Ultrasonic Clues of Chromosome Disorders

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Trie Detection of a chromosomal anomaly at any stage of pregnancy is of great importance in obstetric management. About 6.5% of newborns have a fetal anomaly of some type, and in 3.2% of them, this anomaly is of major significance (1). Recognizable syndromes compose only 0.4% of these anomalies. Of these malformations, the greatest number are in the central nervous system, followed in frequency by the skeletal, cardiac and genitourinary systems. Less common problems are related to the gastrointestinal and respiratory tracts, with eye and ear problems being unusual. If one considers each of these various groups in relation to the chance for chromosomal problems, anomalies affecting the gastrointestinal tract are frequently associated with chromosomal problems (15%). They are followed by the cardiovascular system (14.3%), the central nervous system (7%), and the genitourinary system (1.8%). Particular findings with a strong association with chromosomal abnormalities are cystic hygroma (70%), nonimmune hydrops (14%), duodenal atresia (20%-30%), omphalocele (30%), pleural effusion (10%-15%) and diaphragmatic hernia (20%) (1,2). All these processes have recognizable ultrasonic features.

In this article the focus is on the sonographic features of the five common karyotypic abnormalities. These are trisomies 21 followed by trisomy 18, Turner syndrome (monosomy X), trisomy 13 and triploidy.

TRISOMY 21

Down syndrome is a common disorder occurring in about 1 in 660 births (3). Children with down syndrome are moderately retarded with an average IQ score of approximately 50, although milder or more severe degrees of intellectual handicap can also be observed (4). Children who survive the first year com-

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Table 1. Sonographic findings in Down syndrome

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Thickened nuchal skin fold</td>
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<td>Congenital heart disease (40%)</td>
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<tr>
<td>Ventricular and atrial septal defects</td>
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<tr>
<td>Atrioventricular canal</td>
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<tr>
<td>Cystic hygroma</td>
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<tr>
<td>Esophageal atresia</td>
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<td>Duodenal atresia</td>
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<tr>
<td>Diaphragmatic hernia</td>
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<tr>
<td>Clindactyly of fifth digits</td>
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<tr>
<td>Widely spaced first and second toes</td>
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<tr>
<td>Renal pyeoection</td>
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<td>Short femur and humerus</td>
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Echogenic small bowel has been associated with Down syndrome (16). Echogenic masses that are as echogenic as neighboring bone are intermixed with small bowel (17,18).

Although there is some debate, most authors agree that if the femoral length is less than 0.91 of that expected for the gestational age, or there is an abnormal biparital diameter: femoral length ratio, (12) there is an increased risk of Down syndrome (6,9). Whether this risk is (13) or 1 in 20 (14) is unclear. A shortened humeral length is slightly more sensitive (15).

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Table 2. Sonographic findings in trisomy 18
Table 2. Trisomii 18’in sonografik bulguları

- Third-trimester polyhydramnios
- Congenital heart disease
- Diaphragmatic hernia
- Renal malformations
- Omphalocele
- Umb malformations
  - Clubfoot deformity
  - Generalized arthrogryposis
  - Clenched hands
- Craniofacial malformations
  - Micrognathia
  - Dolichocephaly
  - Prominent occiput
  - Strawberry-shaped skull
- Esophageal atresia
- Intracranial malformations

Benacerraf et al (19) have summarized their work by developing a scoring index that, they claim, will identify 81% of fetuses with Down syndrome. They allot a score of 2 to the presence of a nuchal fold or a major structural anomaly such as cystic hygroma, duodenal atresia, or a cardiac malformation. A score of 1 given to a short femur, short humerus or pyelectasis. If a score of 2 or more is achieved, amniocentesis is recommended.

**TRISOMY 18 (EDWARD SYNDROME)**

Trisomy 18 is the second most common autosomal trisomy, occurring with a frequency of 1 in 3000 births (7). Affected children are severely retarded, fail to thrive, and have reduced survival, with 30% dying with 1 month and 90% dying within 1 year.

Sonographic abnormalities commonly associated with trisomy 18 are listed in Table 2. General features may include second-trimester fetal growth retardation (59%), polyhydramnios, and diminished fetal activity (20). Congenital heart disease is present in more than 90% of affected fetuses, with ventricular and atrial septal defects being most common (21). In one series of 16 fetuses with trisomy 18, there were six VSD, five complete atrioventricular septal defect (cushion defect) and four double outlet right ventricle (22).

Other anomalies in trisomy 18 amenable to sonographic diagnosis include diaphragmatic hernia, hydromephrosis horseshoe kidney, esophageal atresia with or without tracheoesophageal fistula, and omphalocele. Small omphaloceles containing only bowel are more commonly associated with a chromosomal etiology (23); however, fetal karyotyping is recommended regardless of omphalocele content and size.

Trisomy 18 can be associated with a variety of limb malformations, including clubfoot deformity, generalized arthrogryposis, and clenched hands with overlapping digits (24). Head shape changes, such as a diamond or strawberry shape, have reported (25).

Choroid plexus cysts are common in trisomy 18 (Figure 4). They should be distinguished from choroid plexus pseudocysts, which are oval hypoechoic structures located at the inferolateral aspects of the lateral ventricle at the edge of the choroid (26). Fitzsimmons et al (27) showed that approximately 70% fetuses with trisomy 18 have choroid plexus cysts. Benacerraf et al (28), and Gabrielli et al (29) make a decision that the risks of amniocentesis exceed the risk of trisomy 18 if the only abnormality is a choroid plexus cyst, for such cysts are a common normal variant found in between 3% and 18% of pregnancies (28,30). It has been suggested that large, complex, or bilateral choroid plexus cysts carry a greater risk for trisomy 18 than do small unilateral simple cysts (31).

A mildly enlarged cisterna magna (>10 mm) is also associated with trisomy 18 (3) in five patients reported by Thurmond et al (32) the discovery of an enlarged cisterna magna precipitated as dose look at the fetal heart, which was abnormal in two cases. In four of five fetuses there was IUGR with deft lip and rocker bottom feet.

**TURNER SYNDROME**

Most cases of Turner syndrome are caused by a missing X chromosome. The incidence of Turner syndrome among liveborn females is 1 in 2500 (7).
Figures. Posterior cervical edema (arrow) in an 11-week embryo.

Şekil 5. 11 haftalık embriyoda posterior servikal ödem (ok işaretli)

Sonographic findings in Turner syndrome may include cystic hygromas, nonimmune hydrops, renal anomalies, and cardiac malformations. Coarctation of the aorta accounts for nearly 70% of the cardiac defects associated with Turner syndrome (20%) and is usually not detectable during the second trimester (3).

Fetuses with Turner syndrome commonly exhibit cystic hygromas, nuchal edema (Figure 5), or pterygium colli. These abnormalities all result from jugular lymphatic obstruction. Cystic hygroma in which there are usually associated with Turner syndrome (70%) although a few are seen with Down syndrome (33). If the cystic hygroma is associated with nonimmune hydrops, then the process is uniformly fatal, usually during pregnancy. Renal malformations, such as pelvic kidney, horseshoe kidney, or single kidney, are also associated with Turner syndrome (7).

TRISOMY 13

Trisomy 13 is uncommon, an 1 in 4000 to 10,000 births, and is usually lethal. Early death is typical, with 50% of infants with trisomy 13 dying within 1 month and only 18% surviving more than 1 year (3).

Sonographic abnormalities associated with trisomy 13 are shown in Table 3. A typical in utero presentation is fetal holoprosencephaly. Holoprosencephaly is a malformation of brain development in which there is a single horseshoe-shaped ventricle replacing the lateral ventricles (7). There is absence of the third ventricle, with fusion of the thalamus. This anomaly is divided into three forms. Alobar holoprosencephaly is the most severe, with virtually no cortical mantle present. In semilobar holoprosencephaly, there is some malformed cortical tissue, with incomplete fusion of the thalamus. In lobar holoprosencephaly, the appearances are subtle, with fusion of the common ventricle posteriorly only and partial separation of the thalamus (34). All types of holoprosencephaly are associated with very poor mental development; with more severe retardation, the less cortex is present. Trisomy 13 is presented about 50% of the time when holoprosencephaly is found (35).

Craniofacial malformations are also common in trisomy 13 and may include micrognathia, sloping forehead, cleft lip and/or palate (60% incidence) and microphthalmia (3). Typically the cleft palate is a central triangular defect rather than the right or left lateral defect seen with familial cleft palate.

Other features of trisomy 13 include omphalocele (10%-20%), umbilical cord pseudocysts, renal cortical cysts, hydronephrosis, horseshoe kidney (3). Congenital heart disease, most often seen with double outlet right ventricle, hypoplastic left ventricle, ventriculoaortic defect, cushion defect and dextrocardia, is also a frequent finding with trisomy 13(22).

TRIPLOIDY

Many cases of missed abortion and blighted ovum are examples of triploidy. All 23 chromosomes are triplicated. This phenomenon most commonly results from fertilization of an egg by two different sperm, although diandry and digyny are responsible for some cases. Fetal malformation detected in fetuses that survive the first trimester are ventriculomegaly and cystic hygroma (36). Other fetal anomalies include multicystic renal dysplasia, hydronephrosis, ambiguous genitalia, omphalocele, microphthalmia, hydrocephalus and meningocoele. There are also impressive changes present in the placenta. A molar appearance may be seen in the enlarged placenta. Triploidy has an extremely poor diagnosis. Most often, the fetus dies during the course of pregnancy.

Table 3. Sonographic findings in trisomy 13

<table>
<thead>
<tr>
<th>Table 3. Trisomi 13’un sonografik bulgularıS</th>
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<tbody>
<tr>
<td>Third-trimester hydramnios</td>
</tr>
<tr>
<td>Central nervous system malformations</td>
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<tr>
<td>Holoprosencephaly</td>
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<tr>
<td>Agenesis of corpus callosum</td>
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<tr>
<td>Congenital heart disease</td>
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<tr>
<td>Extremity abnormalities</td>
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<tr>
<td>Postaxial Polydactyly</td>
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<tr>
<td>Camptodactyly</td>
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<tr>
<td>Overlapping digits</td>
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<tr>
<td>Craniofacial malformations</td>
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<tr>
<td>Micrognathia</td>
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<tr>
<td>Sloping forehead</td>
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<tr>
<td>Cleft lip and/or palate</td>
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<tr>
<td>renal malformations</td>
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<tr>
<td>Omphalocele</td>
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<tr>
<td>Intrauterine growth retardation</td>
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REFERENCES


