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Review Articles

Neural Tube Defects

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SUMMARY

Neural tube defects (NTDs), are frequently encountered in children. Being congenital defects, they are most frequently seen in the neonatal period. Besides early recognition and quick diagnosis, attention needs to be focussed on prompt treatment, which is mostly surgical. Diagnosis can often be established antenatally Provision of adequate nutrition, and the use of vitamins and folic acid helps in prevention.

DEVELOPMENT OF C.N.S.

C.N.S. begins to develop at the 3rd week of development. At this stage ectoderm has the shape of a flat disc, which is broader at its cephalic end as compared to the caudal end. This elongated disc or slipper-shaped plate is called neural plate.

By the end of 3rd week lateral edges of neural plate become more elevated to form the neural folds, while the depressed middle portion is called the neural groove.

Gradually the neural folds approach each other in the midline where they fuse and form the neural tube, which has open connections at both ends called neuropores.

Failure of closure of neural tube allows the excretion of fetal substances into the amniotic fluid, which serves as biochemical marker for neural tube defects. Histologically closed neural tube consists of 3 layers;

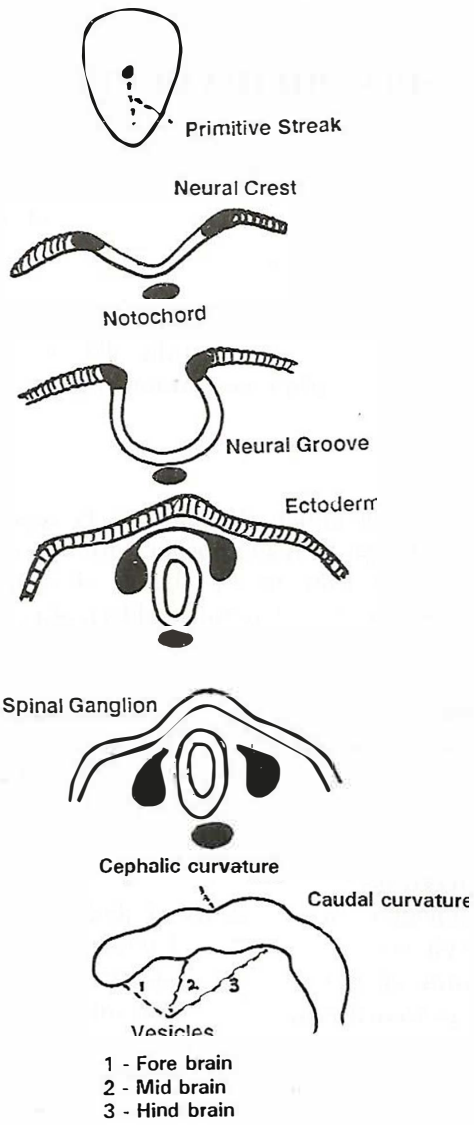
1. Neuro-epithelial layer;
2. Mentale layer
3. Marginal layer

Neural tube defects account for most of the congenital anomalies of C.N.S.

Factors

Major factors associated with different neural tube anomalies include;

- Radiation
- Drugs
- Malnutrition
- Certain chemicals



Maternal selenium (Se) deficiency during pregnancy was thought to be one factor resposible for neural tube defect, as a significant decrease in selenium concentration in serum and hair was observed in the newborn with neural tube defect compared with healthy newborns[1].

Among the major neural tube defects are;

1. Spinabifida occulta
2. Meningocele
3. Myelomeningocele
4. Encephalocele
5. Anencephaly
6. Dermal sinus
7. Disorders of cell migration
8. Agensis of corpus callosum.
9. Agenesis of cranial nerves.

I. SPINABIFIDA OCCULTA

Definition

Failure of fusion of posterior vertebral arches without the protrusion of meningeal and neural tissue.

Etiology

Etiology of this neural tube defect includes genetic and some additional unknown environment factors.

Incidence

Incidence of spinal dysraphism is highest in Ireland and lowest in Asia. Mother with one affected child has about 1.5% to 2% chance of recurrence whereas a mother who has two children affected has recurrence chance of about 6%.

Location

It may occur anywhere along the neuroaxis. The defect commonly occurs in the lumbosacral region and less frequently in the cervical region.

Pathophysiology

Pathology is in the failure of closure of neural tube which occurs in the third week of gestation. Significance of neural tube defects is that it is usually associated with other congenital anomalies. The results of one study support the concept that neural tube defects reside in a primary or secondary maternal or fetal derangement of homocystine metabolism[2].

Clinical Manifestations

This is the most benign form of neural tube defect. Most individuals are asymptomatic with no neurologic signs and the defect is usually of no consequences. It may be associated with other findings which include;

- Patches of hair
- Lipoma
- Skin discoloration
- Dermal sinus

Diagnosis

Diagnosis is usually clinical and spina bifida occulta may be associated with patch of hair, lipoma, sinus and skin discoloration. X-ray shows a defect of closure of posterior vertebral arches. Most common sites are lumbar and sacral vertebrae.

Treatment

No treatment is necessary and infants are usually neurologically normal.

Prognosis

Is usually good.

II. MENINGOCELE

Definition

In meningocele, the meninges herniate from the defect in the posterior vertebral arches.

Etiology

- Genetic factors
- Environmental factors

Incidence

It is about 1/1000 live births. Those with one affected child have an incidence of 1.5-2.0% whereas mothers with two affected children have 6% chance of recurrence.

Location

Most common site is in the lumbosacral region but it may occur anywhere along the neuroaxis. Meningocele may also be anterior, projecting into the pelvis and escape diagnosis. This can only be diagnosed on ultrasound (US) or CT scan.

Pathophysiology

Defect is the failure of closure of posterior or anterior vertebral arches, hence leaving a defect

through which the meninges protrude out of the spinal cord.

Clinical Manifestations

Usual presentation is difficult labour. Most of the infants have a fluctuant mid-line mass which is transilluminant. Most meningoceles are well covered by the skin. A careful neurologic examination is mandatory as the neonate may have weakness of the body below the level of meningocele with loss of sensation and loss of control of the sphincters. Infant may be normal without any obvious neurologic deficit, depending on location of the defect. Female infants may have associated anomalies of genital tract like rectovaginal fistula and vaginal septa.

Diagnosis

Diagnosis is obvious clinically as there is a mass along the midline. Among different tests which help in diagnosis, U/S is most useful in prenatal diagnosis. Others include;

- C.T. Scan
- Plain X-ray
- MRI
- α-fetoprotein; Women who have unexplained elevated maternal serum alfa-fetoprotein level of 2.5 MOM or greater have two fold increased risk of chromosomal abnormalities in their fetuses as compared to general population[3].
- 4F19 enzyme antigen immunoassay;

This identifies the molecular form of acetylcholinesterases (AChE) found in the amniotic fluid of fetus with NTD. This is a simple test and is a good antenatal diagnostic test for neural tube defects in either amniotic fluid or maternal serum[4].

Treatment

Treatment is basically surgical but usually a multidisciplinary approach is advised, the team including a;

- Surgeon
- Physician
- Physiotherapist

Prognosis

Usually good, but few patients may develop neurologic deficits and hydrocephalus following surgical correction.

Prevention

It is thought that frequent use of vitamin and folic acid decreases risk of neural tube defects. But this is useful within 3 months of conception and 1st trimester of pregnancy.

Mechanism of this protective role is not known and this effect is seen with folate doses between 0.4-4 mg. The optimal dose however is unknown[5,6].

III. MYELOMENINGOCELE

Definition

In this form of neural tube defect nerve roots and spinal cord also herniate along with the meninges.

Etiology

The exact cause is unknown but genetic predisposition does occur. Risk of recurrence after one affected child is 3-4% but it may go upto 10% when two or more children are affected. Certain factors increase the incidence of neural tube defects which include;

- Sodium valproate
- Vit. A.
- Hyperthermia

Incidence

1/1000 live births

Location

Anywhere along the neuroaxis but most frequent site is in the lumbosacral region.

Pathophysiology

Myelomeningocele might result from specific biochemical abnormalities in the basement membrane, particularly hyaluronate which plays a role in cell division and shape of primitive neuro epithelium.

Clinical Manifestations

It produces dysfunction of organs and structures which include skin, skeleton, G.U.S. and C.N.S.

Examination of the newborn may reveal;

- Swelling in the midline which may or may not be ruptured.
- The extent and degree of the neurological deficit depends upon the site and extent of the lesion. A lesion in the lower sacral region may cause

bowel and bladder dysfunction which is associated with anaesthesia in the perianal area but there is usually no motor involvement. The higher the lesion, the worst the prognosis.

On examination the infant shows

- Flaccid paralysis in lower limb.
- Absent reflexes
- Disturbed or absent sensations.
- Abnormalities of sphincter control
- Hydrocephalus in 80% of cases.

Fortunately 75% of the myelomeningoceles are located in the lumbosacral area.

Diagnosis

Prenatal diagnosis is usually possible by the use of U/S. At birth diagnosis is usually evident clinically. Other modalities for diagnosis include;

- Plain x-ray spine.
- C.T. Scan spine.
- M.R.I.
- α-fetoprotein level in maternal serum or amniotic fluid.

Treatment

Multidisciplinary approach is required which involves the surgeon, pediatrician and the physiotherapist.

In the past it was recommended that repair should be done as soon as possible after birth, but now it has been shown that results of delayed surgery are the same as that of urgent surgery. Indication for urgent surgery is ruptured meningocele and leaking C.S.F.

Conservative treatment is recommended for neonates with;

- Marked paralysis.
- Thoracolumbar or thoracolumbosacral defect.
- Kyphosis, scoliosis or other associated congenital anomalies.

Most of the patients develop hydrocephalus after surgical correction. For urinary incontinence some surgical implants can be used and fecal incontinence can be helped by treating with timed enemas.

Prognosis

Prognosis of myelomeningocele with marked neurologic involvement is poor. Mortality is 10-15%. About 70% have normal intelligence but hearing problems and seizures may occur.

Prevention

Use of drugs which cause increased incidence should be avoided during pregnancy. On the other hand frequent use of vitamins and folic acid may reduce the incidence.

IV. ENCEPHALOCELE

Definition

This is a type of neural tube defect in which there is protrusion of neural tissue through a bony midline defect called cranium bifidum.

It manifests as either cranial meningocele or cranial encephalocele.

- Cranial encephalocele contains meningeal sac plus cerebral cortex, cerebellum or portions of brain stem.
- Cranial meningocele consists of C.S.F. filled meningeal sac only.

The defect most commonly occurs in the occipital region. Cranial defects are 1/10th as common as those affecting the spinal cord.

Site

Most common site is in the posterior midline. It can be frontal or nasofrontal.

Incidence

1/10th as common as spinal cord defect.

Etiology

Same as that of meningocele.

Clinical Presentation

Children with this deformity usually present with a mass in the posterior or anterior mid line ranging from a small sac to a sac equal to that of the skull. Children with this defect are at increased risk of developing hydrocephalus because of associated anomalies which include Chiari and Dandywalker malformations.

Diagnosis

Diagnosis is usually evident clinically. Labour may be difficult or obstructed.

- It is transilluminant on examination

- Plain x-ray shows the bony defect.
- U/S is helpful in determining the contents of the sac.

Prognosis

Children with cranial meningocele have good prognosis but those with encephalocele are at greater risk of developing visual problems, microcephaly and seizures.

V. ANENCEPHALY

Definition

This is a type of defect in which there is a large bony defect of the clavarium, meninges, scalp and is associated with rudimentary brain stem. It results from failure of closure of rostral neuropore.

Cerebellum and cerebral hemisphere are usually absent and brain stem is rudimentary, pituitary gland is hypoplastic and pyramidal tracts are absent due to absent cerebral hemispheres.

Associated anomalies include;

- Folding ears
- Cleft palate.
- Congenital heart disease in 10-20% cases.

Incidence

Incidence is 1/1000 live births. Recurrence rate is 4% with one affected child and 10% with two affected child.

Etiology

Many factors are implicated which include;

- Low socioeconomic status
- Poverty
- Malnutrition
- Vitamin deficiencies
- Environmental factors
- Toxic factors
- Genetic susceptibility

50% of the pregnancies with this defect are associated with polyhydramnios

Prognosis

Prognosis is bad and most of the infants die within several days of life.

VI. DISORDERS OF CELL MIGRATION

Migration of neural cells are controlled by glial cells which guide them to the proper site. Any failure to do so may result in different abnormalities which include; 1) Lissencephaly, 2) Schizencephaly, and 3) Porencephaly.

1. Lissencephaly

This is also called agyria and is characterized by absence of cerebral convolutions, and poorly formed Sylvian fissure, like the brain of a 3-4 month old fetus.

Clinical Features

These children have typical facies with broad forehead, prominent occiput and anteverted nostrils. There is hypoplasia of the 2nd nerve. These children are usually developmentally slow and are microcephalic and usually have some sort of seizure disorder. Micropthalmia is also associated with this disorder. Lateral ventricles are dilated and enlarged.

2. Schizencephaly

This is characterized by the presence of unilateral or bilateral defects within the cerebral hemispheres.

Clinical Features

Most of the patients with this disorder are mentally retarded and show some type of seizure disorder. C.T. scan is usually diagnostic. Other associations include;

- Microcephaly
- Quardriparesis when cleft is bilateral.

3. Porencephaly

This is characterized by presence of cysts and cavities within the cerebral hemispheres.

Cysts are of two type

1. True porencephalic cysts.
2. Pseudo-porencephalic cysts.

The cysts are mostly located in the region of the Sylvian fissure.

Clinical Features

Some babies are developmentally delayed with microcephaly, encephalocele and are mentally

retarded. Most children have spastic quardriparesis and seizures. Optic atrophy is some times associated with this disorder.

VII. AGENESIS OF CORPUS CALLOSUM

Corpus develops from the commissural plate. An insult to plate during early embryogenesis causes agenesis of corpus callosum. This may result in;

- Mental retardation.
- Microcephaly.
- Hemiparesis
- Diplegia
- Seizures

This may be inherited as x-linked recessive or autosomal recessive or dominant disorder. This is usually associated with trisomy 8 or 18.

Clinically seizures become evident at the age of one year or even before. These seizures are typically resistant to anti-convulsant drugs.

Diagnosis

- C.T. and MRI are diagnostic which show widely separated lateral ventricles and an abnormally high positioned 3rd ventricle.

- E.E.G. is diagnostic which shows independent wave pattern in both hemisphere.

VIII. AGENESIS OF CRANIAL NERVES

The first, 5th, 8th, 9th, 10th, 11th and 12th nerves are frequently involved. There may be hypoplasia, agenesis or decreased number of fibers in the cranial nerves.

These patients present with facial weakness, poor sucking and expressionless face. Prognosis is excellent in this case, since this is an isolated defect.

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