.

Diagnosis was mainly clinical. Treatment comprises of surgery, Laser, sclerotherapy, embolization and debulking operation.

CLOVES syndrome is rare and evident at birth. It affects males and females equally regardless of their race or ethnicity that is primarily characterized by congenital overgrowth of fatty tissue; malformations of the vascular system (the vessels that carry blood and lymph[1-4] throughout the body); epidermal nevi; and spinal or skeletal abnormalities. Other signs and symptoms may include disproportionate fat

distribution, overgrowth of the extremities (arms and legs)[5], skin abnormalities and kidney problems such as an unusually small or absent kidney.

CLOVES syndrome is caused by somatic mutations[6] in the PIK3CA gene. Because these mutations do not affect egg or sperm cells, the condition is not passed on from parent to child. Treatment is based on the signs and symptoms present in each person.

Many of the patients with CS are misdiagnosed as having other syndromes such as Klippel-Trenaunay syndrome or Proteus syndrome.

Related disorders

PIK3CA-related overgrowth syndromes (PROS)[7] refers to a group of disorders caused by PIK3CA gene mutations such as CLOVES and Klippel-Trenaunay syndrome. Somatic mutation but no germ line mutation.

Symptoms of the following disorders can be similar to those of CLOVES syndrome[8,9]:

Klippel-Trenaunay syndrome (KTS) is a rare disorder that is present at birth (congenital) and is characterized by a triad of cutaneous capillary malformation (port-wine stain), lymphatic anomalies, and abnormal veins in association with variable overgrowth of soft tissue and bone. KTS occurs typically in the lower limb. KTS equally affects males and females.

Proteus syndrome is a rare disorder characterized by disorganized overgrowth of various tissues of the body. The cause of the disorder is a mosaic mutation in a gene called AKT1. Disproportionate, asymmetric overgrowth occurs in a mosaic pattern (i.e., a random "patchy" pattern of affected and unaffected areas). Affected individuals may experience a wide variety of complications that may include progressive skeletal malformations, benign and malignant tumors, malformations of blood vessels (vascular malformations), bullous pulmonary disease, and certain skin lesions. In some patients, life-threatening conditions relating to abnormal blood clotting may develop including deep vein thrombosis and pulmonary embolism.

Financial support and sponsorship – Nil

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Tyrosinemia Type I with Unusual Presentation

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Abstract

Tyrosinemia type I is a disease inherited as an autosomal recessive manner and manifests when the enzyme fumarylacetoacetate hydrolase (FAAH) is deficient. It has a prevalence of about 1 in 100,000 newborns[1]. It is a common disorder of tyrosine metabolism with over 30 different mutations identified in the FAAH gene[2]. FAAH deficiency also leads to the formation of blood and urinary succinylacetoacetate and succinylacetone, metabolites of the accumulating maleylacetoacetate[1]. Fumarylacetoacetate that accumulates in Tyrosinemia type I as a result of FAAH deficiency, is toxic to liver and kidney, leading to raised a-fetoprotein early in the disease[1,3]. The laboratory diagnosis of Tyrosinemia type I is based on a tissue deficiency of fumarylacetoacetate hydrolase and / or presence of urinary succinylacetone[3]. The clinical spectrum of the disease is wide, ranging from chronic complications of hepatic failure to hepatocellular carcinoma, renal tubular dysfunction, renal failure, episodes of peripheral neuropathy, and death within the first few months of life[3]. Here we present a unusual presentation at 3 years of age with failure to thrive and rickets with previous diagnosis of cirrhosis of liver of unknown etiology.

Case report

A 3 year old female child born of a non-consanguineous marriage was admitted with a history of inability to stand for last 2 months, failure to thrive and abdominal distension since day 7 of life. There was no history of convulsion, vomiting, jaundice hematemesis, malena. She was investigated in different hospital since age of 1 month for hepatoslenomegaly, diagnosed as cirrhosis of liver from liver biopsy and interpreted as a case of storage disorder at the age of 10 months. She was diagnosed as a case of rickets 1 month back and received megadose of IM vitamin D.

She was delivered normally in institution at 33 weeks of gestational age. Birth wt was 1.25 kg (SGA). She cried immediately after birth. There is no history of similar disease or any genetic or metabolic disorder in the family. She is only child of the parent and there is no history of abortion, still birth or sibling death.

There was delay in motor and language development. DQ in gross motor development is 33 and DQ in language development is 50.

On examination her height was 83cm and weight was 8kg and both of them are below 3rd centile for age. On skeletal survey there was widening of wrist, genu varum, and double malleoli sign. On abdominal examination firm liver was palpable 2 cm below subcostal line. Liver span was 9cm. Spleen was palpable 3 cm below the subcostal margin. Other general and systemic examination was non contributory. Ophthalmoscopic examination was normal.

On laboratory investigation, complete blood count, BUN, creatinine was within normal limit. Alkaline phosphatise level was disproportionately raised (1794IU/l), SGPT, SGOT and serum bilirubin level were normal, total protein was 7gm/dl and albumin were 2.6gm/dl. INR was 1.6. ABG was showing normal anion gap metabolic acidosis with hypokalemia. Serum level of 25 DHCC and parathormone were normal. There was hypouricemia and hypophosphatemia. Serum calcium level was morml. Urinalysis was showing

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aminoaciduria, phosphaturia, glycosuria. An ultrasound study of abdomen revealed parenchymal liver disease (macronodular cirrhosis) with splenomegay. Enlargement of both kidneys were also noted. Xray both knee joint was showing rachitic changes(fig 1). MRI brain was within normal limit (fig 2). Liver biopsy was showing cirrhosis of liver in background of giant cell hepatitis. There was no definite evidence of storage disorder, and necroinflammatory activity was noted raising a suspicion of tyrosinemia.

The serum alpha feto protein (AFP) was markedly raised (1210 ng/ml); urinary level of succinylacetone (by indirect spectrophotometric method of Greiner and Lescault) and the level was found to be elevated 45µmol/l (normal-1.2µmol/l) thus confirming the diagnosis Tyrosinemia type-1. These results confirmed the diagnosis of hereditary tyrosinemia type 1 (HT1). Therapy with 2-(nitro-4-trifluoromethyl-benzoyl)1,3-cyclohexanedione (NTBC) was advised. The family was provided genetic counseling and explained the inheritance with 25% risk of recurrence in a future pregnancy, and informed that prenatal diagnosis would be possible.

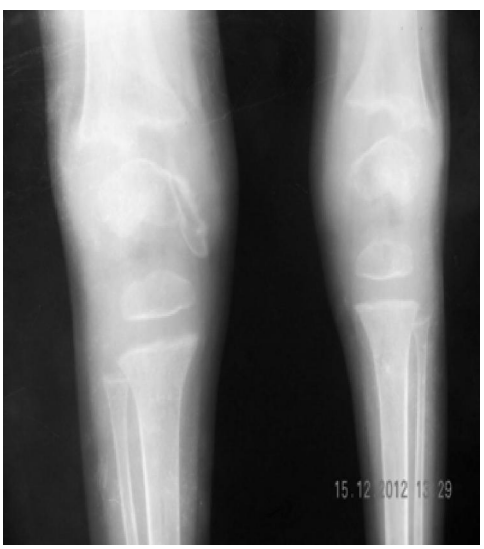

Fig 1. Xray knee joint showing rachitic changes

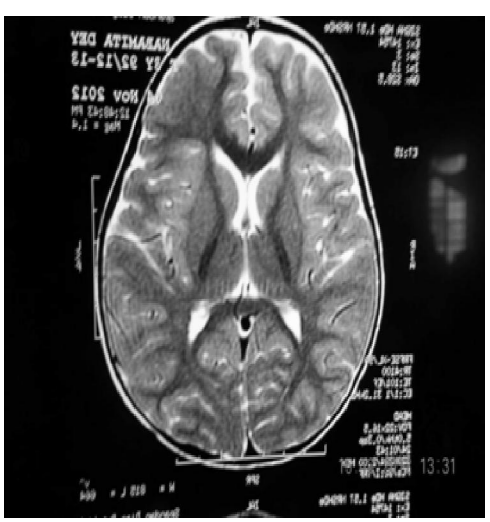

Fig 2. MRI brain

Entire FAH gene sequencing was carried out in both parents and the child, which leads to the identification of two distinct heterozygous point mutations. Mother was heterozygous for nonsense mutation p.R174X in exon 6 c DNA 520C>T . Patient was homozygous for p.Q64H in exon 2 of c DNA 192G>T. . Another heterozygous point mutation was detected in exon 13 as c.1159G>A, which is predicated to result in an amino acid substitution p.Gly387Arg.

Discussion

Individuals with tyrosinemia type 1 typically present with either an acute or chronic form of the disorder.

The so-called acute form is present at birth or during the few first months of life. Infants with the acute form of tyrosinemia type 1 exhibit rapid onset of symptoms, usually beginning with failure to thrive. Additional early symptoms include: fever, diarrhea/ bloody stools, vomiting, enlarged liver, tendency to bruise easily, jaundice, lethargy, irritability. Some infants may have a distinctive cabbage-like odor to the skin and urine. When untreated, tyrosinemia type 1 often rapidly progresses to acute life-threatening liver failure.

The chronic form of tyrosinemia type 1 occurs less frequently than the acute form and is generally characterized by a more gradual onset and less severe expression of the symptoms. Initial signs may include vomiting, diarrhoea, and enlarged liver and spleen, and failure to thrive. Infants with the chronic form may eventually develop progressive cirrhosis of the liver resulting in chronic liver failure, developmental delays, renal Fanconi syndrome characterized by kidney dysfunction, weakness and softening of the bones (rickets) and episodes of vomiting, dehydration, weakness and fever. The most distinguishing characteristic of type I

tyrosinemia is liver and kidney involvement[4] as in our case.

In a study conducted on 32 tyrosinemia type I patients, nephromegaly (47%), hyperechogenicity of kidneys (47%) and nephrocalcinosis (16%), aminoaciduria (82%), hypercalciuria (67%), tubular acidosis (59%), decreased glomerular filtration rate (48%) were found[5]. Our patient had most of these abnormalities including decreased tubular phosphorus reabsorption and aminoaciduria. Another study, conducted on 8 patients, reports nephromegaly, tubulopathy and vitamin D resistant rickets in 50%, 80% and 50% of the patients respectively[6] which are evident in our case.

Succinylacetone, the actual toxic substance in tyrosinemia type I, is responsible for liver and kidney pathologies. This toxic substance accumulation is prevented by NTBC treatment. According to the literature, risk for hepatocarcinoma risk has been markedly prevented following this treatment[7,8]. Furthermore, the results of a study conducted on 101 patients have shown no hepatocellular carcinoma development for two years[9]. There may also be a 10-15 fold increase in the serum AFP level. An abrupt increase in serum AFP is a red flag for detection of hepatocellular carcinoma[4,5]. The diagnosis can be established by determination of succinylacetone in urine or serum and by assay of fumaryl acetoacetate hydrolase in lymphocytes and fibroblasts. Prenatal diagnosis is possible by analysis of succinylacetone in amniotic fluid and by fumarylacetoacetate hydrolase assay in cultured amniotic fluid cells or chorionic villus material. Liver transplantation is as yet the only definite treatment for this disorder.

Our patient is now on tyrosine restricted diet along with oral calcium, phosphate, bicarbonate and vitamin D supplementation. NTBC is now not available in Indian market.

In a child who presents with features of proximal renal tubular acidosis along with hepatosplenomegaly, inborn errors of metabolism need to be considered. Glycogen storage disorders like Von Gierke's and Fanconi–Bickel syndrome along with tyrosinemia are the important differential diagnosis. Hypoglycemia and hyperlipidemia are important markers of Von Gierke's and Fanconi–Bickel syndrome. These glycogen storage disorders show glycogen deposits on liver biopsy.

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A Rare Case of Limb Deformity

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Introduction

Proximal focal femoral deficiency (PFFD) is a rare complex congenital birth defect involving upper part of femur and sometimes acetabulum. The incidence ranges from1:50000 to 1:200000 live births[1]. Clinically the child presents with mild to severe shortening of limb depending on the severity of defect. Sometimes may be associated with bending of femur as in our case which makes it vulnerable for fracture. The defect is usually unilateral but 30% of cases have bilateral deformity.

Several theories have been postulated regarding etiology in various literature but no definite cause is still known. Some stated that this malformation is as a result of cellular nutritional disturbance at the time of cell division during 4-6 weeks of gestation. According to others it may be due to local vascular damage to mesenchymal tissue. Extrinsic factors like irradiation, toxins, ischemia, hormoneor thalidomide may also be responsible[2].

PFFD is mostly an isolated skeletal deformity but at times may be associated with ipsilateral femoral hemimelia, vertebral defects especially in lumbosacral region, caudal dysplasia or caudal regression syndrome[3].

Case report

A full term male baby of birth weight 2.8 kg born by LUCS , a product of non-consanguinous marriage brought to us with complaints of short left lower limb. Mother was 26 yrs of age, without any medical history of diabetes mellitus, hypertension, hypothyroid or any other illness in antenatal period. There was no history of any radiation exposure, intrauterine infection or any drug intake except iron, folic acid and calcium.

On examination, there was apparent shortening of left thigh which was also found to be bulky as compared to right side with a prominent bony point around mid-thigh on palpation. Hip joint was stable bilaterally but adducted and laterally rotated on the affected side (fig 1). No other osseous deformity or any dysmorphism was noted. Systemic examination did not revealed anything significant.

Plain radiograph was done which showed

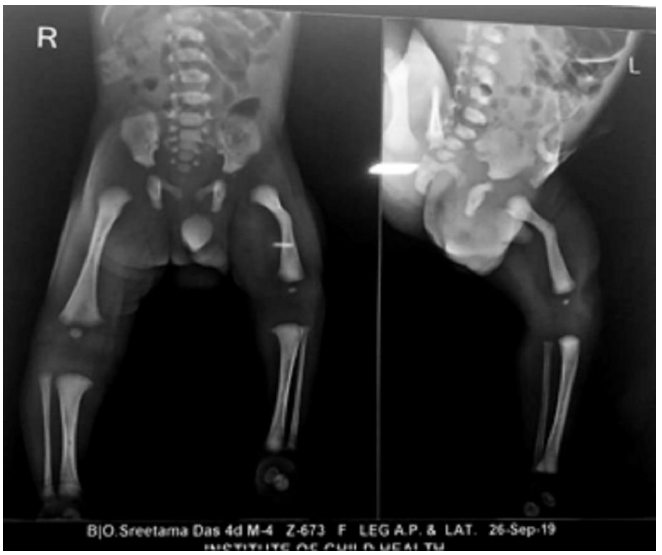

Fig 1. Abducted and laterally rotated left hip

hypoplastic left femur and lateral bowing with concavity on medial aspect. The acetabulum and femoral epiphysis were well formed (fig. 2). The baby was discharged after counselling regarding the possibilities of fracture.

On day 34 of life the baby presented with inability to move the affected limb with swelling and tenderness of left thigh. Plain radiograph was done and it showed fracture shaft femur (fig 3), managed conservatively with closed reduction and plaster

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cast. Complete blood profile, metabolic and biochemical tests were within normal limit. Sepsis screen was also found to be negative. USG abdomen, cranium and echocardiography were done to rule out any other congenital malformations.

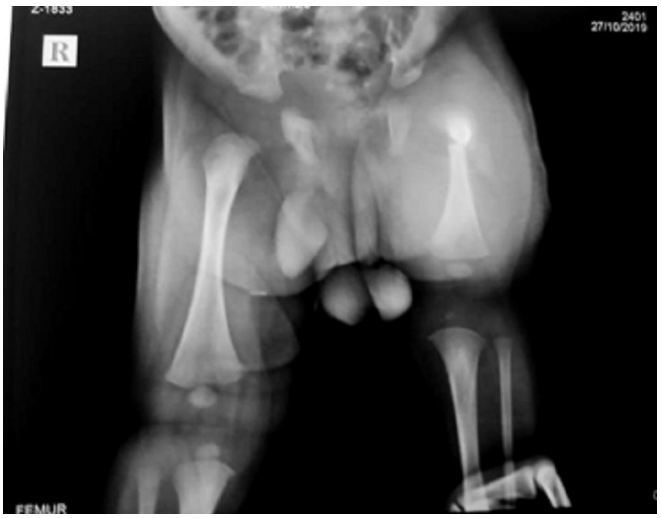

Fig 2. Acetabulum and femoral epiphysis were well formed

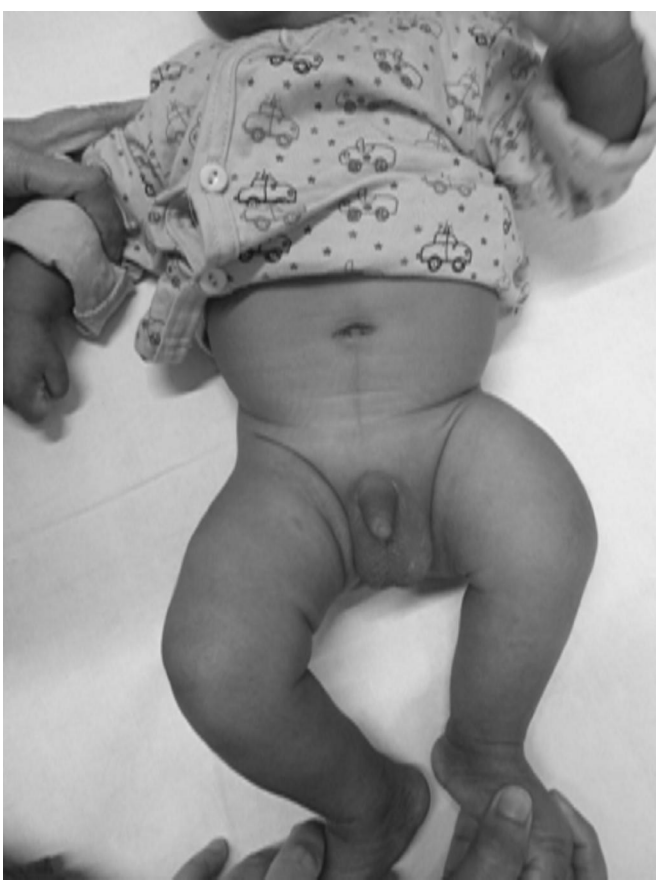

Fig 3. Fracture shaft femur

Discussion

PFFD is mostly a sporadic disease . No chromosomal abnormality have been detected till date although quite a few familial recurrence have been recorded in literature.

There is wide spectrum of clinical presentation of this defect. It may present with varying degrees of shortening of limb with external rotation of femur. There may be associated bending of femur as in our case. Other symptoms include unstable hip or knee joint of the ipsilateral side. in addition, other accompanying skeletal deformities like shortened or absent fibula, flat/club feet and vertebral defects are also found.

Some classification systems are made, mostly based on radiological findings, but few also includes clinical presentation. Aitkin classification is the most widely accepted one which grades the deformity into four types[4,5]. Class A being the mildest form where both femoral head and acetabulum is well formed and only deformity is shortening of proximal shaft of femur. Our case belonged to this class with an additional finding of bowed femur which ultimately got broken after a trivial trauma. Class B has normal femoral head with moderately dysplastic acetabulum. In Class C, entire top half of femur bone is absent including the trochanters as well as femoral head and the acetabulum is also severely dysplastic. Class D is the most severe form where most of the femur bone is absent. Only a small irregular piece of bone above the distal femoral epiphysis is present and in pelvi , acetabulum is completely absent with flattened pelvis on affected side(fig 4).

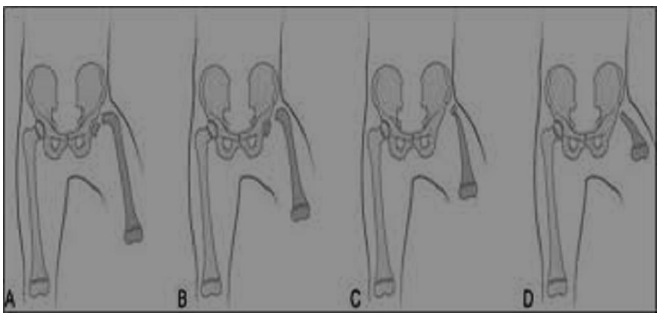

Fig 4 : Aitken's classification for proximal femoral focal deficiency

Besides plain radiograph, MRI is other imaging modality with an additional benefit of evaluating the cartilage and soft tissue better. Hence aids in guiding the plan of management. Antenatal USG is highly effective in early diagnosis. However it is highly subjective and precision comes with practice and experience.

Treatment must collaborate a team of pediatricorrthopedic surgeon, pediatric medicine, prosthetic experts, physical therapist and nurses. . management is complex and must be individualised based on the type of defect , age of presentation, condition and stability of hip, knee and foot, child's general health and medical history.

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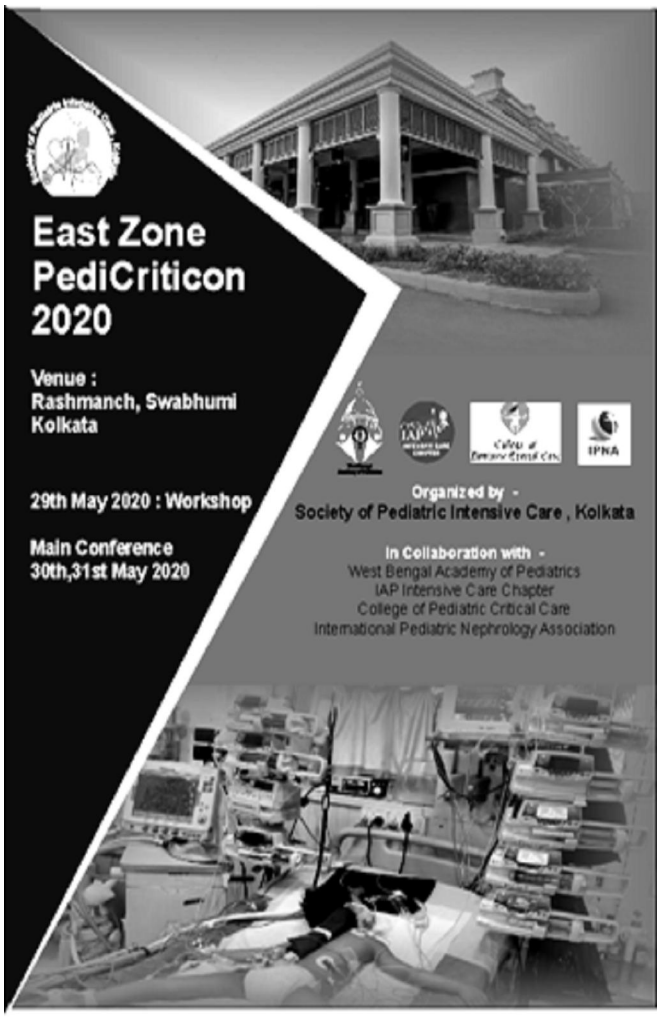

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Cough....Look Beyond Chest

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Abstract

Respiratory symptoms are common in children and often tend to be diagnosed as pneumonia or bronchiolitis and treated with antibiotics and bronchodilators.But sometimes,on meticulous examination, there are certain subtle clues to multisystem involvement by an non-infective disease process,especially in refractory and difficult to manage situations. We describe one such case where a child underwent multiple hospital admissions starting from early infancy because of respiratory symptoms but clues to multisystem involvement were missed resulting in delay in diagnosis.

Keywords

Pneumonia; hypertension; vasculitis

Introduction

We hereby describe the case of an infant in whom meticulous history taking, clinical examination and certain lab parameters prompted us to think out-of-the-box and investigate further to arrive at a non-infection inflammatory diagnosis.

Case report

A one year 5 month old male baby was admitted with complaints of cough and fever for 7 days and difficulty in breathing for 5 days. His parents were first cousins. His elder sibling had died at the age of 6 months due to some respiratory problem, the exact cause was not being clear. This baby had been admitted thrice previously in other hospitals with similar complaints at the age of 3,7 and 12 months. He was born at term without any antenatal or perinatal problem and was exclusively breastfed for first 6 months. Immunisation was uptodate.

On head to foot inspection, no abnormality was detected. Anthropometrically,there was wasting but no stunting. There was tachypnoea with bilateral rales on auscultation of chest. Liver and spleen both were enlarged 4cm below the costal margins. Cardiovascular and neurological examinations were within normal limits. Surprisingly. the blood pressure was 122/70 mmHg – Stage 2 HTN (95th centile + 12mmHg)

With an operational diagnosis of sepsis – bronchopneumonia with hypertension and after initiation of anibioticcs, antihypertensives and other supportive measures, he was investigated which showed a hemoglobin of 7.4gm%, total leucocyte counts 28400 cells/mm^3 with a differential count of N 55%, L 33%, E 4%, platelet count 4.6 lac/mm^3, urea 26 mg/dl, creatinine 0.8 mg/dl, CRP 44.4mg/L, ESR 130 mm 1st hour, bilirubin 0.5mg/dl, liver enzymes were normal and urine RE/ME showed 6 to 8 RBC. Chest x-ray showed patchy infiltrates,CBNAAT from gastric lavage and Mantoux test were negative.On USG Doppler study there were no features suggestive of renal vascular disease. ECHO was normal.

In view of non response to antibiotics, persistent hematuria and refractory hypertension, he was investigated further. CT scan of chest revealed alveolar opacity in upper lobe and ground glass opacity in lower lobe of both sides. Paranasal sinuses revealed maxillary and ethmoid sinusitis on CT PNS. ANA and ANCA were negative.

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From Day 7, his condition started deteriorating with increasing fever spikes and size of spleen and sequentially decreasing blood counts. Serum ferritin was 5826 microgram/L and triglyceride 382 mg/L.With a diagnosis of MAS in an underlying multisystem disease like vasculitis, the child was started on Inj Methyl Prednisolone and other supportive measures. Inspite of aggressive management child succumbed to death on day 10 of admission. Liver and kidney biopsy reports were available post-mortem.Liver bipsy was reported as non-specific reactive hepatitis. Kidney biopsy showed interstitial inflammation, some ischemic glomeruli, endothelial damage, hypercellular glomeruli and pauciimmune deposits on immunofluroscence (fig. 1).

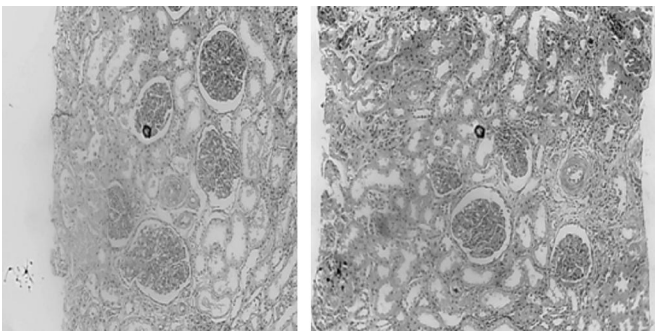

Fig1. HPE kidney showing interstitial Inflammation and endothelial cell degeneration and swelling

Discussion

Repeated chest manifestations with characteristic CT scan changes, associated sinusitis, refractory hypertension and persistent hematuria with consistent histopathology and immunofluroscence findings led us to retrospectively think of granulomatosis with polyangiitis(previously known as Wegener's granulomatosis) as a diagnostic possibility which subsequently succumbed to macrophage activation syndrome. The child a fulfilled 4 out of six EULAR/PRES endorsed classification criteria of WG[1].

The importance of reporting this case lies in the fact that it is important to look beyond the chest in recurrent/persistent cough. Cough or respiratory symptoms may not always be pneumonia or bronchiolitis. Thorough and meticulous clinical examination revealed splenomegaly and hypertension along with hematuria gave us clues to the multisystemic nature of the disease. Also,the importance of measuring BP with a proper size cuff and comparing with percentile charts in every patient needs to be emphasized[2,3]. Sometimes we have to think out of the box to make a diagnosis. Unless we are aware of the possibility of a disease, we will never be able to arrive at a diagnosis. This child was admitted with similar complaints to other hospitals multiple times before presenting to us but the multisystem involvement and hypertension were missed !!

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An Unusual Case of Tuberculosis

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Abstract

Diagnosis of tuberculosis (TB) in child is difficult as there is difficulty in obtaining positive microbiological confirmation of infection. Here, we report a case of fourteen year old adolescent girl who was admitted with fever, cough and chest pain. She had right sided pleural effusion and TST was positive but sputum CBNAAT was negative. Her elder brother was diagnosed as a case of pulmonary tuberculosis five months ago but was on improper therapy. This child responded well to antituberculosis drugs (ATD).

Key words

Pulmonary tuberculosis, antituberculosis drugs (ATD)

Introduction

Tuberculosis infection and disease are much more prevalent in developing countries, where resources for TB control are limited.[1] TB in childhood is difficult to diagnose as it is paucibacillary and due to atypical radiological features and difficulty to expectorate.[2] Most of the cases are completely curable but appropriate therapy with right drugs in right dose for right duration is necessary.[3]

Case report

This fourteen years old adolescent girl admitted in our institute in the month of November 2019 with complaints of cough for 20 days with high spikes of fever for last 10 days and right sided chest pain for the last 2 days. Her mother also noticed gradual weight loss for the last one year. She was completely immunized till date. Her elder brother (16 years) was on inappropriate ATD [low dose (R+I+E)] for the last 5 months]. He was diagnosed a case of TB on the basis of lung imaging (cavitatory lung lesion in chest with hilar lymphadenopathy), his TST and CBNAAT sputum tests were negative.

She was thoroughly examined and physical examinations were suggestive of right sided pleural effusion in an underweight girl without significant respiratory distress. There was no lymphadenopathy, organomegaly and neck rigidity. From the very beginning TB was a differential diagnosis and investigations were done keeping that in mind. Routine blood investigations showed neutrophilic leukocytosis (WBC 16660, N 63, L32,M05) with high CRP (151.3 mg/L). So IV antibiotics with ceftriaxone was started along with other supportive care. Diagnostic pleural tap was done (hazy pale yellow fluid, cell count 1800/ cmm, polymorphonuclear cells 30% and mononuclear cells 70%, glucose 97 mg/dl, protein 5 g/dl, ADA 95.29 U/L, LDH 1509 U/L).TST was strongly positive with 16 mm induration. Chest x-ray suggestive of right sided moderate pleural effusion. Unfortunately sputum AFB was negative and CBNAAT of both sputum and pleural fluid were negative.

After 48 hours injection ampilox was added as high spikes of fever continued. MR scan of chest showed features suggestive of small segmental consolidation in the right upper lobe with streaky and nodular lesion extending upto the right hilum. Large multiloculated pleural collection was noted on the right side with extension into the horizontal and oblique fissures. Thickening of the visceral pleura was noted. Small lymphnodes were noted in the left side of superior mediastinum as shown in figure 1.

After 5 days of treatment there was no significant

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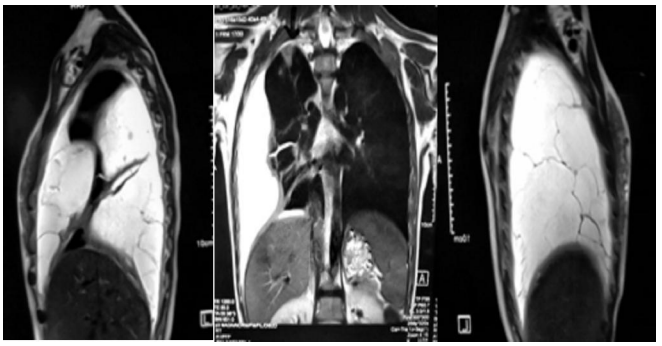

Fig. 1. MR scan of chest showing small segmental consolidation in right upper lobe with streaky and nodular lesion extending upto right hilum. Large multiloculated pleural collection on the right side with extension into the horizontal and oblique fissures. Thickening of the visceral pleura and small lymphnodes noted in the left side of superior mediastinum

improvement of the child and 4 drug ATD was started on clinical ground. Gradually there was clinical improvement with feeling of wellbeing at first and then she became afebrile after 7 days. The diagnosis was further corroborated when the girl showed remarkable improvement on anti-tuberculosis therapy. She was discharged on ATD and now under followup.

Conclusion

Diagnosis of pediatric TB is challenging as collecting proper sample is difficult but every attempt should be made for bacteriological diagnosis of TB.[2] At the start of 2020 the Central Government has renamed the RNTCP as the National Tuberculosis Elimination Program (NTEP).

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