February 2021

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E journal of Paediatrics

Issue. 2

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DEPARTMENT OF PAEDIATRICS, ANDHRA HOSPITALS, VIJAYAWADA
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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**.

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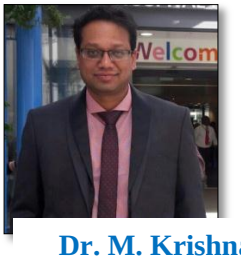

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SUMMARY OF ANTICOAGULATION GUIDELINES

Dr Balakrishna Palnati PICU Consultant

Unfractionated Heparin Infusions

Full Heparinisation:

Loading dose of 75u/kg.

Then start infusion at 25u/k/h.

Aim APTT 60-80 secs.

Monitor 4 hourly till anticoagulation stable.

Making up infusion

Put 1000u per Kg in 50 ml of 0.9% saline. 1ml/hour = 20u/kg/hour.

APTT (in secs)	Bolus (u/kg)	Hold (min)	Rate change (u/kg/h)	Repeat APTT
<50	50	0	Increase by 20%	4 hours
50 – 59	0	0	Increase by 10%	4 hours
60 – 80 (target range)	0	0	No change	8 hours
86 – 95	0	0	Decrease by 10%	4 hours
96 – 120	0	30	Decrease by 10%	4 hours
>120	0	60	Decrease by 15%	4 hours

Warfarin

Warfarin is relatively contraindicated in infants under 1 year of age; milk and formula feeds contain vitamin K which will block the action of warfarin. Since the half lives of the vitamin K dependent coagulation factors vary from 6 to 72 hours, and the half-life of warfarin is 2.5 days, changes made in the dosage will not be full reflected by the INR until day 3 or 4. Maintenance doses are highly dependent upon patient age, vitamin K intake, intercurrent illnesses and concurrent use of other drugs.
The loading period is approximately 3-5 days for most patients before a stable maintenance phase is achieved.

Start Warfarin on day 1 or 2 of heparin therapy. Heparin should be continued for a minimum of 5 days (if treating an extensive thrombus consider a longer period of heparinisation or even thrombolysis).
Consider drugs and feeding regimes which may interfere with anticoagulant effect or control for example – concurrent medication (regular and intermittent), TPN, oral types of feeds etc. If the child is on drugs which potentiate warfarin the loading dose may need adjusting. When the INR has been>2.0 for 2 consecutive days, stop heparin.

Dosing

Initial dosing (day 1)		
If INR baseline is 1.0 – 1.3, start with 0.2 mg/kg orally (maximum of 10mg)		
If INR baseline is more than 1.3 reduce loading dose to 0.1 mg/kg		
Measure INR Day 2 – 6		
If your response is an INR of		
INR	1.1-1.4	Repeat loading dose
INR	1.4-1.9	50% of loading dose
INR	2.0-3.0	50% of loading dose
INR	3.0-4.0	25% of loading dose
INR	>4.5	Omit dose until INR less than 4.5 then restart at 50% less than previous dose
If INR not greater than 1.5 on day 4 contact consultant for help		
Long term control – day 6 onward		
INR	1.1-1.4	Increase by 20% of dose
INR	1.4-1.9	Increase by 10% of dose
INR	2.0-3.0	No change
INR	3.1-4.0	Decrease by 10% of dose
INR	4.1-4.5	Decrease by 20% of dose
INR	>4.5	Hold dose, check INR daily until INR <4.5 then restart at 20% less than previous dose

Target INR levels:

• The target INR is 3.0 (range 2.5 - 3.5) for patients with valvular heart disease, antiphospholipid syndrome and warfarin failure.

• The target INR is 2.5 (range 2.0 - 3.0) for other indications

Low Molecular weight heparin

LMWH may be used for both prophylaxis of thromboembolism, or for treatment of thromboembolic disease.It has much better bioavailability than unfractionated heparin, and can be used in place of warfarin in infants.

Prophylaxis

Enoxaparin

< 2 mon :0.75 mg/kg/dose SC per 12 hours
2 months - 16 years: 0.5 mg/kg/dose SC per 12 hours

Treatment

Enoxaparin

<2 months and <5 kg:1.5 mg/kg/dose subcutaneously (SC) per 12 hours
2 months - 16 years: mg/kg/dose SC per 12 hours.

When using LMWH for treatment doses, anti Xa activity should be monitored in those patients who are under 40kg weight.
Levels should be taken after 2 doses of treatment, 4 hours after the morning dose.

MANAGEMENT OF CENTRAL VENOUS CATHETER OCCLUSION & THROMBOSIS

Introduction:-

Long-term central venous catheters (CVC) facilitate care for patients with chronic illnesses, but catheter occlusions and catheter-related thrombosis (CRT) are common complications. This review summarizes management of CVC and CRT.

Mechanical CVC occlusions require cause-specific therapy; whereas, thrombotic occlusions usually resolve with thrombolytic therapy, such as alteplase. Prophylaxis with thrombolytic flushes may decrease CVC infections and CRT, but confirmatory studies and cost-effectiveness analysis are needed. Risk factors for CRT include previous catheter infections, malposition of the catheter tip, and prothrombotic states. CRT can lead to catheter infection, pulmonary embolism, and post-thrombotic syndrome. CRT is diagnosed primarily using Doppler ultrasound or venography and treated with anticoagulation for 6 weeks to a year, depending on the extent of the thrombus, response to initial therapy, and whether thrombophilic factors persist. Prevention of CRT includes proper positioning of the CVC and prevention of infections; anticoagulation prophylaxis is not recommended at present.

CVC occlusion occurs in 14% to 36% of patients .A CVC occlusion can be partial, such that blood cannot be aspirated but infusion through the catheter is possible, or complete, such that neither aspiration nor infusion is possible. A CVC occlusion can arise from mechanical obstruction, precipitation of medications or parenteral nutrition, or thrombotic causes. CRT occurs in up to 50% of children with a long-term CVC, and can cause long-term vascular complications.

Causes of central venous catheter occlusion:

1)Medication or parenteral nutrition can also cause obstruction, which can be acute or gradual, with increasingly sluggish flow through the catheter.

2)Inappropriate concentrations or incompatible mixtures can cause medications to precipitate within the catheter lumen. An occlusion can result from the precipitation of calcium phosphate crystals when calcium and phosphorus are co-administered at inappropriate concentrations.

3)If the pH of an infusion is too alkaline or acidotic, precipitation can occur. Parenteral nutrition preparations can leave a lipid residue that can obstruct a CVC.

Catheters can also become occluded secondary to a thrombotic process, such as a fibrin sheath around the catheter tip, an intraluminal blood clot, or a venous thrombosis, which can occur separately or in combination. A fibrin sheath is one of the most common causes of thrombotic obstruction. It can occur within 24 hours after CVC placement and usually develops within 2 weeks.

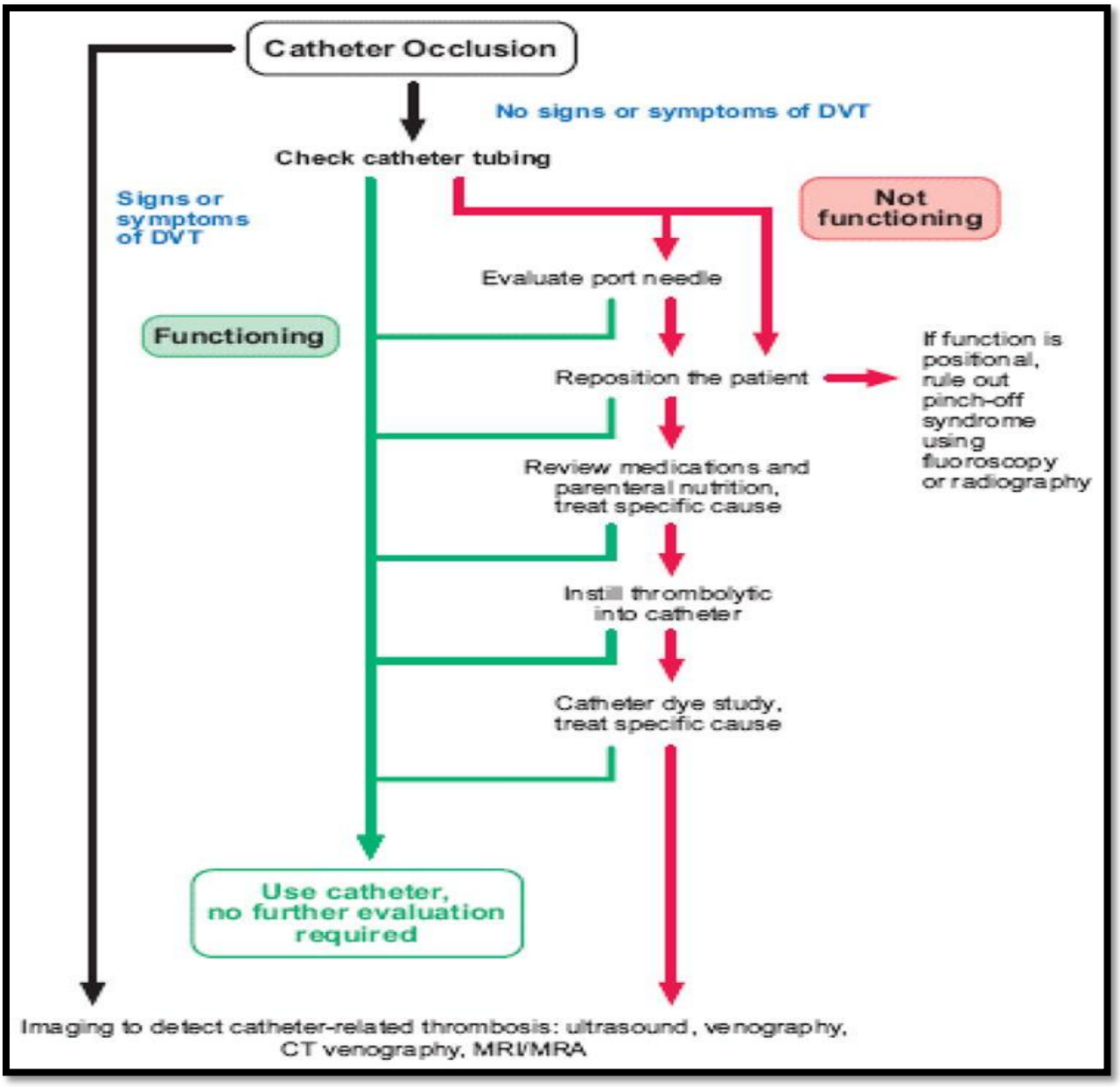
The fibrin sheath does not usually affect catheter function, but may cause a partial obstruction by creating a one-way valve over the catheter tip. The negative pressure created when attempting to aspirate blood creates suction, which pulls the fibrin sheath over the CVC tip and prevents withdrawal of blood.

The obstruction resolves when the negative pressure is relieved (e.g., during infusion or flushing the catheter), allowing for easy passage of fluids into the CVC. Although a fibrin sheath does not usually cause any clinical manifestations, there is a small risk of embolization of the fibrin material.

Management:

Mechanical obstruction of catheter

A standard procedure should be followed to diagnose and manage CVC obstruction. First, any obvious mechanical obstruction (e.g., a kink in the catheter tubing, a suture that is too tight, a clamp inadvertently left closed, a catheter tip blocked by the blood vessel wall, or a malpositioned subcutaneous port access should be ruled out by carefully inspecting the CVC and repositioning the patient.



Catheter obstruction related to medication or parenteral nutrition

If a mechanical obstruction is not found, obstruction by medication or parenteral nutrition should be excluded. The medications and parenteral nutrition preparations administered through the catheter should be carefully reviewed to identify any incompatibility that could have led to the obstruction. Appropriate treatment depends on the suspected cause of the occlusion. Obstructions thought to be caused by precipitation of low-pH medications or calcium phosphate crystals that become insoluble in basic solutions can be treated with 0.1% hydrochloric acid. Obstructions caused by high-pH medications that precipitate in an acidic environment (e.g. phenytoin), are treated with sodium

bicarbonate or sodium hydroxide. A lipid residue from parenteral nutrition can be successfully cleared with a 70% ethanol solution.

Thrombotic catheter obstruction

After ruling out mechanical dysfunction and medication- or parenteral nutrition-related etiologies, the next step is to exclude thrombotic obstruction.A contrast study of the catheter (sometimes referred to as a "linogram"), can be used to detect an intraluminal clot or fibrin sheath. However, a common practice is to treat suspected thrombotic occlusions empirically with thrombolytics.
The current standard treatment for CVC occlusion is instillation of alteplase with a concentration of 2 mg/2mL. A dose of 2 mL, or 110% of the volume of the catheter lumen if less than 2 mL (maximum dose 2 mg), is placed in the catheter lumen.
Alteplase catalyzes the conversion of clot-bound plasminogen to plasmin and initiates fibrinolysis.2 mg dose of alteplase was more effective than urokinase (5000 IU) for treating radiographically proven thrombotic occlusion of a CVC after a dwell time of 120 min.

One 2 mg dose of alteplase cleared the catheter occlusion after 120 min in 74% of patients, compared to only 17% of patients who received placebo.The overall catheter clearance rate for alteplase was 90% after up to 2 doses with no reports of major hemorrhage. Larger studies subsequently confirmed the safety and efficacy of alteplase administered at various time intervals in different long-term catheters, including peripherally inserted central catheters, with major hemorrhage reported in 0.3% of patients

After demonstrating the success of alteplase to treat CVC occlusions in adults, it was proven safe and effective in children as well, with catheter clearance rates of 85–95% and no major hemorrhage. A subsequent subset analysis of pediatric patients in the COOL trial and an open-label, single-arm multicenter trial with the same dosing regimen and dwell times as those of the COOL trial confirmed that alteplase was as effective in children as in adults, with catheter clearance rates of 83–87%, and no evidence of major hemorrhage.
Current recommendations include administration of a thrombolytic agent into the catheter lumen with a dwell time of at least 30 minutes and a repeated dose if needed. If catheter patency is not restored, a low dose of alteplase can be infused over 6 to 8 hours. An ultrasound, venogram, or other diagnostic study is warranted if venous thrombosis is suspected.
If thrombolytic therapy fails to clear the catheter, a guide wire can be inserted through the catheter lumen to dislodge a thrombus at the tip of the CVC. Fibrin sheath stripping has also been used for CVC occlusion that is resistant to medical management. The procedure uses femoral venous access to pass a vascular snare device to dislodge and remove the fibrins heath. Although effective, these procedures are more invasive and are only used as a last resort.

New thrombolytic medications

One promising new thrombolytic is reteplase, a variant of alteplase whose structural differences increase its half-life and penetration of a thrombus. Reteplase effectively restored patency to occluded CVCs, with catheter clearance rates of 67–74% after a dwell time of 30–40 min, as compared to an average 53% with a dwell time of 30 min for alteplase. Reteplase was also effective after longer dwell times, with overall catheter clearance rates approaching 96% and no reports of major hemorrhage.

Recombinant Urokinase

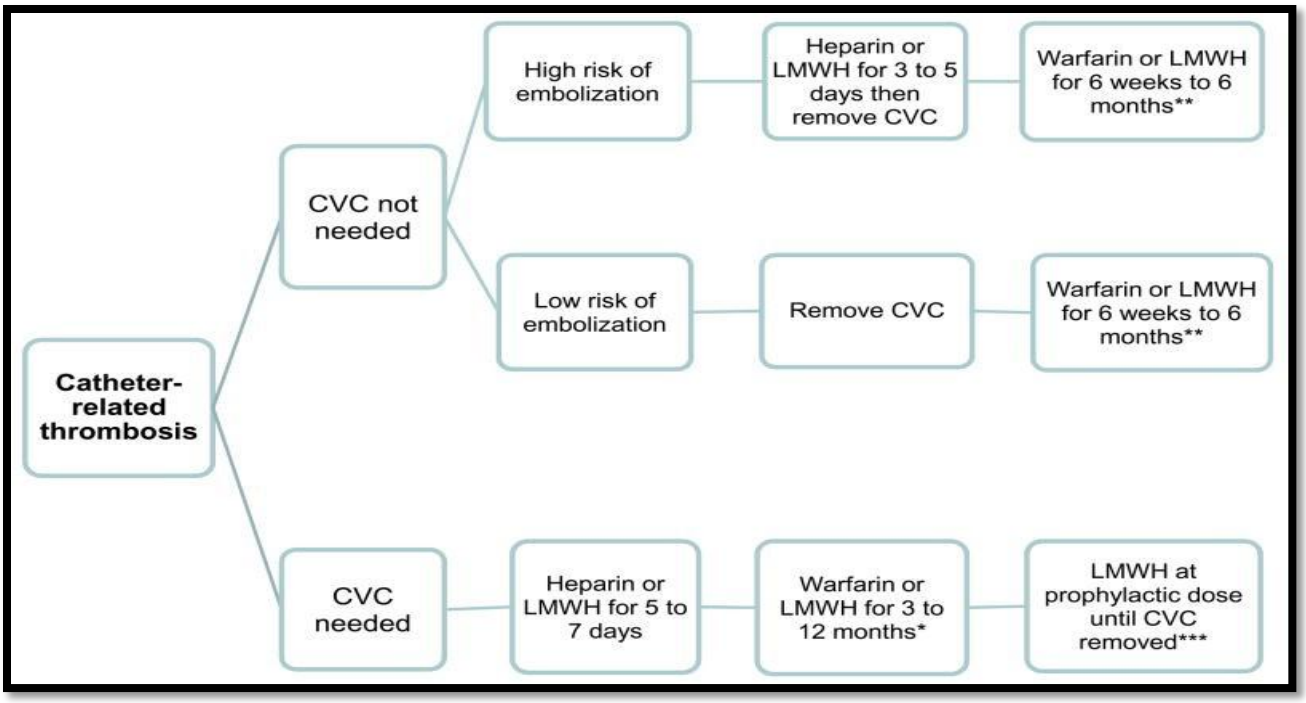
Recombinant urokinase has been studied as a potential candidate for managing CVC occlusions. Compared with the average clearance rate of 53% for alteplase, recombinant urokinase appears to have greater efficacy within the first 30 min, with an average clearance rate of 60%. Whether recombinant urokinase would be more effective than alteplase at time points beyond 30 min remains to be studied. Recombinant urokinase is less effective than reteplase at all time points and the incidence of major hemorrhage was 0.6% within 72 hours and 1.8% within 30 days following administration.

In one study, a higher dose of recombinant urokinase increased the risk of bleeding but did not improve catheter clearance rates. Although only a trial that directly compares the 3 medications can unequivocally determine the most effective and safe treatment, existing data suggest that recombinant urokinase is more effective than alteplase at early time points but less so after 2 doses, and is less effective than reteplase at all time points in treating occluded catheters.

Prophylaxis:

To prevent thrombotic CVC occlusions, most institutions that use long term CVCs have standard protocols regarding the method and frequency of flushing the catheter. However, there is insufficient medical evidence on which to base universal guidelines for these practices, specifically with regard to the type of solution used (10 U/mL heparin vs. 100 U/mL heparin vs. normal saline) and frequency of flushing the catheter.

For CVCs, some studies have suggested that there is no difference between a saline and heparin lock. One study in children showed no difference in catheter occlusion or clot formation when flushing the external catheter twice a day with a heparin solution (10 U/mL) versus once a week with a saline solution.Although there is general consensus that subcutaneous ports should be flushed monthly Although the literature suggests that the current practice of frequent heparin locks for CVC may not be necessary, randomized studies are required to determine the ideal flush solution, its concentration, and its administration schedule for each type of long term CVC.



Conclusion:

Long-term CVCs are important for the medical care of children and adults with chronic illness, but can lead to various complications such as CVC occlusions and CRT. The etiology of a catheter occlusion determines the appropriate treatment, but most occlusions are thrombotic and should be treated with thrombolytic therapy.

Alteplase is most commonly used in North America but new agents have shown promising improvements in efficacy and onset of action. Further studies are required to compare new thrombolytics to those currently available.

Thrombotic CVC occlusions can cause CRT, which can lead to post-thrombotic syndrome, pulmonary embolism, and an increased risk for catheter infections. Although prevention of CRT is the key to decreasing the incidence of subsequent complications, effective prophylactic measures have not been established. Studies in adults have shown sufficient accuracy of ultrasound in diagnosing symptomatic upper extremity DVT, a result that has yet to be confirmed in children

Future research should focus on optimal strategies for prevention, diagnosis, treatment of CVC occlusions and catheter related thrombosis, and the role of new thrombolytic agents in clinical practice.

IMAGE QUIZ

Dr M Krishna Prasad PICU Consultant

A 11-year-old boy presented to Emergency with a history of headache and vomiting following a fall in school. He fell on a hard floor while playing earlier in the day but denied hitting his head and there was no loss of consciousness, although he was later found to be sleepy. On arrival to Casuality, he was complaining of sudden onset frontal headache and he had vomited 4-5 times. He also had been playing Cricket with a friend 2 days previously. He had developed some lower back pain, but this had now resolved. There is no past medical history of note and he was not on any regular medication. On examination his GCS was 15/15. On neurological examination there was mild right-sided upper motor neuron facial weakness, with no other abnormality.He was apyrexial and all other observations were normal.

Questions

1.What would be your top three differential diagnoses?

a) Intracranial haemorrhage
b) Other space occupying lesions (e.g. tumour)
c) Epilepsy
d) Cerebro vascular accident (stroke)
e) Migraine
f) Behavioural problem
g) Encephalitis
h) Drug toxicity
i) Cardiac arrhythmia

2. What will be your two initial investigations?

a) Blood glucose
b) Blood culture
c) CT head
d) EEG
e) Lumbar puncture
f) Urine for toxicology
g) ECG
h) Echocardiography

He was admitted to the ward for neurological observation.His initial investigations including CT head were normal.The following day he developed some right-sided shoulder droop and his mother felt that he was more lethargic than before.He also had an episode of urinary incontinence during sleep. His lumbar puncture result was unremarkable. Urine toxicology was negative. The EEG was reported as showing unilateral encephalopathic changes on the left.

2. What would you do next?

a) Continue observation
b) Reassure and discharge with review plan
c) IV acyclovir and antibiotics
d) MRI head
e) Seek mental health team opinion

His facial palsy resolved after 72 hours. Following review by the Paediatric neurologist, an MRI and MRA of the Brain were performed (Figures 1 and 2).

4. What is seen in Figures 1 and 2?

a) Extradural haemorrhage
b) Haemorrhage in right internal capsule
c) Aneurysm of right internal carotid artery
d) Left internal carotid artery dissection with resultant Left Sided Middle Cerebral Artery ischaemic stroke
e) Normal scan

5. What would your treatment be?

a) Transfer to neurosurgical unit
b) Referral for assessment by vascular surgeons
c) Start anticoagulant and follow-up
d) Thrombolysis
e) Conservative treatment with follow-up

Figure-2

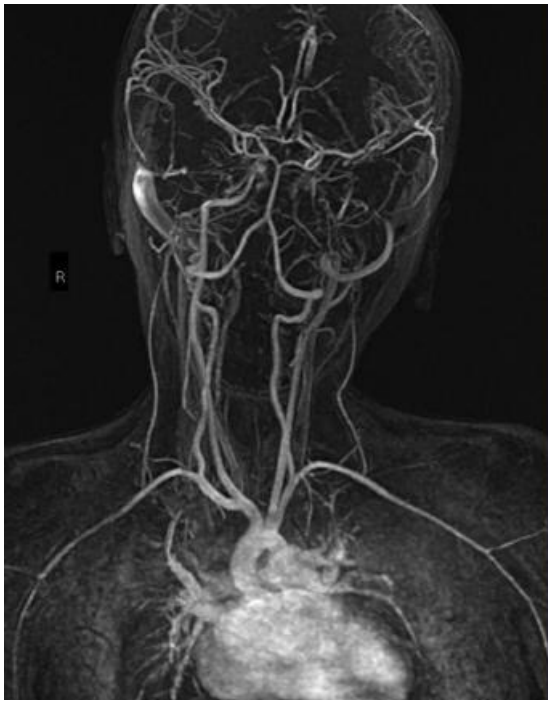
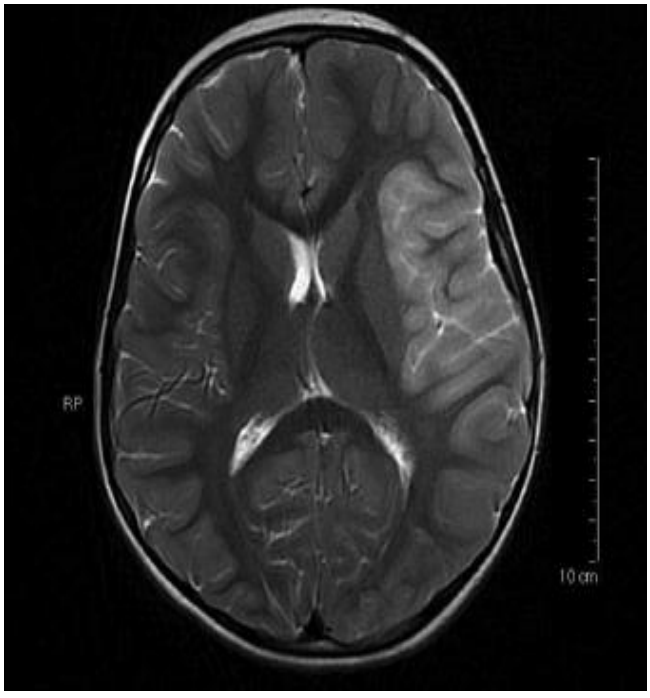


Figure-1



Answers

1. a, d, g
2. a, c
3. d
4. d
5. c

Arterial dissections are a common cause of arterial ischaemic stroke in children.Dissections occurwhen there is compromise to the structural integrity of the arterial wall allowing blood to breach the intima and collect between layers of the artery wall as an intramural haematoma. This can be spontaneous or can be secondary to (often minor) degrees of trauma. The average annual incidence rate for spontaneous internal carotid artery dissection is 1.72 per 100,000 individuals.The clinical presentation of stroke is variable depending on the age of the patient. Infants often present with seizures and altered mental status such as irritability, reduced conscious level or coma. Older children may have hemiparesis or other focal neurological signs, but can also present with seizure, headaches and lethargy. The differential diagnosis of stroke is very broad as many conditions can present with acute neurological deficit, these include intracranial haemorrhage, aneurysm, tumour, migraine, epilepsy, intracranial infections and drug toxicity. Clinical features may raise suspicion of stroke and dissection; however the diagnosis is confirmed by neuroimaging. Current guidelines from the Royal College of Physicians (RCP) recommend neuro-imaging with MRI for the investigation of children presenting with clinical stroke, and this should be as soon as possible after admission. A CT head is an acceptable initial alternative if an MRI is not available within 48 hours. Imaging of the cervical and proximal intracranial arterial vasculature should be performed in all children with arterial ischaemic stroke and imaging of the cervical vasculature to exclude arterial dissection should be undertaken within 48 hours of presentation with arterial ischaemic stroke. As part of the initial work up following an ischaemic stroke children should be investigated for an underlying prothrombotic tendency. This should include evaluation for protein C, protein S deficiency, activated protein C resistance, increased lipoprotein (a), increased plasma homocysteine, factor V Leiden, prothrombin G20210A and MTHFR TT677 mutations and antiphospholipid antibodies. Providing there is no evidence of haemorrhage on brain imaging, anticoagulation should be considered in children with confirmed extracranial arterial dissection associated with arterial ischaemic stroke. There is currently no evidence to support the use of thrombolytic agents in children (and this is contraindicated in infants where the risk of resultant haemorrhage is much higher).

CONGENITAL METHEMOGLOBINEMIA IN NEONATE – AN EASILY MISSED CAUSE OF CYANOSIS – A CASE REPORT

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ABSTRACT.

Cyanosis in newborn is a common finding in day to day practice. It often points to either Cardiac or Respiratory system problems. Congenital methemoglobinemia presenting in newborn period is rare, and associated with severe disease. This case report highlights the importance of considering Methemoglobinemia even in a newborn baby. The interesting feature in this case is that though the methemoglobin levels were only mildly deranged, the baby was significantly cyanosed and required treatment from birth.

CASE REPORT

A Near term (35 weeks), male neonate, product of a non-consanguinous marriage, was born to a primigravida mother through emergency LSCS in view of Oligohydramnios and Anemia complicating pregnancy.The baby was vigorous at birth. But was visibly cyanosed and oxygen saturation being 78% in room air. There was mild respiratory distress. Baby was managed in referral hospital with oxygen and IV antibiotics. In view of persistent oxygen requirement baby was referred to our hospital on day 6 of life.

On examination, the baby was nearterm gestation (35 weeks) with anthropometric parameters within 70th-80th centile for age. The neonate had peripheral and central cyanosis with oxygen saturation of 78% in room air, which improved to 90% with 2 liters of oxygen. He was normotensive. Systemic examination was normal. Complete blood picture and routine biochemistry were normal except for a marginally elevated CRP(1.2). Chest radiograph showing normal lung fields and normal cardiac shadow. On2D-Echocardiography structurally normal heart with no evidence of pulmonaryarterialhypertension.
Retrospectively, Antenatal exposure to drugs such as nitrites, nitrates, Aniline dyes, Antimalarial drugs, Phenacetin, Topical anaesthetic agents were ruled out[1, 2]. Family history is also not significant with no post-natal deaths.

In view of persistent cyanosis in the absence of significant pulmonary or cardiac disease, the rare possibility of methemoglobinemia was suspected.

ABG IN ROOM AIR

PH	7.507
PCO2	37.8 mmhg
PO2	156 mmhg
LACTATE	1.5 mmol/L
FMETHB	5.7%
FCOHB	0.0%
BASE EXCESS	6.3 mmol/L
BICARBONATE	30.4 mmol/L

BROWN COLORED ARTERIAL BLOOD

ABG revealed methemoglobin levels to be 5.7% (Normal-1-3 %) with good PaO2 levels in presence of clinical cyanosis. The arterial blood sample was chocolate brown in color. Filter paper test was inconclusive as both the control and test sample were bright red. Parents were screened with ABG which showed normal methemoglobin levels. Clinical Exome Assay Analysis for methemoglobin genes was also sent and no abnormalities detected. HB Electrophoresis report was normal.G6PD deficiency levels are within normal limits.

Baby was treated with Oxygen and oral Vitamin C (5mg/kg 6th hourly) and could be weaned off to room air on 14th day of life. IV antibiotics were given for 3 days (Blood culture and sensitivity –Negative). Intravenous Methylene blue was not considered as methemoglobin levels were not more than 10%.

Baby was later discharged on oral daily ascorbic acid therapy on 16th day of life and followed up after 1 month and has SPo2 98% in room air and Methemoglobin level 2% on ABG. His growth and development are normal with no clinical cyanosis.

BEFORE TREATMENT AFTER TREATMENT

DISCUSSION

Congenital Methemoglobinemia in neonates is rarely reported.Hence its incidence is largely unknown. Methemoglobinemia is of two types Congenital and Acquired. Methemoglobin is produced from oxidation of ferrous iron (Fe^{2+}) to ferric iron (Fe^{3+}) within the heme moiety of hemoglobin. Methemoglobin, which normally constitutes <1% of the total hemoglobin, has an increased affinity for oxygen causing a shift to left in the oxygen dissociation curve. These phenomena contribute to a reduction in the delivery of oxygen to tissues there by, causing hypoxemia and lactic acidosis.

Congenital methemoglobinemia is differentiated into[3]:

a) **Cytochrome b5 Reductase Deficiency–** Most cases of hereditary methemoglobinemias are autosomal recessive and are due to homozygous or compound heterozygous deficiency of cytochrome b5 reductase. Cytochrome b5 reductase participates in the transfer of electrons to cytochrome b5 from the NADH generated by glyceraldehyde-3-phosphate dehydrogenase. The gene for NADH-CB5R is located on chromosome 22.

b) **Hemoglobin M Disease**– isAutosomal dominant hemoglobin M disease due to mutations in either the alpha or beta or, rarely, gamma globin gene. Administration of methylene blue (MB) does not correct this type of congenital methemoglobinemia.

c) **Cytochrome b5 Deficiency–** Rarest form of congenital methemoglobinemia.

There are two pathways for reduction of methemoglobin back to hemoglobin:

a)The physiologically important pathway is the NADH-dependent reaction catalyzed by cytochrome b5 reductase (b5R).

b) An alternative pathway which is not physiologically active utilizes NADPH generated by glucose-6-phosphate dehydrogenase (G6PD) in the hexose monophosphate shunt. However, there is normally no electron carrier present in red blood cells to interact with NADPH methemoglobin reductase. Extrinsically administered electron acceptors, such as methylene blue (MB) and riboflavin, are required for this pathway to be activated. This non-physiologic pathway becomes clinically important for the treatment of methemoglobinemia.

Clinical manifestations of MetHb reflect the reduction in oxygen carrying capacity, leading to tissue hypoxemia. In general, MetHb under 10% causes only a grayish pigmentation of the skin, but the condition is

frequently overlooked.

Clinical symptoms in relation to MetHb blood concentration.

MetHb % of total Hb	Symptoms
<10	Asymptomatic
10-20	Cyanosis
20-40	Headache, fatigue, weakness, tachycardia, and dizziness
40-50	Dyspnea and lethargy
50-70	Acidosis, arrhythmias, hypoxia, seizures and coma
>70	Death

MetHb, methemoglobin; Hb, hemoglobin.

DIAGNOSIS:

1. ABG

Blood gas analysis will give falsely high levels of oxygen saturation in the presence of methemoglobin. Methemoglobinemia is strongly suggested when there is clinical cyanosis in the presence of a calculated normal arterial pO2 (PaO2) as obtained by arterial blood gases. Arterial blood gas analysis is deceptive because the partial pressure of oxygen is normal in subjects with excessive levels of methemoglobin[4].

2. FILTER PAPER TEST

In a case of methemoglobinemia, when an arterial blood gas is drawn, the colour of blood is commonly a brown or chocolate colour. Upon exposure to air, the colour of the blood does not change in a case of methemoglobinemia. Rapid screening test can be done bedside by placing a drop of blood on filter paper allowing the blood to dry. Deoxygenated normal hemoglobin turns red, whereas methemoglobin remains brown. Using this technique, methemoglobin levels of 10% or more can be detected.

In our case, both case and control samples turned red, suggesting ours is a case of mild methemoglobinemia.

3. CO-OXIMETRY

Co-oximetry is the gold standard for the diagnosis of Methemoglobinemia which has peak absorbance at 631 nm[5].Methemoglobin detected by the co-oximeter should be confirmed by the specific Evelyn-Malloy method[6].

4. HB-ELECTROPHORESIS

Hemoglobin electrophoresis will identify hemoglobin M, ahemoglobin variant that causes cyanosis. Cyanosis is noticed at birth orwithin 4 to 6 months thereafter.

5. CLINICAL EXOME ASSAY

Clinical exome assay for methemoglobin genes helps in confirming the genetic defects.

TREATMENT:

In the neonatal period, there is a persistence of fetal hemoglobin which has got increased affinity for oxygen. Methemoglobinemia also causes a leftward shift of the oxygen-hemoglobin dissociation curve. These factors, contribute to decreased oxygen delivery at tissue level in newborns with methemoglobinemia. Methylene blue (MB) is the treatment of choice for severe methemoglobinemia (0.5-2mg/kg over 5 min). In neonates it is recommended to start at lower end of the dose, as it might be as effective as higher and carries lower risk of hemolysis. In the presence of nicotinamide adenine dinucleotide phosphate (NADPH), methylene blue is converted to leucomethylene blue, which results in nonenzymatic reduction of methemoglobin. Methylene blue is not indicated in cases of HbM[7].MB should not be administered to patients with known G6PD deficiency, since the reduction of methemoglobin by MB is dependent upon NADPH generated by G6PD. As a result, MB may not only be ineffective, but it is also potentially dangerous since MB has an oxidant potential that may induce hemolysis in G6PD-deficient subjects precipitating acute hemolysis, thus, further decreasing oxygen delivery. N-acetyl-cysteine (another electron donor) has been used on those cases[8].Ascorbic acid(5mg/kg/dose/ 6th hourly) directly reduces methemoglobin, but the rate of the reaction is too slow for it to be effective when used alone[4,9].Finally, if the combination of ascorbic acid and methylene blue fails to reduce the methemoglobin level, then hyperbaric oxygen and exchange transfusions are alternative therapy[10].

CONCLUSION:

Congenital methemoglobinemia is a rare diagnosis. Because of its rare occurrence in the neonatal period, its incidence is not usually reported. This diagnosis should be considered in any newborn with mild to severe cyanosis, after ruling out cardiopulmonary pathologies. Our case is an example of congenital methemoglobinemia which presented with cyanosis at birth, and showing minimal increasein saturation levels on oxygen administration which was misleading initially. The Clinical signs which help to clinch the diagnosis are

1. Cyanosis not responding or minimal response to oxygen administration in absence of cardiopulmonary problems.
2. ABG showing good PaO2 levels in presence of clinical cyanosis.

The idea to present this case is to highlight varied presentation and clinical manifestations in congenital methemoglobinemia with less than 10% methemoglobin levels. Baby needed ascorbic acid to remain acyanotic as well as to ensure normal growth and development.

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