Ultrasonic Clues of Cromosome Disorders

FETAL KROMOZOMAL ANOMALİLERİN ULTRASONOGRAPH BULGULARİ

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Trie Detection ot a chromosoi te anomaly at any stage of pregnancy is of gieat importance in obstetric management. About 6.5% of newborns have a fetai 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, cardicac 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 anomalies 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 disorer occuring 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 commonly live to adulthouud, although mortality rates exceed those for normal persons at any given age (5). There is a definitive association with advanced maternal age; however. 80% of Down syndrome occurs in patients who are younger than age 35(3).

Table 1 is a summary of recognizable sonographic abonrmaiities in trisomy 21. There are two pathologic processes with obvious sonographic features associated with trisomy 21. Cardiac defect, particularly endocardial cushion defects of the heart, are relatively easily recognizable with ultrasound (Figure 1).

The second anomaly with obvious sonographic features is duodenal atresia in which there is obstruction of the duodenum causing the "double bubble sign" (Figure 2). About one third of fetuses with duodenal atresia are associated with Down syndrome (6). The obstructed stomach adopts a c-like shape and can be connected to the dilated duodenum by judicious transducer positioning.

Nonimmune hydrops is a common second-trimester presentation of many chromosome abnormalities, including trisomies 13, 18 and 21 as well as Turner syndrome. Overall, 14% to 18% hydropic fetuses will have an undei lying cytogenetic disorder (7). Fetal karyotyping should therefore be included as a part of teh diagnostic evaluation of this pregnancy compication.

Loose skin at the back of the neck is a feature of newborns with Down syndrome. Nucha! thickening ts considered present if *"-e* si- n at the back of the neck is over 6 rum thick on an . • ;il view of the skull taken through the cerebellum (Figure this standard is only valid if the pregnancy is between 15 and 20 weeks (8). Accuracy in the detection of Down syndrome using the sign is at best 39% (9).

More recently, Benacerraf and colleagues reported an association between mildly dilated renal pelves and down syndrome (10) 25% fetuses with Down syndrome had pyelectasis as compared with only 2.8% of normal subjects. Corteville ef al (11) confirmed an increased frequency of trisomy 21 among fetuses with pyelectasis but noted that other sonographic abnorma-

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Table 1, Sonographic findings in Down syndrome
Tablo 1. Down sendromunun sonografik bulgulari

Thickened nuchal skin fold
Congenital heart disease (40%)
  Ventricular and atrial septal defects
  Atrioventricular canal
Cystic hygroma
Esophageal atresia
Duodenal atresia
Diaphragmatic hernia
Cllnodactyly of fifth digits
Widely spaced first and second toes
Renal pyeiectasls
Short femur and humerus

Figure 1. Four -chamber view of heart m a fetus with Down syndrome and atrioventricular canal

Şekil 1, Down sendromlu fetusun kalbinin görüntüsü ve antrio-ventriküler kanal

lities were also commonly observed. The sensitivity (4%) and predictive value (1 in 340) of isolated pyeiectasls would not appear to warrant invasive testing.

Although there is some debate, most authors agree that if the femoral length is less that 0.91 of that expected for the gestational age, or there is an abnormal blparletal 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).

Echogenic small bowel has been associated with Down syndrome (16). Echogenic masses that are as echonegic as neighboring bone are intermixed with small bowel (17,18).

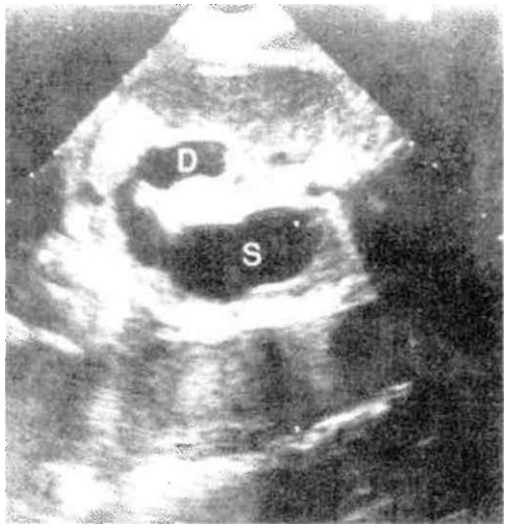


Figure 2. **'• vs.**-erse axial view tnrougn fetai atxjomen snowing dilatée stomach ,S) ana proximal duodenum (D). secondary to duodenal atresia

Şekil 2. Fetal abdomenin transvers axial görüntüsü, duedonal aire; ye sekonder olara* dilate mide ;S) ve proksımal duodenum

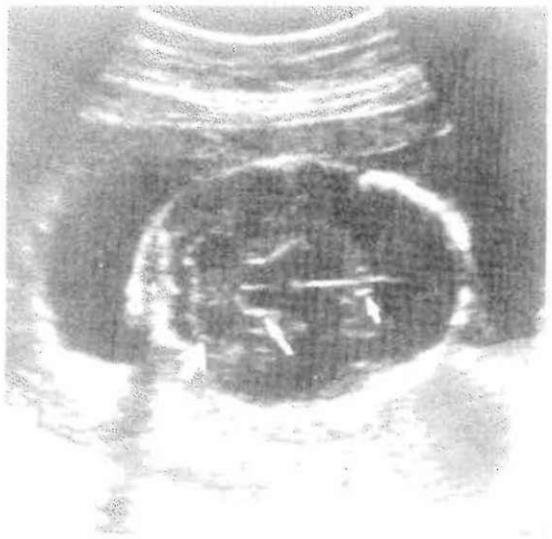


Figure 3. Correct plane for measuring nucna, win '->a thi-ckness. Calipers (+) are placed from the outer skull taoie to the outer skin surface

Şekil 3. Ense ödemini ölçmek için doğru pıan İşaretler skullın dışından, deri seviyesinin dışına yerleştirilmiştir

Table 2. Sonographic findings in trisomy 18
Table 2. Trisomi 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

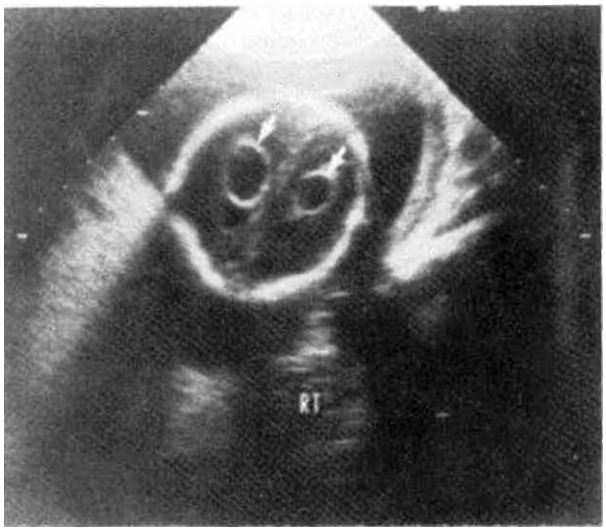


Figure 4. Choroid plexus cysts (arrows)
Şekil 4. Korold plexus kisti (oklar)

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 precence 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.

TRISC MY 18 (EDWARD SYNDROME)

Trisomy 18 is the second most common autosomal trisomy, occuring 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, hydronephrosis 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 recommented regardless of omphalocele content and size.

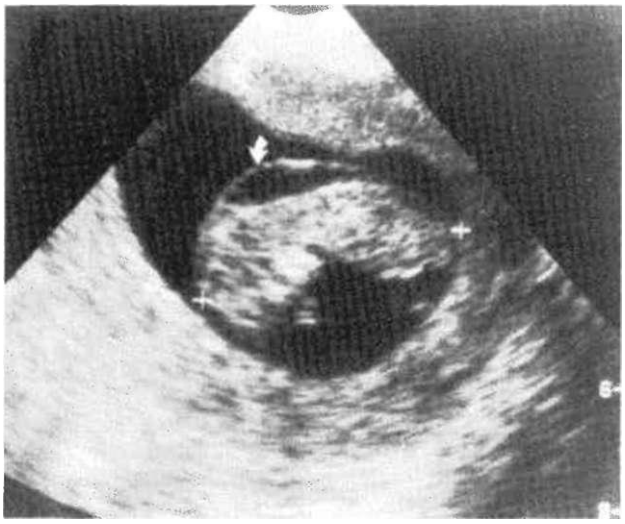
Trisomy 18 can be associated with a variety of limb malformations, including clubfoot deformity, generalized arthrogryposis, and clenched hands with overlapping digits (24). Head shape changes, such as a diamond or strawberry shape, have reported (25).

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 amniocen tesis 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. 3 The inddence of Turner syndrome among liveborn females Is 1 in 2500 (7).



Figures. Posterior cervival edema (arrow) in an 11-week embryo.

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

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 exlbit 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 typicam in utero presentation is fetal holoprosencephaly. Holoprosencephaly Is a malformation of brain development In which there is a single horseshoe-shaped ventlcle 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 peresent. In semllobar 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 migrognathia, sloping forehead, cleft lip and/or palate (60% incidense) and microophtalmia (3). Typically the cleft palate is a central triangular defect rather than the right or left or bilateral 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, ventriculoseptal defect, cushion defect and dextrocardia, is also a frequent finding with trisom 13(22).

TRÎPLOiDY

Many cases of missed abortion and blighted ovum are examples of triploidy. All 23 cromosomes 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, microophtalmia, hydrocephalus and meningocele. There are also impressive changes present in the placenta. A molar apperance may be seen In the enlarged plasenta. Triploidy has an extremely poor diagnosis. Most often, the fetus dies during the course of pregnancy.

Table 3. Sonographic findings in trisomy 13
Tablo 3. Trlsomi 13'un sonografik bulgulariS

Third-trimester hydramnios
Central nervous system malformations
Holoprosencephaly
Agenesis of corpus callosum
Congenital heart disease
Extremity abnormalities
Postaxial Polydactyly
Camptodactyly
Overlapping digits
Craniofacial malformations
Micrognathia
Sloping forehead
Cleft lip and/or palate
renal malformations
Omphalocele
Intrauterine growth retardation

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