THE NEW BORN

JOURNAL OF NNF KERALA

Theme : Case Reports

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Contents

Message

Dear Colleagues in Neonatology,

This little baby of an E-magazine awaits your perusal. All the contributions are of a high standard and we at the editorial desk extend our sincere appreciation. As always, I say a big thank you to the editorial team with me and hasten to add that all deficiencies are unintentional and solely mine.

God bless our little state who is bravely bouncing back from the shock of the august floods!

Sincerely,

Preetha

Message

Dear friends

I'm pleased to see Dr Preetha and team coming out with first magazine of NNF Kerala 2017.

NNF Kerala has taken a big leap this year by forming 8 district branches with in a short span of 6 months. Strength of an organisation lies is membership and branches. We had a very good start in February when we started traveling all over kerala in connection with new district branch formation. Response from each & every corner was uniformly. encouraging,so much so that we are actually far ahead of our action plansfor this year!

When we started at the grass root level, we have managed to identify a lot of things which require our urgent attention.The neonatal transport system is in very primitive level in kerala.15 states in India have very good neonatal transport system in place whereas in this vital aspect Kerala is literally floundering. We have very good (albeit few in number) tertiary care neonatal intensive care units in kerala. To reach these centres, a sick neonate has to be transported, that too most often in an ordinary vehicle.We have submitted a proposal to the government in this regard on July 1st at the health minister's office in Thiruvananthapuram. I am very very happy to learn that they have already taken initial steps to implement this project.

In Kerala, there are 464 delivery points in private sector and 72 delivery points in public sector. 28% deliveries take place in public sector and the major share of 72 % occurs in private sector. To reduce our IMR we have to reduce NMR, which as we know is the major contributer of IMR. For this we must develop a good neonatal resuscitation team at all delivery points.

We,NNF Kerala can easily train the available work force in each delivery point with the help of our state government. This suggestion alsowas well taken by the government and we hope to start our work soon. We now have to accredit all existing neonatal care unit according to the level of care they are expected to deliver. Each & every baby delivered in Kerala should get uniformly expert care irrespective of where they are born.

We do not have any cardiothoracic surgery unit for neonates and children in northern kerala beyond Ernakulam till Kasarakode. We should have at least one in government sector attached to Calicut Medical College. We hope to start our website and E magazine during midneocon in August 2017. Wealso hope to start work on our data bank shortly.

As I wind down this message,I do so with the realisation that we have much much more to do in the field of neonatal care. Hope God almighty will give our team bith courage and strength to achieve more and more during our tenure. I'm grateful to one and all who contributed to the growth and development of NNF in Kerala.

'Our little state is slowly rallying around after the unprecedented fury of nature.We now stand united in pledging our support in a timely fashion'.

Thank you and best wishes!

Jai NNF Jai IAP

Dr.Santosh M K
President NNF Kerala
Dear Colleagues,

Message

Greeting from NNF Kerala.

Its my pleasure and privilage to write a forward to the NNF Kerala journal with a theme of Neonatal emergencies. NNF Kerala is going through its Golden period. The team of office bearers are doing a very dedicated team work with SMART goals and this will take NNF Kerala to greater heights. Let me take this opportunity to congratulate Dr.Preetha & Team for preparing this journal and team Trivandrum for organising Mid Neocon 2018.

Best regards

Dr. AK.Jayachandran MBBS, DCH, MRCPCH, CCT

Secretary.NNF Kerala

Pathogenic bacteria distributions and their antibiotic sensitivity pattern in the neonatal intensive care unit

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Dr. A.K. Jayachandran

Abstract

Objective: To examine the microbiological patterns of neonatal sepsis and specify their antibiotic susceptibility pattern in NICU.

Methods: This is a retrospective study carried out in regional referral centre in Kerala. A total of 108 blood culture positive neonatal sepsis cases during a two-year period from January 2016 to December 2017 were analyzed for type of organism and antimicrobial sensitivity pattern.

Results: The incidence of sepsis was 8.6%. The percentage of early-onset sepsis (EOS) was 58.7% and that of late-onset sepsis (LOS) was 41.3%. Sepsis due to Gram-negative organisms was more common (60.6%). Sepsis related mortality was 9.3%. The most common organism isolated was Klebsiella pneumoniae (21%) followed by Acinetobacter baumannii and Staphylococcus haemolyticus (13.8% each). Coagulase negative Staphylococci (CoNS) exhibited penicillin and Ampicillin resistance rates as high as 100%. Acinetobacter strains were 100% sensitive to Colistin but resistant to most of the other antibiotics.

Conclusions: Klebsiella pneumoniae was most common organism in neonatal sepsis having

maximum sensitivity for Amikacin and Meropenem. Most of the gram positive sepsis was due to coagulase negative Staphylococci which had maximum sensitivity for Vancomycin. Most of the organisms were resistant to penicillins and cephalosporins. This indicates that previously used penicillins and cephalosporins could not be used as preferred medications for neonatal sepsis. Ongoing surveillance of local epidemiology and antimicrobial susceptibility is essential to ensure appropriate empiric and targeted antimicrobial therapy.

Keywords: Neonatal sepsis, blood culture, antibiotic sensitivity, Klebsiella pneumoniae, Acinetobacter baumannii, coagulase negative Staphylococci.

Introduction:

Sepsis is one of the commonest causes of neonatal morbidity & mortality and it is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes(1). Neonatal sepsis is a clinical syndrome in an infant 28 days of life or younger, manifesting with a diversity of non-specific systemic signs and symptoms and isolation of a pathogen from the bloodstream(2). Early onset sepsis (EOS) refers to infections during the first 72 hrs of life; whereas late onset sepsis (LOS) refers to postnatal acquisition of infections after the first 3 days of life(3).

Early-onset infection is usually due to vertical transmission by ascending contaminated amniotic fluid or during vaginal delivery from bacteria in the mother's lower genital tract. Late-onset infections can be acquired by either vertical transmission, resulting in initial neonatal colonization that evolves into later infection or horizontal transmission from contact with care providers or environmental sources. It is important to identify neonates with risk factors for sepsis and to have a high index of suspicion for sepsis because the signs and symptoms of sepsis can be subtle and nonspecific(4).

Precise estimates of neonatal sepsis burden vary between countries of different incomes. Defining the rate of neonatal sepsis has been complicated by variation in the denominators used. It is important to consider if population-based or hospital-based rates of neonatal sepsis are reported(5). Pathogens encountered in neonatal sepsis vary worldwide; Gram negative organisms are more commonly encountered in developing countries, but Gram positive organisms have been also reported(6–9).

Resistant organisms can potentially grow in the community with inappropriate use of antibiotics typically in developing countries. Understanding of the pathogens in neonatal sepsis cases admitted in our NICU and their antibiotic sensitivity pattern would be necessary for implementation of antibiotic stewardship program. Therefore, this retrospective study was done to examine the microbiological patterns of neonatal sepsis and to specify their antibiotic susceptibility.

Method:

It is a retrospective study carried out in regional referral centre accredited by IAP and NNF "Neobless" Moulana Hospital, Perinthalmanna, Malappuram district Kerala. This study was approved by Hospital Ethical committee of Moulana Hospital. Patients with episodes of blood culture-proven sepsis, admitted in the NICU during a two-year period (From January 2016 to December 2017) were included in the study. Positive blood cultures for recognized pathogens were included in the study. We excluded episodes of positive blood cultures for organisms that were considered contaminants, such as bacillus species, diphtheroids and non-speciated streptococci. We also excluded the cases which were culture positive from outside laboratory. Blood samples were incubated in blood culture incubator (BACTEC- 9120, Beckton-Dickenson) in our Microbiology department.

Sepsis before the age of 3 days (<72 hrs after birth) was defined as early-onset sepsis (EOS) and that after the first 3 days of life (>72 hrs after birth) was defined as late onset sepsis (LOS) (3). All data was collescted using our electronic medical records database. We collected data including demograph-

ics, gestational age, mode of delivery, birth weight, indication for sending blood culture, co-morbidities, presence of central venous catheter, types of respiratory support, type of nutrition, total WBC count, platelet count and CRP value at time of sepsis, microbiology data (i.e. type of organism and antimicrobial sensitivity pattern). Collected data was tabulated in a spreadsheet using Microsoft word and Excel. Statistical analysis was done using appropriate tests.

Results:

General information:

In our NICU 2477 babies were admitted from 1st Jan 2016 to 31st Dec 2017. During this 2 years period blood cultures were sent in 1256 cases (842 inborn and 414 out-born). This study included a total of 108 neonatal sepsis cases and isolated a total of 109 pathogenic bacterial strains (two strains were cultured from one sample and one neonate had both EOS as well as LOS); the male-female ratio in this study was 1.06:1, including 55 males (51.4%) and 52 females (48.6%). This study included 56.1% preterm babies and 43.9% term babies. Fifteen babies were extremely low birth weight (14%), 17 babies were very low birth weight (15.9%), 36 babies had low birth weight (33.6%) and 39 babies were of normal birth weight (36.5%). Early-onset sepsis was detected in 64 cases i.e. (58.7%) and late-onset sepsis was present in 45 (41.3%) cases. Out of 107 neonates 10 (9.3%) died due to sepsis.

In this study the incidence of sepsis was found to be 8.6%. The incidence was 6.2% in inborn babies compared to 13.3% in out-born babies. Respiratory support in the form of ventilation, CPAP or oxygen by nasal prongs required for 90 (84.1%) babies. High CRP (≥6 mg/L), high TC (≥20000 per mm3), thrombocytopenia (<1.5 lack per mm3), respiratory distress and feeding intolerance were most common reasons for sending blood culture in decreasing frequency.

Pathogens distribution:

From the 108 cases, 109 pathogenic bacterial strains were identified. Incidence of sepsis due to Gram-negative organisms was 60.6%, and that of due to Gram-positive organisms was 39.4%. Among Gram negative bacteria, Klebsiella pneumoniae accounted for 34.8% and Acinetobacter baumannii accounted for 22.7%, whereas Pseudomonas accounted for 9.1% and Escherichia coli for 7.6%; additionally 17 (25.8%) strains of Enterobacter and other species were detected. Among Gram positive bacteria, Staphylococcus haemolyticus accounted for 34.9% and Staphylococcus epidermidis for 23.3%, whereas Staphylococcus aureus accounted only for 4.7%. Other CoNS accounted for 30.2% cases whereas other bacteria (Aerococcus viridians and Enterococcus) accounted for 6.9%. Distribution of bacterial strains detected in 108 neonatal sepsis cases is presented in Table 2.

Drug sensitivity pattern:

Among 23 case of Klebsiella pneumonia 91% were sensitive to Amikacin, 87% to Imipenem, 83% to Levofloxacin, whereas sensitivity to Piperacillin + Tazobactam and Meropenem was 78% each. All were resistant to Ampicillin whereas only 30% were sensitive to Amoxicillin + Clavulanate and Cefotaxime. Acinetobacter strains were 100% sensitive to Colistin. Meropenem and Gentamicin showed 80% sensitivity for Acinetobacter whereas Amikacin and Levofloxacin showed 67% sensitivity. Piperacillin+ Tazobactam and Cefotaxime showed 53% and 13% sensitivity respectively. Acinetobacter strains showed 100% resistance for Ampicillin and Amoxicillin + Clavulanate. E. coli showed 100% sensitivity for Meropenem, Imipenem and Colistin whereas 80% for Amikacin and Piperacillin+ Tazobactam. Ampicillin, Amoxicillin + Clavulanate, Cefotaxime, Ceftazidime and Ciprofloxacin had only 20% sensitivity for E.coli. Pseudomonas had zero resistance rates against Imipenem, Colistin, Aztreonam and fluroquinolones, whereas aminoglycosides, Piperacillin + Tazobactam, Ceftazidime and Meropenem showed 83% sensitivity. Pseudomonas had 100% resistance for Ampicillin and Amoxicillin + Clavulanate. Enterobacter and other strains (Burkholderia cepacia, Rhizobium radiobacter,

Achronobactor species, Pantoe agglomerans, Aeromonas hydrophila, Stenotrophomonas maltophila) were mostly sensitive to Cotrimoxazole (87%) and Levofloxacin (88%). These strains showed high resistance for Ampicillin (100%), Amoxicillin + Clavulanate (94%), Aztreonam (89%) and Imipenem (86%). Sensitivity pattern of gram –ve organisms is presented in Table 3.

Out of 43 cases of Gram-positive organisms, Staphylococcus haemolyticus showed 100% sensitivity for Linezolid and Daptomycin whereas 86.7% and 83% sensitivity for Vancomycin and Tiecoplanin respectively. Staphylococcus haemolyticus showed 100% resistance rate against Penicillin, Gentamicin, Ampicillin, Cefazolin and Cefoxitin. Staphylococcus epidermidis was 100% sensitive for most of the antibiotics (Vancomycin, Linezolid, Daptomycin, Tiecoplanin, Clindamycin, Erythromycin and Oxacillin). Penicillin, Ampicillin and Cefoxitin had 100% resistance rate for Staphylococcus epidermidis and Gentamicin showed only 40% sensitivity. Most of the other CoNS species are sensitive to Vancomycin (92%), Linezolid (85%), Levofloxacin (85%) and Tetracycline (85%). Only 2 cases of Staphylococcus aureus were detected and both were sensitive for Vancomycin, Gentamicin and Linezolid. Enterococcus faecium, Enterococcus faecalis and Aerococcus viridians were sensitive for Vancomycin whereas Linezolid was sensitive against Aerococcus viridians. Enterococcus faecalis showed sensitivity for Penicillin and Ampicillin. Sensitivity of Gram + ve organisms is presented in Table 4.

Discussion:

Neonatal sepsis is a severe illness and remains among the main causes of neonatal death. On many occasions empirical antimicrobial therapy needs to be started immediately pending investigations. The long-term hospitalized neonates had high prevalence of sepsis (30%), with mortality rate as high as 50%, and survivors experience serious sequelae. Blood culture is the gold standard for diagnosis of neonatal sepsis (10). Early onset sepsis (EOS) is caused by maternally transmitted pathogens and the risk factors are chorioamnionitis, maternal intrapartum fever, prematurity, prolonged rupture of membranes and inadequate intrapartum antibiotic prophylaxis(11). Late-onset sepsis (LOS) is more common in preterm and in newborns with prolonged hospitalizations, use of central lines, parenteral nutrition and mechanical ventilation and is caused by nosocomial infections(12).

In our study 108 cases of neonatal sepsis were included with incidence of sepsis being 8.6% (6.2% in inborn and 13.3% in out-born). Verma et al. found 7.6% incidence of sepsis in their study, but they used total live birth as a denominator whereas we used only admitted babies whose blood cultures were sent as a denominator. Joseph et al. observed 7.8% incidence which is almost comparable to our study. The incidence of sepsis was found to be low in our study when compared to study conducted by Choudhary et al. which reported a much higher incidence of neonatal septicemia of 11.2% in live births. The male: female ratio was 1.87:1 in a study by Verma et al. but we found male: female ratio 1.06:1 which was lower compared to their study(13–15).

Preterm neonate is more susceptible for sepsis which was reflected in our study, as 56.1% were preterm neonates. Similar finding were reported by Verma et.al, who found pre term babies had more sepsis (58.15%) than term babies (41.8%). Khatua et al. also had similar findings in their study. In our study 63.5% babies had birth weight less than 2.5 kg. Our results were comparable with study by Verma et al. who found 60.94% neonates less than 2.5 kg and a study by Shitaye et al. who observed 60% LBW neonates(13,16,17). Compared to our study higher incidence of early onset was reported by Verma et al. in their study(13). In our study case fatality rate due to sepsis (9.3%) was lower than reported by Verma et al (23.43%) and Mohsen et al (22.3%) (13,18).

In our study incidence of sepsis due to Gram-negative organisms was 60.5% and that of due to Gram-positive

organisms was 39.5%. Yusef D et al. reported 62% incidence of gram negative sepsis, which is similar to our study(19). Compared to our study higher incidence of gram negative sepsis (71%) was reported by Mohsen et al.(18).

Klebsiella pneumoniae and Acinetobacter baumannii accounted for 21.1% and 13.8% of total neonatal sepsis cases respectively in our study. Higher incidence of Klebsiella pneumoniae sepsis and lower incidence of Acinetobacter baumannii sepsis was reported by Mohsen et al. whereas similar incidence of Klebsiella pneumoniae sepsis (22%) and higher incidence of Acinetobacter baumannii sepsis(27%) was reported by Yusef et al. (18,19). Among Gram positive bacteria, Staphylococcus haemolyticus accounted for 13.8% and Staphylococcus epidermidis accounted for 9.2%, whereas Staphylococcus aureus accounted only for 1.8%. Dong et al reported similar incidence of sepsis due to Staphylococcus haemolyticus (14.4%) and Staphylococcus aureus (2.1%) but much higher incidence of Staphylococcus epidermidis sepsis (44.3%) in their study(10).

The principles of antibiotic application and issues related to antibiotic resistance should be strictly controlled and drugs should be selected according to individual sensitivity to reduce bacterial resistance to antimicrobial drugs and improve drug efficacies. In current era, the extensive application of antibiotics could quickly control infections or prevent neonatal sepsis to a limited extent, but it could also easily induce highly drug-resistant strains(20). In our study Klebsiella pneumoniae showed highest sensitivity for Amikacin, Imipenem, Levofloxacin and Meropenem and was least sensitive for Ampicillin, Amoxicillin + Clavulanate and Cefotaxime. Dong et al in their study found that Klebsiella pneumoniae was completely resistant to penicillin and cephalosporins, whereas highest sensitivity was reported to Meropenem and Amikacin, similar to our results(10). Doare et al. reported that Klebsiella pneumoniae had maximum resistance to Ampicillin and cephalosporins in Asia and Africa (21). Acinetobacter species, mainly Acinetobacter baumannii had highest sensitivity for Colistin, Gentamicin and Meropenem. In a study by Al-Lawama et al. with 21 patients with culture-proven Acinetobacter baumannii sepsis, 90% were resistant to carbapenems(22). In a study by Yusef D et al Acinetobacter baumannii strains were resistant to all groups of antibiotics except Colistin, and a few were susceptible to Tigecycline(19). E. coli and Pseudomonas species were sensitivity to Amikacin, Piperacillin+ Tazobactam, Meropenem and fluroquinolones.

The data in the present study revealed that Gram-positive cocci exhibited higher resistance rates to Penicillin, Ampicillin, Cefazolin, Cefoxitin and erythromycin while showing maximum sensitivity to Linezolid and Vancomycin. Coagulase negative Staphylococci (CoNS) such as Staphylococcus epidermidis and Staphylococcus haemolyticus exhibited penicillin and Ampicillin resistance rates as high as 100%. Dong et al. reported similar results in their study(10). Mohsen et al. reported that gram positive organisms were most resistant to Ampicillin, a wide variety of cephalosporins, carbapenems, piperacillin-tazobactam, and erythromycin(18).

Conclusion:

In our NICU the incidence of sepsis was found to be 8.6%. Out-born babies had higher incidence of sepsis compared to inborn babies. Klebsiella pneumoniae was most frequently isolated organism in LOS as well as in EOS which showed maximum sensitivity for Amikacin, Meropenem and Imipenem. Acinetobacter baumannii was sensitive to Colistin, Meropenem and Gentamicin. Coagulase-negative Staphylococci were the main Gram positive bacteria isolated in both EOS and LOS which showed highest sensitivity for Vancomycin and Linezolid. Most of the organisms were resistant to Penicillin, Ampicillin and Cefotaxime. Septicemia threatens survival during first few weeks of life. Considering the few resources available in developing countries a reduction in sepsis related morbidity and mortality may be possible

by using hygienic measures in labor room and NICU. The frequent emergence of resistant bacteria is a worrisome problem. One of the important steps to prevent antibiotics resistance and to achieve judicious use of antibiotics in the NICU is to implement antimicrobial stewardship programs. Ongoing surveillance of local epidemiology and antimicrobial susceptibility is essential to ensure appropriate empiric and targeted antimicrobial therapy.

What is already known?

Neonatal sepsis is one of the leading causes of neonatal death. Sepsis due to gram negative organisms is more common in India.

What this study adds?

As most of the organisms were resistant to penicillins & cephalosporins, they can no longer be used as preferred medications for neonatal sepsis.

Benign Familial Neonatal Seizure

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Benign familial neonatal seizure is a rare, autosomal dominantly inherited condition characterized by multiple episodes of brief seizures occurring within the first few days of life.1 The seizures tend to occur in clusters over several days to weeks and remit spontaneously. They are usually never generalized. It is a relatively benign condition with no significant neuro-developmental outcome.2,3 EEG changes are not specific for the condition. Here we report a family affected with this rare disease with 5 members of family affected.

Case Report

The proband was a term female baby born to a non-consanguineously married couple. She was the 2nd child born to a G2P2L1 mother via normal vaginal delivery with no significant immediate post natal complications. On day 2 of life baby had one episode of seizure followed by a second episode one hour later characterized by staring look and stiffness of both upper limb lasting for 1 minute following which baby started on anticonvulsant-phenobarbitone. Baby continued to have multiple episodes of seizures and was started on 2nd anticonvulsant following which baby improved and seizures settled. Baby was active with good cry and tone. Neurosonogram done was normal. There was a strong history of similar seizures in family.

Case 2: Proband's brother had similar history of multiple episodes of seizures during neonatal period and was on carbamazepine for 6 months. Child was investigated in detail. Neuro-imaging and EEG were normal. He had no further episodes of seizure after weaning off anti epileptic drug and psychomotor development was normal.

Case 3: Proband's father had experienced similar seizure clusters in neonatal period, controlled with anti epileptic drug given for short period. Again no further episodes of seizure and psychomotor development was normal.

Case 4: The proband's paternal aunt had similar episodes of seizures in neonatal period with no long term deficits.

Case 5: Proband's first cousin also had similar history.

None of the cases had history of febrile seizures and no other members had a history of seizure.

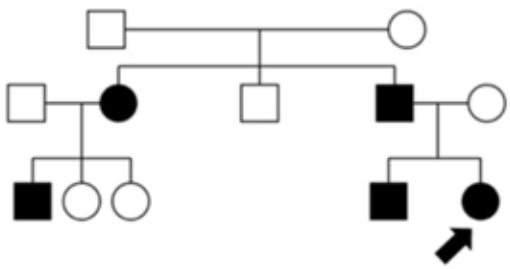

Fig 1. Pedigree of the family with benign familial neonatal seizure.

Discussion

Benign familial neonatal seizure represents a rare epileptic syndrome of neonatal onset and a favorable prognosis. Occurrence of unprovoked partial or generalized tonic-clonic seizures typically starting around 1 week of life and often disappear after several weeks or months. However, about 10-15% of patients have febrile or afebrile seizures later in childhood, often provoked by unexpected stress5, but none of the members in this family had seizures beyond infantile period. Seizures observed in these newborns are brief and of a mixed type, starting with tonic posturing, and other symptoms such as apnea, and other autonomic features may occur. Cyanosis can also occur in case of prolongation of tonic phase of seizures, which may be seen in some cases. The post-ictal state is brief and the neonates look normal in the inter-ictal period.6 Our case presented with generalized tonic seizure with normal inter-ictal period. The seizure frequency (5-6 in week) was considerably less as compared to 20-30/day as reported in earlier literature.1 As reported previously both sexes are affected in this condition.1 EEG findings may not be specific to this disorder but, 60% of cases show minimal focal or multifocal abnormalities or a pattern of 'Theta Pointu alternant'.7 None of the affected members whose EEG were available showed any changes. Benign familial neonatal seizure is a diagnosis of exclusion; hence family history is very important pointer to this condition. Other laboratory investigations such as serum electrolytes, glucose, calcium and magnesium are in normal range. Treatment of BFNC is not clear because many seizures remit spontaneously. These seizures remit in majority by 6 months of age. Usually treatment is not needed in all cases, if initiated can be discontinued by 3 or 6 months. Psychomotor development remains normal. Risk of epilepsy and febrile seizure is increased and is approximately between 13 and 20%.

BFNC though a rare cause, should be considered as a differential diagnosis of neonatal seizure. Although already known this disorder emphasizes the importance of good and detailed history as a positive family history will clinch the diagnosis and further unwanted tests and prolonged treatment with potentially toxic agents can be avoided.

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Cutis marmorata telangiectatica congenita

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Figure 2: Cutis Marmorata Congenita.

Cutis marmorata telangiectatica congenita (CMTC) is a rare, sporadic, congenital cutaneous anomaly characterized by discoloured patches of skin caused by dilated blood vessels. As a result, the skin has a purple or blue "marbled" or "fishnet" appearance.

It is often confused with a physiological mottling due to hypothermia-cutis marmorata, which disappears on rewarming the child while CMTC does not.

Virtually all cases of CMTC occur sporadically. It is associated with body asymmetry, vascular anomalies (Sturge-Weber syndrome, Klippel-Trenaunay syndrome, Adams Oliver syndrome etc.). Glaucoma, retinal detachment, cutaneous atrophy and Neurologic anomalies.

The diagnosis is by clinical examination and the skin lesions achieve spontaneous remission. Treatment is directed at treating any associated anomalies.

Fig. 1. Cutis marmorata Telangiectatica congenita, left upper arm.

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Alobar Holoprosencephaly

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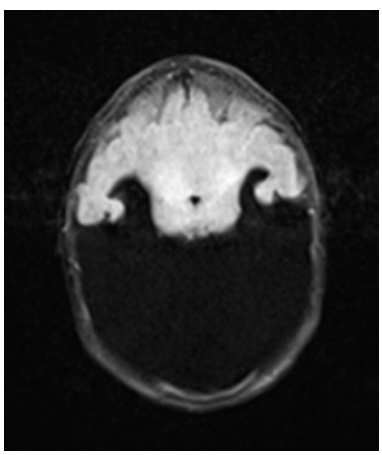

Figure 1: Alobar Holoprosencephaly. T2 image shows fused (uncleaved) frontal lobes with absent anterior midline falx/ fissures. Fusion of the basal ganglia and thalami noted. Large monoventricle posteriorly in contact with skull vault with absent covering brain parenchyma. (Dorsal cyst)

Background: Holoprosencephaly (HPE) is a developmental disorder of the brain that results from defective formation of the prosencephalon and inadequate induction of forebrain structures [1].

Case report: This female infant was born by LSCS at 36 weeks of gestation, to a 30yr old G3P2L2 mother. Antenatal USG at 24 weeks was suggestive of HPE, but no other congenital anomalies. Termination of pregnancy was refused by the parents and hence pregnancy continued till 36 weeks, before delivery.

The baby cried immediately after birth with APGAR 8 at 1min, 9 at 5min. with birth wt-2.910kg, head circumference-35.5cm length 50 cm. On examination cry, tone and activity were normal with anti-mongoloid slant of eyes, with no other obvious dysmorphic features or systemic abnormality. There was no hypoglycemia, convulsions or any neurological deficit. The baby had physiological jaundice in the neonatal period which did not require any treatment. She was breast feeding well and hence discharged after 4th day and is kept under follow up.

Introduction:

Holoprosencephaly is a congenital induction disorder of the brain occurring at 3- 6 weeks gestation, with failed segmentation of the neural tube. This leads to incomplete separation of the prosencephalon (forebrain).

Although rare in absolute terms, HPE is the most common brain abnormality and is seen in 1 per 5,000-16,000 live births [1,2]. The early embryonic occurrence may be even higher but may not be detected due to most fetuses aborting in early gestation. A failure of the developing brain to divide into left and right halves (which normally occurs

at the end of the 5th week of gestation), results in variable loss of midline structures of the brain and face as well as fusion of lateral ventricles and the 3rd ventricle.

Classification: HPE has 4 subtypes: alobar HPE, semilobar HPE, lobar HPE and a middle interhemispheric fusion variant (syntelencephaly). Alobar HPE is the most severe form, with no separation of the cerebral hemispheres; it is characterized by a single ventricle, absence of the corpus callosum and inter-hemispheric fissure and fused thalami. In semilobar HPE, the cerebral hemispheres are fused anteriorly, while lobar HPE is characterized by fusion of the cerebral hemispheres at the frontal lobes. A middle interhemispheric fusion variant results from non-separation of posterior frontal and parietal lobes. [3]

The etiology of HPE includes genetic and environmental factors. Among the environmental causes there are: maternal diabetes mellitus, maternal alcoholism, TORCH infections, some drugs (retinoic acid, cholesterol synthesis inhibitors). HPE can be transmitted in an autosomal dominant way. About 25% of people with nonsyndromic HPE have a mutation in one of these four genes: SHH, ZIC2, SIX3, or TGIF1. Mutation of SHH gene is the most frequent cause of familial HPE. HPE is also associated in 40% of cases with numerical chromosomal anomalies, the most frequent one being trisomy 13. HPE is associated with Smith-Lemli-Opitz, Pallister Hall or velocardio- facial syndrome.

Clinical features associated are cyclopia, synophthalmia, or a proboscis include microcephaly (although hydrocephalus can result in macrocephaly), Ethmocephaly, Cebocephaly Closely spaced eyes, Anophthalmia or microophthalmia , cleft lip, depressed nasal ridge, Relatively normal facial appearance.

Clinical manifestations commonly observed in children with HPE include the following:

• Developmental delay, Seizures, Hydrocephalus, swallowing difficulties and instability of temperature, heart rate, and respiration, partial or complete pan-hypopituitarism, short stature and failure to thrive.

Prenatal ultrasound of the face and falx cerebri can be used to diagnose alobar and semilobar HPE as early as the first trimester, while fetal MRI provides more sensitive diagnosis for milder forms of HPE during the third trimester. Ultrasound remains the gold standard, other tests include-Cytogenetic analysis, and Molecular analysis of fetal DNA.

Medical management should focus on hypothalamic and endocrinologic dysfunction, motor and developmental impairment, respiratory issues, seizures, and hydrocephalus.

Pediatricians should follow up medical management by

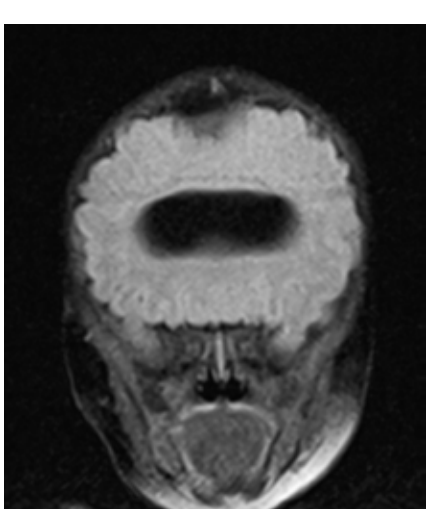

Figure 2: Fused frontal lobes with absent anterior midline falx.

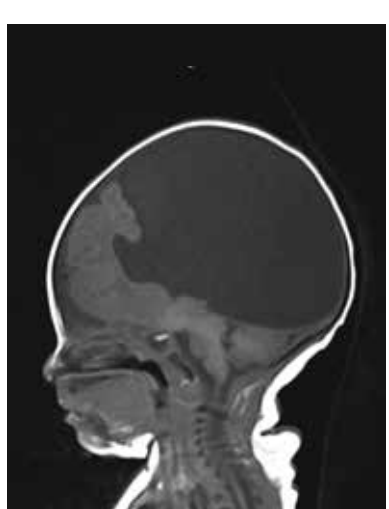

Figure 3: Large monoventricle posteriorly in contact with skull vault with absent covering brain parenchyma (Dorsal cyst).

collaborating with a genetic specialist, with the aim of performing genetic testing, determination of associated syndromes, and genetic counseling.

The prognosis depends on the sub-type. The alobar variety usually presents as stillbirth, or die soon after birth, or during the first 6 months of life. However, a significant proportion of more mildly affected children (as well as some severely affected children) survives past age 12 months. More than 50 percent of children with semi-lobar or lobar HPE without significant malformations of other organs are alive at age 12 months. The life expectancy for individuals with semi-lobar HPE depends on the underlying cause of the condition and the presence of associated anomalies.

References:

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2. Winter TC, Kennedy AM, Woodward PJ. Holoprosencephaly: a survey of the entity, with embryology and fetal imaging. Radiographics. 2015;35 (1): 275-90. doi:10.1148/rg.351140040 –
3. Medscape.

Incontinentia Pigmenti

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INCONTINENTIA PIGMENTI is a rare, X-linked dominant neurocutaneous syndrome with cutaneous, neurologic, ophthalmologic and dental manifestations. The phenotype is produced by functional mosaicism caused by random X-inactivation of an X-linked dominant gene that is lethal in males (IKBKG [kappa B kinase gamma, previously NEMO] gene).

This disease has 4 phases, not all of which may occur in a given patient.

The 1st phase is evident at birth or in the 1st few wk of life and consists of erythematous linear streaks and plaques of vesicles that are most pronounced on the limbs and circumferential on the trunk. It generally resolves by 4 mo of age.

In the 2nd phase, as blisters on the distal limbs resolve, they become dry and hyperkeratotic, forming verrucous plaques. They generally involute in 6 months.

The 3rd or pigmentary stage is the hallmark of incontinentia pigmenti. Hyperpigmentation is more often apparent on the trunk than the limbs and is distributed in macular whorls, reticulated patches, flecks, and linear streaks that follow Blaschko lines. They generally begin to fade by early adolescence and often disappear by age 16 yr.

In the 4th stage, hairless, anhidrotic, hypopigmented patches or streaks occur as a late manifestation of incontinentia pigmenti. The lesions develop mainly on the flexor aspect of the lower legs and less often on the arms and trunk.

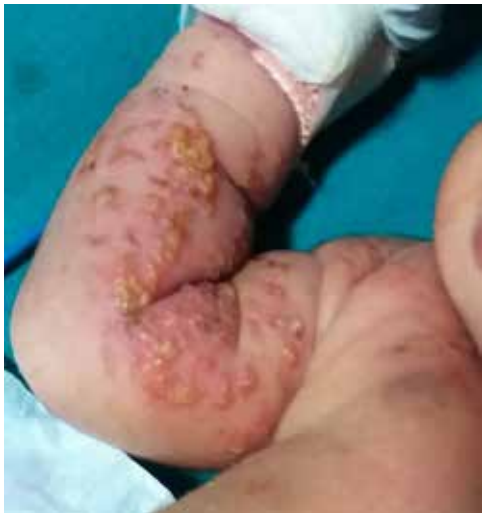

Figure 1: Incontinentia Pigmenti. Phase 1 lesion. Note erythematous linear streaks and plaques of vesicles that are most pronounced on the limbs.

Approximately 80% of affected children have other defects. Alopecia is seen in 40% and dental anomalies in 80% of the patients. Central nervous system manifestations, including seizures, intellectual disability, hemiplegia, hemiparesis, spasticity, microcephaly and cerebellar ataxia are found in up to 30% of affected children. Ocular anomalies, such as neo-vascularization, microphthalmos, strabismus, optic nerve atrophy, cataracts and retrolenticular masses, occur in >30% of children.

Diagnosis is clinical, although genetic testing may be done. Identification of a heterozygous IKBKG pathogenic variant in a female proband or a hemizygous IKBKG pathogenic variant in a male proband confirms the diagnosis if clinical features are inconclusive. IP is inherited in an X-linked manner. The male fetus who carry the mutation do not survive unless they have 47XXY or are mosaics. Prenatal testing for pregnancies at increased risk is possible if the familial pathogenic variant has been identified. Management is aimed at treating other associated anomalies as the skin lesions are benign.

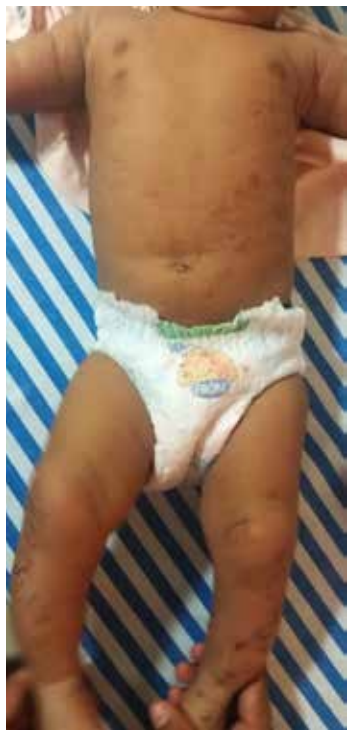

Figure 2. Incontinentia Pigmenti, Pigmentary stage.

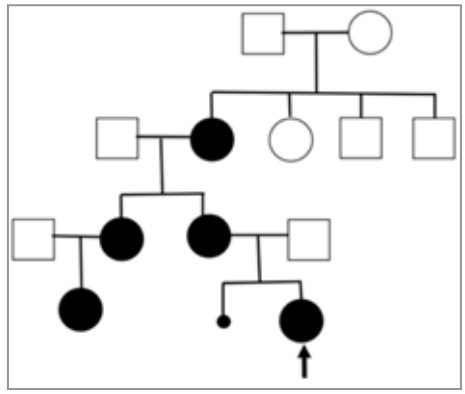

Fig 3. Pedigree of the baby with Incontinentia Pigmenti. Note that only females are affected.

True umbilical cord knot

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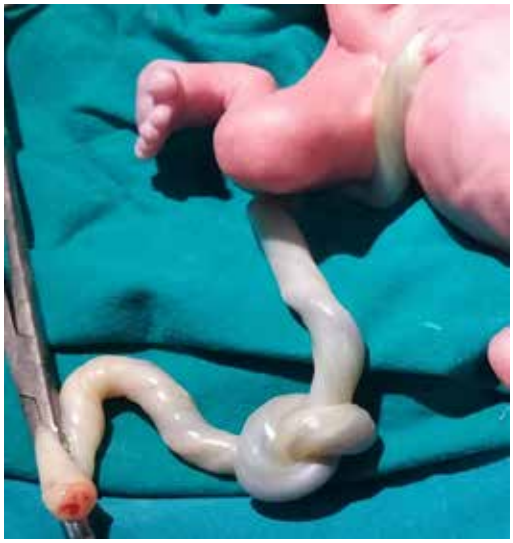

Figure 1. True Umbilical cord knot.

True knots and false knots can form in the umbilical cord. True knots occur in approximately 1% of pregnancies, with the highest rate occurring in monoamniotic twins [1]. False knots (Kinks in the umbilical cord vessels) are more common and have no known clinical significance.

True knots increase the fetal loss to a 4 fold, because of compression of the cord vessels when the knot tightens. Detection of umbilical knots has been reported with ultrasonographic imaging. True knots has been identified commonly in antenatal ultrasonograpy of mononamniotic twins, when the condition was specifically sought [2]. Cesarian delivery is indicated if a diagnosis of true cord knot is made.

Reference:

1. Medscape
2. Ramon y Cajal CL, Martinez RO. Four -dimensional ultrasonongraphy of a true knot of the umbilical cord. Am J Obstet Gynecol. 2006 Oct. 195(4):896-8.

Antenatal Infections - Effect on Fetus and Newborn

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How do the fetus get infection? 3 mechanisms

i. Transplacental- Intra-uterine infection
ii. Perinatal - Acquired intra-partum
iii. PROM- Chorioamnionitis. In-utero bacterial infection of the fetus

TORCH Infections -Rubella:
Mild infection in the mother – Fever, rash and post auricular lymphadenopathy. May even be missed.

Infection in the first 10 weeks of gestation-100% chance to have cardiac defects & hearing loss. Infection around 20 wks – only hearing loss

Congenital Rubella Syndrome – Devastating illness

Main manifestations are: Intra-uterine growth restriction microcephaly, cataract, mental retardation, CHD –PDA, PPAS

(Peripheral pulmonary artery stenosis), hepatomegaly, jaundice

anemia, thrombocytopenia, metaphyseal bone lesions and rash-blue berry muffin spots .

No specific treatment.

Prevention: Rubella vaccine:
Effective universal immunization-decreased incidence of Cerebral Palsy in US. Currently in Kerala MMR is being given at 9 m, 15 m ; 4 & 1/2 yrs so that in the near future rubella may be washed off from Kerala. Rubella monovalent vaccine also available for adolescent girls

Cytomegalovirus: 90% congenital infection in infants are asymptomatic

10% à IUGR, microcephaly, chorio-retinitis, sensory neural

hearing loss (SNHL –most common), thrombocytopenia ; hepatosplenomegaly, jaundice

Virus shed in body secretions (saliva) & in urine

Diagnostic: CMV-specific IgM antibody ; CMV DNA by PCR

CMV Rx: Antiviral agents-Intravenous(IV) Ganciclovir 6 mg/kg per dose IV q12h for 2 to 6 wks & its orally available pro-drug, Valganciclovir 16 mg/kg /dose orally q12h for 6 months. Start treatment within the first month of life. Foscarnet and Cidofovir - reserved for refractory cases.

CMV specific monoclonal antibody available.

CMV prevention: CMV vaccine –under trial.

Pregnant women at risk in Day care centres – good hand-washing after contact; avoid kissing, avoid sharing food, eating & drinking utensils. Premature & acutely ill neonates : Use CMV -ve or irradiated leuko-depleted blood products.

Congenital Toxoplasmosis: Contact with infected cats (definitive host)and ingestion of undercooked meat.

Intermediate host: Man, Live stock and mice

Triad of Congenital toxoplasmosis: Hydrocephalus, diffuse intracranial calcifications and chorio-retinitis.

Treatment: Vertical transmission reduced by Spiramycin .

After 18 weeks Pyrimethamine + Sulfadiazine + Folinic acid 10-20mg daily

In the infant : Pyrimethamine (1mg/kg 12 hourly for 2 days, daily for 2-6 months for age, 3 times weekly till 1 year of age)

Sulfadiazine (50mg/kg 12 hourly until 1 year)

Folinic Acid: prevents bone marrow suppression

Herpes simplex - HSV - TYPE 1, TYPE 2 (80% Neonatal Disease). Primary genital HSV infection in pregnancy can lead to life-threatening disseminated HSV infection

Treatment: Acyclovir. If genital herpes, LSCS is advocated within 6 hours of rupture of membranes

Guidelines for TORCH screening(-FOGSI)

Routine screening –not recommended.

Screening Indicated in pregnancies with 1) fetal hydrops, 2) fetal brain lesions, 3) unexplained IUGR 4) other sonographic markers of fetal infection 5) Non-vesicular rash (screen for Rubella & Parvovirus B19)

Serology

IgM+ve & IgG –ve: A/c primary infection

IgM & IgG both –ve: Unexposed/unvaccinated

IgM –ve & IgG +ve: Past infection

Chicken Pox (Varicella Zoster): Incubation period: 10-21 days

Contagious 1-2 days before & 5 days after onset of rash

Varicella during pregnancy:

1.Congenital varicella syndrome: If mother gets infection before 20 weeks, but is very rare . Baby with Congenital varicella syndrome may have cicatrical skin scarring, limb hypoplasia, microcephaly, cortical atrophy, seizures, mental retardation chorioretinitis, microphthalmia, cataract, hydroureter and hydronephrosis

Perinatal varicella – If mother develops rashes 5 days before & within 2days of delivery, risk of severe disease in newborn à Pneumonia, Sepsis, Multi organ failure, DIC, Fulminant hepatitis. Mortality:30%

POST NATAL INFECTION: Usually mild disease.

If mother has rashes 5 days before to 2 days after delivery -Give Varicella Zoster immunoglobulin to the infant 125 units (1 vial) IM within 96 hrs (4 days); not later than 10 days after exposure.

Post exposure prophylaxis will prevent, ameliorate or delay infection. Premature infants are at increased risk. Active transfer of maternal IgG antibodies occurs primarily during third trimester of pregnancy

Recommendations for

VZIG(Current ACIP & CDC guidelines)

1.Mother having varicella around time of delivery (five days before to two days after).

2. Preterms < 28 wks gestation or wt < 1000 g

3. Exposed infants within first 2wks of life whose mothers do not have evidence of immunity to varicella

Isolate mothers & infants with active disease. Newborns exposed to VZ Virus who remain in the hospital should be cohorted & placed in protective isolation from 7 to 21 days after exposure.

Symptomatic neonate – treat with Acyclovir .

Breastfeeding encouraged in newborns exposed to or infected with varicella (antibody in Breast Milk protective.)

If VZIG not available Consider – pooled IVIG (Dose 400 mg/kg, IV) .

No clinical data available demonstrating effectiveness of pooled IVIG for post exposure prophylaxis of varicella

Acyclovir Prophylactic acyclovir beginning 7days after exposure may prevent or attenuate disease.

A Pregnant mother comes in contact with a Chicken Pox case in the family. What should she do?

If immune status of mother unknown, test for varicella antibody (IgG). If result negative or unavailable within 96 hrs of exposure, give VZIg . Varicella vaccine (live virus vaccine) is contraindicated in pregnancy.

HBsAG positive mother:

Peri-natal transmission risk is as high as 90%. Take universal precautions. Give Hep B vaccine & HBIG 0.5 ml IM to the baby at two different sites as early as possible after delivery (within 12 hrs)

Birth weight > 2 kg-

Second & third doses give at 1-2 & at 6 m of age, respectively

Birth weight < 2 kg - 3 additional doses should be given (1, 2-3 & 6 m of age or at 2, 4, & 6m).The final dose in the vaccine series should notbe administered before 24 wks (6 m) of age.

Breastfeeding - No additional risk. Transmission of HBV through breastfeeding is unlikely, particularly in infants who received HBIGand hepatitis B vaccine at birth.

HBV + HBIG < 24 hrs after birth + completion of vaccine series: 85-
95% effective in preventing both acute & chronic HBV infection
Hepatitis B vaccine administered alone < 24 hours of birth: 70-90% effective .

HUMAN IMMUNO-DEFICIENCY VIRUS (HIV)

Incidence of vertical transmission - 25-30%.

90% of Pediatric HIV follows mother to child transmission

Universal screening for HIV infection in pregnancy .

HIV transmission from mothers to their infants:

1) Antipartum 2). Intrapartum 3). Postpartum 4). Breast feeding

C.section reduces the risk of mother to baby HIV transmission

Postpartum ARV prophylaxis for infant for minimum 6 wks.

Start daily Nevirapine plus twice-daily Zidovudine immediately & continue for at least 6 wks. Co-trimoxazole prophylaxis from 6 wks of age. Confirmation of HIV status of all babies at 18 months using all 3 Antibody (Rapid) Tests

Immunization schedule:

BCG, Hepatitis B, DTaP, Rotavirus, IPV, HiB, PCV. Hepatitis A - give as routine. Caution in giving MMR, Varicella – if low CD4 counts

Test for HBsAg and Anti-HBs at 9-18 m. Anti-HBs < 10 mIU – repeat schedule of HBV

Influenza vaccine – 0.25ml up to 3 years & 0.5 ml over 3 years

Baby born to a mother with tuberculosis

About 300 cases of perinatal TB described in literature

Mode of transmission: Hematogenous; aspiration of infected amniotic fluid and

post natal transmission Mortality of 40-60%. Start treatment for mother as early as possible. If mother treated for 2–3 wks- she is no longer infectious

TB work up for baby. If negative, give INH for 6 months (10mg/kg/d)

Mantoux test & Chest X-ray. Baby vaccinated with BCG at 6 months if tests are negative. Any sign of active TB - full course of ATT

RNTCP Recommends breast-feeding. ATT drugs excreted into breast milk, esp INH. Breast feeding is safe. No separation from mother .Mother should wear mask when in close contact with her baby

Parvovirus B19: (Erythema infectiosum ; Fifth disease)

Fetus : Severe anemia & Non-immune hydrops

Ureaplasma urealyticum: In sexually active young females- Recurrent abortions; Chorioamnionitis, preterm delivery, LBW, Still Birth. Neonatal disease : Pneumonia; CLD

Diag : culture-special broth; PCR

Antibiotic: Erythromycin; Doxycycline

Intra-amniotic infection:Chorioamnionitis

PROM: 4- 7% ; Term baby - immediate induction

PPROM(Preterm prelabour rupture of membranes)- 30% of all preterm births- RDS; Sepsis; Asphyxia, Pulmonary hypoplasia

High index of suspicion for sepsis to start antibiotics.

Group B streptococcal infection: Asymptomatic GBS colonization: 5-40%. Universal screening of pregnant women for GBS at 35-37 wks is suggested.

Intrapartum antibiotic prophylaxis (IAP) : for perinatal GBS infection

1.GBS positive screening test

2. Heavy maternal colonization

3. Spontaneous preterm onset of labour <34 wks

4. Maternal chorioamnionitis (fever>380 C); PROM >18 hrs

5. Previous sibling with GBS infection

6. GBS in the mother's urine during current pregnancy

Maternal GBS –treatment: Penicillin preferred drug for IAP. Ampicillin acceptable alternative.

IV Penicillin G: 5 mU stat, 2.5 mU every 4 hrs until delivery. IV antibiotics during labour atleast 4 hrs before delivery. Minimum 2 doses prior to delivery.

Penicillin allergy- Erythromycin or Clindamycin.

Effective Intra-partum Rx- 90% Early onset GBS in NB prevented.

Congenital Malaria:

Low birth weight / Preterm 4-6 weeks fever, anemia, jaundice, hepatosplenomegaly. Similar to transfusion malaria- no exo-erythrocytic cycle;

Treatment – Chloroquine

Mumps in mother → Endocardial fibroelastosis

Coxsackie B virus → Myocarditis

Congenital Zika syndrome; Transmission by Aedes Aegypti and Albopictus mosquitoes. Microcephaly ,Intracranial calcifications, Arthrogryposis; Hypertonia/spasticity, Ocular abnormalities, SNHL

<u>Congenital syphilis</u>

Dark field microscopy - motile spirochetes

Serology – VDRL; Rapid plasma reagin (RPR)

Specific : FTA –ABS; TPHA

VDRL with positive TPHA – Treat with Penicillin promptly

Chlamydia : purulent conjunctivitis

Conclusion: Myriads of infection in the mother can affect the baby. A shrewd Obstetrician and a caring Neonatologist can intervene early and timely to prevent or treat the infection successfully.

Neonatal Thrombosis - A case series

Dr. Fadiya Rasheed, Dr. Vishnu Mohan, Dr. Divya Nath, Dr. Anand MR, Dr. Preetha Remesh

Introduction

Newborn infants are most vulnerable to development of thrombosis and serious thromboembolic complications. Amongst newborns, those neonates who are critically ill, both term and preterm, are at greatest risk for developing symptomatic thromboembolic disease. The most important risk factors are inflammation, DIC, impaired liver function, fluctuations in cardiac output, and congenital heart disease, as well as exogenous risk factors such as central venous or arterial catheters. In most clinically symptomatic infants, diagnosis is made by ultrasound, venography, or CT or MRI angiograms. However, clinically asymptomatic vessel thrombosis is sometimes picked up by screening investigations or during routine imaging for other indications. We describe 3 such cases over the past 1 year.

Case Report

CASE 1 :-

Term/ AGA/ 2.6 kg female baby born to G2A1 mum by NVD, developed respiratory distress, referred at 8 hours of life with features of congestive cardiac failure, ECHO done revealed severe LV dysfunction, dilated left atrium with a large thrombus. Baby was electively ventilated, initiated on anti-failure measures along with LMWH. Gradually weaned off ventilation once LV function improved. Discharged at 2 weeks of life on LMWH. Cardiac evaluation prior to discharge showed decreasing size of thrombus, and complete resolution documented at 1 month of life.

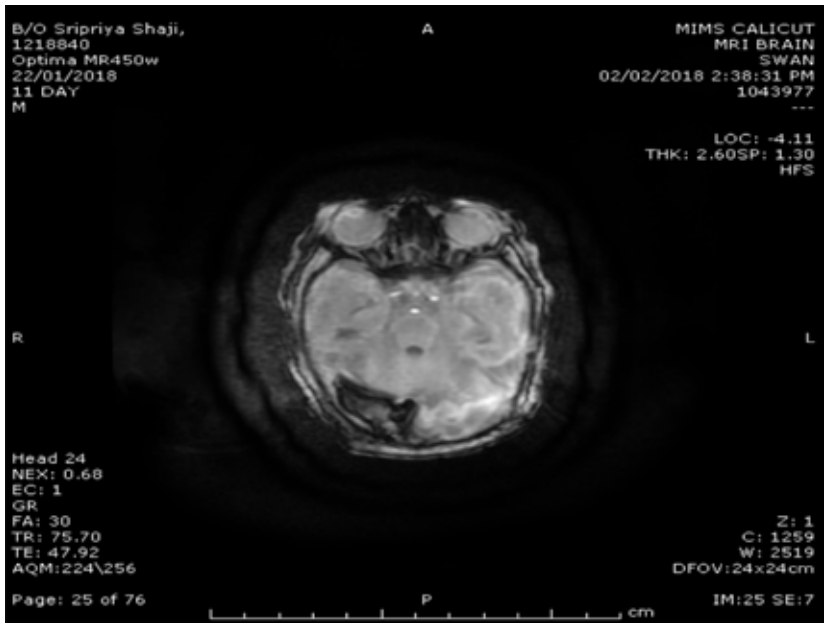
CASE 2 :-

Late preterm (35weeks)/LGA/ 3.7 Kg male baby born to primi mum with overt DM by LSCS (Ind: Uncontrolled DM, PIH), cried at birth, referred at 7 hours of life with persistent respiratory distress. At admission, baby had moderate respiratory distress, with low saturations, cardiovascular system examination revealed a grade 2-3 systolic murmur, impaired perfusion left lower limb with absent femoral pulses. Evaluation proceeded :- ECHO showed severe ASH, with dyanamic LVOTO, with persistent pulmonary

hypertension. Left lower limb arterial Doppler revealed Thrombosis of the common femoral, superficial femoral, popliteal, anterior tibial and posterior tibial arteries with absent flow. Baby was stabilised on hood oxygen. Medical thrombolysis ensued for the thrombosis. Beta blockers for the ASH with LVOTO. Cardiology review at 72 hours confirmed improvement. Complete re-canalisation of left lower limb vessels confirmed at 3 months of life.

CASE 3 :-

Late preterm (33weeks)/ LGA/ 2.4 Kg male baby, born to G3A2 gestational diabetic mum by LSCS (Ind: Absent FM), had history of hypoglycemic seizures at 2 hours of life. Presented to us on Day 11 of life with refractory seizures needing mechanical ventilation & multiple anti-epileptic agents. Baby had no further hypoglycaemic events. No evidence of dyselectrolytemia / coagulopathy/ polycythemia/ sepsis. Metabolic screening was normal. MRI suggestive of hypoglycaemia induced brain injury. MRV:- Filling defect in distal SSS extending to right transverse sinus. LMWH started following the MRI. Weaned off ventilation by D3 of admission. Feeds established and roomed in by DOL22. Baby discharged by DOL25 on LMWH and AED. Neuroimaging at 1 month of life, showed resolved thrombus. LMWH stopped after 3 months & AED's gradually tapered off.



Discussion

Haemostatic system as a dynamic development first introduced by Andrew et al (Andrew et al 1988; Andrew et al 1990). The changes in plasmatic, cellular & vessel wall components of haemostasis vital in diagnosis, treatment and prevention of thrombosis in a critically ill neonate.

Why neonates at risk for thromboembolism?

Although neonates have decreased plasma activity of pro-coagulant factors (Vitamin K-dependent coagulation factors), they are also met with significantly reduced anti-coagulant factors (vitamin K-dependent inhibitors of coagulation, protein C & protein S) along with reduced activity of the fibrinolytic system (decreased plasma activity of plasminogen & increased levels of plasminogen activator inhibitor).

Other risk factors include :- Inflammation, sepsis/ disseminated intravascular coagulation, fluctuations in cardiac output, exogenous risk factors such as central venous or arterial catheters, polycythemia, dehydration, perinatal asphyxia & Congenital thrombophilia. Almost 90% of thromboembolic events in neonates are caused by intravascular device.

Clinical Features

Extremely variable clinical picture in neonates with vascular events. Depends on the location and size of the thrombus. May range from discrete symptoms or asymptomatic events to life or limb threatening acute events.

Arterial thrombosis accounts

for ~ 50% of all thromboembolism in neonates. It is directly related to arterial catheterisation in neonates. Obvious signs include Ischemia of limbs or trunk, pale / cold extremities distal to the catheterization site, weak or absent palpability of the pulse, decreased or unmeasurable blood pressure. A neonate may present with features of NEC consequent to mesenteric ischaemia, or unexplained hypertension with features of AKI consequent to renal artery thrombosis, all secondary to a UAC in situ.

Venous thrombosis presents with limb swelling, pain, and cyanosis or hyperaemia. Abdominal mass & hematuria in renal vein thrombosis, Impaired liver function test with hepatosplenomegaly in portal vein thrombosis are the cardial features. A neonate with cerebral sino-venous thrombosis may present with irritability & seizures or obtundation. The impact on neurodevelopment morbidity in these neonates varies from 10 -80 %.

Diagnosis

Ultrasound with Doppler flow is THE most employed imaging study. MRI with MRV for suspected cerebral sinovenous thrombosis & acute ischemic stroke. Other relevant Lab studies:- Complete blood count (polycythemia, thrombocytopenia as an indicator of micro & macro-circulatory thrombosis, Coagulation studies, D-dimers (acute phase reactant), thrombophilia work up (only if indicated).

Treatment

Anticoagulation, thrombolysis, surgery, and observation forms the mainstay of treatment in thromboembolism. The goal of anticoagulation is to reduce the risk of embolism, halt clot extension, and prevent recurrence. Most commonly used anti-coagulant is Low molecular weight heparin. Ease of dosing & monitoring makes it the most preferred agent. The recommended starting dose :- 1.5 mg/kg/dose SC every 12 hour. Monitored via the anti-Xa activity. No clear consensus on the duration of therapy. May range from 6 weeks to 3 months. The effectiveness of thrombolysis is neonates is controversial. Minimal data exists in newborn populations regarding all aspects of thrombolytic therapy.

Prevention

Identifying risk factors & adopting appropriate strategies to prevent thrombus formation are of utmost importance in critically ill neonates. Prevention of catheter related infection is vital :- Insertion only if necessary, minimise the time in-situ, low dose heparin infusion to maintain patency. UAC-related thrombosis can be prevented by high umbilical positioning & end-hole and single-lumen construction. Above all, regular clinical assessment of all peripheral pulses mandatory.

Retinopathy of Prematurity: A Study Report of Incidence and Risk Factors

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Background:

Retinopathy of prematurity (ROP) is a vasoproliferative disease that affects premature infants. The World Health Organization's "VISION 2020" programme has identifiied ROP as an important cause of blindness in both high and middle income countries1 . WHO estimates that there are 15 million preterm births(<37 weeks) in a year and India has the largest number of preterm births in the world.(2). The reported incidence of ROP in the Western world ranges from21% to 65.8%, in India it ranges from 38% to 51.9% among low birth weight babies.(3) ROP is on a rise in India as a result of the improved neonatal care and better neonatal survival rate. Approximately 2 million babies out of 26 million annual live births in India are born with birth weight <2000 g and are at risk of developing ROP. Hence the study is undertaken.

Aim:

To evaluate the incidence of retinopathy of prematurity (ROP), identification of pre-and postnatal risk factors which predispose for development of ROP, and to assess the treatment outcomes in newborns admitted in Neobless NICU, IAP and NNF accredited regional referral centre, Moulana Hospital, Perinthalmanna, Kerala.

Type of study: Prospective study on infants fulfilling the screening criteria admitted to Neobless between November 2017 to April 2018.

Materials & Methods:

Babies admitted to Neobless who met the following criteria for ROP screening , according to Neobless guidelines for screening, were included in the study : (a) ≤34 weeks of gestation, (b) ≤1800 g of birth weight, (c) Babies >1800g or born after 34 weeks with unstable clinical

course requiring cardio respiratory support.

ROP was graded into stages and Zones as per International Classification of ROP (ICROP)4

Type I ROP or Threshold ROP ,is defined as Zone 1 any stage ROP with plus diseaseone 1 stage 3 ROP without plus disease and zone II stage 2 or 3 ROP with plus disease.

Aggressive Posterior ROP (APROP) is defined as severe plus disease,flat neovascularization in Zone I or Posterior Zone II, intraretinal shunting,hemorrhages and rapid progression to retinal detachment.

Type I ROP and APROP have been grouped into Severe ROP Group,who required treatment for ROP.

Type 2 ROP or prethreshold ROP is defined as zone 1 stage 1 or 2 ROP without plus disease and zone II stage 3 ROP without plus disease.

ROP screening was done by experts from Aravind Eye Hospital, Coimbatore using RETCAM. Treatment was offered for Type I ROP and APROP with intravitreal Injection Bevacizumab(Avastin) and LASER.

Results:

Total number of admissions in our NICU during the 6 month period was 698 , out of that 91 babies ,who fulfilled the screening criteria, were included in the study .The average weight of the babies requiring ROP screening was 1.589 Kg and the average gestation was 32.6 weeks.Out of the 91 babies screened 36 (39.5%) were males and 55 (60.5%) were females.

Out of 91 infants screened 9 (9.8%) were diagnosed as Severe ROP and required treatment , the remaining 82 babies (90.2%) did not require treatment(Non ROP group).

The average duration of oxygen requirement was 103 hours in babies who required treatment compared to average duration of 22 hours in those who did not require treatment for ROP.

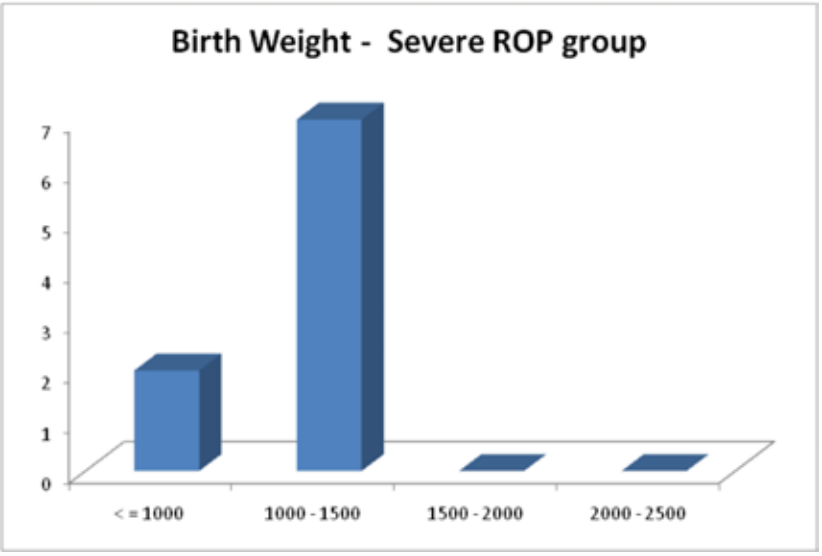
Seven babies (77.78%) received blood transfusion in Severe ROP group, in comparison 5 babies (6.10%) needed blood transfusion in Non ROP group.

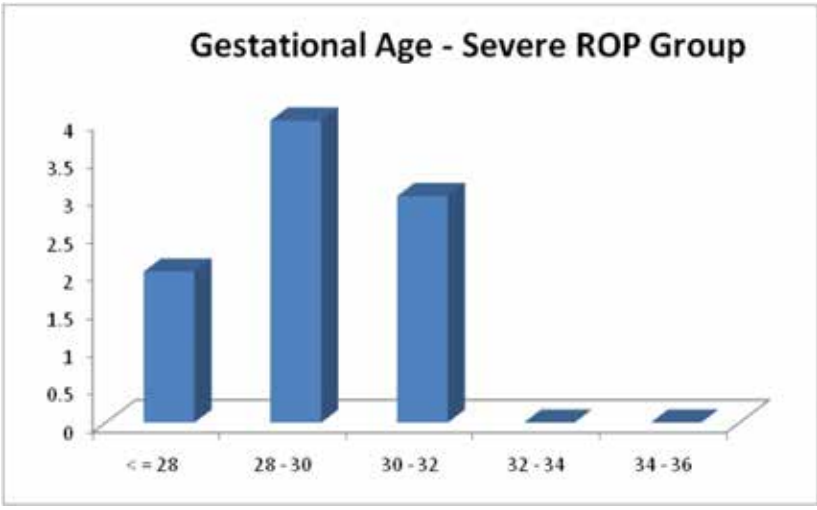
5 babies(55.5%) had sepsis in Severe ROP group, whereas only 11 babies (6.17%) out of 82 in non ROP group had sepsis.

Surfactant administration was required in 66.67% babies who were in Severe ROP group for treatment of Respiratory distress syndrome owing to their prematurity . In comparison only 13.41% required surfactant therapy in Non ROP group.

Out of the 9 cases with Severe ROP, 8 were treated with intravitreal injection of Bevacizumab (Avastin) and only one case required Laser treatment. All of them had good outcome on subsequent follow ups.

	Severe ROP Group	Non ROP Group	
Gestational Age (weeks)	....	32.99 ± 2.05	< 0.005
Birth Weight	1.14 ± 0.2	1.64 ± 0.39	< 0.005
NPO2	206.67 ± 203.36	43.35 ± 37.3	< 0.005
Ventilator	37.89 ± 42.83	5.99 ± 21.84	< 0.005
CPAP	65.56 ± 38.6	16.66 ± 20.79	< 0.005
Sepsis	5 (55.56%)	11 (13.41%)	0.002
Blood Transfusions	7 (77.78%)	5 (6.17%)	< 0.005





Conclusion:

Incidence of Severe ROP was 9.8% in our study. Incidences of ROP in various studies in India have been reported to be 51% from Delhi (79 patients), 47% in a study from Chandigarh (165 patients), 44% from north east (50 patients), 38% from Chennai (50 patients), 22% from Bangalore (7106 images), 22.3% from Pune (552 infants) and 11.8% from AIIMS, Delhi (704 patients).5-11

All treated cases had good outcome and no case had visual impairment on follow up. Those Severe ROP Group that required treatment had smaller gestation age (average 29 weeks) and lower birth weight (average 1.142 kg). There was found to be significant association between duration of oxygen therapy(p value <0.005), sepsis(p value <0.005) and blood transfusions(p value 0.002) with Severe ROP.

Recommendations:

Improved survival outcomes of Extreme preterm and very low birth weight babies due to advances in Neonatology warrants stringent screening, follow up and treatment of at risk babies. Better oxygen control ,judicious use of blood transfusions and sepsis prevention remain the most important strategies in prevention of blindness caused by ROP.

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