Prenatal Sonographic Findings in Trisomy 21

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Prenatal imaging: Menu of tests

**Ultrasound**

**Advantages**
- Non-invasive
- Not harmful to fetus, even in first trimester
- Cost-effective
- Main modality for screening

**Disadvantages**
- Operator-dependent
- Unable to detect many anomalies in fetus
Prenatal imaging: Menu of tests

**MRI and Maternal Radiography**

**MRI**
- Better characterization of anatomic details (e.g. brain)
- Better tissue contrast
- Large field of view
- Safety for fetus still not well characterized (avoid first trimester)

**Maternal Radiography**
- Used historically for limited survey of structural anomalies
- Currently investigated for use in additional studies (e.g. to evaluate fetal bone)

Shinmoto H, et. al. Radiographics 2000, 20
Estroff, JA Semin Roentgenol. 2004, 39:2
Prenatal Ultrasound

- Full fetal survey: ~18 weeks gestation (structural anomalies can be detected)
- Early ultrasound: 10-14 weeks gestation
  - Nuchal translucency measurements
Down Syndrome

- Common: overall incidence about 1 in 700
- Trisomy 21 (47XX or 47XY)
- Most Trisomy 21 caused by non-disjunction event in maternal meiosis
- Strong association with advancing maternal age

Karyotype with 3 copies of Chromosome 21

http://www.biotechnologyonline.gov.au
Down syndrome: Clinical features

- Characteristic facies, transverse palmer crease
- Newborn: excess nuchal skin
- Atrial and ventricular septal defects
- Small middle phalanx of 5th finger
- Duodenal atresia
Ultrasound detection of Down syndrome

**Structural anomalies**

*NB: found in less than 20% fetuses with Trisomy 21*

- Cardiac defects: e.g. VSD, ASD
- Duodenal atresia
- Ventriculomegaly

**Sonographic markers**

- Shortened proximal long bones (humerus/femur)
- Echogenic intracardiac focus
- Echogenic bowel
- Absent nasal bone
- Nuchal thickening
- Pyelectasis (renal pelvis dilation)

Adapted from Table 1: Estroff, JA Semin Roentgenol. 2004, 39:2
Our Patient 1: JM
11 wks 2 days

- 36 yo G1P0 female who presents for her initial visit to the OB
- 11 weeks and 2 days pregnant and otherwise healthy
- No known history of inherited genetic or chromosomal disorders
- Expresses a desire to have first trimester screening.
Our Patient JM: Early OB ultrasound
12 wks 4 days

- Transabdominal ultrasound
- Crown rump length corresponding to appropriate gestational age

- Significant abnormal finding: Thickened nuchal translucency (NT)
Our Patient JM fetus: Sagittal Ultrasound Demonstrating Thickened NT of 4.2 mm
The following images show another example of thickened nuchal translucency in a 12-week fetus with Trisomy 21 (right), as well as an example of the corresponding subcutaneous fluid collection which can be seen behind the neck (left).
Companion Images of Nuchal Translucency: image of embryo & 12-week sagittal ultrasound

Thickened Nuchal Translucency
Nuchal translucency

- Normal subcutaneous fluid-filled space found between the back of the fetal neck/upper trunk and overlying skin.
- Measurements must be made between 10 wks 3 days and 13 wks 6 days.
- With maternal age and biochemical markers, can detect Trisomy 21 to 90% with false positive rate of ~1%.
- Possible pathophysiology of enlarged NT: abnormalities in extracellular matrix, delayed development of lymphatics, cardiac abnormalities.

Malone FD and D’Alton ME, Obstetrics and Gynecology 2003, 102:5
Estroff JA, Semin Roentgenol. 2004, 39:2
Differential diagnosis for increased NT

- Trisomy 21
- Trisomy 13, trisomy 18
- Turner Syndrome (XO)
- Triploidy
- Structural heart disease
- Other anomalies
Our Patient JM: Plan for further studies to confirm risk of Down syndrome in fetus

• First-trimester screen positive for Down syndrome, risk of 1 in 5
• Too late for CVS diagnosis- Amniocentesis planned
• Full fetal ultrasound scheduled
Our Patient JM: Full fetal Ultrasound demonstrated 3 additional findings in fetus 15 wks 2 days

- Short femur
- Echogenic focus in heart
- Ventricular septal defect
Our Pt JM fetus: Femur length measurement-
Anatomic orientation

Landmarks:  
1 & 2: Inner thighs  
3: Posterior
Two fetal length measurements were made for our Patient JM fetus as shown in the following two slides.
Our Pt JM fetus: Femur length measurement 1 - Short for gestational age
Our Pt JM fetus: Femur length measurement 2- Short for gestational age
The second finding in our Patient JM fetus was an Echogenic Intracardic focus (EIF). In Trisomy 21, this is thought to be due to calcification of the papillary muscle.
Our Pt JM fetus: 4 chamber view of heart demonstrating echogenic intracardiac focus

Landmarks:
1: Spine
2: Ribs
3: Left Atrium
4: Left Ventricle
The following companion images show two other examples of echogenic intracardiac foci and a normal 4-chamber heart for comparison.
Companion images: Echogenic intracardiac foci and normal 4-chamber heart view

Landmarks:
1: Spine
2: Ribs
3: Left Atrium
4: Left Ventricle

http://www.fetal.com
http://www.centrus.com.br
The third finding in our Patient JM fetus was a suspected endocardial cushion defect. No normal 4-chamber views of the hearts could be obtained.
Our Pt JM fetus: 4-chamber views of the heart demonstrate a probable endocardial cushion defect.
The following companion image shows an example outlining a full endocardial cushion defect.
Companion image: Full endocardial cushion defect
Differential diagnosis for each finding

**Short Femur:** Nonlethal osteogenesis imperfecta, Diabetic embryopathy, trisomy 21, fetal hypoplasia-unusual facies syndrome, ethnic variation

**Echogenic intracardiac focus:** Fetal cardiac tumors, endocardial fibroelastosis, trisomy 21, trisomy 13

**Ventricular septal defect:** Trisomy 21, trisomy 13, trisomy 18, prematurity, other chromosomal abnormalities and syndromes

Our Patient JM: Summary of findings

- U/S 12 wks 4 d: Thickened NT in fetus
- U/S 15 wks 3 d: Short femur, echogenic intracardiac focus, probable endocardial cushion defect in fetus
- Amniocentesis performed and confirmed Trisomy 21 in fetus
- Pt. elected to have pregnancy termination
Our Patient 2: LG
16 weeks 6 days

- 40 yo who is 16 weeks 6 days pregnant and otherwise healthy
- Presents for full fetal ultrasound and amniocentesis
Our Patient LG: Full fetal ultrasound demonstrated 2 significant findings in fetus 16 wks 6 days

- Echogenic bowel
- Short femur
The following image demonstrates the echogenic bowel seen in our Pt LG fetus. Note the echogenicity of bowel compared to bone.
Our Pt LG fetus: Sagittal ultrasound
demonstrating Echogenic bowel
The second finding for our Pt LG fetus was a short femur, shown on the next slide.
Our Pt LG fetus: Short femur

Short femur
Differential Diagnosis for each finding

**Echogenic Bowel:** Normal variant, Trisomy 21, Meconium ileus (cystic fibrosis), CMV infection

**Short Femur:** Nonlethal osteogenesis imperfecta, Diabetic embryopathy, Trisomy 21, fetal hypoplasia-unusual facies syndrome, ethnic variation

Reeder and Felson’s Gamuts in Radiology, 3rd ed.
Our Patient LG: summary

- U/S 16 wks 6 d: Short femur, echogenic bowel in fetus
- Amniocentesis performed and confirmed Trisomy 21 in fetus
- Pt. elected to have pregnancy termination at 19 wks
Pathology report from our Pt LG fetus included findings of GI tract with calcifications and small ventricular septal defect.

Note that one hypothesis for echogenic bowel in Trisomy 21 includes calcified meconium due to hypomotility of bowel leading to increased water absorption, thickening, and subsequent calcification. Also note that ventricular septal defect was not seen in ultrasound performed earlier.
Main Summary

- Thickened nuchal translucency, (10-14 wks), when combined with maternal age and biochemical markers, can detect Trisomy 21 to 90%.
- Structural anomalies, e.g. endocardial cushion defects, found in less than 20% of fetuses with Trisomy 21, may be seen in the full fetal scan.
- Sonographic markers, e.g. shortened femur, echogenic intracardiac focus, and echogenic bowel can be normal variants but also seen frequently in Trisomy 21 fetuses.
References

- Estroff JA. Prenatal Diagnosis and Imaging of Genetic Syndromes, Seminars in Roentgenology 2004; 39: 323-335.
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