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A Rare Case of Cyclopia & Hypotelorism

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Abstract: *Cyclopes are rare congenital abnormalities; a severe form of holoprosencephaly resulting in children being born with just one eye. It results from failure of the cerebral hemisphere to separate during fetal development which is incompatible with life. The incidence is 1 in 13,000 live births but present in 1 in 2500 pregnancies that end up as miscarriage. We report on the ultrasound (US) detection of holoprosencephaly with cyclopia at a gestational age of 30 weeks. The sonographic diagnosis was based on the intracranial finding of fused thalami with no visible midline structures and facial abnormalities, including cyclopia and proboscis. Ultrasonography was able to identify the cyclopia below the proboscis. These findings are characteristic of alobar holoprosencephaly. The use of 3D prenatal US made additional diagnostic images possible. With the informed consent of the patient, the pregnancy was terminated by prostaglandin induction after proper counseling. Chromosome study of the abortus revealed a normal karyotype (46, XY). Postmortem examination of the abortus confirmed the presence of cyclopia and a proboscis.*

Key words**:** *cyclopia, holoprosencephaly, proboscis*

I. Introduction:

Cyclopia is an extreme fetal malformation which includes a single palpebral fissure as well as proboscis associated with severe brain malformations. Its rate of occurrence is almost 1 in 100,000 births, including stillbirths identified as cyclopean [1]. The ethmoid complex, rooted in the prechordal mesoderm, plays an important role in the development of the midline and symmetry of the fetal face. Flaws in the development of the ethmoid complex lead to severe malformations of the whole, middle or upper parts of the face. In situations without ethmoid process, a structure called the proboscis, develops above the eyes. This structure is a hollow tube made of cartilage coated with respiratory epithelium. Histologic findings show the proboscis is a similar structure to the nose, which includes respiratory epithelium. This indicates that it results from a problem during development of the frontal region of the nose.

II. Case Presentation:

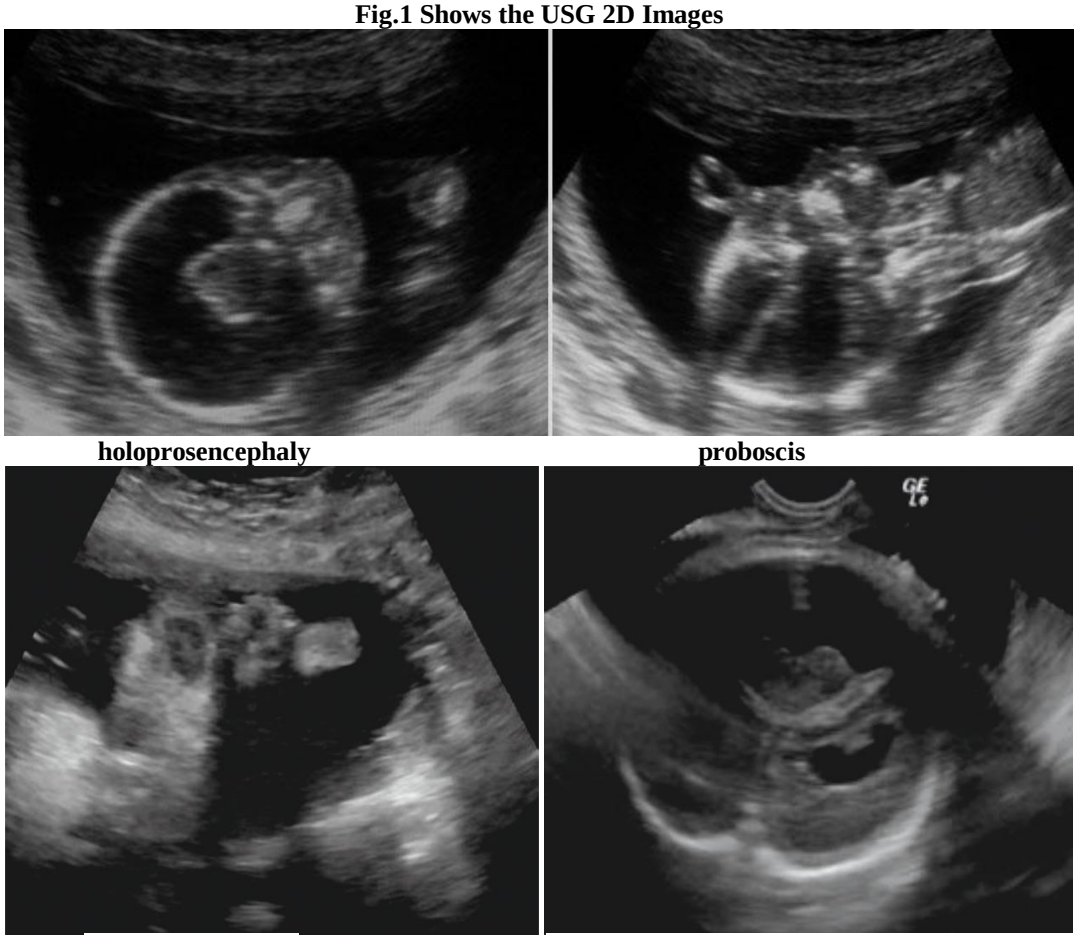
26 years old second gravida at 30 weeks of gestational age presented with disproportionate increase in abdominal girth and breathlessness on mild excretion since 3 days. She had regular Antenatal Checkup (ANC) starting from 6th week of Gestational Age (GA) at CHC. She was given folic acid and doxylamine during her 1st trimester. She was immunized with 2 doses of Inj. T.T and taking iron and calcium regularly. Towards the end of her 2nd trimester, she noticed gradual increase in her abdomen and breathlessness on with mild excretion. No history of hypertension, diabetes mellitus, renal disease and TB. No significant drug history; She had 3-4/28-30 days regular menstrual history. On examination, she had average body built, Pulse Rate-88/min, Weight -58 kg, Respiration rate -42/min; Pallor +, P. edema + bilateral, Heart and chest –NAD; Per abdomen: Height of uterus TS, Cephalic, Liquor increased, Fetal movement – Felt.

Investigation report said: Hb% - 10.2mg/dl, FBS -82mg.dl.VDRL-Non reactive, Blood group –'O'+ve; Urine R/M – NAD, USG at 16-18 weeks done; some where the diagnosis was missed. She was advised repeat sonography which revealed Single Intrauterine live fetus with cephalic presentation. AFI – 22 weeks, HC – 22 weeks,AC – 28 weeks, FL -31 weeks. The anomalies detected by Ultrasonography were as follows: abnormal development of the brain with an appendage protruding from the forehead being noted (Fig. 1). Fused thalami were seen, and no mid-line echo could be identified. The fetal face was evaluated by 3D US with a transabdominal transducer (VOLUSON E8, GE) 1-5-MHz probe and were able to identify cyclopia below the proboscis at 31st week of gestation These findings are characteristic of alobar holoprosencephaly.

To summarize the usg findings; a male fetus with

- Microcephaly.
- Hypotelorism (both eye balls were close to each other and placed at midline).
- Cyclopia (Single median bony orbit with a supraorbital fleshy proboscis above it).
- Nose absent at mid line and present over forehead as single elongated proboscis.
- Hexadactyly on right hand at radial side. (preaxial polydactyly on right hand)
- 4D sonography confirmed the findings.

Fig.1 Shows the USG 2D Images

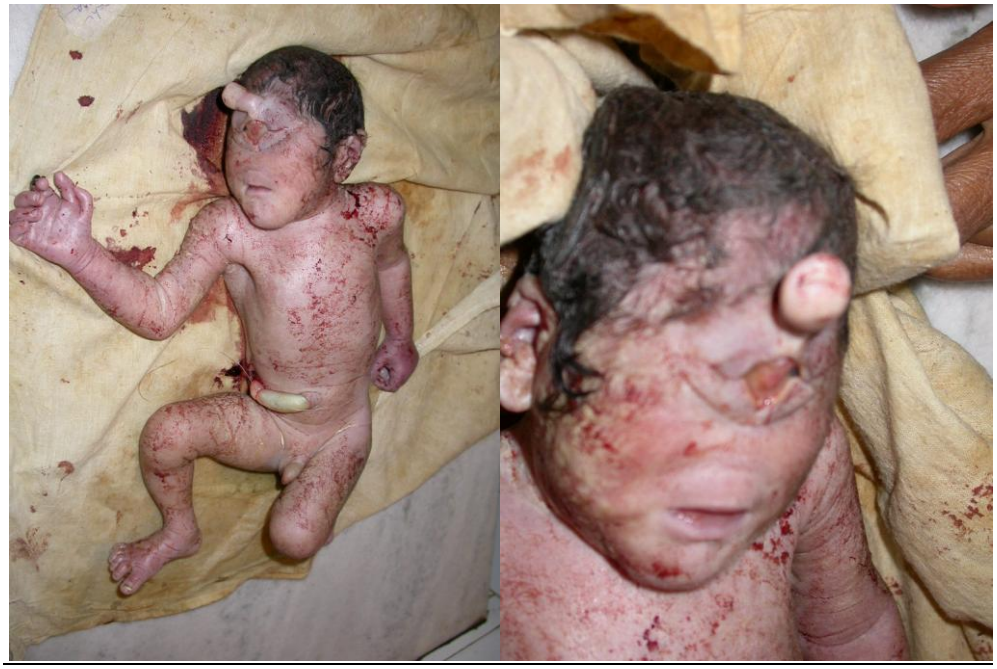


holoprosencephaly **proboscis**

proboscis, cyclopia **single ventricle, fused thalamic nuclei- coronal section**

Counseling regarding termination of pregnancy was done. The patient delivered a preterm male baby weighing 1.3 kg who had multiple abovementioned congenital malformations. Patient was stable after abortion and was discharged uneventfully. The abortus findings were consistent with Ultrasonography findings.

Fig. 2 shows the follow up Photographs:



III. Discussion

Holoprosencephaly embraces a variety of abnormalities of the brain and face resulting from incomplete cleavage of the primitive prosencephalon (forebrain). Microcephaly is usually present because of decreased cortical mass. A spectrum of midline facial anomalies may be seen due to defective embryonic development of the prechordal mesoderm [2].

3.1. History: Thomas Bartholin described in 1656 the clinical picture of a patient that may with certainty be classified as trisomy 13 [3]. Later clinical descriptions were reported by Feichtiger in 1943 and Otto Ullrich in 1951. In 1960, Klaus Patau made the first cytogenetic description in one patient [4].

3.2. Mechanism of pathogenesis: Trisomy 13 occurs when extra DNA from chromosome 13 appears in some or all of the body's cells. Trisomy 13- the presence of an extra (third) chromosome 13 in all of the cells. Trisomy 13 mosaicism- the presence of an extra chromosome 13 in some of the cells. Partial trisomy - the presence of a part of an extra chromosome 13 in the cells. The extra material interferes with normal development. Chromosome studies show trisomy 13, trisomy 13 mosaicism, or partial trisomy.

3.3. Symptoms: Infants with trisomy 13 are small for gestational age and microcephalic and have numerous malformations:-midline facial defects such as: cyclopia (single orbit), with microphthalmia or anophthalmia, cebocephaly (single nostril) and cleft lip and palate (60-70%); midline CNS anomalies such as: alobar holoprosencephaly- ears are often small and malformed -a punched out scalp lesion over the left or right occiput called "aplasia cutis congenita".-malformations of the limbs: postaxial polydactyly of the hands (75%), club feet, rocker bottom feet -abnormalities of the genitalia: hypospadias, criptorchidism are common in boys whereas girls generally have hypoplasia of the labia minora -congenital heart disease (>80%). [5, 6] -Severe mental retardation -decreased muscle tone.

Since fetuses with trisomy 13 have severe abnormalities, the sensitivity of prenatal sonography for detection of this aneuploidy is very high, most studies reporting sensitivities greater than 90% [7, 8, 9, 10]. Some of the most common findings included: central nervous system anomalies (58%), cardiac defects (48%), facial anomalies (48%), growth restriction (48%), holoprosencephaly (39%) and renal abnormalities (33%) [7].

On the other hand, a study performed via routine scanning reported a sensitivity of only 68.2% for the detection of 85cases of trisomy 13 [10] and the authors believed that when detailed scanning is undertaken, the performance would be better.

3.4. Paraclinic exams and tests: Gastrointestinal x-rays or ultrasound may show rotation of the internal organs. MRI or CT scans of the head may reveal a problem with the structure of the brain. The problem is called holoprosencephaly. It is the joining together of the two sides of the brain. Chromosome studies show trisomy 13, trisomy 13 mosaicism, or partial trisomy.

3.5. Differential diagnosis: The main differential diagnosis of Trisomy 13 is Meckel Grubber syndrome because of the similarity of the findings polydactyly, neural tube defects (posterior encephalocele) and enlarged echogenic kidneys [11].

3.6. Prognosis: The syndrome involves multiple abnormalities, many of which are not compatible with life. It accounts for approximately 1% of spontaneous first trimester miscarriages and has an extremely poor prognosis.

More than 80% of children with trisomy 13 die in the first month and less than 5-10% of them pass the first year of life. For the living babies with trisomy 13, complications begin almost immediately after delivery and may include: Deafness, Feeding problems, Heart failure, Seizures, Vision problems.

3.7. Recurrence: Recurrence of trisomy 13 is almost unknown, with zero being the most common percentage figure in formal series. However, there is a small risk of recurrence increasing with the maternal age, with the cutoff at age 31 and there are also women at increased risk for meiotic errors in general, compared with other women of the same age with an increased risk of spontaneous abortion or life births with trisomies [12]. So, in general, an empiric risk of approximately 1% is usually given to patients [13].

IV. Conclusion:

Cyclopia is alobar (severe form) holoprosencephaly which is a very rare form of congenital malformation. It can be diagnosed in early 2nd trimester of pregnancy by ultrasonography and amniocentesis with chromosome studies of the amniotic cells. Termination is the only option as this form of malformation is not compatible with life. Parents of infants with trisomy 13 caused by translocation should have genetic testing and counseling which may help them prevent recurrence.

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