

Case Presentation of Open Neural Tube Defect: What Does it Index to ?

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Neural tube defects (NTDs) are in the top list of birth defects in India. Neural defects may involve brain or spinal cord or both and happens in 1st month of pregnancy due to certain known or unidentified risk factors. One of the clinical evidenced risk factor is folic acid deficiency. NTDs are estimated in around 4.5 per 1000 total births in India (Allagh et al, 2015). Globally, an estimated 88,000 deaths and 8.6 million disability-adjusted life years (DALYs) are due to NTDs (WHO, 2015).

The neural tube defects are due to defective closure of dorsal midline structures in the back during embryogenesis. Generally in early human development, the *neural tube* which is the embryo's precursor to CNS, develops by primary and secondary neurulation. Primary neurulation begins after neural tube plate is formed which includes inner neural tube, middle neural crest cells (migrates later to new location) and external epidermis. The edges start to thicken and lift upwards forming neural folds. The centre of the neural plate remains grounded, allowing a U-shaped neural groove. Ultimately, the folds unite in the middle line and convert the groove (Fig.1) into the closed neural tube. In secondary neurulation, the cells of the neural plate form a cord like structure that migrates inside the embryo and hollows to form a tube.

The neural epithelial cells of neural tube subdivides to form *prosencephalon* which further develops into telencephalon (forming forebrain/cerebrum) and diencephalon (developed optic vesicles and hypothalamus), *mesencephalon* (developed midbrain), *rhombencephalon* (developed metencephalon: form pons and cerebellum) and myelencephalon (the medulla oblongata) and *spinal cord* (Fig 2). For a short time, the neural tube is open on both cranially and caudally. These openings called neuropores which closes between 18 and 26 days after conception. Improper closure of these neuropores leads to NTD. The dorsal part of neural tube contains alar plate associated with sensation while ventral plate contains basal plate which is associated with motor /

muscle control.

NTDs are categorised into open or closed neural tube defects. Open defect occurs when the brain/spinal cord exposed through skull or vertebrae at birth. It includes *anencephaly* (absence of cranial vault), *encephaloceles* (herniation of brain / meninges), *hydranencephaly* (sacs filled with CSF instead of cerebral hemispheres), *iniencephaly* (extreme bending of the head to the spine, usually neck is absent), *schizencephaly* (slits or clefts in the cerebral hemispheres) and *spina bifida* (meninges may or may not protrude owing to defective closure of the bony encasement of the spinal cord). Spina bifida is further classified into *Spina bifida cystica* and *Spina bifida occulta*. The cystica arises due to non-union of one or more vertebral arches, results in protrusion of meninges and its contents which may be meningocele (herniation of meninges but no spinal cord involvement) and myelomeningocele (herniation of meninges as well as spinal cord). In contrast, Spina bifida occulta is hidden split spine where meninges do not herniate. Untreated NTD may manifest hydrocephalus with mental retardation, blindness, deafness, motor deficit or paralysis, lack of sphincter control, cutaneous symptoms (hypertrichosis / haemangioma / dermal sinus tract), orthopaedic complaints (scoliosis/ club feet) and death.

The risk factors are multifactorial/polygenic trait. Conclusive evidence from clinical trials proved few risk factors such as family or previous history of child birth with anencephaly (2% to 3% in later pregnancies), known genetic syndromes (trisomy 13, trisomy 18 Meckel-Gruber syndrome / occipital encephalocele), folic acid deficiency, maternal cigarette smoking (which result in hyperhomocysteinemia -Homocysteine: produced at the conversion of methionine to cystein), maternal diabetes, obesity or drugs during pregnancy (anti-seizure - valproic acid/ anti folate - aminopterin folate / antimetabolites - Methotrexate) (Suarez et al, 2008), hyperthermia in early development (Moretti et al, 2005), mycotoxins in contaminated corn meal, arsenic intake and radiation.

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Case Presentation

This is 22 years old female with obstetric score $G_3P_2L_1A_0$ presented for the treatment of medical termination of pregnancy after knowing poor prognosis of her foetus with menigomyelocele at L3 - L4 level. Three years ago, she delivered a live single normal male newborn by normal vaginal delivery (NVD) at home. Within a year, she delivered anencephaly newborn by NVD at a private nursing home. She consulted the gynaecologist when she exceeded the expected date of delivery (EDD). There was no

significant family history of NTDs.

Obstetrical examination revealed 26 weeks of gestational age, cephalic presentation, longitudinal lie, stable FHR and relaxed uterus. Per vaginal examination showed closed Os and soft cervix. She had USG assessment at 14 and 28 weeks which illustrated unwavering FHR, normal fetal movements and adequate amniotic fluid. The crown rump length was 90mm at 1st trimester whereas the biparietal diameter was 71 mm and dilated lateral ventricles with free fluid seen in brain at 28 weeks. Finally, she was diagnosed to have foetus with menigomyelocele.

Management and Outcome

Subsequent to acceptance of termination of pregnancy by the client, induction of labour was initiated by Misoprostol 200mg P/V stat followed by 100 mg Q4h for 3 doses. A single live female newborn with APGAR 3/6 was delivered by NVD. Newborn was diagnosed to have menigomyelocele at L3 - L4 level, respiratory distress and prematurity. The clinical assessment demonstrated 700 gm birth weight, heart rate 144 beats/min, respiratory rate 68 breath/min, 83% SpO_2 , presence of bilateral crepitus on lung auscultation, subcostal and intercostals retraction, periphery cold on touch, <3 sec of capillary refill time, normal fontanel and CNS/cry activity tone low. Overall, the general condition was critical. Hence, newborn was shifted to NICU.

In NICU, newborn was kept NPO; oxygen was administered through bubble oxygenator and shifted to C-PAP with PEEP 5cm of H_2O . Prophylactic antibiotics, bronchodilators and Isolyte P IV fluid was on tract of treatment. Although corrective surgeries such as Ventriculoperitoneal shunt in hydrocephalus, suboccipital craniotomy and decompression of the posterior fossa and tonsils in symptomatic chiari malformations, laminectomy and placement of syringosubarachnoid stent to divert the CSF out of central canal or surgical separation of the spinal cord from surrounding tissue for tethered spinal cord can be considered, no surgeries could be performed as the condition was

Figure 1: Neural tube formation

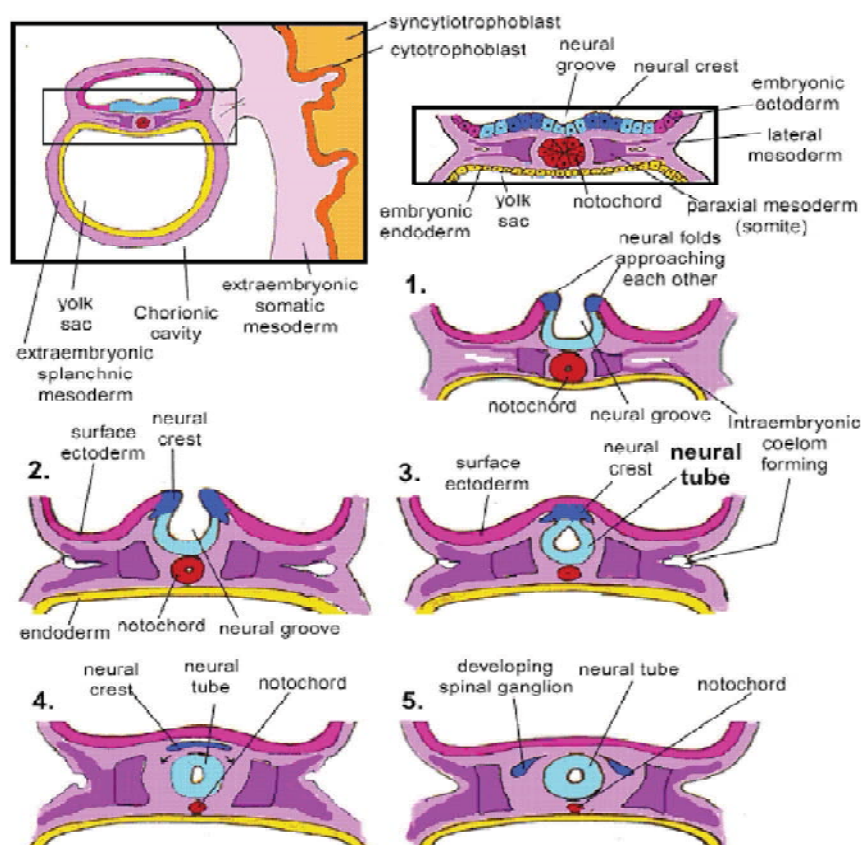
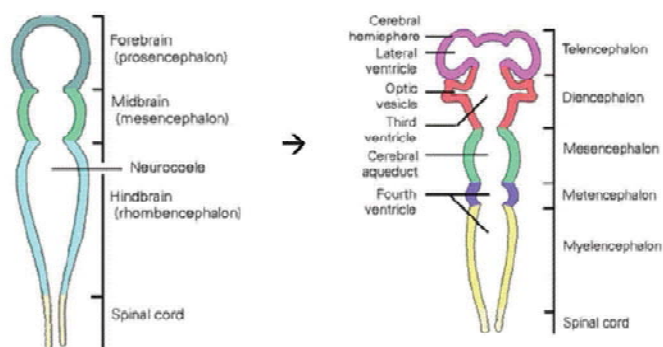


Figure 2: Neural epithelial cells



gradually deteriorating after birth. Anyhow, the newborn expired after 5 hrs of birth due to incapability to maintain vital parameters to thrive.

Nursing Management

Adequate information, support and counselling for parent were made available to make a future decision which indeed is necessary.

Infant was laid in Trendelenburg or prone position with sufficient aids so that there would be minimal pressure on the defect, feet and toes. This was managed by placing a pad between the legs. Newborn was kept warm and the exposed area was dressed with a sterile saline dressing every 2-4 hrs and as required. Plastic bag and sterile linen was placed between anus and sac to avoid soiling (McLone, 1998). Signs of infection or the appearance of opening with leakage of spinal fluid were noted in turn to prevent meningitis and brain stem herniation. In addition, meningocele apron, oblong piece of plastic wrap, also can be applied over the defect and fixed.

The significant setback related to meningocele is the neurogenic bladder resulting in urinary retention. Further, distended bladder may lead to hydronephrosis, hydronephrosis and renal failure. Crede's method of suprapubic manual expression of urine by applying gentle and firm pressure over umbilical area slowly progressing under the symphysis pubis towards the anus may be considered to disallow urinary stasis and reflux. Indwelling catheter with administration of urinary tract antiseptics may be optional. Intake Output chart was maintained to determine dehydration or excessive hydration. Surgical urinary diversion such as cutaneous uretostomy, ileal conduit or cystostomy are considered in case of hydronephrosis. Signs of urinary infection such as an elevated temperature, vomiting or cloudy/foul smelling urine noted and also must be reported immediately. Infection control measures, for example, clean catheterisation were practiced.

Direct pressure against the area of the defect was avoided. Contracture or stretching those that are present can be avoided by gentle passive range of motion exercises on the knees, ankles and feet with caution as the bones are very fragile. These must be excluded in unstable hip joints because of the danger of subluxation.

Adequate nutrition and formula foods, could be fed through a holed nipple by turning infant's head to a side in tolerable cases. Intermittent feeding must be done to allow air to be expelled. Gentle shoul-

der rub can have a soothing effect and may aid in bubbling.

Skin massaged with liniment periodically to stimulate circulation, particularly, pressure areas (ankles, knees, elbows and chin), buttocks and genitalia to prevent skin break down.

Substitute pleasure such as fondling, talking or singing of parents may help in bonding. For sensory stimulation, bright colour toys of various textures can be encouraged. En face position encouraged to stimulate the infant and to facilitate bonding.

Discussion

NTDs are one of the most common birth defects affecting over 300,000 births each year worldwide. Prevention stands in the high priority to control this lofty mortality rate. Certainly folic acid deficiency has significant role in the development of NTDs. Folate, an essential water soluble B vitamin, has certain vital function in the production and maintenance of new cells for DNA and RNA synthesis. The folates in natural forms are 5-methyltetrahydrofolate (5-MeTHF) and 10-formyltetrahydrofolate (10-formylTHF). It can donate a methyl-group to methionine (essential amino acid) by methionine synthase for homocysteine remethylation. The methionine, subsequently converted to S-adenosyl-methionine, also called the universal methyl donor. S-adenosyl-methionine is the substrate for almost all methylation reactions in mammals such as methylation of proteins, nucleic acids, lipids, neurotransmitters and creatine synthesis. During the reduction process of 5, 10-MTHF to 5-MeTHF in homocysteine remethylation, it is vital for the riboflavin (vitamin B2) dependent enzyme methylenetetrahydrofolate reductase (MTHFR) for advance process. The outcome of diminished folate mechanism is reduced methylation of protein resulting in altered protein function. The end result is NTD.

In order to detect NTDs in the intra uterine stage and to prevent the birth of baby with multiple defects, latest technologies are being widely used. Increased Maternal Serum Alpha Feto protein (MSAFP) between 14 and 20 can detect 90% anencephaly/ 80% spina bifida. Normal MSAFP in amniotic liquor around 16 weeks of gestation is 20mg/L. If screening positive, karyotyping is considered. Raised Acetyl Choline esterase (AChE) is made known in open NTDs. USG is capable to detect anencephaly at 12th week and spinal cord anomalies at 16- 20 weeks.

NTDs account for 29 percent of total neonatal

deaths due to congenital defects. Conclusive evidence from clinical trials has led to the recommendation for adequate periconceptional folic acid intake to reduce the incidence of NTDs. To prevent NTDs, 4 mg of folic acid daily is advised in pregnancy. In case of previous history of NTD, 4 or 5 mg of folic acid daily should be started 4 weeks prior to the conception and continued till 12th week of pregnancy (CDC, 1992). A cohort study pointed that women planned for pregnancy were given multivitamin containing folic acid of 0.8 mg a month before conception. The report communicated that occurrence of 1 NTD in 3056 subjects who took folic acid supplements and 9 NTD in 3056 subjects who did not (Digra, 2009). Mandatory fortification of selected foods with folic acid in Canada has been reported to reduce the incidence of NTD by 46 percent.

Conclusion

The untreated NTDs may result in obstetric complications such as hydramnios, malpresentation (face or breech), premature labour (in hydro-aminos), post-maturity, shoulder dystocia, obstructed labour (in short neck) or infant complications, for instance, infections, associated motor and sensory problems especially lower limb, learning disability, developmental delay, hearing impairment, and bladder / bowel dysfunction. Nearly 70 percent of NTDs are caused by folic acid deficiency. To conclude, more active and public involved health education strategies need to be implemented as an urgent intervention.

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