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STUDY OF VARIOUS CONGENITAL ANOMALIES IN FETAL AUTOPSY – A CASE SERIES

Pathology

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ABSTRACT

Introduction: Congenital anomalies are structural, functional and/or biochemical-molecular defects present at birth whether detected at the time or not. In India, congenital anomalies account for 10-15% of perinatal fatalities. A significant fraction of fetal losses and early neonatal mortality are linked to congenital anomalies. Only a small percentage of them are amenable to prenatal diagnosis via USG, different maternal serum testing, etc. But perinatal autopsy continues to be the most reliable method of research. **Materials And Method:** The present study of 10 congenital anomalies in fetal and neonatal deaths was done in Pathology department at tertiary care centre over a time of 1 year from January – December 2023. Consent for autopsy was taken. **Results And Conclusion:** Overall result suggested that Neural tube defects are the most common congenital anomalies. Fetal autopsy provide us an important information about pattern of anomalies, their incidences, genetic counseling and prenatal diagnosis in successive pregnancies.

KEYWORDS

INTRODUCTION

The incidence of congenital anomalies has been increasing in recent past. The worldwide incidence of congenital anomalies is estimated at 3-7%, but the actual numbers vary widely due to under reporting of cases in developing countries. The presence of congenital anomalies in a baby has an emotional impact not only on the mother but also on the family[1]. Congenital malformations remain a common cause of perinatal deaths accounting for 10-15% in developing countries like India. In spite of antenatal diagnostic modalities still the fetal autopsy plays the vital role in the confirmation as well as identification of congenital anomalies and also for the counseling of the parents, to prevent the fetal congenital anomalies in further pregnancies. Every effort should be made to identify the etiology of the perinatal death so that appropriate genetic counseling can be given[1].

Fetal autopsy includes an external, internal and histopathological examination of dead fetus along with placental examination. There are two types of autopsy:
1) Medicolegal autopsy : Conducted on requisition of police under section Crpc-174 to know the cause of death, age, sex and viability of fetus for which police inquest and panchnama is required.

2) Academic autopsy/Clinicopathological autopsy : Conducted on request of obstetrician, pediatrician, radiologist or family members of fetus to know the cause of congenital anomaly if any and cause of repeated abortions[2].

MATERIALS AND METHODS

The present study is descriptive study of 10 congenital anomalies in fetal and neonatal deaths was done in Pathology department at tertiary care centre over a time of 1year from January – December 2023. Consent for autopsy was taken.

Inclusion And Exclusion Criteria

The present study included dead fetuses and neonates with gestational age between 15-40weeks of intrauterine life. All fetuses <14weeks and and all neonates from 7days of gestation were excluded from the study. Autopsy was performed by standard technique.

AUTOPSY PROCEDURE

1) External Examination:

This is done for inspection of cyanosis, injuries and maceration, skin lesions. All major and minor developmental anomalies were described. The 'Y' shaped incision was taken which extend from the anterior aspect of each shoulder to the xiphoid process. Umbilical cord was examined for one vein and two arteries. Later the autopsy protocol included the removal of thoracic, cervical, abdominal and pelvic organs en block and subsequently dissected into organ block.

2) Internal Examnination:

All internal organs position, size and weight were examined. The internal genitalia are inspected. As the testis will be undescended in younger fetuses, they are removed with the abdominal contents. Each lungs will be examined for developmental changes carefully. Heart was examined in situ, while anatomic relationship with the structures were intact, inspected externally and internally in a systemic fashion that follows the flow of blood. All major vessels were examined. Later, all the organs were removed en bloc by the Rokitansky method of evisceration. Neck structures like trachea and esophagus were examined. The scalp, fontanels and cranial sutures were examined by palpation. The brain was removed and examined on all sides and placed in a fixative.

3) Histopathological Examination:

The organs after evisceration and external examination were fixed in 10% formalin. Blocks of tissues for microscopic examination were taken. One block from each lobe of both lungs, one each from thymus, heart, stomach, liver, spleen, pancreas, small intestine, large intestine, kidneys, adrenals and very doubtful lesions were taken. Sections were studied in the routine way with Haematoxylin and Eosin stains. Special stains were done whenever necessary. Autopsy findings were compared with ultrasound findings whenever available.

RESULTS

	Period Of Geststion	WEIGHT	USG FINDINGS	AUTOPSY FINDINGS
1). MALE	Primigravida, 28wk+5days	1000g	Open NTD's, large thoracolumbar meningomyelocele. Spine- severely deformed. Gross hydrocephalus with Chiari-2 malformation.	Spinal defects at thoracolumbar region of 5x2.5cm. Skull- bulging fontanelle. Drained CSF and brain matter removed.
2). FEMALE	Primi, 27wk+4d	1000g	Calvaria & brain parenchyma not visualized. Frog like bulging of eyes & absent frontal bones - Anencephaly.	Head - absence of Calvaria and brain tissue. Face - frog like appearance

3). FEMALE	G2P1L1 with 20wk+4d	600g	Large occipital encephalocele across a bony gap of 23mm comprising 65% of brain mass Native skull cavity is underdeveloped – Microcephaly.	Occipital region of skull showing a bulging mass of 6x6x4cm. Head circumference is reduced.
4). FEMALE	G2P1L1 20wk+4d	250g	Calvaria & brain parenchyma not visualised. Frog like bulging of eyes & absent frontal bones – Anencephaly.	Head- absence of calvaria and brain tissue. Face- frog like appearance.
5). FEMALE	Primi, 20wk+1d	360g	Spina bifida - NTD	Cystic lesion noted at lumbar region measuring 1x1cm.
6). FEMALE	Primi, 24wk+1d	560g	Anencephaly & short neck with abnormal spine-NTDs	Anencephaly & short neck. Mass measuring 3x2.3cm on the umbilical cord near fetal end. C/S – Liver like s/o Ectopic liver.
7). FEMALE	G3A2, 16wk	100g	Head shows excencephaly with spinal malformation & facial abnormality – NTDs.	Spinal deformity measuring 3x2cm at cervicothoracic area. Head - absence of Calvaria(excencephaly) Face - frog eye appearance.
8). FEMALE	A3, 20wk+4d	500g	Short lowered/fractured long bones, deformed hypoplastic chest, hypomineralised skull - S/O Lethal skeletal dysplasia possibly Osteogenesis imperfecta -2.	Skull- Fontanelle are separated. Hypoplastic chest. Fractured long bones.
9). MALE	G3P1L1A1, 20wk+5d	700g	Small & rotated vermis. Enlarged 4th ventricle - s/o Dandy Walker malformation.	Externally normal except that there are 6 digits and 6 toes in all 4 limbs.
10).MALE	Primi, 24wk+3d	760g	Long bones are lagging by 3-4wk compared to BPD, AC, HC - s/o skeletal dysplasia. Increased frontonasal angle s/o Chondrodysplasia punctata.	Depressed nasal bridge. Underdeveloped mandible mainly left side. Flat nose.

Key notes:

- G – Gravida, P – Para
- L – Live child, A - Abortion

In The Present Study,

- Many studies have documented male preponderance.
- However, we observe 3male babies and 7female babies with congenital malformations (F>M), irrespective of the mother's age & fetal weight.
- CNS malformation is the most common congenital anomaly of which Neural Tube defects are the commonest.
- Ectopic liver within the UC where studies done in last 60years are <35mm. However, in this study it was 3cm which was confirmed by histopathology.
- All other anomalies are rare.

Fig 1 – Anencephaly(Case-4)

Fig 2 – Dorsolumbar Spina Bifida(Case-1)

Fig 3 – Occipital encephalocele(Case-3)

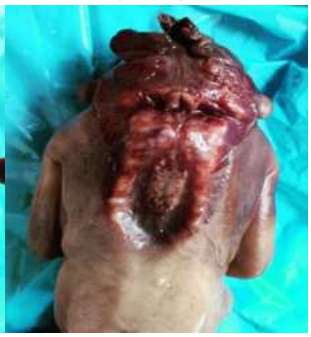

Fig 4 – Cervicothoracic spinal defect(Case-7)

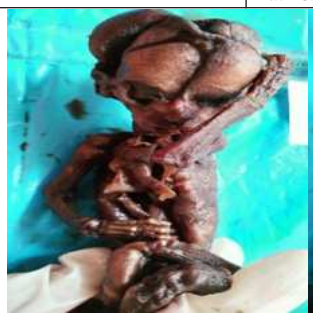

Fig 5 – Separated fontanelle s/o skeletal dysplasia (Case-8)

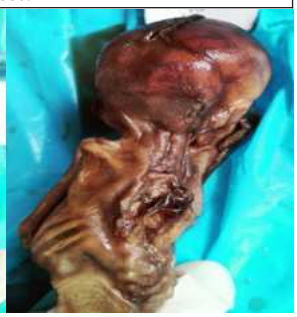

Fig 6 –Spina bifida(Case-5)

Fig 7 – Underdeveloped mandible s/o Chondrodysplasia punctata (Case-10)

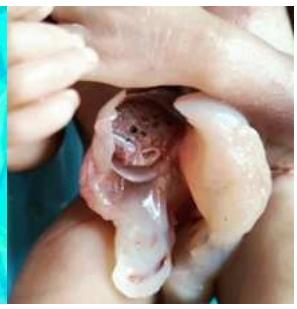

Fig 8 - Ectopic liver within the umbilical Cord (Case-6)

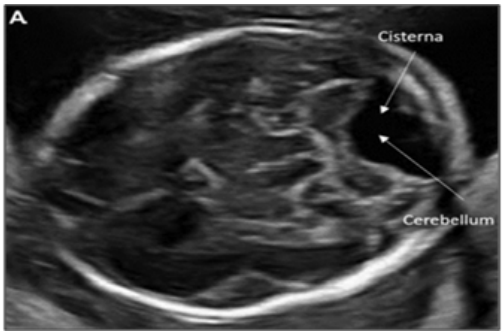

Fig 9 – Dandy walker malformation[5] (Case 9)

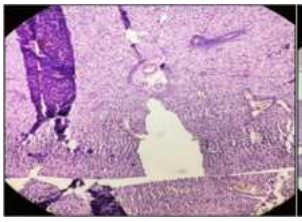

Fig 10 – Portal triad in an Ectopic liver.

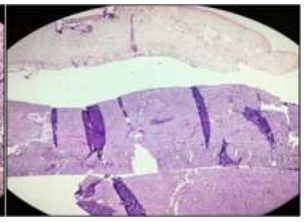

Fig 11 – Wharton's jelly s/o Ectopic liver within Umbilical cord.

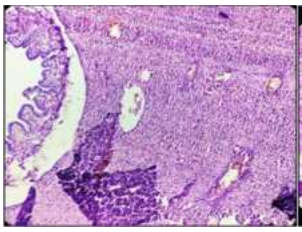

Fig 12 – Bile duct epithelium in a case of Ectopic liver tissue.

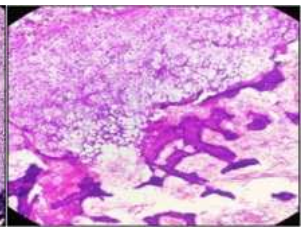

Fig 13 – Cortical bone with increased number and overcrowding of of osteocytes(Case 8).

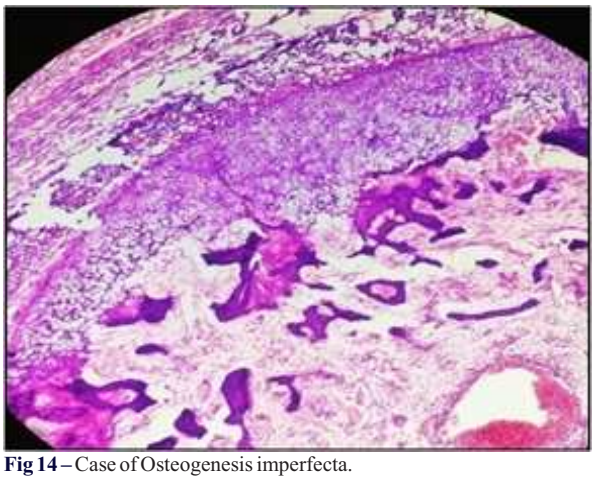

Fig 14 – Case of Osteogenesis imperfecta.

DISCUSSION

1. Neural Tube Defects:

NTD's arise as result of incomplete closure of neural tube during early embryonic development. This leads to miscarriage, stillbirth in many cases and abnormalities of central nervous system function in most affected individuals who survive. NTD's can be classified according to the type or position of the lesion, most common types being anencephaly and spina bifida (meningocele and myelomeningocele). The current recommendations to reduce the chances of NTD's is daily supplementation of 4-5mg of Folic acid prior to pregnancy and during pregnancy[3].

The incidence of NTD's in Indian subcontinent is much more higher than in developed countries where prenatal screening is the standard medical protocol. However in India, unplanned pregnancies and unawareness regarding benefits of folic acid supplementation are the main reason for higher incidence. Anencephaly and spina bifida comprise 95% of NTD's and remaining 5% is encephalocele[3]. In the present study, out of 10 fetal autopsies, 7 cases comprised of NTD's.

SPINA BIFIDA: Spina bifida cystic is a term used to describe failure of closure of the neural tube in its spinal portion and defects may be classified as meningoceles, in which meninges herniated out forming a cyst like structure and myelomeningoceles, in which the spinal cord also herniates out. These may be divided into upper and lower spinal lesions. Lower lesions in the lumbar region of the spine occur most commonly. Spina bifida occulta is of different etiology and is the result of the incomplete fusion of vertebral arches in the spine[3].

ANENCEPHALY: Congenital malformation of the central nervous system that results to the failure of the cranial end of the embryonic neural tube, usually occurs between the 23rd to 26th days after conception, affecting 1 in 1000 pregnancies. It represents 40% of NTD's which is the 2nd leading cause of nervous system abnormalities after spina bifida. A baby born with anencephaly is usually blind and deaf[4].

Diagnosis is made by 1st trimester ultrasound between 11th and 14th week of amenorrhoea by the demonstration of exencephaly which results in the non-visualisation of the ossification of cranial box. In the second trimester scan, the typical appearance of "frog eyes" due to absence of visible brain tissue above the eye sockets[4].

Anencephaly is a lethal congenital anomaly for which prognosis is grim. Termination of pregnancy is the most legal approach, but is not practiced in our context due to religious beliefs. Prevention is therefore essential and creating awareness among the people about the preventable causes of nutritional deficiency. Therefore, folic acid plays an important role in preconception or in the 1st trimester[4]

2. DANDY WALKER MALFORMATION:

It is a complex malformation involving the posterior fossa and cerebellum. It is rare condition with an estimated incidence of 1 in 10000-30000 births. Hydrocephaly is the common finding, seen approximately 80% of cases. Most of the cases are sporadic, although first degree relatives have an increased risk. The classic triad of DWM is defined by 1). Enlargement of posterior fossa with upward displacement of the tentorium, transverse sinus and torcular. 2). Complete or partial agenesis of the vermis. 3). Cystic dilatation of the fourth ventricle. The pathogenesis of DWM involves an intricate developmental anomaly of the cerebellar vermis in which fourth ventricles fails to close, causing persistent Blake's pouch[5].

It is usually diagnosed during second trimester on ultrasound examination. The typical finding is an enlarged cistern magna measuring >10mm in the axial plane. DWM is frequently associated with other central nervous system and non-CNS anomalies, chromosomal abnormalities such as Trisomies 9, 13, 18 and 21, Triploidy etc. Genetic evaluation by amniocentesis, chromosomal microarray analysis should be offered when DWM is detected[5].

PROGNOSIS: Evidence regarding long term prognosis is conflicting. One study reports that all children with DWM had some degree of cognitive impairment, whereas other studies report a more favourable outcome. Overall, it appears that upto one-third of survivors with DWM develop normally. It also depends on presence or absence of associated malformations[5].

3. OSTEOGENESIS IMPERFECTA:

Osteogenesis imperfect (Brittle bone disease) is the most common heritable disorder of connective tissues. In 1833, Jean Lobstein described OI Type-1 as Lobstein's disease. The estimated incidence is approximately 1 per 20000 live births. Persons with OI caused by collagen mutations have 50% risk of having an affected child[6].

ETIOPATHOGENESIS: Individuals with OI have less or poorer quality of type-1 collagen than unaffected people, causing their bones to deform or fracture(or both). The nosology for OI was devised by Sillence et al. in 1979. However, DNA-based findings have subsequently provided critical information concerning the genetic transmission patterns, especially for the severe form by revealing that autosomal dominant(AD) inheritance explains most OI patients[6].

The International Nomenclature group for constitutional disorders ICHG of the skeleton proposed that the OI syndromes are classified as five different groups based on phenotype alone(OI type 1 to 5)[6].

TYPES	PHENOTYPE
Type-1	Mild, non-deforming
Type-2	Severe, seen as perinatal and lethal forms
Type-3	Moderately severe, progressively deforming.
Type-4	Moderate
Type-5	Moderate, calcification of the interosseous membrane seen.

Clinical Features:

It Can be divided into Skeletal and Extraskeletal. Skeletal features include excess/ atypical fractures, short stature, scoliosis and basilar skull deformities. Extraskeletal malformations include hearing loss, abnormal dentin leading to appearance of small deformed teeth.

Cardiovascular abnormalities and neurological manifestations include macrocephaly, hydrocephalus, cervical bone kyphosis[6].

Clinical diagnosis of OI is based on the signs and symptoms. There are no definitive tests for OI. Treatment includes Bisphosphonate therapy, IV pamidronate, IV Zoledronic acid. Genomic test useful for collagen analysis from fibroblasts and the prognosis is variable[6].

4. CHONDRODYSPLASIA PUNCTATA:

It is a rare disorder of peroxisomal metabolism with an estimated incidence of 1:100000. Chondrodysplasia punctata is a rarely occurring skeletal dysplasia characterized by stippled, punctuate calcifications around the joints and within cartilages. It is associated with the number of disorders including inborn errors of metabolism. Growth and development are severely restricted. Life expectancy is considerably reduced. Spinal stenosis is the most frequent sign of bone dysplasia. Spasticity, psychomotor retardation, growth retardation, seizures, thermoregulatory instability, feeding difficulty, recurrent otitis media and pneumonia have been reported in CDP cases[7].

Prenatal diagnosis of CDP is possible from the first trimester onwards by demonstration of peroxisomal dysfunction in cultured chorionic villous or amniotic fluid cells. Imaging of the brain and spinal cord may aid in prognosis and guide management decisions[7].

5. ECTOPIC LIVER TISSUE IN UMBILICAL CORD:

A solid mass in the umbilical cord is a very rare finding. A neonate with an ectopic liver tissue found in the umbilical cord is reported. Ectopic liver tissue has been identified in thorax, pericardium, esophagus, pylorus, gallbladder, testicles and retroperitoneum. The liver arised from an outgrowth of the most caudal part of the forgut in th fourth week. Because of the recent developments in prenatal ultrasonography, early detection of such lesions has become relatively easy. Abnormalities in the position or number of the liver parts are considered rare developmental anomalies. They are typically asymptomatic and incidentally detected[8].

The underlying basis for ectopic liver in cord is not known. It is possible that a part of normal liver gets entrapped outside the abdomen by umbilical ring closure or there may be aberrant differentiation of the endoderm, which is common to the allantois, urachal progenitor and liver[8].

PURPOSE:

- No complications attributed to UC mass.
- To describe a lesion that it is a rare within umbilical cord.
- To consider a previously unaccounted mechanism of origin[8]

CONCLUSION:

Fetal autopsy provide us an important information:

- Cause of death during perinatal & neonatal period.
- Patterns of congenital anomalies.
- Their incidences.
- Genetic counseling.
- Prenatal diagnosis in successive pregnancies.

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