June 2020

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E journal of Paediatrics

Issue.1

Vol.1

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Dr. P.V.Ramana Murthy M.S.FRCS (UK)
Managing Director, Chief Surgical Gastroenterologist

Prakasam Road,Govenorpet.	Heart & Brain Institute, Suryaraopet	Bhavanipuram, Vijayawada.
On Call Paediatrician : 8466996310	On Call Paediatrician : 8466998754	On Call Paediatrician : 9603066888
Ph : 0866-2574757,2576757	Ph : 0866-2442333	Ph : 0866-2415757, 2414167

DEPARTMENT OF PAEDIATRICS, ANDHRA HOSPITALS, VIJAYAWADA
E-JOURNAL

VOLUME 01 ISSUE 01 JUNE 2020

Foreword

Greetings from the Andhra Hospitals!

For the past two decades, we are delivering excellence in terms of quality health care in the field of Paediatrics including Paediatric and Neonatal intensive care, Paediatric cardiac intensive care and other allied Paediatric sub-specialities.We take pride in introducing ECMO in pediatric specialty for the first time in the state of Andhra Pradesh. In this context, we convey our heartfelt thanks to you for your continued support and encouragement which played a pivotal role in our success.

As a token of our commitment to contribute to continuous medical education, we are introducing this monthly E-journal to showcase important clinical guidelines, recent advances in paediatric sub-specialties, interesting case reports, image quiz, OSCE scenarios etc, gathered from our patient database.
We hope this endeavor would prove to be useful to practicing paediatricians, intensivists, neonatologists and post-graduate students.

Please send your valuable feedback and suggestions to ***maramkp@gmail.com*.**

Dr. P. V. Ramana Murthy M.S. FRCS (UK)

Managing Director & Chief Surgical Gastroenterologist

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Dr. M. Krishna Prasad
Consultant in PICU & ECMO

Dr.Bhoojata N
Consultant Neonatologist

Dr. Revanth. B
Consultant Paediatric intensivist

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Management of Dilated Cardiomyopathy in Children

Dr.Vikram Kudumula[a] **Dr Krishna Prasad M**[b]
[a]*Consultant Pediatric Interventional Cardiologist*
[b]*Consultant in PICU & ECMO*

Key messages:

1) In a child with respiratory illness, DCM or myocarditis should be suspected if the child has tachycardia which is disproportionate to the degree of respiratory distress.

2) When there is a suspicion, chest x ray and ECG should be done.

3) Treatable causes of dilated cardiomyopthy (like ALCAPA, tachyarrhythmias, renal artery stenosis, nutritional causes like thiamine deficiency etc) should be ruled out before labeling the case as idiopathic DCM.

Epidemiology: Dilated cardiomyopathy (DCM) is a myocardial disorder characterized by a dilated left ventricular (LV) chamber and systolic dysfunction that commonly results in congestive heart failure (CHF). It is the most common form of cardiomyopathy and reason for cardiac transplantation in adults and children. The incidence of DCM in adults is reported as 2 to 8 per 100,000 in the United States and Europe, with prevalence of 36 per 100,000 population. The incidence of paediatric DCM in USA is 0.56 cases/100,000/year, and in Australia (1.09/100,000 aged 10 years). Boys have a higher incidence than girls, related to X-linked genetic causes and neuromuscular disorders. Dilated cardiomyopathy is significantly more likely to present in the first year of life than at older paediatric ages. Infants had more than 13 times the incidence of older children.

Aetiology: Only 30% of paediatric patients have an identifiable cause for DCM in different studies. In familial DCM, autosomal dominant transmission is the most frequent inheritance however autosomal recessive, X-linked and mitochondrial inheritance patterns have been reported.

Viral	Coxsackie, HIV, Echovirus, Rubella, Varicella, Mumps, Ebstein-Barr virus, Cytomegalovirus
Bacterial	Diphtheria, Meningococcal, Pneumococcal, Mycoplasma, Tuberculosis
Rickettsia	Psittacosis, Rocky Mountain spotted fever
Parasites	American trypanosomiasis (Chagas disease), Toxoplasma, *Toxocara*, *Cysticercus*
Fungi	Candidiasis, Aspergillosis, Histoplasma, Coccidioidomycoses, *Actinomyces*
Neuromuscular disorders	Duchenne or Becker muscular dystrophies, Barth syndrome (Cardioskeletal myopathy), Friedreich ataxia, Kearns-Sayre syndrome, other muscular dystrophies
Connective tissue disorders	Rheumatic fever, Rheumatoid arthritis, Systemic lupus erythematosus, Dermatomyositis, Kawasaki disease
Infiltrations and granulomas	Leukaemia, Sarcoidosis, Amyloidosis
Haematological diseases	Thalassemia, Sickle cell disease, Iron deficiency anaemia
Endocrine diseases	Hypothyroidism, Hyperthyroidism, Hypoparathyroidism, Pheochromocytoma, Hypoglycaemia
Metabolic disorders	Glycogen-storage diseases, Carnitine deficiency, Fatty acid oxidation defects, Mucopolysaccharidoses, Sphingolipidosis
Drugs	Anthracycline, Cyclophosphamide, Chloroquine, Iron overload
Nutritional factors	Kwashiorkor, pellagra, Thiamine deficiency (Infantile Beriberi), Vitamin D deficiency and Selenium deficiency
Coronary artery diseases	Anomalous left coronary artery from pulmonary artery (ALCAPA), Post vasculitis (Kawasaki), Familial hypercholesterolemia
Tachyarrhythmias	Supraventricular tachycardia and ventricular tachycardia

Clinical features:

History:

1. Onset is usually insidious but may be acute in as many as 25% of patients with dilated cardiomyopathy, especially if exacerbated by a complicating lower respiratory tract infection.
2. The common presenting symptoms are cough, poor feeding, irritability, and shortness of breath. Some children may present with pallor, sweating, easy fatigability, failure to gain weight, and decreased urine output. Other symptoms at the time of presentation are chest pain, palpitations, orthopnea, hemoptysis, frothy sputum, abdominal pain, syncope, and neurologic deficit.
3. Some children presenting as sudden unexplained death have a diagnosis of DCM in post-mortem examination.
4. In some cases DCM is diagnosed incidentally when cardiomegaly is detected on a chest radiograph or an arrhythmia is detected on an ECG.
5. Approximately 50% of patients with DCM have a history of preceding viral illness. A detailed family history for familial cardiomyopathy is revealing in as many as 25% of cases.

Physical signs:

1. A patient with established disease will have features of congestive heart failure like tachypnoea, tachycardia with weak peripheral pulses, and has cool extremities and hepatomegaly. Blood pressure is low with a decreased pulse pressure. In extreme cases, patients may present in shock. *Wheezing may be an important clinical sign, suggesting congestive heart failure manifestation in infants.*

2. Older children may show dependent oedema, elevated jugular venous pulses, and fine basal crepitations in the lungs.

3. Major cardiac findings include cardiomegaly, quiet precordium, *tachycardia which is disproportionate to the degree of respiratory distress*, gallop rhythm (S_3 and/or S_4), accentuated P-2, and murmurs of mitral and tricuspid regurgitation. Murmurs may be inconspicuous initially if the patient presents with acute heart failure.

Investigations:

1) Chest X ray:

i) Cardiomegaly (Increased cardiothoracic ratio)

ii) Pulmonary plethora and pulmonary oedema

iii) Evidence of lateral displacement of bronchi due to left atrial enlargement

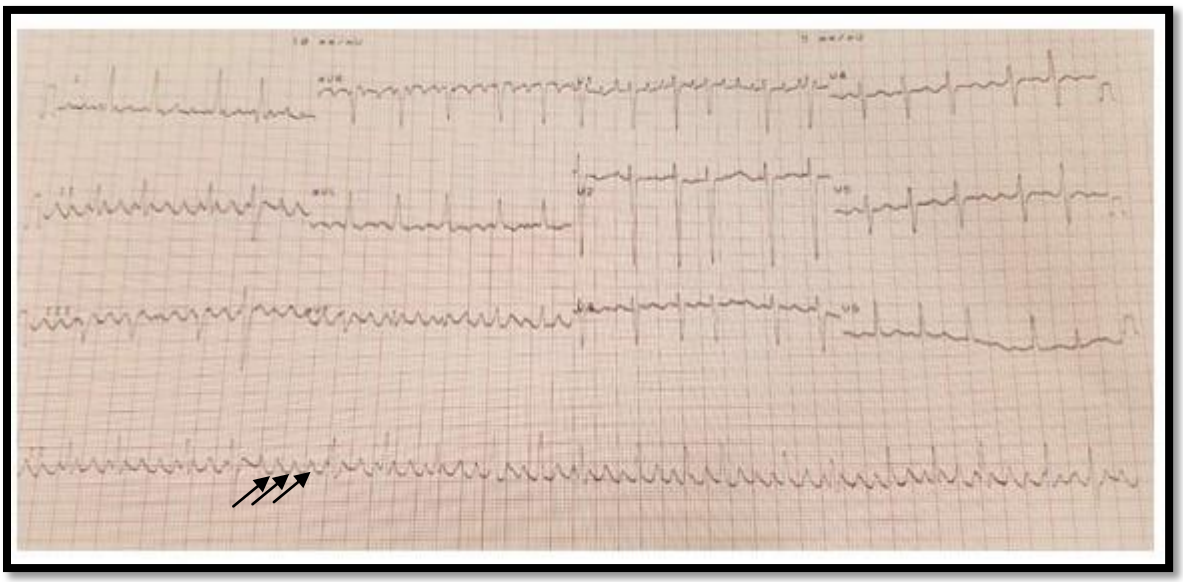
iv) Pleural effusion

2) ECG:

A) Every patient with dilated cardiomyopathy should have a 12 lead ECG to rule out tachycardiomyopathy. Long standing tachyarrhythmias like ectopic atrial tachycardia can cause dilated cardiomyopathy**.**

Below ECG showing tachycardiomyopathy secondary to incessant atrial flutter.

(Arrows showing P waves)



B) ECG signs of DCM:

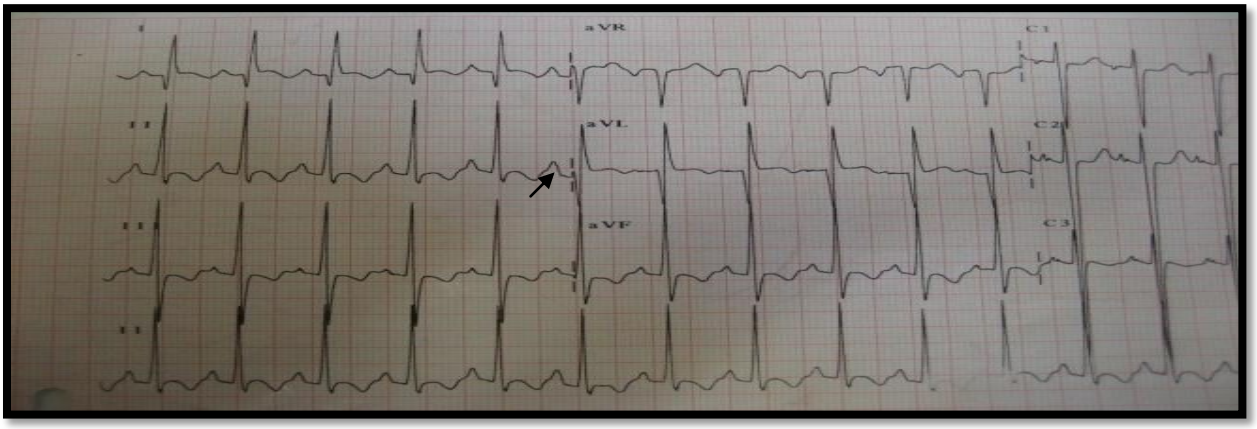
i) Sinus tachycardia

ii) Increased left ventricular voltages and ischemic ST and T wave changes

iii) Prolonged PR interval and broad QRS complexes

iv) Left and right atrial hypertrophy pattern.

v) Deep Q waves in lead I, wide Q waves in AVL, suspect ALCAPA (see the arrow in the ECG below)

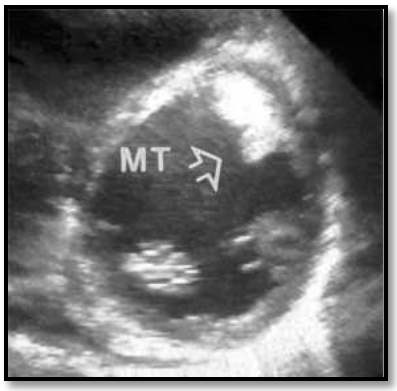


3) Echo:

i) Dilated left ventricle and left atrium with or without mitral regurgitation

ii) Decreased left ventricular function (decreased fractional shortening and ejection fraction)

iii) Exclude mural thrombus (MT)



iv) Both coronary arteries should be identified to exclude *Anomalous left coronary artery from pulmonary artery (ALCAPA).* If in doub aortic angiography is needed to rule out ALCAPA.

v) Other structural causes like coarctation of aorta and aortic stenosis should be ruled out.

4. Renal ultrasound: Chronic untreated hypertension can cause hypertrophic LV and later DCM. Our practice is to do ultrasound abdomen as a routine in all cases of DCM to rule out any renal pathology like renal artery stenosis, dysplastic or multicystic kidneys etc. We should have strong suspicion of renal pathology if you observe hypertension in a case of DCM

5. Specific Tests:

Diagnostic Test	***Rationale***
Cardiomyopathy Viral serology	Identification of possible viral etiology
Free carnitine levels Urine carnitine excretion	Diagnosis of acyl carnitine transferase deficiency, Conditions associated with increased carnitine loss
Serum ammonia levels.	May be elevated in a variety of metabolic defects
Blood Erythrocyte transketolase activation assay	To diagnose Thiamine deficiency associated DCM. Erythrocyte transketolase activation assay is expensive, time consuming and not easily available. Therapeutic trial with IV/oral Thiamine is considered the most feasible approach as patients with Thiamine deficiency cardiomyopathy will show rapid response to Thiamine repletion therapy.
Lactate levels, pyruvate levels urine organic and amino acids, succinyl acetone, urine MPS	Hyperketotic states, Barth syndrome, Metabolic myopathies
Endomyocardial biopsy	Diagnosis of myocarditis, Pre-transplant work-up Certain metabolic myopathies
Troponin T	Nonspecific index of myocardial injury, may indicate the presence of myocarditis
Thyroid Function Tests	To rule out Hypothyroidism
Vitamin D levels	Vitamin D deficiency
DNA studies, Cytogenetics	Inherited forms of DCM
ANA, dsDNA	Connective tissue disorders
CPK	To diagnose Dystrophin gene defect

Treatment:

Management of dilated cardiomyopathy involves 3 aspects.

A) Management of cardiac failure

B) Arrhythmias

C) Anticoagulation

A) Management of cardiac failure:

***1) PICU management of acute heart failure*:** If a patient is very sick, intubation and ventilation should be considered depending on the clinical condition. Use sedation and muscle relaxation to decrease metabolism and oxygen consumption. *Consider using sedation with minimum negative inotropic effect like Ketamine. (If possible avoid using Propofol and inhalation gases like sevoflurane)*

i) Inotropes: Catecholamines are the most potent positive inotropic agents available but they also have chronotropic properties and complex effects on vascular beds of the various organs of the body. So the choice of an agent may depend as much on the state of circulation as it does on the myocardium. Try avoiding child becoming unduly stressed. Consider using peripheral inotropes like dobutamine initially for stabilisation in the initial phase.

ii) Inodilators: Milrinone and Amrinone, phosphodiesterase III inhibitors, are particularly useful in the treatment of cardiogenic shock as they increase myocardial contractility and reduce afterload by peripheral vasodilatation without increasing the myocardial oxygen consumption.

iii) Diuretics: Consider intravenous route initially. Commonly used diuretics are Furosemide and Spiranolactone. Change to oral diuretics when signs of pulmonary and systemic venous congestion have decreased. Check regular fluid balance and electrolytes and correct any imbalance.

iv) Levosimendan: Levosimendan is one of a new class of inodilators, the calcium sensitizers. Its primary action is to enhance cardiac contractility by binding to cardiac Troponin-C in a calcium dependant manner and stabilize Troponin-C. It does not increase intracellular concentration of free calcium. Unlike dobutamine and milrinone, it doesn't increase myocardial oxygen consumption and has less potential for cardialarryhtmias. It exerts its effect during systole sparing diastolic relaxation of ventricle and causes venous, arterial and coronary dilatation.

It is 98% bound to plasma proteins and completely metabolized prior to excretion. Approximately 5% of the drug is converted to a highly-active metabolite with a very long elimination half life of 75-80 hrs (compared to 1 hr elimination half life of levosimendan itself).Because of this long half life, the effects of levosimendan last for 7 to 9 days after discontinuation of 24 hours IV infusion. The usual dose of Levosimendan used for congestive heart failure is 6 -12 micrograms/kg loading dose over 20 minutes followed by a continuous infusion at a rate of 0.05 -2 mcg/kg/min for 24 hours. Main side effects include first dose hypotension and headache which are dose related and rarely prolongation of QTc interval and ventricular tachycardia.

Many studies demonstrated its efficacy in improving myocardial performance, hemodynamics and results in rapid myocardial cell recovery in decompensated heart failure. It has been shown to reduce requirement of other inotropes and delay the need of mechanical heart support in patients awaiting cardiac transplantation. Repetitive levosimendan infusions appear to be well tolerated in children with dialated cardiomyopathy without severe adverse effects.

V) L-Carnitine: The primary role of carnitine is to shuttle fatty acids across the mitochondrial membrane, delivering them for beta oxidation and the production of ATP. Carnitine deficiency results in muscle myopathy, accumulation of lipid in the muscle resulting in muscle weakness.

Carnitine deficiency can be primary, resulting from a recessively inherited defect in muscle transport of carnitine, or secondary to decreased availability of free carnitine with many causes. Primary or secondary carnitine deficiency syndrome as the only concomitant entity accompanying DCM is rare but, some clinicians consider it as one of the many contributory factors. Hence, L- carnitine is routinely administered to all children with DCM irrespective of carnitine levels. Oral dose is 100-200 mg/kg/day in 2 -4 divided doses.

Vi) Immunoglobulins: A few retrospective studies on the role of Immunoglobulins (IgG) in viral myocarditis/DCM demonstrated improved recovery of LV systolic function and reduction in the episodes of fulminant arrhythmias but didn't have an impact on the transplant free survival. However, more evidence is needed to routinely recommend this therapy in acute myocarditis/early DCM. The usual recommended dose is 1gm/kg/day for 2 days.

Vii) Corticosteroids:

Myocarditis accounts for 30% to 35% of children with dilated cardiomyopathy phenotypes where chronic inflammation of the myocardium secondary to auto-immunity is thought to play a role. This forms the basis of various studies on the role of steroids (with or without other immunosuppressive agents like Azathioprine, Cyclosporin etc.) in the management of viral myocarditis/DCM. Various uncontrolled studies, case series showed the use of steroids (Methylprednisolone, oral Prednisolone) was associated with improvements in LV function, reduction in mitral regurgitation although, a recent meta-analysis demonstrated non superiority of steroids over conventional therapy in viral myocarditis. Further RCT's are needed to clarify the role of steroids in the management of myocarditis with DCM phenotype.

viii) Thiamine :

The recommended dose of Thiamine in heart failure secondary to Thiamine deficiency (wet Beriberi) is 100 mg IV once daily for several days which can be converted to oral form at discharge. The clinical effect of thiamine therapy seen in wet Beriberi patients will be dramatic with improvement in LVEF in 48 to 72 hours.

Thiamine has multiple effects on the CV system. It has important hemodynamic effects on the circulatory system as well as direct positive pharmacologic effects on the heart. Thiamine deficiency has been shown to cause cardiac hypertrophy, dilated cardiomyopathy, and dysrhythmias. Clinical trials in patients with CHF have shown that thiamine supplementation increases systolic, diastolic, and central venous pressures, with a decline in heart rate and increase in LVEF. Thiamine acts as a vasodilator and reduces the afterload on the heart, thus improving cardiac function. Thiamine has also been reported to increase diuresis and natriuresis in patients with HF receiving diuretics, an effect that is of considerable benefit in this population.

ix) Vitamin D (Cholecalciferol):

Calcium plays a crucial role in myocardial contraction coupling while, hypocalcemia reduces myocardial function. Congestive cardiac failure due to hypocalcemia is rare and few cases of hypocalcemia-induced cardiomyopathy have been reported. Hypocalcemia causing DCM is reversible with complete recovery after normalization of serum calcium. Vitamin D deficiency is the main cause of hypocalcemia in infants and old children. Nutritional rickets secondary to vitamin D deficiency is still rampant in the breastfed infants and children in our country. Hence, we routinely administer oral Vitamin D suppliments to all dilated cardiomyopathy children pending Vitamin D levels. The recommended oral dose is 1000 IU/day for <1 month, 1000 -5000 IU/day for 1 -12 months and 5000 IU/day for >1 year for 2 to 3 months.

2) Once patient is stable

I) Continue diuretics

ii) ACE inhibitors: Enalapril is the most commonly used drug in our centre. First dose hypotension and renal impairment are common side effects. In children >1month of age, give a test dose of 100mcg/kg and monitor ½ hrly blood pressure for 2 hours. If tolerated well, start with 100mcg to 200mcg/kg/dose BD and increase gradually over a period of 5 to 7 days to 500 mcg/kg/dose BD. Monitor BP and U&E regularly during escalation of dose. After stabilising the dose of Enalapril stop Spiranolactone.

Cautions:

a) First dose hypotension, so needs regular blood pressure monitoring after starting and adjustment of the dose.

b) Hyperkalemia and renal impairment: regular U&E monitoring after starting and adjustment of the dose.

c) Non productive cough

Contraindications:

a) Suspected renovascular disease

b) Hypersensitivity to ACE inhibitors.

iii) β blockers: Increased sympathetic drive that occurs as a compensatory mechanism in cardiac failure has inverse relationship in prognosis. Long term adrenergic stimulation results in receptor desensitization, maladaptive proliferative response like myocyte hypertrophy and fibrosis. This is collectively called as remodelling. β blockers down regulates sympathetic drive and increases the prognosis and outcome.

The use and efficacy of beta-blockers on decreasing morbidities and mortality in adults with dilated cardiomyopathy has been well described. The role of beta-blockers in the treatment of children with dilated cardiomyopathy remains under

investigation. The most commonly used drug in our centre is *Carvedilol* which should be started only at the discretion of cardiologist.

Initial Dose: 50microgram/kg (max 3.125mg) twice daily for 1-2 weeks

Monitor blood pressure and heart rate 1 hourly for 6-8hours after the first dose

Maximum dose: 350 micrograms/kg (max 25mg) twice daily

Dose escalation: Increase dose by 50-100microgram/kg increments e.g. if previous dose 50 micrograms/kg twice daily, increase dose to 100-150micrograms/kg twice daily.

Monitor FBC, U&E and LFTs

Carvedilol comes as 3.125mg, 6.25mg, 12.5mg and 25mg tablets (they are all scored and may be halved).

Monitor blood pressure and heart rate during escalation of dose.

Side effects: Hypotension, dizziness, headache, fatigue and sleep disturbance.

Contraindications:

a) Severe bradycardia, sick sinus syndrome and second or third degree heart block

b) Children with asthma

iv) Digoxin: Oral inotrope but failed to actively reduce mortality and morbidity in adults. So it is used as second line medication. Dose: 3 micrograms/kg/dose/twice daily.

V) Ivabradine:

Ivabradine is a **s**elective and specific inhibitor of the hyperpolarization-activated cyclic nucleotide-gated (HCN) channels (f-channels) within the sinoatrial (SA) node of cardiac tissue resulting in disruption of I_f ion current flow prolonging diastolic depolarization, slowing firing in the SA node, and ultimately reducing heart rate. It is commonly used to reduce the heart rate and proven to lower the incidence of cardiovascular death and hospitalization for worsening HF in adult patients.

In a RCT evaluating Ivabradine in children with DCM and symptomatic heart failure, adding ivabradine to stable HF therapy (including beta-blockers) could reduce heart rate by more than 20% in a clear majority of children without inducing bradycardia. Ivabradine has a good safety profile and was associated with a significant reduction in resting heart rate of children with chronic HF and DCM in all age subgroups tested from 6 months to 18 years. Children treated with ivabradine also showed significant improvement in echocardiographic indexes (LVEF and LVESV) and a favorable trend for clinical status and quality of life (QOL) compared with placebo.

The usual starting dose is 0.02mg/kg twice daily for children 6 to 12 months and 0.05 mg/kg twice daily for children aged 1 to 18 years which can be titrated upto a maximum of 0.3mg/kg twice daily. Patients weighing >40 kg, can be started on 2.5 mg twice daily (tablet form), could be uptitrated to 5, 7.5, 10, and 15 mg twice daily.

B) Management of arrhythmias: Arrhythmias are common in dilated cardiomyopthies so, careful monitoring of U&E, Calcium and Magnesium levels is important. In patients with tachycardiomyopathy (tachyarrhythmias causing DCM), treatment of underlying tachycardia is very important to improve LV function. Many antiarrhythmic drugs are negatively inortropic. Of the available anti-arrhythmics, Amiodarone has been shown to be effective and relatively safe in children. Management should be started after consultation with cardiology team.

C) Anticoagulation: DCM patients are more prone to develop mural thrombus due to stasis of blood. So patients with very poor left ventricular function should be given prophylactic Heparin until oral Aspirin is established.

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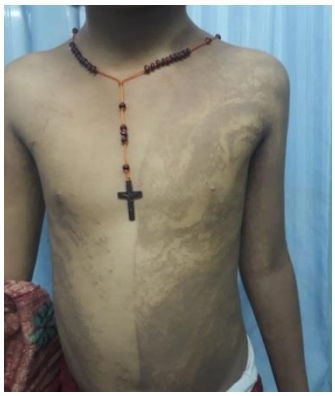
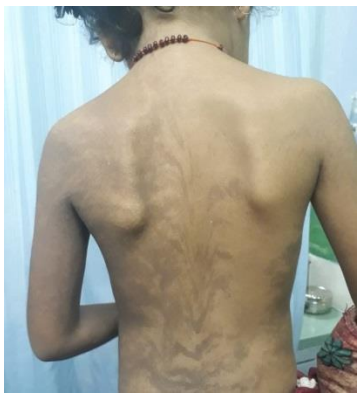
Dr.Pavan satyam[a]

[a]**Junior Consultant in Pediatrics**

A 7 yr old female child brought to OPD with complaints of hyperpigmentary lesions on the trunk and extremities for the past 6-months.The lesions were non-itchy and painless, progressively spreading with increased pigmentation overtime.Child also had a history of seizures 4 yrsagowhich were treated with Levetiracetam for 2 years before discontinuation.Shehad no recurrence of seizures.Therewas no other significant relevant history

General Examination: Significant for a diffuse hyperpigmented, with occasional vesicles. The rash was noted to be linear and appears to follow the lines of Blaschko on her trunk. Neurologic Examination: Mental Status:GCS 15/15. Cranial Nerves: Her pupils were equal, round, and reactive to light. Her extraocular muscles were intact. Facial expression is symmetric. She had positive gag and her tongue is in midline. Motor: She had normal bulk,tone and power. Reflexes: 2+ throughout with bilateral plantar flexor responses.





What is your diagnosis?

a.Molluscum contagiosum

b.Varicella

c.Hypomelanosis of Ito

d.Naegeli syndrome

e.Incontinentiapigmenti

Answer in the next page

Answer: ***Incontinentiapigmenti (IP)***

The characteristic skin lesions of IP must be distinguished from other dermatologic possibilities. These include infections such as molluscum contagiosum, as well as other neurocutaneous disorders such as hypomelanosis of Ito and Naegeli syndrome. Molluscum contagiosum has umblicated vesicles and In hypomelanosis of Ito, abnormal hypopigmentation is the primary skin manifestation. Naegeli syndrome is an extremely rare autosomal dominant skin disorder without different stages of skin lesions.

Incontinentiapigmenti (IP),also known as Bloch-Sulzberger syndrome, is an X-linked dominant neurocutaneous disorder that affects the skin, hair, teeth, nails, and eyes, as well as the central nervous system. IP occurs in 1 in 40,000 individuals and is usually lethal in males. The characteristic skin findings evolve over four defined stages that occur along the lines of embryonic and fetal skin development known as Blaschko lines. Blaschko lines are linear on the extremities and circumferential on the trunk. The rash is usually present at birth or shortly afterwards.

This disease has 4 phases, not all of which may occur in a given patient. Stage 1 (bullous stage) is characterized by blister or vesicular-like eruptions that can be erythematous and appear infectious. Stage 2 (verrucous stage) is characterized by keratotic, warty papules and plaques that continue to follow the Blaschko lines. Stage 3 (hyperpigmentation stage) is noted for macular hyperpigmented whorls along the Blaschko lines (“marbled cake” appearance). The hyperpigmentation usually fades in the teens and early 20s, leading some individuals to proceed to stage 4. Stage 4 (atretic stage) is characterized by hairless hypopigmented streaks and patches with skin atrophy that may persist into adulthood. Ocular manifestations are seen in almost 80% of affected individuals. They include mottled, hypopigmentation of the retina and abnormal peripheral vascularization of the retina, which can result in retinal detachment. Dental findings occur in 65% to 90%, with delayed tooth

eruption, hypodontia, microdontia, and round, peg-shaped teeth. Dysplastic nails with ridging, pitting, onychogryposis, or subungual dyskeratomas occur in 40% to 60% of individuals. Woolly hair or alopecia may also be seen. Central nervous system manifestations occur in 10% to 40% of individuals with IP. They include microcephaly, mental retardation, spasticity, seizures, and strokes.

Management

Diagnosis of incontinentia pigmenti is made on clinical grounds, although major and minor criteria have been established to aid in diagnosis. Wood's lamp examination may be useful in older children, and perform skin biopsy confirmation and adolescents to highlight pigmentary abnormalities. Neuroimaging and Ophthalmologic evaluation is recommended. Clinical molecular testing is available, and in 80% of the affected patients a deletion that removes exons 4 through 10 of *IKBKG* gene can be detected.

Dermatologic consultation is recommended for supportive skin care to minimize skin irritation, prevent infection. Ophthalmologic evaluation is recommended to identify ophthalmologic findings and monitor for retinal detachment. In addition, neuroimaging, preferably with a brain MRI, should be done to evaluate for underlying structural abnormalities that might explain seizures. Magnetic resonance (MR) angiography of the head is also recommended as cerebrovascular abnormalities have been rarely reported with IP. Surveillance evaluations by ophthalmology, dermatology, and dentistry are recommended to monitor for retinal detachment, complications associated with skin lesions, and dental care, respectively. Genetic counseling is encouraged for parents and family as deletions of the *IKBKG* gene can be inherited or from a de novo gene mutation (commonly of paternal origin by germ line mosaicism). As the deletion is lethal in most males, a history of multiple miscarriages (males) is common in familial IP. Skewed X-chromosome inactivation in females can result in variable presentations.

Care of newborn after delivery with suspected/ confirmed COVID19 positive mother

Dr Rama Rao Paturi[1]
[1] **Chief of Children's services & Director**

Obstetric team:

- PPE including eye shield & N95 mask.
- Delivery mode: Dictated by obstetric team based on indications.
- Neonatal team: PPE including eye shield & N95 mask.

  Neonatal management:
- Consider temporarily separating infant from the mother.
- Consider expressed breast milk.
- If mother & baby are not separated, breast feeding while wearing N95 mask and after hand hygiene may be considered.
- Isolation pending test results.
- Nasopharyngeal/ throat swab for RTPCR at 24 hrs& repeat at 48 hrs.
- Majority are asymptomatic or with mild symptoms and recovered without complications.
- Presents with non specific symptoms like temperature instability, apnoea, respiratory distress, fever, lethargy, rhinorrhea, cough, tachypnea, vomiting, diarrhea and feeding intolerance or decreased intake.
- Transmission of COVID19 to neonates is thought to occur primarily through respiratory droplets during the postnatal period when neonates are exposed to mothers, other care givers, visitors or health care personnel with COVID19.

- Limited reports have raised concerns of possible intrapartum or peripartum transmission, but the extent and clinical significance of vertical transmission by these routes is unclear.
- As majority of neonates are asymptomatic, all neonates born to mothers with confirmed or suspected COVID19 should be considered as having suspected COVID19 when testing results are not available.
- Infants with suspected COVID19 should be isolated from other healthy neonates.
- Temporary separation in the clinical setting can be achieved in many ways including a separate room, maintaining a physical distance of > 6 ft between the mother & neonate and placing the neonate in a temperature controlled isolette if the neonate remains in the mother's room. For mothers whose test results are negative, separation precautions may be discontinued.
- If the neonate tests positive for COVID19, separations is not necessary.
- Face mask should not be on neonates or any children younger than 2 years of age.
- Newborn discharge: Based on clinical condition, precautions based on baby test results.
- Neonates with suspect or confirmed COVID19, require close outpatient follow up after discharge.

  Potential for postnatal infection:
- Take precautions/ follow guidelines for aerosol generating procedures while doing suction, intubation, extubation, HFNC, CPAP, droplet or contact spread from mother.
- All staff should wear PPE.
- All babies requiring respiratory support should be nursed in an incubator.

Feeding in babies with COVID19 positive mothers:

- Benefits of breast feeding currently outweigh the risks of passing infection from mother to infant.
- No evidence to say that corona virus secreted in breast milk and transmitted to the infant.
- Mother to child transmission of COVID19 during pregnancy in unlikely.
- We do not know for sure if mother with COVID19 can spread the virus to babies with their breast milk, but the limited data available suggest this is unlikely.
- If mother insists on direct breast feeding, then advice mother to wear protective gear ie mask, apron & gloves while breast feeding.

1. If you have COVID19 & choose to breast feed:

- Wear a face mask covering while breast feeding and wash your hands before each feeding.
- Continue to breast feed while taking care with hygiene.

Three 'W's

- **W**ear a mask during feeding
- **W**ash hands with soap before & after touching the baby.
- **W**ipe & disinfect surfaces regularly.

2. If you have COVID19 & choose to express breast milk:
   - She may wish to express her breast milk and feed the baby using a clean cup & spoon.
   - Use a cup & spoon to feed babies with expressed breast milk when too sick to breast feed.
   - Use a dedicated breast pump.

- Wear a face mask and wash your hands before touching any pump or bottle parts and before expressing breast milk.
- If possible, expressed breast milk should be fed to the infants by healthy care giver who does not have COVID19, is not at high risk for severe illness from COVID19, and is living in the same home.

3. Take extra care when formula feeding:

Breast feeding is the best way of providing ideal food for the healthy growth & development of babies. However, there are instances where a mother is unable to breast feed or where she has decided not to breast feed, and then extra care is taken with thoroughly washing bottles, teats and any other equipment used.

Reference:

CDC

UNICEF

BMJ

IAP

RCPCH, UK

FOOD PROTEIN INDUCED ENTEROCOLITIS SYNDROME (FPIES) IN A NEWBORN – A SEPSIS MIMIC

Dr.Bhoojata N[1] Dr Upender Shava[2] Dr Vamsi Krishna G[3]

[1]Consultant Neonatologist

[2]Consultant Pediatric Gastroenterologist

[3]Neonatal Fellow

Introduction.

Milk protein allergy in infancy is widely reported in western population with an overall prevalence of 2 to 3% in less than 1 yrold(1,2). 0.5% of breast fed infants show reactions to CMP. Until the last decade, this disease was generally believed as a disease of west. Since a decade milk protein allergy is being increasingly reported in Asian children attributed to the increased awareness and diagnostic facilities (endoscopic biopsies.) But still information about this disease from India is scanty.

Yachha*et a(3)l.* has highlighted a prevalence of 13% among Children < 2 years of age with malabsorption. Poddar et al., showed a 30% prevalence rate of CMPA in Indian children (2) with chronic diarrhoea

Milk protein allergy presenting in new born period is also not uncommon presenting as early in the first week of life. This case report highlights the importance of considering milk protein allergy in a new born presenting with colitis.

CASE REPORT

A term, female baby of birth weight 2.7 kilograms born to a non consanguineous marriage presented on day 24 of life with complaints of Loose stools for last 3 days, 9 to 10 episodes per day, watery in consistency, large in volume, yellowish in color with no blood in stool; Excessive and Irritable, nonconsolable cry since 1 day, Fast breathingfor 1 day .Baby was seen at local hospital and was referred to our hospital for further management.

Further history suggested of vomiting at 10days of life, 3 to 4 episodes per day, nonbilious, nonprojectile, subsisded with some local medication. H/o red colored mucoid stools – 1 episode at 10 days of life.

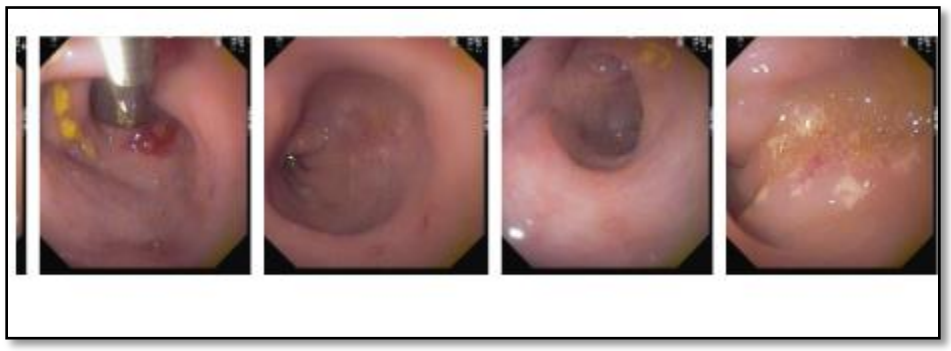
Baby was admitted in postnatal period in NICU at local hospital and was treated for sepsis with IV antibiotics for 7 days of life.

Baby is on breast feeds with top up formula feeds since birth.
On admission to NICU, baby was irritable, with signs of severe dehydration, weight of 2.5 kg. blood gas analysis showed severe metabolic acidosis, PH - 7.03,Lactate - 2.3,Base deficit : -Baby was started on IV fluids as per the unit guidelines and blood reports showed raised TC (32000, N- 74 L- 16 , E- 03, M- 07), positive CRP (2.4) , Acute gastroenteritis with sepsis was considered and baby was started on iv antibiotics,

Blood gas was normalized once dehydration got corrected. But baby continued to have loose stools 7 to 8 episodes per day. Hence ZEROLAC feeds were started in v/o secondary lactose intolerane (stool for reducing substance came negative.)Baby seemed to improve with decrease in the number of stool frequency and improvement in stool consistency, but on day 5 of admission baby had 3-4 episodes of blood stained mucoid stools, Blood counts repeated showed a decrease in TC (26000), with normal platelets and normal coagulation.

Hence other differential diagnosis for dysentery was considered, stool culture was sent, (came negative,), milk protein allergy was considered. Feeds changed to amino acid formula feeds, and stool became normal in colour and consistency in 24 hrs. Gastroenterologist opinion was taken and sigmoidscopy was planned which showed multiple aphthous ulcers in rectum and biopsy report also was suggestive of allergic proctocolitis. Baby was ischarged on 35 day of life with good weight gain of 2.84kg.

Blood stained Mucoid Stool



SIGMOIDOSCOPY

DISCUSSION

Milk protein allergy can effect various organ systems skin (eczema, atopicdermatitis, anaphylaxis) respiratory (wheeze), GI manifestations (diarroea, colitis, FTT,GERD). It can present even in exclusively breast fed infants and in infants on formula feeds. Age of presentation can vary between 1 week to 6 months of life.

Cow's milk protein has two main proteins: casein (80%) and whey (20%). The major proteins in whey are α-lactalbumin (α-Lac; Bos d 4), β-lactoglobulin (β-Lg; Bos d 5), Immunoglobulins (Bos d 7) along with bovine serum albumin (BSA; Bos d 6) and lactoferrin(4). Cas, β-Lg and α-Lac are considered major allergens in cow's milk. Breastfed baby can develop CMPA due to secretion of bovine protein (beta lactoglobulin) through breast milk when the mother is ingesting bovine milk.. In nonbreast-fed infants, cow's-milk–based formula or supplementary foods containing CMP or other unmodified animal milk proteins (eg, goat's milk, sheep's milk)can cause CMPA.

Milk allergy can either be immunoglobulin mediated (IgE) or non-IgE mediated. Non IgE mediated immune reactions mainly involve GI tract.Manifestations of CMPA include IgE-mediated urticaria, angioedema, acute flare-up of atopic eczema and gastrointestinal symptoms like vomiting, diarrhoea, colic reactions. Atopic dermatitis is observed in approximately 10–15% of young children. There is an increased risk of developing atopic diseases such as asthma, atopic dermatitis and rhinoconjunctivitis in children with a history of IgE-positive CMPA(5).

Non IgE mediated manifestations of GI includes:

1. Food protein induced entercolities syndrome (FPIES)

   Occurs in young infants presents as vomiting, diarrhea, metabolic acidosis, dehydration, lethargy, bloody stools.

   Milk and soy protein are the most common causes.

2. Food protein – induced enteropathy syndrome:

   Uncommon disorder in young infants.

   Presents as chronic diarrhea with generalized malabsorption.

   With weight loss and growth failure.

   Milk allergy in most cases

3. Food protein induced allergic proctocolitis (FPIAP)

   Infants seem generally healthy

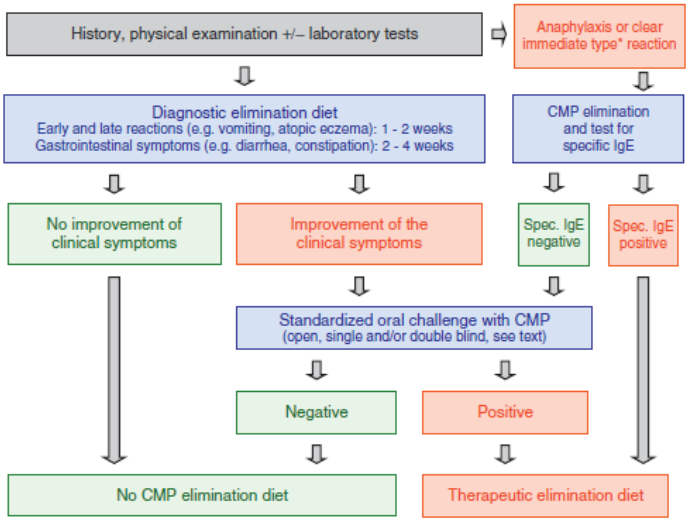
   Stool has visible specks of blood mixed with mucus, casual food allergen is milk or soy, maternally ingested proteins in breast fed.

4. Eosinophilic Gastroenteritis or esophagitis are manifestations of mixed IgE and non IgE mediated reactions

Hematochezia in a newborn carries the differentials of Necrotizing enterocolitis, infectious colitis (Salmonella, Shigella, Campylobacter, Yersinia, or parasites), volvulus, and intussusception in a sick baby(6). In a well-baby with hematochezia we need to rule out the differentials of swallowed maternal blood, perianal dermatitis, anal fissure after the passage of first meconium, vit k deficiency,

coagulation disorders, vascular malformations. Hematochezia early in newborn period with in one week of neonatal life also points to the common but largely unreported cause of food protein-induced enterocolitis syndrome, and also rare but known entity of transient neonatal eosiniphilic colitis.FPIAP has been described as the trigger of hematochezia in well-looking neonates, in the absence of any of the other possible causes of early rectal blood loss.

Diagnosis



ESPHGAN guidelines on CMPA in infants

CMPA is suspected when there is history of chronic diarrhea or dysentery, failure to thrive, GERD, with other differentials excluded. And infants show response to withdrawal of milk and milk products.

Endoscopic duodenal biopsy shows shortening of villi (mild to moderate or partial villous atrophy) with excessive eosinophilic infiltrates in the lamina propria and sigmoidoscopy shows aphthous ulcers (small discrete ulcers with surrounding erythema and normal intervening mucosa) and rectal biopsy shows focal eosinophilia (>6 eosinophils/HPF in the lamina propria of one or two crypt regions)

or eosinophilic proctitis (focal eosinophilia + eosinophilic infiltrates in the muscularis mucosa and/or eosinophilic crypt abscess).

Presence of aphthous ulcers and abnormal rectal biopsy (eosinophilic proctitis) are supportive for diagnosis.

Treatment

Bloody diarrhea typically disappears within 72 to 96 hours, but endoscopic and histologic can take several weeks. Most babies tolerate subsequent reintroduction of the protein by the age of 1 to 3 years (8).

Elimination diet:

- Maternal elimination of CMP diet in breast fed infants.
- eHF in formula fed infants.
- In more than six month infants – soya formula
- > 2 yrs solid foods and liquids free of CMP
- In sick infants AAF are of choice.

In our case the newborn presented with acute gastroenteritis with sepsis like symptoms and signs. Blood cultures were negative with persistence of dysentery inspite of treatment for sepsis which made us think of FPIES.

Conclusion-

CMPA is common even in a developing country like India. It should be suspected even in a newborn with chronic diarrhoea or colitis while ruling out other differentials. Presence of aphthous ulcers and abnormal rectal biopsy (eosinophilic proctitis) are keys to initial diagnosis. Mainstay of treatment includes elimination of allergen.Once trial of elimination diet for 2-4 weeks is given,if child responds then same diet is continued for 12 -18 months depending on severity of disease.The milk challenge confirms the diagnosis in all cases if it is done in time.

The idea to report this case is that without a proper diagnostic workup, including food challenge procedures, there is a high risk of both over- and under diagnosis and thus over- and under treatment. A correct diagnosis allows the appropriate diet to be given to affected infants,thus supporting normal growth and development. In contrast, a diet that is not indicated or continued when the child may have already developed tolerance may impair growth and quality of life for both infant and family along with financial concerns.

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