Neural tube defects

Challenging, yet preventable

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Neural tube defects (NTDs) constitute one of the most common malformations of human structure with a major public health burden (0.5-2/1000 pregnancies worldwide).[1-3] They remain a preventable cause of still birth, neonatal and infant death, or significant lifelong handicaps. The underlying pathology is the consequence of a defect in the neurulation process very early in pregnancy, between 21 and 28 days after conception, leading to failure of the neural folds to fuse in the midline and form the neural tube.[1] Secondary abnormal development of the mesoderm, responsible for forming the skeletal and muscular structures that cover the underlying neural structures, follows resulting in dysraphism, which indicates persistent continuity between the posterior neural ectoderm and cutaneous ectoderm. Based on embryological considerations and the presence or absence of exposed neural tissue, NTDs are classified as open or closed types. Cranial dysraphism (failure of cranial neural tube closure) includes anencephaly and encephaloceles, whereas spinal dysraphism (due to failure of caudal neuropore closure) is divided into open spinal dysraphisms (myelomeningocele, myelocele, hemimyelocele, and hemimyelomeningocele) and closed spinal dysraphisms. The latter can be associated with subcutaneous mass and includes lipomas with dural defect and meningocele. Complex dysraphic states are disorders characterized by aberrant formation or integration of the notochord, which is the inductor of the neural ectoderm and constitutes the foundation of the axial skeleton.[1] These include caudal regression syndrome, which ranges from agenesis of the coccyx to absence of the sacral, lumbar, and lower thoracic vertebrae; to sirenomelia (or mermaid syndrome) characterized by fusion of the lower limbs and other major organ malformations.[4] Complex dysraphic states due to aberrant integration of the notochord include split cord malformation (SCM) or diastematomyelia: a congenital spinal anomaly in which there is longitudinal splitting of the spinal cord.[5,6]

Causes of NTDs are multifactorial and defects in several different genes can underlie the genetic basis of this disease.[1] However, inheritance is commonly polygenic with strong influencing environmental factors with strong implication of genes that regulate folate one-carbon metabolism and planar cell polarity. In Saudi Arabia and several other countries, consanguinity was suggested to contribute to the high incidence of NTDs.[7] A higher proportion (20%) of syndromic NTDs, often associated with chromosomal anomalies, has also been documented compared with <10% elsewhere.[7]

The average incidence of NTDs is 1/1000 births, with a marked geographic variation and declining incidence in developed countries over recent decades. However, it remains high in the less-developed countries in Africa, Latin America, the Middle East, Asia, and the Far East (>1 to 11/1000 births).[2] Recognized risk factors associated with NTDs include folate deficiency, maternal diabetes, obesity, maternal exposure to certain teratogens such as valproic acid and carbamazepine taken by mothers who have epilepsy, lead and tetrachloroethylene-contaminated drinking water, in utero exposure to arsenic, pesticides, mycotoxins, and fungus contaminants of maize, heat exposure, influenza, certain parental occupations, and low socioeconomic status.[2]

Most open NTDs are readily apparent at birth. Closed NTDs can present early with a cutaneous marker

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such as a fluid-filled cystic mass, congenital dermal sinus, or hairy patch (hypertrichosis).[1] Later they may present with symptoms related to cord tethering mainly neurological deterioration, urodynamic changes, or spine and feet deformity.[1,5]

Children with NTDs require comprehensive follow-up in a multidisciplinary setting involving numerous specialties and subspecialties. These include neonatology, pediatric neurology, neurosurgery, urology, pediatric orthopedics, and physical medicine.[5,6,8,9] A model of this is depicted by the Spina Bifida Clinic (SBC) at King Khalid University Hospital, College of Medicine, King Saud University, Riyadh, Saudi Arabia, which was established in 1999.[9] Through optimum urologic care, the SBC managed to maintain normal renal function and normal social life for children with NTDs by maintaining their urinary and stool continence.[9] On the other hand, NTDs registries, similar to that operating at King Faisal Specialist Hospital and Research Center, Riyadh,[10] have met their objectives by becoming a source of data that may significantly contribute to the improvement of quality of care for NTDs patients through active publication of registry findings and management approaches.

Screening for NTDs[2] is based on biochemical testing of maternal blood for alpha-fetoprotein and the use of ultrasonography, which is around 97% sensitive, and 100% specific in diagnosing open NTDs. Further prenatal management requires parental decisions regarding fetal karyotyping and whether to continue or terminate the pregnancy (with the local ethical and legal backgrounds in perspective). Recently, endoscopic repair of myelomeningocele by intrauterine approach resulted in significant improvement at 30 months in the composite score for mental development and motor function of children with NTDs.[2] Nevertheless, periconceptional folic acid supplementation is the corner stone of prevention and decreased the prevalence of NTDs by 50-70%. Since awareness of the benefits of folic acid is still not optimum even in advanced industrialized countries, and to reach women with unplanned pregnancies and those facing social deprivation, an obligatory folic acid fortification of food was adopted in several countries including Saudi Arabia.[2] Prevention of NTDs can gain faster momentum if low income countries adopted fortification of the staple food in their communities.

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