

Very Early Diagnosis of Holoprosencephaly

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BACKGROUND

- Holoprosencephaly is a severe forebrain developmental abnormality associated with poor outcome.
- It is often associated with trisomy 13 (T13).
- There is increasing trend to perform ultrasound prior to cfDNA testing between 9-11 weeks' gestation.
- This provides an opportunity to detect major fetal abnormalities early, facilitating clinical management, diagnostic pathways and timely reproductive choices.

AIM

To present a case series of four very early prenatal diagnoses of holoprosencephaly.

METHODS

- We present four cases of very early diagnosis of holoprosencephaly made on ultrasound prior to cfDNA screening.
- All cases had gestational age based on crown rump length (CRL) < 45 mm.
- Fetal karyotype was investigated with chorionic villous sampling (CVS) or in the products of conception (POC) after pregnancy termination.
- 2D and 3D Images were obtained using a GE Healthcare Voluson™ E10.

| Case | Gestation age in weeks (based on CRL) | Ultrasound findings | Outcome | Karyotype |
|------|---------------------------------------|---|--------------------------|-----------|
| 1 | 9+1 | Crown rump length (CRL) 25.0 mm, fetal heart rate (FHR) 178 beats per minute (bpm) <i>Single anterior monoventricle, dilated fourth ventricle, bilateral polydactyly</i> | Termination of pregnancy | T13 (POC) |
| 2 | 10+0 | CRL 29.4 mm, FHR 189 bpm <i>Single anterior monoventricle, fused choroid plexuses</i> | Termination of pregnancy | T13 (CVS) |
| 3 | 9+6 | CRL 30.0 mm, FHR 173 bpm <i>Single anterior monoventricle, bilateral polydactyly, NT 2.9mm</i> | Termination of pregnancy | T18 (POC) |
| 4 | 10+1 | CRL 34.1 mm, FHR 194 bpm <i>Holoprosencephaly, midline facial cleft, cardiac anomaly (AVSD, tachycardia), subcutaneous oedema, small omphalocele</i> | Termination of pregnancy | T13 (POC) |

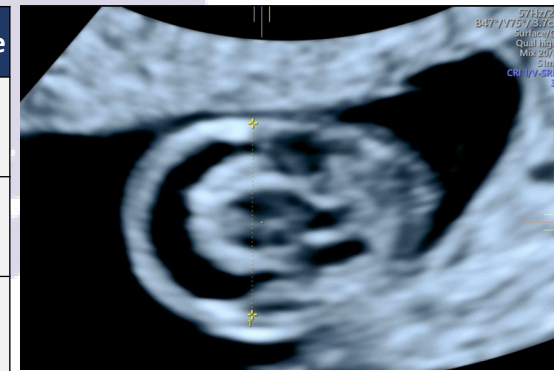


Figure 1 [Case 4]. 2D image demonstrating holoprosencephaly – incomplete cleavage of forebrain resulting in single anterior monoventricle.

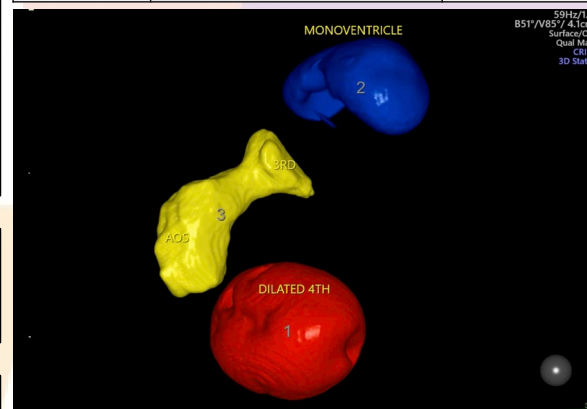


Figure 2 [Case 1]. Monoventricle and dilated 4th ventricle; 3D rendered image using Virtual Organ Computed-aided Analysis™ (VOCAL)

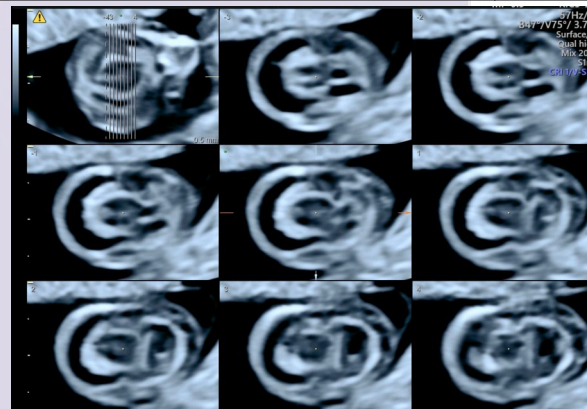
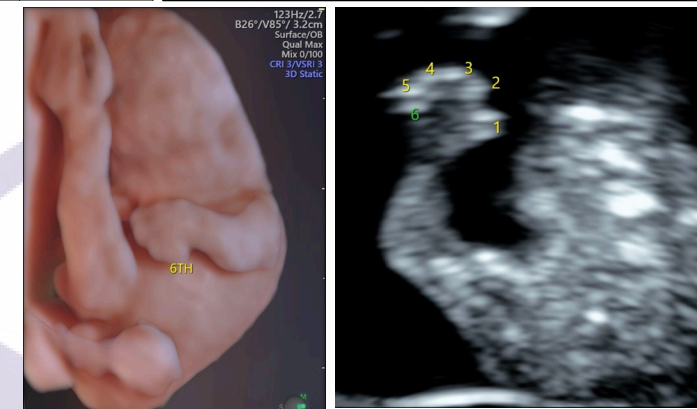


Figure 3 [Case 4]. Tomographic ultrasound imaging (TUI); axial slices demonstrating a monoventricle, fused thalami and dilated 4th ventricle.



Figures 4 and 5. 3D rendered image [left, Case 1] and 2D image [right, Case 3] demonstrating polydactyly.

DISCUSSION

- High-definition transvaginal imaging, novel modalities and training of providers may be crucial to identify major life-limiting abnormalities such as holoprosencephaly at an early gestational age
- This allows for prompt follow-up and pregnancy management
- Timely intervention is associated with better psychological outcomes for women and reduced medical complications
- Caution must be taken given the current lack of evidence for detection rate and cost-effectiveness