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CONTENTS

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Dear Esteemed Members,

Greetings from NNF Delhi!

It gives me a feeling of immense pleasure about the success of our Monthly Bulletin **NeoClips** (Neonatal Clinical Practice). This idea has emerged as a unique proposition from the minds of experienced neonatologists teaming up with young budding counterparts.

This section covers a few important topics like a review article on retinopathy of prematurity and an interesting case of refractory seizures in diamniotic dichorionic twins. A case of Kasabach Meritt syndrome has been covered in the picture of the month section.

My sincere congratulations to the NeoClips team for their continuing efforts in publishing this monthly bulletin.

With Best Regard

L Bharti

Dr. Lalan Bharti
President, NNF Delhi

From Secretary's Pen

DR KUMAR ANKUR

Secretary, NNF Delhi

Dear friends,

Warm greetings from National Neonatology Forum, Delhi!

It gives me immense happiness to see the success of NNF Delhi monthly E- Bulletin, launched in February 2022 with the name of '***NeoClips' (Neonatal Clinical Practice)***. Every month it's getting better & better. And credit goes to the Chief editor Dr Naveen Gupta & his exceptional team. OSCE as system wise which would be very helpful for Neonatal fellows/Residents/Postgraduates. This month we have included some interesting topics like retinopathy of prematurity. An interesting image of the vein of Galen malformation has been covered in the image section. Few questions on CNS are covered in OSCE section.

We are requesting all the esteemed members to contribute to these E-bulletins. We shall be giving the due credits to all the contributors.

We eagerly look forward to your feedback and hope to give you an experience that you will cherish forever!

Dr. Kumar Ankur
Secretary, NNF Delhi

Editor's Desk

DR NAVEEN PARKASH GUPTA

Chief Editor, Neo Clips

Dear Friends,

Greetings from the NeoClips team.

As Editor I would like to start by thanking the editorial team for the effort and the authors for their contribution to this and previous issues.

I am sorry for the delay in publishing this edition.

In the present issue, we have covered some interesting topics.

An interesting case of refractory seizures in twins has been covered in case report section.

Retinopathy of prematurity is an important cause of severe visual impairment in childhood. Screening and treatment of ROP has been discussed in review section by Dr Ashok Deorari.

An interesting case of Kasabach Meritt syndrome has been covered in the picture of the month.

The image section describes a case of vein of galen malformation.

Few questions on CNS are covered in OSCE section.

We hope that you will enjoy reading this issue. Please share your feedback with us. It will help us improve the journal.

Dr Naveen Parkash Gupta

Refractory Neonatal Seizures in Di-chorionic Di-amniotic (DCDA) twins

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A 25-day-old Di-chorionic Di-amniotic (DCDA) twins, both female, were admitted to our neonatal intensive care unit (NICU) in view of repeated episodes of jerky movements of all four limbs. Twin 1 had these episodes since day 7 of life and in twin 2, these episodes occurred since day 13 of life. The neonates were born at 36 weeks of gestation, to a 29 year-old primigravida mother by caesarian section. Antenatal period was uneventful. The neonates weighed well at birth, with twin 1 weighing 2500 g and twin 2 weighing 2600 g. Both were mixed-fed with formula and breast milk. The neonates were air-lifted on day 25 of life, due to repeated episodes of multifocal clonic seizures. On evaluating the history, these episodes were of abrupt onset, brief -lasting for less than a minute, occurred 5-6 times in a day and had no relation with sleep. There was no history of any post-ictal phase/alteration of sensorium, fever, rash or feeding difficulty. On examination, the general physical and neurological findings were unremarkable in both neonates. There were no signs of dysmorphism, rash, hepatosplenomegaly or abnormal skin/urinary odour. The infants were active and alert, anterior fontanelle was at normal level. There were no tone abnormalities or signs of focal deficit. Neonatal reflexes were appropriate for age. Fundus examination was normal.Based on history and examination, our differential diagnoses were of metabolic and electrolytes abnormalities, late onset sepsis with meningitis, infantile epilepsy, structural abnormalities of brain and inborn error of metabolism. Sepsis work up including blood culture and lumbar puncture was done, which revealed no signs of infection. Cranial ultrasound and cerebral function monitoring was normal. Laboratory investigations showed normal serum electrolytes, renal function test, serum magnesium and glucose levels (Table 1). However, serum calcium was low in both babies (twin 1, 6.3 mg/dl and twin 2, 5.8mg/dl) with high phosphate levels (twin 1, 9.5mg/dl and twin 2, 9.2mg/dl). Parathyroid hormone (PTH) levels were inappropriately low against an expected high level in response to hypocalcemia (twin I, 50 pg/ml and twin II, 59 pg/ml with a normal reference range: 10-65pg/ml). Vitamin D levels were within normal limits (twin I, 29 ng/ml and twin II, 31 ng/ml, compared to a normal reference range of 10 to 55 ng/ml). Chest X rays of both neonates showed normal thymic shadow. Serum creatinine and urine Calcium creatinine ratios were normal.

Table-1- Laboratory Reports of Neonates at admission

	Twin 1	Twin 2
S. Calcium	6.3 mg/dl	5.8 mg/dl
S. Phosphate	9.5 mg/dl	9.2 mg/dl
S.Magnesium	1.9 mg/dl	2 mg/dl
Vit-D	32ng/ml	35 ng/ml
PTH level	50 pg/ml	56 pg/ml
Renal function test	Normal	Normal
Serum electrolytes	Normal	Normal
Blood sugar	89 mg/dl	78 mg/dl

In view of refractory hypocalcemia with hyperphosphatemia and inappropriately low PTH, a provisional diagnosis of hypoparathyroidism was made in the DCDA twins. Activated Vit-D (1 alpha-OH

D3) was started at a dose of 0.06 ug/kg/day (0.25 ug/day) and oral calcium was given at a dose of 50 mg/kg/day. Because of unexplained neonatal hypocalcemia and hypoparathyroidism, maternal evaluation was done. Maternal laboratory evaluation revealed normal vitamin D levels (40ng/ml) and hypercalcemia with hypophosphatemia (serum calcium 11 mg/dl and serum phosphate 2.1 mg/dl). Parathyroid hormone (PTH) level was 484 pg/ml (normal reference range is 10-60 pg/ml). Based on the above findings, maternal hyperparathyroidism was diagnosed. Ultrasonography of the neck (Figure 1) revealed a hypoechoic nodule of size 14x6 mm in the left paramedian location closely abutting the left lobe of thyroid gland.

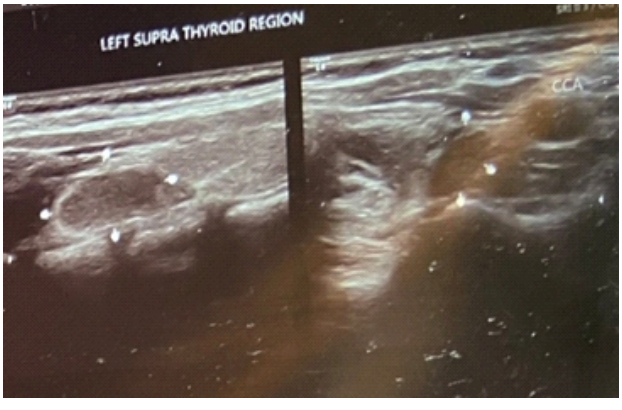

Fig. 1. Hypoechoic nodule of size 14x6 mm in left paramedian location, closely abutting the left lobe of thyroid gland.

Tc 99m sestamibi scintigraphy revealed focally increased uptake in the corresponding site suggestive of parathyroid adenoma. Ultrasonography of the abdomen showed bilateral nephrocalcinosis in the mother. Mother was referred to endocrinology department for further management.

Both the neonates responded well to therapy. Seizures resolved after 48 hours. Serum calcium and phosphorus levels normalized in a week. Both babies were discharged after 7 days of NICU stay. Currently, both babies are under follow up and have appropriate growth and developmental milestones.

Neonatal seizures are one of the most common neurological emergencies in neonates. In addition to sepsis work up, lumbar puncture, neuro-imaging and metabolic screen to exclude inborn errors of metabolism; laboratory parameters should also include sodium, potassium, calcium, magnesium and phosphorus in all cases. [1] Once hypocalcemia is detected, the cause of neonatal hypocalcemia should be investigated. Differentials of late onset hypocalcemia with hyperphosphatemia includes high phosphate diet, chronic kidney disease (CKD), hypoparathyroidism and PTH resistance. Parathyroid hormone is one of the major hormones that regulate serum calcium (along with vitamin D) via direct effects on bone and kidney and indirect effects on the gastrointestinal tract. Hypoparathyroidism occurs when there is abnormal parathyroid gland development, altered regulation of PTH production or impaired PTH action. Isolated congenital hypoparathyroidism can occur as a sporadic or familial disorder with inheritance by autosomal dominant, recessive or X linked modes of transmission. DiGeorge syndrome has also association with hypoparathyroidism.

In our case, both neonates were on breastfeeds (rules out high phosphate diet), blood urea and serum creatinine were normal (rules out CKD) and PTH level were not high (rules out PTH resistance). In neonates, with refractory hypocalcemia, workup for hypoparathyroidism and Vitamin D deficiency should be undertaken. Chest X ray should be done to look for absence of thymic shadow.[2] Mother should be investigated for hyperparathyrodism and Vitamin D deficiency in all patients with refractory neonatal hypocalcemia.[3]

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Retinopathy of prematurity: Must know for Every pediatrician!

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Introduction

Retinopathy of prematurity (ROP) is a retinal vascular disease characterized by an aberrant vascular formation and proliferation in neonates born premature. India has the highest numbers of preterm babies with at-least 10% of them requiring ROP treatment annually. About a third of the neonates born below 1500 grams develop any ROP, with rates as high as 60% in those less than 1000 grams. (1) Fortunately, most regress on their own but screening to detect those who might need intervention is critical. The greatest challenge faced in India is the availability of a skilled ophthalmologist to screen and treat ROP. An increased survival of the smaller and sicker neonates has placed ROP as the leading cause of potentially avoidable childhood blindness.

Pathogenesis

Due to the physiologically hypoxic state in-utero, retinal vessels develop (*vasculogenesis*: 14-21 weeks) and proliferate normally under influence of vascular endothelial growth factor (VEGF) (*angiogenesis*: 22 weeks till term). Retinal vessels continue to proliferate from the optic disc to the peripheral retina nasally by 32 weeks and temporal area by 44 weeks. Disruption of these processes in preterm and exposure to high oxygen milieu leads to suppression of angiogenic factors like VEGF and erythropoietin. Compounded by a low omega-3-polyunsaturated fatty acid and Insulin-like Growth Factor-1 (IGF-1) in a nutritionally deprived environment, the retinal vessels fail to proliferate (*Phase 1:* Hyperoxia or vasoconstriction). Retinal hypoxia commences and progresses to a stage where sufficient VEGF production is induced (along with IGF-1) leading to formation of aberrant and fragile vessels at the transition of avascular and vascular retina, worsening the hypoxia further (*Phase 2:* Hypoxia or vasoproliferation). If unrecognized and untreated, a vicious cycle is created leading to progressive retinal detachment, and blindness.

Risk factors

The most important risk factors are prematurity and low birth weight. Each 100 g increase in weight below 1250 g, decreases the odds of developing severe ROP by 27%. Further, the risk decreases by 19% with each extra week added in gestation. (2) Other modifiable risk factors include use of supplemental oxygen, ventilation (both invasive and non-invasive), liberal blood transfusions, presence of systemic sepsis, need for inotropes and poor weight gain.(3)

Diagnosis and Classification of ROP

ROP has been traditionally classified as zone, stage, extent and presence of plus disease. International Classification of ROP (ICROP) has been recently updated with an aim to decrease subjectivity and incorporate challenges presented by innovations in imaging and anti-VEGF medications. (4) The updated classification is summarized in table 1 and figure 1.

Another rapidly progressive and severe form of ROP called **Aggressive ROP (A-ROP)** is seen in smallest and sickest of preterm neonates. It is an ill-defined retinopathy characterized with no sequence of progression and prominence of plus disease resulting in early retinal detachment. Previously called aggressive posterior ROP (AP-ROP) mostly localized in posterior zones I and II, an increasing recognition that this may occur beyond posterior zones has led to this change in nomenclature.

Table 1. Classification of ROP based on ICROP-3

	Description
Zone	*Location of the most posterior vascularization denotes the zone for the eye*
I	A circle whose radius is twice the distance from the centre of the optic disc to the centre of macula
II	A circle whose radius is the distance from the centre of the optic disc to the nasal margin of the retina *Posterior Zone II:* begins at the margin between zone I and zone II and extends into zone II for 2 disc diameters*
III	The remainder of the retina, from Zone II to ora-serrata on nasal side and equator on temporal side
Notch*	*Incursion by the ROP lesion of 1–2 clock hours into a more posterior zone. Most posterior zone with the qualifier "notch" defines the zone.*
Stage	
1.	Appearance of demarcation *line* between avascular and vascular retina
2.	Appearance of demarcation *ridge* between avascular and vascular retina
3.	Presence of *extra-retinal neovascular proliferation* or flat neo-vascularization
4. 5.	*Retinal detachment* with fovea attached **(4A)** and fovea detached **(4B)** Total retinal detachment* A. Optic disc is visible by ophthalmoscopy (*open-funnel detachment)* B. Optic disc is not visible because of retrolental fibrovascular tissue *(closed-funnel detachment)* C. 5B, with anterior segment changes *(closed-funnel configuration)*
Extent	Defined as sectors using clock hour designation
Plus disease	Presence of increased venous dilation and arterial tortuosity of posterior retinal vessels.

The asterisk (*) denotes changes updated in ICROP, 3rd edition

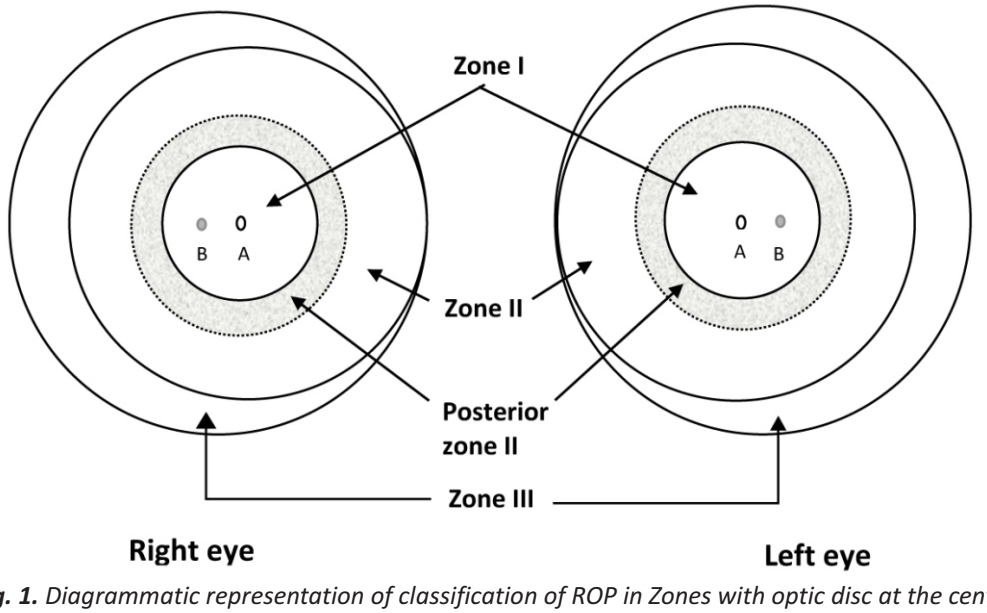

Fig. 1. *Diagrammatic representation of classification of ROP in Zones with optic disc at the centre* ***(A)*** *and macula* ***(B)*** *lying temporally to optic disc. The shaded area represents a circular rim between Zone I and Zone II, extending for 2 disc diameters into Zone II*

The updated ICROP also defines two sequelae: *regression* (spontaneous or after treatment with laser or anti-VEGF) and *reactivation* (appearance of new ROP lesions and vascular changes, with a suffix 're-activated').

Screening

All preterm neonates must undergo timely ROP screening to prevent development of sight-threatening complications and facilitate early treatment. Use of western guidelines recommending to screen only smaller babies like those <30 weeks may not be generalizable to a resource challenged country like ours where larger babies are also sick and develop ROP. Application of AAP and British guidelines would miss 17.7% and 22.6% neonates > 32 weeks or > 1500 g with ROP. (5) Taking these factors into consideration, a set of Clinical Practice Guidelines(6) were released by NNF as summarized below.

a. Whom to screen?

All neonates less than 2000 grams or gestation less than 34 weeks should be screened. Neonates born between 34-36 weeks should be screened in presence of following risk factors:

i. Cardio-respiratory instability

ii. Oxygen therapy beyond 6 hours

iii. Blood transfusion

iv. Systemic sepsis

v. Poor postnatal weight gain

b. When to screen?

Screening should be performed at 4 weeks postnatal age. For neonates below 1200 grams, an earlier screen at 2-3 weeks after delivery should be performed to particularly screen for A-ROP.

c. How to screen?

A thorough examination using indirect ophthalmoscope should be performed by a trained ophthalmologist. An area inside the newborn unit should be dedicated for screening. The baby should be kept nil per oral for 2 hours. Tropicamide drops (0.5-1%) should be instilled every 15 min prior to procedure for 3-4 times. Topical phenylephrine (2.5%) and topical paracaine (0.5%) should be instilled as 1 drop each just prior to procedure. Since ROP examination is a painful procedure especially with use of scleral indentation, all non- pharmacological measures must be taken to allay the peri-procedural pain. Neonates should be monitored for pain and apnea, following screening.

d. Follow up after ROP screening

Regular follow up is essential to prevent progression of ROP and its related complications. Frequency of follow up depends on the classification of ROP:

- Stage 1-2 for zones I and II: 1-2 weeks
- Regressing ROP: 2-3 weeks
- Stage 3, any zone, without plus: 1 week or less
- If ROP vascularized: 1-2 weeks for zone 1 and 2-3 weeks for zone 2 and 3

e. Indications of treatment

The treatment is indicated in cases of threshold ROP defined as any stage, zone I ROP with plus disease, zone I stage 3 with or without plus disease or zone II stage 2 or 3 with plus disease[7]

Role of tele-medicine and Artificial Intelligence (AI)

Use of innovations like RetCam for retinal imaging has made it possible for all retinas in remote areas to be screened and confirmed by a trained ophthalmologist. With increasing survival of preterm neonates in smaller units like SNCUs, telemedicine can come handy in face of a compromised ophthalmologist: patient ratio in India. Use of wide-angle digital field imaging helps in better resource utilization, overcome geographic barriers and improve cost-effectiveness. The KIDROP (largest of its kind) is an exemplary program reaping the benefits of tele-medicine based screening for diagnosis, treatment and referral.(8)

A disease with an image-based diagnosis sets up a platform for AI techniques to identify complex patterns, invisible even to a trained eye. Use of neural networks on 5500 retinal images led to a high performing predictive model with 94% sensitivity and 94% specificity. [9] Although still in infantile stages, these findings pave way for a huge predictive

generalizable potential for AI-based algorithms, especially in resource challenged countries.

Treatment

The treatment modalities are laser photocoagulation, cryotherapy, anti-VEGF medications and retinal surgery.

a. *Laser photocoagulation* is the modality of choice. It involves ablation of the avascular retina using double frequency Nd-YAG or diode laser (810 nm) to decrease the hypoxic drive for VEGF induction. The treatment gained wide popularity over cryotherapy (first tested treatment for ROP) with significant reduction in unfavorable outcomes and need for general anesthesia.(10)

b. *Anti-VEGF medications* are another possible treatment option, due to role of VEGF in the pathophysiology. The drug bevacizumab, surfaced as a great modality after the BEAT-ROP study (11) where it led to significant reduction in retinal detachment and recurrence rates till 54 weeks' postmenstrual age with no adverse effects. Another dug Ranibizumab, was tested in RAINBOW trial (12) for two dosage strengths and resulted in significantly improved outcomes compared to laser, with a possible dose-response effect. Despite advantages of decreased need for anesthesia and personnel along with lower rates of refractive error, they are not routinely recommended. The possible concerns underlie the role of VEGF as a neurotropic and neuroprotective factor for not only eye, but also kidneys, lungs and brain. Reports suggest a risk of cognitive decline due to VEGF suppression in these preterm neonates.(13) Further, there is lack of consensus on choice, dosage and timing of these agents, precluding their widespread use. Due to these possible concerns, they are only recommended in Zone 1 ROP if laser therapy fails or the centre of macula is not vascularized.(6)

c. *Retinal surgery* is indicated in stages 4 and 5, where scleral buckling or lens sparing vitrectomy is usually performed.

Medicolegal aspects

Due to potentially avoidable blindness, the comprehensive management of ROP brings great responsibility to the care-givers and poses them at risk of litigations. Various cases have been described in literature to address the medico-legal concerns in ROP screening, referral and treatment. (14,15) Although many aspects like timing, methods and mode of screening or treatment are an active area of research, reports suggest that a large proportion of malpractice litigations point to inefficient system processes. Therefore, there is a need for a coordinated effort from the healthcare personnel and parents to provide high quality standard of care. A few recommendations for medicolegal protection are highlighted below(15):

1. Adapt to the most recent region-specific recommendations. NNF 2020 guidelines can serve as a guidance.(6)
2. Screening must be conducted timely, irrespective of sickness or available resources. Telemedicine may be used as an aid.
3. Always counsel the caregivers regarding the need of timely screening and follow up to prevent complications. A formal consent should be taken.
4. A scientific, legibly written documentation of complete diagnosis should be ensured.
5. Laser remains the gold standard; anti-VEGF agents are still a debatable choice.
6. When in doubt, additional opinion from peers should be sought.

Prevention

ROP is a devastating sight-threatening condition with a huge impact on the long-term outcomes of a child and her family. As treatment of ROP is not devoid of adverse effects, prevention of ROP remains the cornerstone for its management. Interventions in maternal and neonatal care that are evidence-based for prevention of ROP are tabulated below.

The obstetrician, pediatrician, ophthalmologist and nurses need to collaborate for prevention and early diagnosis. Healthcare professionals must ensure clear communication with family. The role of neonatal nurses is pivotal in implementation of best practices in the unit.

Table 2. Evidence based strategies for prevention of ROP

Maternal	**Delivery room: care during the 'Golden hour'**	**Neonatal (POINTS)**
Standard treatment protocols in neonatal unit		
Prevent preterm birth	Delayed cord clamping	**P**ain control
Antenatal corticosteroids	Use of plastic bag or wrap	**O**xygen management
	Gentle ventilation strategies	**I**nfection control
	Oxygen saturation targeting	**N**utrition with mother's own milk
	Thermoregulation	**S**upportive care: Minimize blood transfusions

Conclusion

Management of ROP requires multi-disciplinarian approach with timely screening and treatment. Family education & counselling is of utmost importance, so as to avoid medico- legal litigations. A stringent follow-up is crucial to improve outcomes extending up to childhood. Preventive strategies especially judicious use of oxygen, blood transfusion, asepsis and provision of mother's own milk, are the key.

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Kasabach Meritt Syndrome

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Clinical presentation: A 4-day-old term born neonate presented with a diffuse, firm, erythematous to violaceous, non-pulsatile, indurated swelling that was present over the whole of the left lower limb extending onto the perineal and lower abdomen regions (Figure 1). Pallor and icterus were present. The vitals were stable and there was no bleeding from any of the orofacial sites. The systemic examination was normal.

Suspicion: Kassabach Meritt Syndrome

Course: Investigations revealed anemia (Hb 8.4 gm/dl and severe thrombocytopenia (platelet count 20,000/µL). The coagulation profile revealed prolonged prothrombin (INR 2.8), activated partial thromboplastin time (prolonged 30 seconds above control) and elevated D-dimer levels (4.0 mg/dl, normal <0.4 mg/dl). Fibrinogen level was decreased (90 mg/dl, normal 160-400 mg/dl). Unconjugated hyperbilirubinemia was present with normal liver enzymes. Ultrasonography with Doppler flow imaging confirmed the presence of hemangioma. The baby was managed with blood transfusion and oral prednisolone. Initially, the response was noted. The patient eventually left against medical advice (LAMA). There is no follow-up available.

Condition: Kasabach-Merritt syndrome (KMS) is a rare disorder characterized by a vascular tumour leads to profound thrombocytopenia, microangiopathic hemolytic anemia, and an acute or chronic consumption coagulopathy in association with a rapidly enlarging hemangioma, particularly kaposiform hemangioendothelioma (KHE) or tufted angioma (TA). Therefore, KMS is also known as hemangioma-thrombocytopenia syndrome.

This was described in 1940 by Kasabach and Merritt as "capillary hemangioma. KMS accounts for about 1% of cases of hemangioma. About 80% of patients present within 1 year after birth, and the reported mortality rate ranges from 10% to 37% [1]. Mortality and morbidity are usually associated with visceral involvement, haemorrhage related to aggressive invasion, profound thrombocytopenia, DIC, severe infections and iatrogenic complications [2]. Males and females are equally affected [3]. The pathophysiology is believed to be consumption of platelets and fibrinogen by intralesional thrombosis [4]. The lesions are typically superficial and solitary, but may involve internal structures such as the visceral organs, retroperitoneal organs, the mediastinum, the pelvis or the mesentery.

Blood work including a CBC with differential and platelets, fibrinogen, D-dimer, PT, and PTT should be ordered. The best imaging modality to assess the extent of the lesion is a MRI with contrast though ultrasound can reveal an infiltrative high flow lesion. A biopsy will confirm the diagnosis.

Treatment

For large, nonresectable tumors with KMS, initial treatment with sirolimus and systemic corticosteroids can be done. (Grade 1C)

Sirolimus is typically given at the dose of 0.8 mg/m2 per dose with close monitoring of blood levels and supportive care. Neonates and infants may need a lower dosing regimen due to physiologic differences in drug metabolism.

Oral prednisolone 2 mg/kg/day is given for two weeks and then weaned over a two- to four-week period.

Hemostatsis support, in particular platelet transfusion and fibrinogen replacement, should be based upon careful evaluation of the acuteness of the clinical presentation and the patient's needs (eg, active bleeding, upcoming surgery).

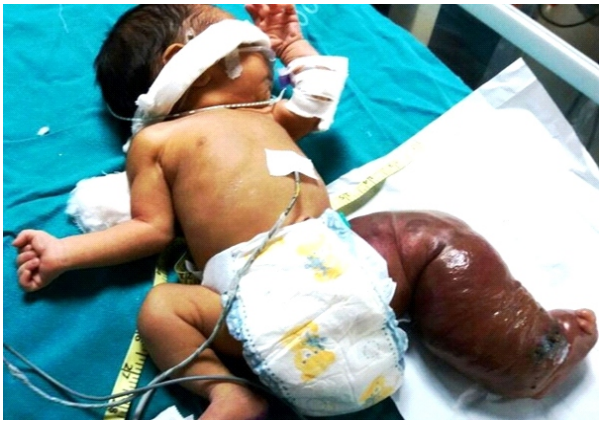

Fig.1 : Large tumour involving the whole lower limb

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Vein of Galen aneurysmal malformation in neonate

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A 33 years old pregnant lady came at 33 weeks of gestation to the fetal medicine department with suspicion of vein of Galen malformation in an antenatal scan done one week prior (32 weeks GA). The vein of Galen malformation (14 x 18 x 14 mm) was confirmed on an antenatal scan at our centre (Figure 1). Antenatally mother had GDM which was controlled on diet. Amniocentesis was done which showed no chromosomal abnormality.

Birth detials: A male baby was delivered through elective cesarean section at 38 weeks of GA with birth weight of 3.328 kg. Baby was vigorous at birth with APGAR of 8/9 at 1 min and 5 min respectively. Baby was shifted to mother. In view of antenatally suspected Vein of Galen malformation (VGM), USG cranium and 2D Echo was planned.

Diagnosis: Vein of Galen malformation

Clinical course:

Baby was on direct breast feeds from birth on mother's side. On day 2 of life, baby developed tachypnea for which baby was shifted to NICU. 2D Echo revealed dilated right atrium and ventricle suggestive of congestive cardiac failure. USG cranium showed vein of Galen malformation measuring about 27.9 x 16.8 mm (Figure 2). Baby was started on oral furosemide and spironolactone in view of persistent tachypnea with congestive cardiac failure. Interventional neurologist opinion was taken. We planned to monitor for head circumference serially and elective embolization of VGM was planned at 5 months of age. Baby was discharged on day 3 of life on direct breast feeds and oral furosemide/ spironolactone. MR angiography was done first at age of 3months (Figure 3) and then at 12 months of age. Baby is under regular follow up. Repeat MR angiography showed lesion of smilar size with no hydrocephalus. Presently, child is 16 months old, weighing 9.5 kg. He was continued on diuretics which were stopped later on at 12 months of age. Plan is to do endovascular embolization in coming months.

Review of literature:

The vein of Galen aneurysmal malformation(VGAM) is a choroidal type of arteriovenous malformation involving the vein of Galen. The vein of Galen is located under the cerebral hemispheres and drains the anterior and central regions of the brain into the sinuses of the posterior cerebral fossa. The congenital malformation develops during weeks 6-11 of fetal development. VGAM causes high-output heart failure in the new born resulting from the decreased resistance and high blood flow in the lesion. Associated findings include cerebral ischemic changes such as strokes or steal phenomena that result in progressive hemiparesis. It may result in mass effects, causing progressive neurological impairment or may cause obstruction of the CSF outflow resulting in hydrocephalus. Typically, in the neonatal period, VGAM presents with congestive heart failure, a cranial bruit, and marked carotid pulses. Cranial ultrasound and /or MRI with or without contrast are done to identify the lesion. 2D echo should be done to assess

the cardiac status in a child with VGAM. Cardiac management of high-output heart failure is essential. Seizures should be managed with antiepileptic medications. Head circumference measurements should be obtained regularly and monitored carefully to detect hydrocephalus. Assessment of the child's development is an important part of medical care.

Surgical management: Endovascular embolization is the treatment of choice. Vaso-occlusive therapy like selective catheterization and therapeutic embolization of feeding arteries in the vein of Galen malformation, can be performed. . If the child develops hydrocephalus, ventriculoperitoneal shunt may need to be done Death usually results from cardiac failure or cerebral decompression.

Key messages

1. Vein of galen malformation is a choroidal type of arteriovenous malformation involving the vein of Galen.
2. Neonate usually presents with congestive cardiac failure.
3. USG cranium, MRI brain and echocardiography should be done in neonatal period.
4. Endovascular embolization is the treatment of choice.

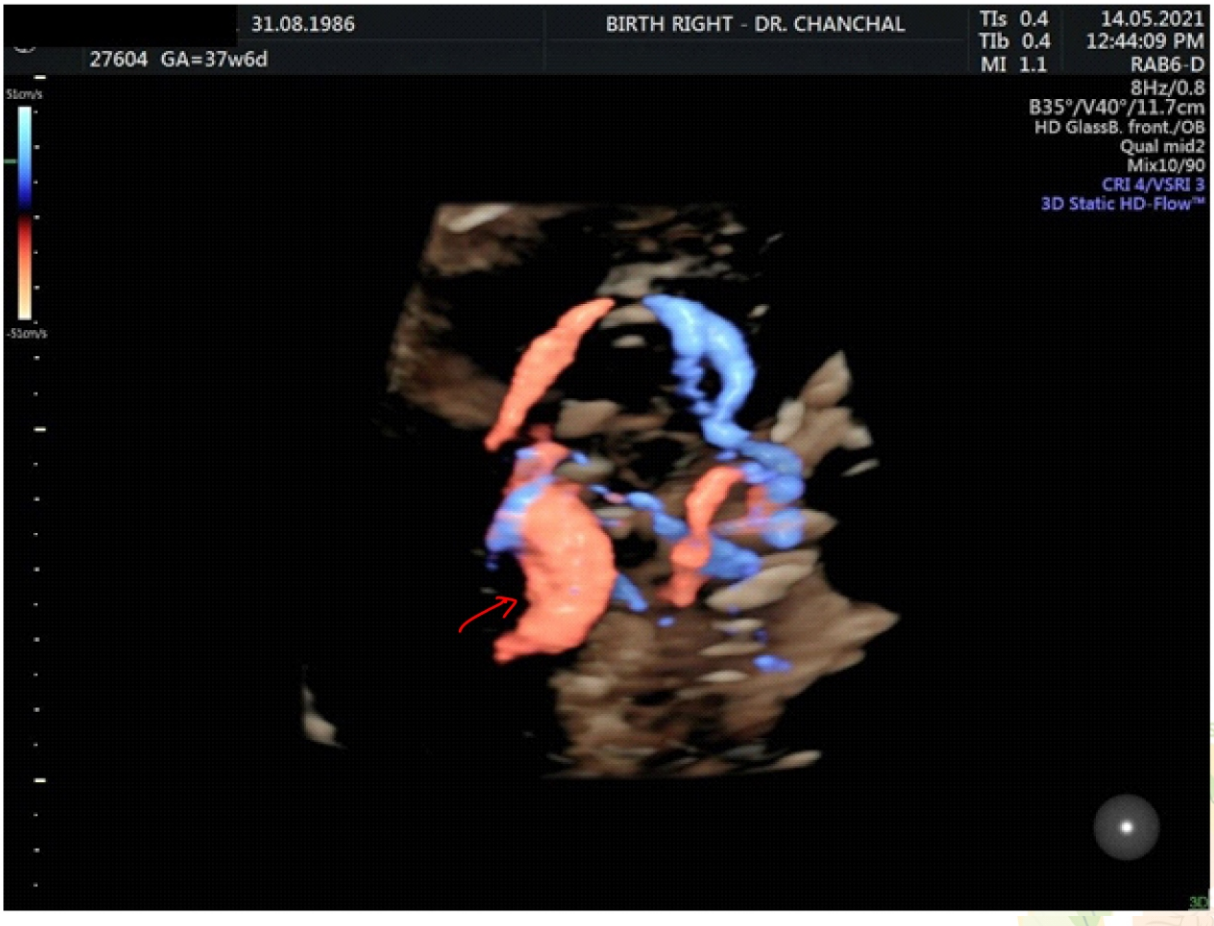

Fig. 1 : Antenatal scan depicting vein of Galen malformation (arrow)

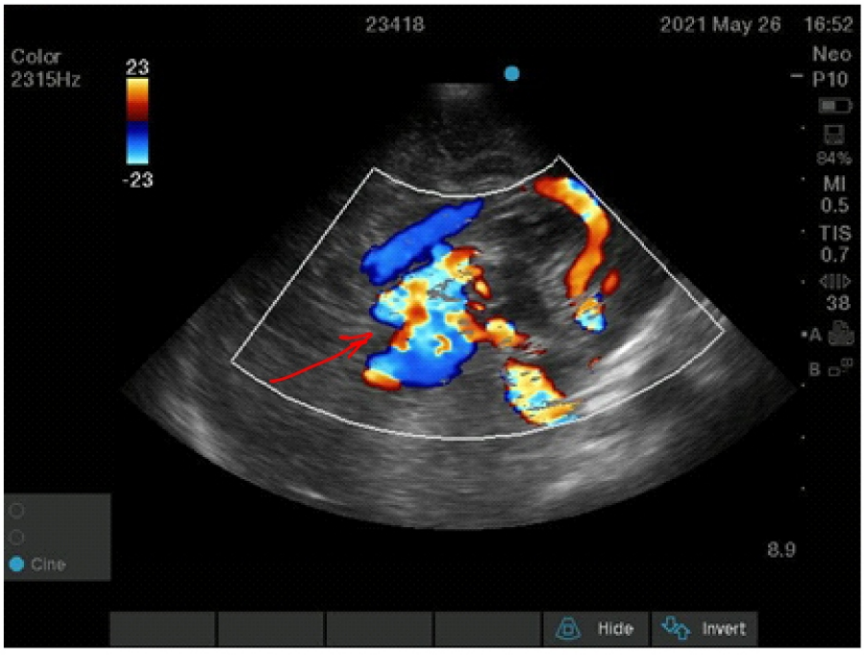

Fig. 2 : Postnatal Ultrasound doppler showing vein of Galen aneurysmal malformation (arrow)

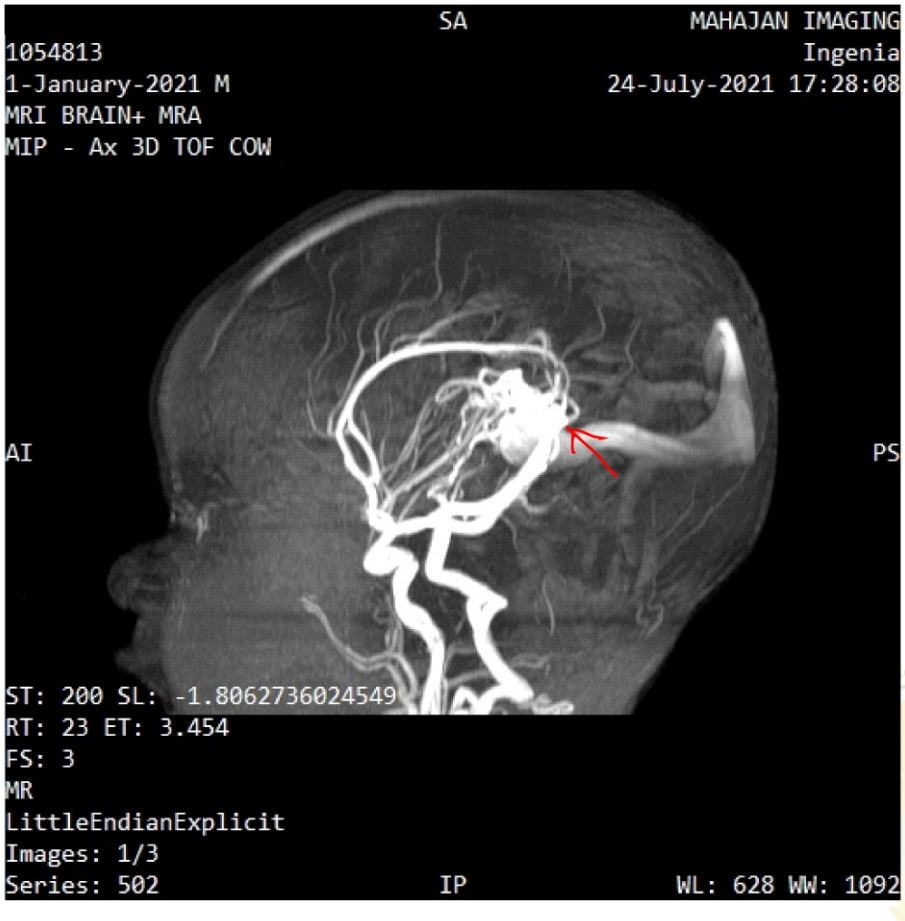

Fig. 3 : MR angiography demonstrating vein of galen aneurysmal malformation (arrow)

Reviewed by
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Journal Scan

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nasal High-Flow Therapy during Neonatal Endotracheal Intubation

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N Engl J Med2022;386:1627-1637

Background:

Neonatal endotracheal intubation often involves more than one attempt, and oxygen desaturation is common. It is unclear whether nasal high-flow therapy, which extends the time to desaturation during elective intubation in children and adults receiving general anaesthesia, can improve the likelihood of successful neonatal intubation on the first attempt.

Hypothesis :

Population	Neonates undergoing intubation in delivery room or neonatal unit.
Intervention	Nasal high flow during first intubation attempt
Control	Standard care (no high flow or oxygen while intubation)
Outcome	Successful first attempt intubation without physiological instability
Time	November 2018 through April 2021

Methodology:

Definitions:

1. Intubation attempt: Time from insertion of the laryngoscope blade beyond the infant's lips until its removal from the infant's mouth
2. Successful intubation: Completion of the intubation attempt and confirmation of correct placement with a colorimetric expired CO2detector
3. Physiological instability:
   a. Desaturation -absolute decrease in oxygen saturation >20% from baseline
   b. Bradycardia -HR <100 beats per minute

Design: Randomized, controlled trial.

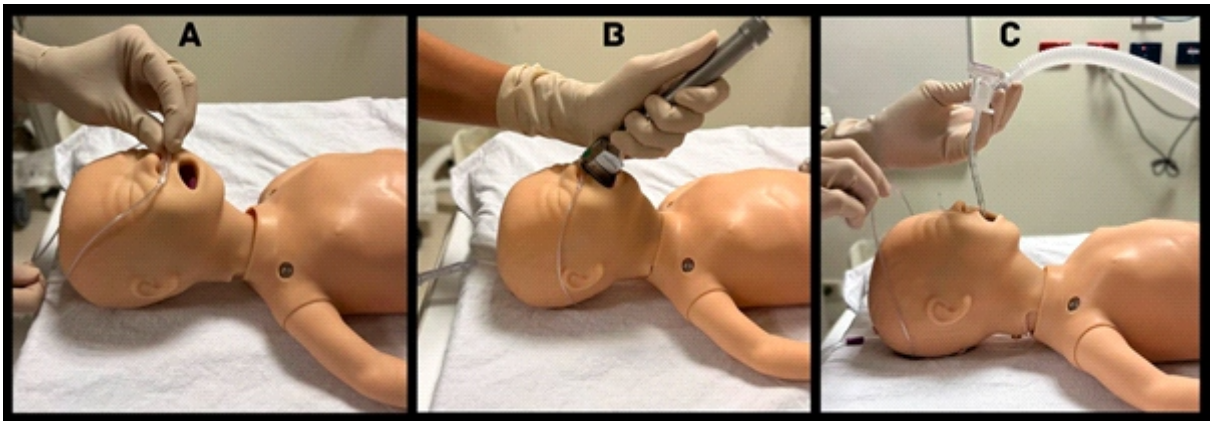
Study population: Neonates undergoing intubation in delivery room or NICU.

Primary outcome: Successful first attempt intubation without physiological instability

Sample size: The estimated rate of the primary outcome was 30%. To demonstrate and increase from 30 to 50%, 123 babies in each group were needed with 90% power.

From November 2018 through April 2021, a total of 258 intubations in 209 infants were randomly assigned to the high-flow group (129 intubations) and the standard-care group (129 intubations). Seven intubations were excluded after randomization, with 251 intubations (124 in the high-flow group and 127 in the standard care group).

Procedure:



Randomization was performed with the use of a computer-generated random-assignment sequence.

Results:

The infants had a median postmenstrual age of 27.9 weeks and a median weight of 920 g at the time of intubation.

Primary outcome i.e successful first attempt intubation without bradycardia or desaturation was 50% in high flow group as compared to 31.5% in standard care group [Adjusted risk difference 17.6% (95% CI 6.0% to 29.2%)]. Number needed to treat was 6 (95% CI 4 to 17)

Successful intubation on the first attempt regardless of physiological stability was accomplished in 68.5% of the intubations in the high-flow group and in 54.3% of the intubations in the standard-care group.

The median oxygen saturation during the first intubation attempt was 93.5% in the high-flow group and 88.5% in the standard-care group, with a 5.0 percentage-point difference in the median values.

Among the infants with an episode of oxygen desaturation, the mean time to desaturation was longer in the high-flow group (44.3 seconds) than in the standard-care group (35.5 seconds), for a mean difference of 8.8 seconds.

Authors Conclusion:

Nasal high flow during neonatal endotracheal intubation improves successful intubation at the first attempt. This intervention has the potential to improve care

Reviewer comments:

Overall a well-designed randomized controlled trial demonstrated better successful first-attempt intubation in the group receiving high flow during intubation.

A few things however raise concern. The Control group didn't receive oxygen while intubation though the indication of intubation was hypoxemia in 60% and apnea in 20% of episodes. In such a population, the omission of oxygen during intubation appears to put the comparison group neonates at a disadvantage. Providing high flow in one group and oxygen in another group could have been more reasonable for comparison purposes.

Few issues need more research. It is unclear whether it is pressure or oxygen which leads to successful first attempt intubation.

Part 2

QUESTIONS

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Question1.

A full term 3.2 kg baby boy delivered by elective LSCS to a primi mother, was admitted with complaints of poor feeding, lethargy, fast breathing, and unresponsiveness on day 3 of life. There were no maternal risk factors for early onset sepsis. Ultrasound scans in antenatal period were normal. Baby cried soon after birth and did not require resuscitation. He was being nursed with mother before the illness. On examination at the time of admission, baby was encephalopathic. Baby's respiratory rate was 70/min and baby had fast deep breathing. Heart rate was 158/min. Pulse volume was good and CFT was 2 seconds. Temperature was normal. RBS was 74 mg/dl.

A. What are your differential diagnoses? How would you like to evaluate this baby?

B. What preliminary basic investigations would you do when suspecting inborn error of metabolism?

C. This baby's counts were normal, CRP was negative and blood culture was sterile. CSF analysis revealed no meningitis. USG cranium was normal. RBS was 74 mg/dl. Serum electrolytes (sodium, potassium, calcium, magnesium) were normal. Blood gas revealed pH 7.47, pCO2 24, BE -1. Lactate was 4 mmol/l and serum ammonia 1000 micromol/l (1785 microgram/dl). Urine ketones were negative. What is the interpretation? What is the probable diagnosis?

D. How would you confirm the diagnosis? How would you manage this baby?

E. TMS showed high glutamine and decreased levels of citrulline. Urine GCMS showed increased orotic acid. What is the probable diagnosis?

F. What is the long-term therapy for this condition?

Question2.

A term born 3 kg baby girl was admitted on day 5 of life with history of difficulty in feeding, lethargy, abnormal movements, and fast breathing. Her temperature was 37 degrees Celsius, heart rate 180/min, respiratory rate 80/min, mean BP 68 mm Hg. Pulses were well felt. She had hepatomegaly (3 cm below right costal margin). RBS was 90 mg/dl. Treatment for congestive cardiac failure and probable sepsis was initiated while awaiting evaluation. Chest x-ray revealed cardiomegaly. 2D ECHO showed normal cardiac morphology. CRP was negative and blood culture sterile. Electrolytes (sodium and calcium) were normal. USG Brain and MRI were done, and images are as shown in Fig. 1 and 2.

A. What is the probable diagnosis?

B. What are the potential complications associated with this condition?

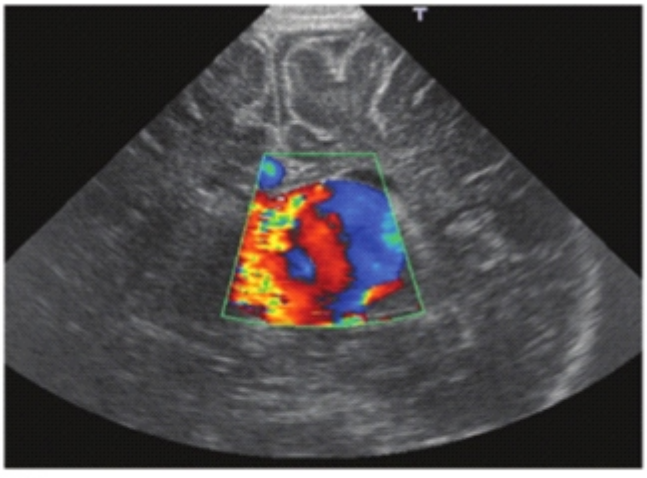
C. What is the pathophysiology of cardiac failure in this condition?

D. What is the treatment modality?

E. What are few complications that can happen after treatment?

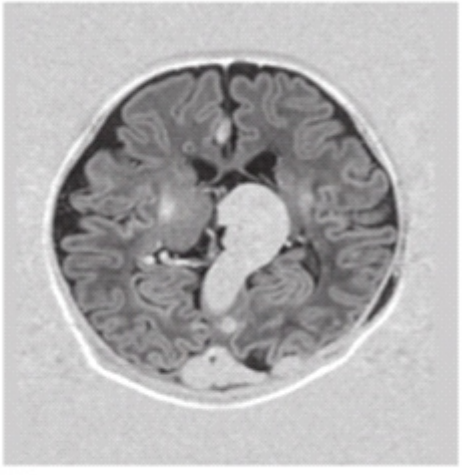
Question 3.

A 5-day old term born neonate was admitted with history of abnormal movements in form of multiple, successive, unilateral, clonic movements affecting the



a

Fig. 1. USG Brain Doppler



b

Fig. 2. MRI Brain

face and the limbs. It was a full term normal vaginal delivery and immediate perinatal period was uneventful. APGAR scores were 8, 9, 9 at 1, 5 and 10 minutes respectively. Baby was discharged to home at 48 hours. There were no risk factors for sepsis and baby was being exclusively breast fed.

A. How would you evaluate this baby?

B. After admission, RBS was 90 mg/dl. Electrolytes (sodium, calcium, magnesium) were normal. Sepsis work up was negative. Basic metabolic work was negative. Phenobarbitone and phenytoin were administered for repetitive seizures. USG Brain and MRI Brain were normal. EEG was done and is as shown in Fig. 3. It showed "theta pointu alternant pattern". What would be the probable diagnosis?

C. How would you differentiate between familial and non-familial variant of this disease?

D. What is the long-term prognosis of this condition?

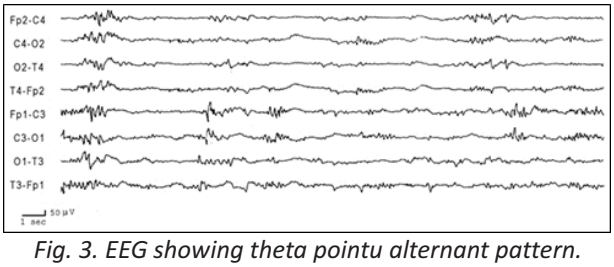


Fig. 3. EEG showing theta pointu alternant pattern.

Question 4.

A full term 2.9 kg baby boy developed marked hypotonia and refractory seizures requiring multiple anti-epileptic drugs on day 3 of life, after an uneventful normal vaginal delivery. It was an un-booked pregnancy and antenatal scans were not available. Baby had not required any resuscitation at birth. RBS, Electrolytes were normal, and sepsis work up was negative. MRI Brain is as shown in Fig. 4.

A. What is the diagnosis?

B. Name few conditions with which it is associated?

C. At what gestational age during pregnancy is this brain malformation likely to occur?

D. What are the other disorders of neuronal migration?

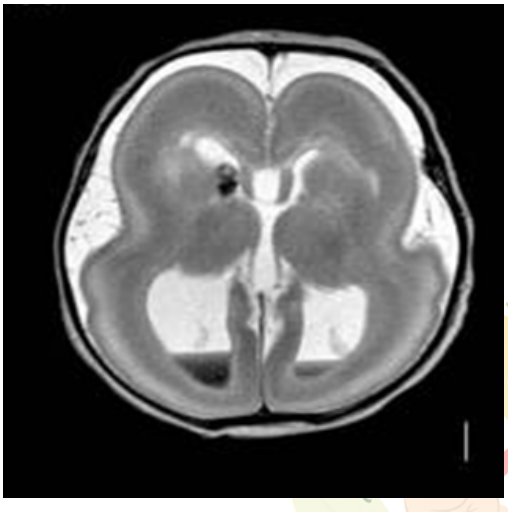


Fig. 4 MRI Brain

Question 5.

A full term 3.1 kg baby girl developed feeding difficulty

and increased sleepiness on day 2 of life, followed by refractory seizures requiring multiple anti-epileptic drugs within next 12 hours. It was an uneventful normal vaginal delivery. Baby had not required any resuscitation at birth. RBS, Electrolytes were normal, and sepsis work up was negative. MRI Brain on day 3 of life is as shown in Fig. 5.

A. Describe the MRI findings.

B. On simultaneous DWI images (not shown here) there was restricted diffusion. What is your diagnosis?

C. What are the maternal and neonatal risk factors associated with this neonatal thromboses?

D. How would you manage this baby?

E. What are the indications for using anticoagulants?

F. What additional imaging would you do to evaluate this baby?

G. What additional lab tests would you do to evaluate this baby and what is the timing of evaluation?

H. The MRI Brain of same baby on day 75 of life is as shown in Fig. 6. Describe the findings.

I. What are the long-term problems expected in this baby?

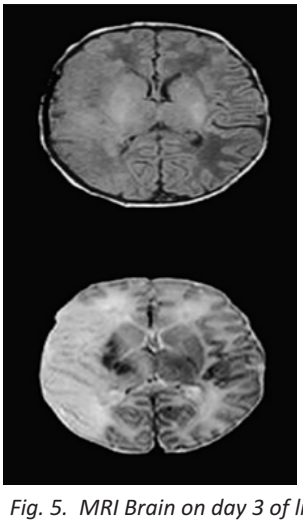


Fig. 5. MRI Brain on day 3 of life.

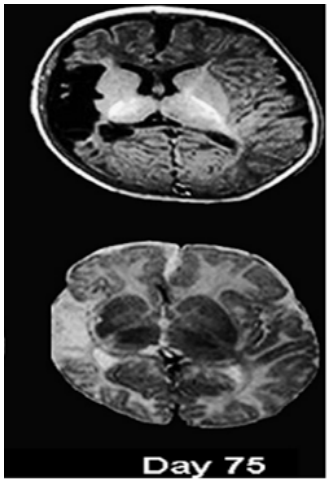


Fig. 6. MRI Brain on day 75

Question 6.

A 25-day old neonate with culture positive sepsis (Acinetobacter), was referred to you due to worsening sensorium and clinical condition. At the time of admission, baby had temperature of 38.5 degree C and poor sensorium. Perfusion was stable. RBS was 82 mg/dl. The baby is stabilised, and antibiotics are administered as per blood culture sensitivity report. You decide to perform lumbar puncture. CSF analysis showed 60 cells with 10% neutrophils, sugar 25 mg/dl and protein 170 g/dl. CSF culture also grew Acinetobacter and appropriate antibiotics were being given. After 3 days of antibiotic treatment, the baby became afebrile, and sensorium improved. However, during the second week of treatment, the baby developed bulging fontanelle and multiple episodes of seizures.

A. What are the possible complications of meningitis?

B. What is the utility of USG brain in evaluating meningitis and its complications?

C. How would you diagnose ventriculitis?

D. What is the recommended duration of treatment for ventriculitis?

E. Cranial ultrasound of this baby showed a large cystic mass with internal debris and shaggy wall in the parietal region of the right cerebral hemisphere. MRI brain is as shown in Fig. 7. Describe the findings. What is your diagnosis?

F. How would you manage this baby further?

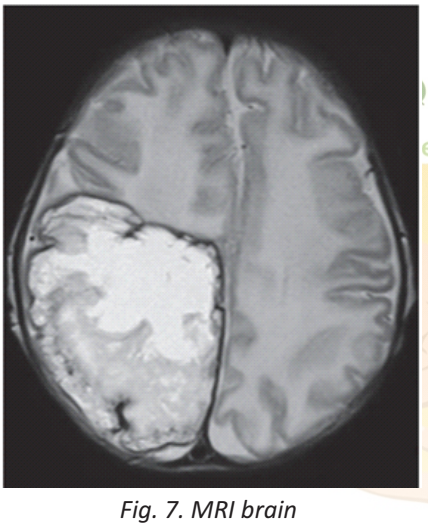


Fig. 7. MRI brain

Question 7.

A 2-month-old baby is brought to you with paucity of spontaneous movements and difficulty in feeding for last 2-3 weeks. Mother had noted looseness while handling the baby. Baby sucked intermittently for few minutes and mother was struggling with breast and bottle feeding. Baby otherwise looked around and was responsive. Antenatally, there was H/O reduced foetal movement compared to earlier pregnancy. There was polyhydramnios in 3rd trimester. No H/O any drug exposure in mother. No H/O fever, rash suggestive of intrauterine infection. Antenatal scans were normal. Baby was delivered in breech presentation with no perinatal complication. There was no history of NICU admission. There was no H/O consanguinity or similar condition in family. On examination, baby had normal sensorium, had an alert look, marked hypotonia with absent deep tendon reflexes. There is weakness and paucity of movements in upper as well as lower limbs. There was no dysmorphism, no microcephaly, no neurocutaneous markers and no other external visible malformations.

A. How would you differentiate between central and peripheral hypotonia?

B. What are the possible sites of involvement and respective differential diagnoses in peripheral hypotonia?

C. What are the differential diagnoses for central hypotonia?

D. What is the probable diagnosis in this child?

E. What would be your approach in managing this baby?

F. Name 2 FDA approved drugs for use in infants with SMA.

Question 8.

A term baby is admitted with seizures on day 1 of life. Mother had no antenatal check-ups. There was no history of perinatal asphyxia and need for resuscitation. Initial blood and lab investigations (RBS, blood gas, electrolytes, CRP, blood culture and CSF analysis) were all normal. MRI scan is as shown in Fig. 8.

A. What are the findings in this MRI scan?

B. What is the diagnosis?

C. What are the three characteristic features of this condition?

D. What are the associated abnormalities in this condition?

E. What are the differential diagnoses of posterior fossa abnormalities that may be associated with hydrocephalus?

F. How would you manage this baby?

G. What is the prognosis of this disease?

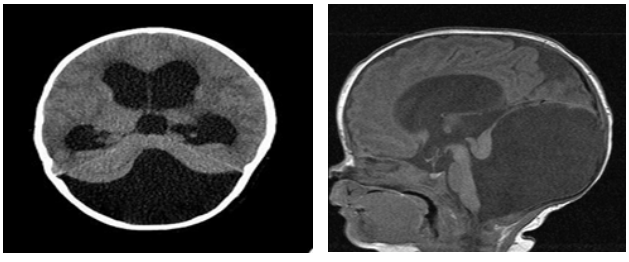


Fig. 8.

Question 9.

Identify the amplitude integrated EEG patterns as shown in Fig 9-12:

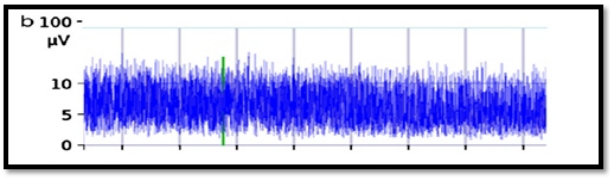


Fig. 9

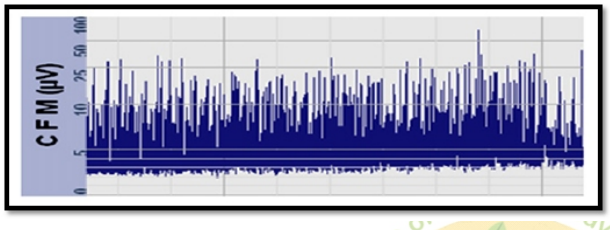


Fig. 10

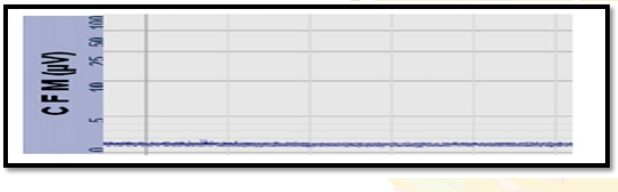


Fig. 11

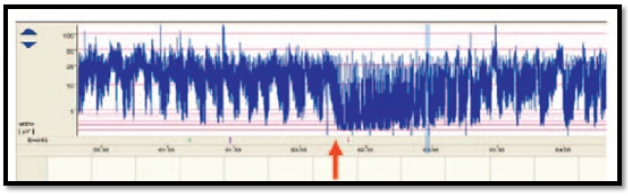


Fig. 12

Question 10.

A 25-year-old primigravida is referred to you for antenatal consultation as foetal ultrasonography at 25 weeks of gestation is showing bilateral ventriculomegaly of 16 mm size.

A. Define foetal ventriculomegaly.

B. How would you grade its severity and what is the severity in this case?

C. What further evaluation would you plan in this mother?

D. How would you counsel and prognosticate the family?

E. What are the 3 most common causes of congenital hydrocephalus?

F. This baby was delivered at 36 weeks of gestation in view of rapidly increasing ventriculomegaly. Baby cried soon after birth and had birth weight 3.2 kg and head circumference 41 cm. How would you evaluate further?

G. Post-natal MRI showed gross hydrocephalus and aqueductal stenosis. What would be the mainstay of treatment?

Answer 1.

A. Differential diagnoses: Sepsis with meningitis, dyselectrolytemia, intracranial bleed, neonatal stroke, cranial malformations, inborn errors of metabolism.

Evaluation: RBS, Electrolytes (sodium, calcium, magnesium), CBC, CRP, Blood culture, CSF analysis for meningitis, USG cranium/ MRI Brain, IEM work up.

B. Preliminary basic investigations when suspecting IEM: Glucose, Electrolytes, Lactate, Ammonia, Arterial blood gas, urinary ketones ("GELAAK"), liver function tests, urine for reducing substances.

Second line investigations for confirmation: Gas chromatography mass spectrometry (GSMS) of urine, Plasma amino acid and acylcarnitine profile by Tandem Mass Spectrometry (TMS), CSF amino acid analysis, Neuroimaging and MRS, EEG. Genetic testing for final confirmation.

C. Baby has respiratory alkalosis and hyperammonaemia. Probable diagnosis is Urea cycle defect.

D. Confirmation of diagnosis: Gas chromatography mass spectrometry (GSMS) of urine, Plasma amino acid and acylcarnitine profile by Tandem Mass Spectrometry (TMS).

Management:

- Stabilise baby, maintain airway/breathing/ circulation, stop protein intake.
- Start IV glucose (GIR 8-10) or TPN with lipids but no protein initially
- Start first line medications (sodium benzoate/ sodium phenylbutyrate/l-arginine)

Sodium benzoate: Loading dose 250 mg/kg IV/ oral. Maintenance dose: 250-400 mg/kg/day in 4 divided doses (IV/ oral) (IV preparation is not available in India).

Sodium phenylbutyrate: Loading: 250 mg/kg. Maintenance: 250-500 mg/kg/day (Not available in India)

Arginine: 300 mg/kg/day oral/ IV

- Peritoneal dialysis should be started as soon as possible with routine monitoring of ammonia levels. Haemodialysis is better.
- Energy intake- 120% age adjusted requirements
- Use of special infant formula feeds (initially protein free) and later with reduced proteins.

E. Probable diagnosis: OTC (Ornithine transcarbamylase) deficiency. Further molecular genetic testing should be done to confirm the diagnosis.

F. Long term therapy: Lifelong low protein diet and nitrogen scavenger therapy (sodium benzoate)

Answer 2.

A. Vein of Galen Aneurysmal Malformation (VGAM).

B. Potential complications: Hydrocephalus, cardiac failure, refractory PPHN, Stroke.

C. High output cardiac failure due to high-flow AV shunts of VGAM.

D. Treatment: Coil embolization. Both arterial and venous embolization is possible depending on number of feeders. Hydrocephalus is typically not shunted, as this may exacerbate cerebral ischemia by altering cerebral hemodynamics and increases risk of intraventricular hemorrhage.

E. Post-embolization complications included cerebral hemorrhage/hematoma, cerebral ischemia, macrocephaly or hydrocephalus, leg ischemia, vessel perforation, pulmonary embolism, and non-target embolization.

Answer 3.

A. RBS, Electrolytes (sodium, calcium, magnesium),

CBC, CRP, Blood culture, CSF analysis, USG cranium/ MRI Brain.

B. Benign neonatal seizures (non- familial).

C. Difference between familial and non-familial variants:

	Benign (non-familial) neonatal seizures	Benign familial neonatal seizures
Main seziures	Mostly donic	Tonic-donic
Onset	Fifth day of life	Second or third day of life
Duration of seizures	Status epilepticus (median 20 hours)	Repetitive isolated seizures
Main causes	Unknown, probably environmental	Autosomal dominant
Subsequent seizures	Practically nil (0.5%)	Relatively high (11%)
Psychomotor deficits	Minor	Practically non-existent
Ictal EEG	Usually localised spikes	Usually generalised flattening
Interictal EEG	Usually theta pointu alternant	Normal or focal abnormalities

D. Long term prognosis: The prognosis is usually excellent with normal development and no recurrence of seizures. Minor psychomotor deficits and occasional febrile or afebrile seizures (0.5%) have been reported.

Answer 4.

A. Lissencephaly (smooth brain)

B. Associations:

- Type I Lissencephaly with chromosomal defects of 17p (LIS1), Xq (XLIS)
- Fetal CMV infection
- IEMs like pyruvate dehydrogenase deficiency, Zellweger syndrome, Glutaric aciduria

C. The peak time period for neuronal migration disorders to occur is from 3rd to 5th month of gestation (12-24 weeks)

D. Other disorders of neuronal migration:

Schizencephaly

Pachygyria

Polymicrogyria

Heterotopias

Focal cerebrocortical dysgenesis

Answer 5.

A. MRI findings: Axial T1 (upper row) and T2 (lower row) images of the brain at the level of basal ganglia. It shows T2 hyperintense signals in right frontal and parietal lobes with effacement of sulci. Involvement of the right middle cerebral artery (MCA) in its cortical area, sparing deep grey matter.

B. Diffusion restriction in DWI suggests right sided acute infarct. Diagnosis: Neonatal stroke/ Perinatal arterial ischemic stroke

C. Maternal risk factors: Infertility, oligohydramnios, prothrombotic disorder, preeclampsia, Diabetes, IUGR, Chorioamnionitis, PROM, autoimmune disorders.

Delivery risk factors: Fetal HR abnormalities, Meconium Stained Amniotic Fluid (MSAF), placental infarcts

Neonatal risk factors: Central venous/ arterial catheters, congenital heart disease, sepsis, meningitis, birth asphyxia, RDS, dehydration, congenital nephritic/ nephrotic syndrome, NEC, polycythemia, pulmonary hypertension, ECMO, Medications like steroids

D. Management: Mainly supportive.

Neuroprotective management—maintain oxygenation, ventilation, and fluid status.

Correct metabolic parameters—sugar and electrolytes.

Treat specific causes like infection.

Treat seizures—usually easily controlled and in most cases, medications can be stopped before discharge.

Aspirin, unfractionated, or LMW heparin can be given if the risk of recurrence is high (thrombophilia, complex cyanotic heart disease)

E. Current guidelines from American College of Chest Physicians recommend anticoagulation for neonates with perinatal arterial ischemic stroke (PAIS) only if there is ongoing cardioembolic source or if there is evidence of recurrent PAIS

(thrombophilia, complex cyanotic heart disease).

F. MR Angiography, 2D ECHO

G. Baseline CBC, PT, aPTT, Thromboplastin time and fibrinogen levels should be obtained shortly after the acute event. Additional tests for evaluation of thrombophilia (particularly in absence of any other cause or risk and strong family history) which may be considered:

- Antiphospholipid antibody panel, anti-cardiolipin and lupus anticoagulant
- DNA based assays: Factor V Leiden mutation, Prothrombin G
- Protein based assays: Protein C, protein S levels, Antithrombin activity, Lipoprotein (a), Fasting homocysteine, Plasminogen, Factor VIII activity, Factor XII activity.

Timing: Baseline CBC, PT, aPTT, Thromboplastin time and fibrinogen levels should be obtained shortly after the acute event.

Antiphospholipid antibody panel, anti-cardiolipin and lupus anticoagulant may be performed from maternal serum during first few months of life

DNA based assays may be obtained at any time.

Certain protein-based assays may aid in treatment (AT III and plasminogen) and may be performed during neonatal period. However, most other protein-based assays are affected by acute thrombosis and must be repeated at 3-6 months of life before definitive diagnosis is made. Therefore, it is recommended that complete evaluation (excluding DNA based assays) be performed at ***3-6 months*** of life. If anticoagulation is being given, then these assays should be obtained 14-30 days after discontinuing the anticoagulant.

Lipoprotein (a) concentrations increase during the first year of life and should be repeated at 8-12 months of life if values obtained at 3-6 months of life are low.

H. Findings: Axial T1 and T2 images at the level of basal ganglia. There is atrophy with encephalomalacia changes in right fronto-parietal and insular lobes - likely sequelae of ischemic insult.

I. Long term problems: Motor deficits (Perinatal stroke is the most known cause for hemiplegic cerebral palsy (30%). About 50–60% of neonatal acute stroke and 80–90% of presumed strokes have unilateral weakness of some degree. Extent of disability is decided by location, size, and number of lesions), cognitive impairments, seizure disorder, behavioral abnormalities, visual impairment, delay in language development.

Answer 6.

A. Complications of meningitis: cerebral edema, ventriculitis, brain abscess, infarction, haemorrhage, hydrocephalus.

B. USG brain can help in diagnosing IVH and in grading of type of IVH (Grade 1-4) which helps in prognosticating patients. USG brain also helps in monitoring Levene Index and thalamo-occipital distance in post haemorrhagic and post meningitis hydrocephalus, which helps in determining need of serial lumbar puncture or neurosurgical intervention (shunt surgery).

In ventriculitis in USG brain, we find ventricular dilatation with irregularity of ventricular margin and echogenic material.

USG brain can also help in picking up brain abscess, which will be seen as cystic mass with internal debris and shaggy wall.

C. Diagnosis of ventriculitis: Failure to respond to appropriate antibiotics clinically or bacteriologically (no clinical improvement/ clinical worsening/ worsening CSF counts/ persisting positive CSF culture or cytology) and signs of elevated ICP may suggest the diagnosis of ventriculitis. The definitive diagnosis is by ventricular tap and cytological, biochemical and microbiological analysis of ventricular cerebrospinal fluid (CSF). As this is invasive procedure, various non-invasive modalities in the form of neuroimaging have been used. In USG Brain, there may be ventricular dilatation with irregularity of ventricular margin, ventricular septations, echogenic material. USG Brain is usually the first imaging modality.

Contrast enhanced MRI findings include

intraventricular debris, pus, abnormal periventricular and subependymal signal intensity, and enhancement of the ventricular lining. MRI is usually not necessary for initial management.

D. Recommended duration of treatment for ventriculitis: 4-6 weeks. Intraventricular antibiotics via EVD (external ventricular drain) or reservoir, may be needed in case baby is not responding to intravenous antibiotics alone and CSF counts/ culture are worsening or persistent.

E. T2-weighted image showing temporo- parieto-occipital mass lesion with a central hyperintense signal and a peripheral linear irregular hypointense wall signal. Perilesional oedema and mass effect with midline shift towards the left. Diagnosis is Brain Abscess.

F. Management: Neurosurgical consultation for need for surgical intervention (needle aspiration or excision). Duration of antibiotic therapy may need to be extended to 6-8 weeks, depending on clinical and radiographic response. Serial brain imaging at weekly or biweekly intervals should be performed to monitor the evolution of lesion.

Answer 7.

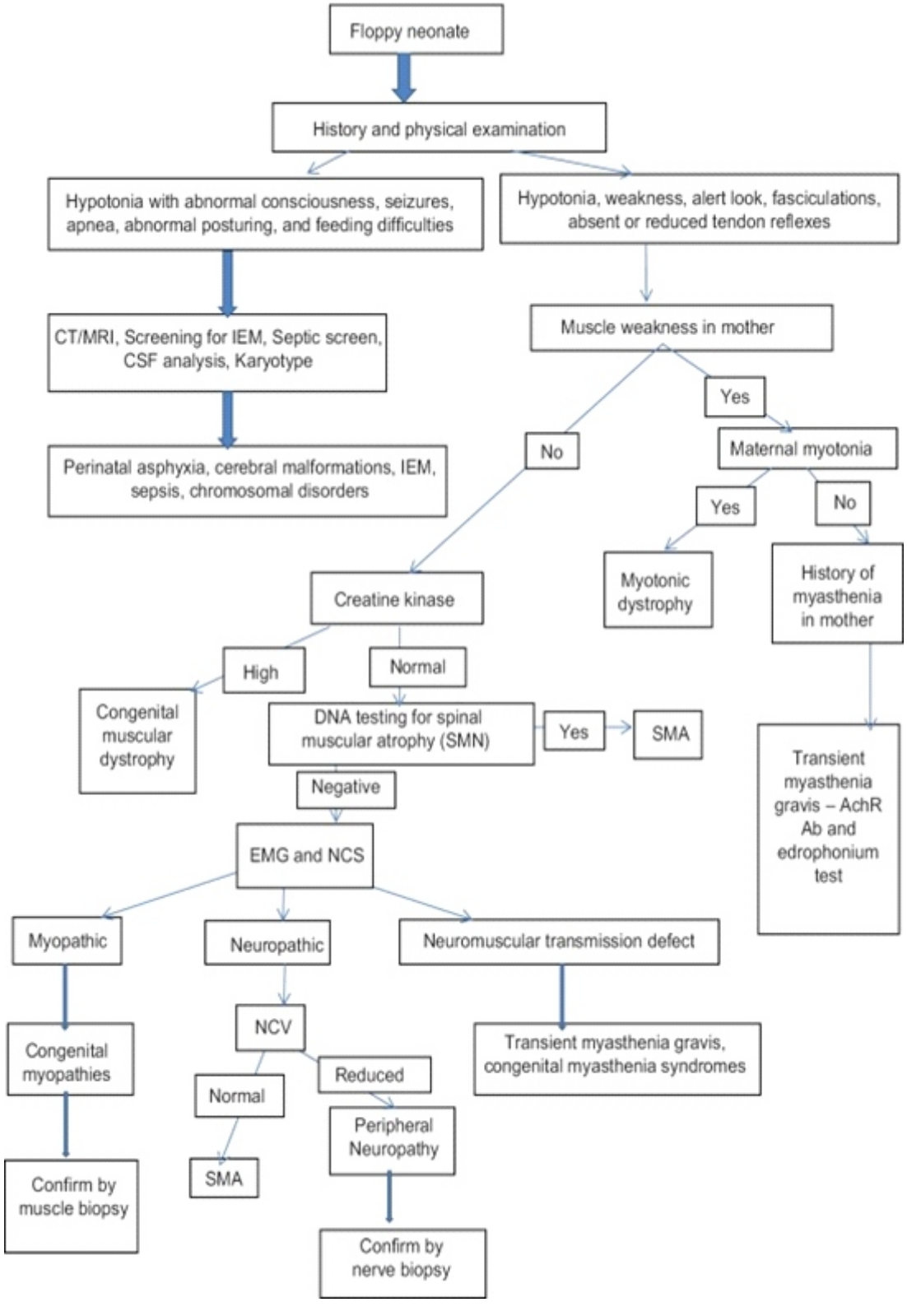
A. Difference between central and peripheral hypotonia:

Central hypotonia: These hypotonic neonates show signs of abnormal consciousness, seizures, apnea, abnormal posturing, and feeding difficulties. Muscle power is relatively preserved, and axial weakness is a significant clinical feature. The tendon reflexes are normal or hyperactive, and there is no evidence of muscle fasciculations. Postural reflexes are generally preserved in infants with cerebral hypotonia despite a paucity of spontaneous movements. In some acute encephalopathies, the Moro reflex may be exaggerated.

Peripheral hypotonia: These infants appear more alert in comparison to those with CNS involvement. Babies with anterior horn cell disease usually have sparing of extra-ocular muscles while the disorders of neuromuscular junctions may have ptosis and extra-ocular muscle weakness. There is weakness in the antigravity limb muscles along with diminished or absent reflexes. They can have deformities of

Anterior horn cell	Generalized weakness and absent deep tendon reflexes	Spinomuscular atrophy
Nerve	Distal muscle weakness and wasting Decreased tendon reflexes	Peripheral neuropathy
Neuromuscular junction	Involvement of facial muscles with or without generalized weakness	Myasthenia gravis botulism
Muscle	Weakness Decreased tendon reflexes Fasciculations joint contractures	Congenital muscular dystrophy Congenital myotonic dystrophy Congenital and metabolic myopathy

bones or joints (arthrogryposis). Fasciculations maybe observed in the tongue. Postural reflexes are absent or diminished, and limbs that lack voluntary movement also cannot move reflexively.



B. Possible sites of involvement and D/D in peripheral hypotonia:

C. D/D for central hypotonia: Brain malformations, perinatal asphyxia, chromosomal disorders, stroke, inborn errors of metabolism.

D. Probable diagnosis in this child: Peripheral hypotonia with areflexia.

E. Approach to management:

F. FDA approved drugs for use in infants with SMA: Nusinersen, Zolgensma

Answer 8.

A. Ventriculomegaly and posterior fossa cyst

B. Dandy Walker Syndrome

C. Agenesis or hypoplasia of cerebellar vermis, cystic dilatation of the fourth ventricle, enlargement of posterior fossa.

D. Hydrocephalus, atresia of foramen of magendie

E. D/D of posterior fossa abnormalities: Retrocerebellar arachnoid cysts, cystic hygroma, Blake's pouch cyst, mega cisterna magna, and vermian hypoplasia. Additionally, several syndromes correlate with DWM, such as Aase-Smith, cerebro-oculo-muscular syndrome, Coffin-Siris, Cornelia de Lange and Aicardi.

F. Treatment consists of treating the manifestations and associated comorbidities. AEDs need to be given for seizure control. Most patients present with signs and symptoms from increased intracranial pressure, most commonly related to hydrocephalus and posterior fossa cyst. For this reason, therapy generally aims to control intracranial pressure, usually through surgery. Surgical treatment may include ventriculoperitoneal (VP), or cystoperitoneal (CP) shunts. Few patients may be candidates for endoscopic procedures, including endoscopic third ventriculostomy (ETV).

G. Prognosis: Patients with DWM may present with different degrees of hydrocephalus, which if untreated may lead to severe neurological deficits and death. Fifty percent of children with untreated hydrocephalus die before age 3, and only around 20 to 23% will reach adult life. From the patients with untreated hydrocephalus who reach adult life, most will have motor, visual and auditory deficits. The diameter of the fetal lateral ventricle through obstetric ultrasound may have substantial prognostic value. Lateral ventricles measuring between 11 to 15 mm correlate with a 21% risk of developmental delay. If the diameter measures more than 15 mm, the risk of developmental delay is above 50%. Overall risk for epilepsy is approximately 30%. Functional outcome is subject to several factors, which include other structural brain abnormalities, extra-CNS manifestations, epilepsy, motor, visual or hearing impairment, and other congenital abnormalities.

Answer 9.

Fig. 9: Discontinuous pattern/ moderately abnormal background

(Minimum amplitude/ lower margin < 5 microvolt and maximum amplitude/ upper margin > 10 microvolt)

Fig. 10: Burst suppression pattern

(Lower margin < 5 and upper margin < 10 and bursts with amplitude > 25 microvolt)

Fig. 11: Isoelectric trace/ primarily inactive background

(Minimum amplitude/ lower margin < 5 microvolt and maximum amplitude/ upper margin < 5 microvolt)

Fig. 12: Seizures

(Abrupt rise in the minimum amplitude and simultaneous rise in the maximum amplitude/ sawtooth pattern; Raw EEG is a must to corelate findings)

Answer 10.

A. Foetal ventriculomegaly: Lateral ventricular width >/= 10 mm on fetal ultrasonography.

B. Grading of severity:

Mild: 10-12 mm

Moderate: 13-15 mm

Severe: > 15 mm

This is a case of severe fetal ventriculomegaly.

C. Prenatal Evaluation:

Comprehensive sonographic evaluation for complete search for associated CNS and non-CNS anomalies.

Foetal MRI, Foetal echocardiography

Serological tests for TORCH infections

Amniocentesis – Karyotype or CMA/ CMV and Toxoplasmosis PCR. For known syndromic forms of primary congenital hydrocephalus, targeted gene testing can be done. For unknown syndromic or non-syndromic forms, SNP array and L1CAM gene mutation evaluation is suggested.

D. Prognosis and counselling: In mild isolated ventriculomegaly ≤ 12 mm size, the outcome is usually good. The risk for abnormal outcome increases when there are associated anomalies, the atrial width is >12 mm, or there is a progressive increase of the lateral ventricular width. The outcome of severe ventriculomegaly depends mainly on the presence of associated pathologies. When associated pathologies are diagnosed, the prognosis is usually poor unless the cause is intraventricular hemorrhage. Ventricular size does not seem to correlate with outcome and caution should be used in prognosticating outcome in isolated ventriculomegaly. Even when isolated, the risk of perinatal death or severe neurologic sequelae is in the range of 50% in survivors.

E. 3 most common causes of congenital hydrocephalus: Aqueductal stenosis, Myelomeningocele with Chiari type II malformation, Dandy Walker malformation.

F. We would do postnatal MRI Brain for detailed evaluation.

G. Ventriculoperitoneal shunt would be the mainstay of treatment in this baby.

Instructions for Authors

Review Article	**The article should be approximately 2-3 pages long with a word count of 2000-2500 words. Author should summarize key practice points at the end. Please include 5-6 references as suggested reading.**
Case Report	**This would be a summary of the case discussed in that months clinical meeting. Interesting cases even if not presented may also be submitted. It should include the clinical presentation and a brief discussion about the condition. Word count should be 1000-1500. Please include 2-3 references at the end.**
Journal Scan	**Some recent research paper of interest to pediatricians and neonatologists. The structure should include Introduction, Research question, Hypothesis, Methods, Results, Limitations and strengths of study, Reviewers comments. Word count should be approximately 1000 words. Please include 2-3 references if needed at the end.**
Picture of Month	**An interesting case related to neonatal practice. It should have a brief case history and a commentary, all fitting on one page along with the pictures.**
Image section	**Any interesting Xray, Ultrasound, CT or MRI of clinical interest. Brief clinical presentation and about the condition should be summarized on one page along with image.**
OSCE	**About 10-12 questions would be included in this section along with answers.**

Contact Us

On behalf of committee, I request all members of NNF, Delhi to actively contribute to various sections of the newsletter.

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