



The Fetal Study on Cranial and Spinal Dysraphism of Neural Tube

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ABSTRACT:

Neural tube defects (NTD) are more common congenital birth defect affecting the babies all over the world. .It is one of the causes of fetal mortality and morbidity .Defective neurulation process during embryonic period leads to this condition. Based on the level of neural tube involvement the defects are divided as cranial dysraphism and spinal dysraphism.Cranial dysraphism include lethal anencephaly ,encephalocele and iniencephaly .In spinal dysraphism ,failure in the fusion of caudal end of neural tube leads to meningocele and myelomeningocele.These conditions are associated with mesodermal involvement leading to bony defects .The present study was done on 50 human fetuses that were collected for development of museum in Anatomy.In this process more number of fetuses with neural tube defects were identified. The fetuses were separated based on the level of neural tube involvement. In anencephaly,encephalocele and rare iniencephaly in which the cranial end of neural tube is involved and in meningocele and myelocoele the caudal end neural tube is involved. All these fetuses were studied further. Manifestation of NTD is multifactorial that have genetic or environmental basis with high recurrence rate. Neural tube defects are usually diagnosed in early weeks of intrauterine life by ultrasound examination .In the various forms of neural tube defects,anencephaly is incompatible with life and depending on the level of exposure of neural tissue ,open spinal defects will survive with permanent disability.Folic acid is given as a supplement to prevent the neural tube defects and the role of folic acid in NTD's was studied by authors and they expressed that folic acid is important in nucleic acid formation and in the metabolic activity of enzymes. The deficiency of folic acid blocks all this process and leads to formation of neural tube defect. So pregnant woman with previous history of neural tube defect are advised to take folic acid before planning the pregnancy and continue for three months after conception to prevent the recurrence of neural tube defects..

KEY WORDS: Neural tube,Mesoderm, Anencephaly, Meningocele, Folic acid

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I. INTRODUCTION

Neural tube defects(NTD) are most common congenital anomalies .It affects approximately 300,000 babies

every year worldwide.NTD are most serious congenital anomaly involving the nervous system leading to fetal mortality and morbidity.Its incidence is 1-5 /1000 live births. Development of nervous system starts in the embryonic period of intrauterine life. Under the influence of notochord, neural groove is formed from neuroectoderm.The two ends of neural groove forms neural tube that closes in the middle and extends cranially and caudally leaving anterior neuropore and posterior neuropore .The anterior neuropore closes by 25th day and posterior neuropore closes by 27th day ,that closes the neural tube .Neural tube formation and closure occur at 4th week of intrauterine life.Failure in the closure of the neural tube disrupts the differentiation of central nervous system and formation of vertebral arches that derives from mesoderm. This leads to developmental malformations along the neuroaxis and manifest as neural tube defects .Neural tube defects are in the form of open type if the neural tissue is exposed and closed type if the defect is covered by skin. Failure of cranial neural tube closure leads to cranial dysraphism which manifests as anencephaly with defective brain development ,encephalocele with midline skull defects and iniencephaly with defective folding of

embryo. Failure of caudal neuropore closure leads to spinal dysraphism that manifest as myelocele and myelomeningocele. A rare form of NTD is craniorachischisis that results from failure of the neural tube closure over the entire body axis. The two most common neural tube defects are spina bifida and anencephaly (1). Spina bifida is an open form of spinal dysraphism in which the fetal spinal column does not close completely with exposed neural tissue and anencephaly is most common cranial dysraphism with absence of parts of brain and the overlying skull.

Anencephaly is a cephalic neural tube defect associated with absence of the mesodermal tissue dorsal to the neural elements leads to failure in the bony skull development. The condition is lethal and the baby dies within few hours. It can be diagnosed easily in the antenatal period by ultrasound imaging.

Encephalocele with midline skull defects, can be termed as crania bifida. Crania bifida is less common compared to spina bifida. Encephaloceles are two types -anterior and posterior. The anterior encephalocele is more common with protrusions from the face as proboscis and posterior encephalocele present in the occipital region as occipital encephalocele. It may have present with infratentorial or supra tentorial brain contents. Iniencephaly is a very rare neural tube defect, characterized by an occipital bone defect, cervical dysraphism, fixed retroflexion of the fetal head and severe lordosis of cervicothoracic spine.

Spinal dysraphisms is due defective caudal neural tube closure associated with mesenchymal defects. They can be diagnosed at birth or in early infancy. Open spinal dysraphisms include meningocele, meningomyelocele with exposed neuronal structures without skin covering and accounts for 95% of spinal dysraphism. This caudal neural tube defect may present at any region but lumbosacral involvement is more common. Closed spinal dysraphisms are minor defects that do not have any exposed neural structures and it is covered by skin.

II. MATERIALS AND METHODS

Fetuses were collected from Victoria General Hospital, Visakhapatnam for the development of Anatomy museum. During this process anomalous fetuses of various system were found. Of these fetuses with neural tube defects were separated and studied further. The fetuses were separated based on the level of neural defect that was present in the cranium and spinal column. The fetuses that were presented with cranial defects were studied to know the level of defect and involvement of nervous system and the same was observed in the fetuses of spinal defects. The extent of involvement of nervous system and level of bony involvement was studied and noted.

III. OBSERVATIONS

The present study identified fetuses with cranial dysraphism like anencephaly, encephalocele and rare iniencephaly. This study found more number of fetuses with spinal dysraphism that manifested as meningomyelocele at various regions, more commonly at lumbar region.

Out of 50 fetuses collected, two fetuses with anencephaly, one fetus with encephalocele and a fetus with a rare neural tube defect of iniencephaly were observed. Fifteen fetuses presented with spinal and bony defects at various vertebral levels. The defect may be at cervical, thoracic, lumbosacral region, more commonly at lumbosacral region.

A male fetus was presented with anencephaly with absent cranial vault. The face was presented with typical frog eye appearance of anencephaly. The cranial fossae appeared empty with macerated brain tissue. Few contents of hind brain were observed close to the foramen magnum and it continued in the vertebral canal. (fig.1)



Fig.1 Showing Anencephalic fetus

Encephalocele was observed in a full term female fetus with a bulky mass at occipital region. No other external anomaly was found in this fetus. On dissecting the mass, at occipital region, brain tissue of infratentorial components were found. The spinal cord was exposed in the cervical region due to defective vertebral bodies. In this defect, the skeletal elements were not formed properly due to defective mesoderm. So the skeletal defect leads to herniation of brain tissue.



Fig.2 fetus showing posterior encephalocele

A rare neural tube defect of this study was iniencephaly. This was found in a male fetus which was presented with huge face with retroflexion of head, the face pointed towards the roof. The neck was absent and the skin of chest is continuous with face. Normally iniencephalic fetus presents with huge head with normal cranial vault, but this study presented an iniencephalic fetus with anencephaly and craniorachis a rare association. (fig.3)



Fig.3 Iniencephalic fetus-A Rare neural tube defect

Spinal dysraphism was observed in the form of spina bifida, myelocele and myelomeningocele. More number of fetuses were identified with myelocele with bifid spine with exposed spinal cord to the surface. This defect was observed in cervicothoracic and more commonly at lumbosacral region. These fetuses showed unfused lamina of vertebra with exposed vertebral canal leading to exposed spinal cord and spinal nerves. (fig.4a)

Meningomyelocele was also observed in this study. In these fetuses the contents of vertebral canal were exposed and covered by meningeal layers. So a sac with neural structures was observed through the vertebral defect. (fig.4b)



Fig.4 fetuses with spinal dysraphism

IV.DISCUSSION

Neural tube defect is a multifactorial disorder that occurs due genetic or environmental factors with high recurrence rate. Monogenic inheritance of NTD shows that the disease may be produced by single genes, particularly genes present in the X gene. Environmental factors such as socio-economic status, nutritional deficiency, hypothermia, gestational diabetes, use of anticonvulsant drugs and insulin are well known risk factors.(2)

Neural tube defects are usually diagnosed in early weeks of intrauterine life through imaging techniques. Of all NTDs, anencephaly is incompatible with life and the fetus will die few hours after birth and the child with open spinal defects will survive with permanent disability

Neurulation is the process by which neural tube is formed around 22-23 days (2). In mammals, neurulation occurs in two phases: primary and secondary neurulation. Primary neurulation occurs at 3rd and 4th week of intrauterine life and forms the entire neural tube leaving cranial and the caudal neuropore. Secondary neurulation occurs at tail bud region (3). Earlier it was proposed that the fusion of neural tube starts from a single initiation site and progresses both cranially and caudally towards the cranial and caudal neuropores. Later multiple sites of neural tube fusion were proposed and extensive studies were made in rats and mice. According to Sakai (4) in mice there are four sites at which fusion of neural tube takes place. Site 1 appears in the cervical region at the caudal part of hindbrain and proceeds bidirectionally. Site 2 appears at the junction of prosencephalon and mesencephalon and proceeds bidirectionally. Site 3 appears at the cranial end of neural plate and proceeds caudally. Site 4 appears at the caudal end of neural plate and proceeds cranially. Van Allen et al., (5) proposed multisite closure model of neural tube with five sites of closures in humans based on the observation of types and occurrence of NTDs. Of the five sites 3 are present in the cranial region and 2 are present in the spinal region

Anencephaly occurs in 3 phases, initially the cranial part of the neural tube fails to close followed by protrusion of the developing brain parts and its exposure to the amniotic fluid and at last degeneration of the exposed part results in anencephaly (6). Occipital encephalocele occurs when the surface ectoderm does not separate from the developing neural tube at the occipital region. This leads to defects in the formation of occipital bone. Encephalocele is associated with other syndromes like Meckel – Gruber syndrome, Walker – Warburg syndrome, Dandy – Walker syndrome, Joubert syndrome, Trisomy 13 and Amnion rupture sequence (6). Iniencephaly was derived from greek word inion that means back of the neck and encephalos to brain. Persistence of the embryonic cervical lordosis at the third week leads to failure of closure of the neural tube and abnormal development of the rostral portion of the notochord and somites of the cervicooccipital region is the cause for iniencephaly .(7)

Open neural folds in the spinal region prevent the sclerotome-derived vertebral arches from covering the neuroepithelium, the consequent opening in the vertebral column giving rise to the term spina bifida (8). The neural tissues may be contained within a meninges-covered sac that protrudes through the open vertebrae or exposed directly to the amniotic fluid. Babies born with open spina bifida usually survive with appropriate medical care but suffer with neurological impairment, the severity depends on the level of the lesion. A less well-defined group of closed spinal NTDs in which the vertebral arches are malformed but covered by skin may lead a normal life.

Open defects affecting the brain like anencephaly, craniorachischisis are lethal before or at birth. Encephalocele can also be lethal depending on the extent of brain damage during herniation.

Open spina bifida is compatible with life leaving neurological impairment below the level of the lesion.

Closed spinal lesions are generally less severe and can be asymptomatic, as with spina bifida occulta which is considered a variant of normal. However, lumbosacral spinalcord tethering can lead to lower limb motor and sensory deficits, and a neuropathic bladder.

Clinical observations suggest a higher frequency of NTDs in offspring of consanguineous couples as well as in twin pregnancies(9), pointing towards a strong genetic contribution to the etiology of NTD. Consanguinity is thought to contribute to Mendelian autosomal recessive conditions by inheritance of pathological mutations and also to polygenic multifactorial disorders such as NTDs by increasing the load of risk alleles.(10)

Folic acid deficiency during antenatal period is thought to be a cause of NTD. The relation between folic acid deficiency and NTDs in humans was first reported by Hibbard in 1964. (11) He observed higher incidence of aberrant folate metabolism in women who had pregnancies associated with foetal malformations. Smithells and co-workers in 1976 observed that maternal red blood cell folate levels were significantly lower in fetus with NTDs in comparison to those who did not have NTDs.(12) This observation led to the possibility of preventing neural tube defects by periconceptional vitamin supplementation(13).

Folic acid is present in the blood as tetrahydrofolate .THFA has an important role in the metabolism of one carbon (1C) groups and THFA is the carrier of one carbon groups which are involved in metabolic pathways and nucleic acid synthesis. So genetic defects of the enzymes involved in folate and 1C metabolism

have been identified in NTDs in clinical and experimental settings. Supplementation of folic acid may overcome these metabolic blocks and reduce the risk of NTDs.(14)

A study conducted by the British Medical Research Council on women with earlier neural tube defects and the effect of supplementing folic acid in subsequent pregnancies. This study showed that supplementation of 4 mg folic acid significantly reduced the risk of recurrence of NTDs.(15) In our country, women are more prone to infections, anemia and other deficiency conditions, so it is preferable to recommend the folic acid on a regular basis to women of child bearing age especially to those who are at high risk state.

V. CONCLUSION

Neural tube defects are most common congenital anomaly of defective neural tube formation during embryonic period of intrauterine life. It is one of the causes of fetal mortality and morbidity with high recurrence rate. It may have either genetic and environment factors in causation of this condition. Folic acid deficiency was identified in the manifestation of various forms of neural tube defects and supplementation of folic acid during pre and post conceptional period will help in the prevention of this anomaly

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