Chapter 10

FETAL SKELETAL SYSTEM ANOMALIES

Şadan TUTUŞ[1]

Skeletal system anomalies are a group of diseases that affect the healthy growth and development of both bone and cartilage and cause morphological disorders. When normal embryological development is somehow disrupted, the severity of the disorder and anomaly that will occur according to the current gestational week will also be different. The sooner the damage starts, the more complex the anomaly will be[1]. Anomalies may develop as a result of a chromosomal disorder, a single gene mutation, or the mother's exposure to teratogenic substances used during pregnancy. Fetal skeletal system anomalies are a very large group of diseases and their number is increasing with each new update.

In this article, it will be first focus on the embryology and development of the skeletal system, and then will be explain how to approach fetuses with skeletal dysplasia. I will try to explain by giving some examples that we frequently encounter in daily obstetric ultrasonography practice about extremity and skeletal system dysplasia anomalies from my personal archive.

EMBRYOLOGY

In the embryonic period, ossification occurs in two forms as enchondral and intramemranous ossification. In enchondral ossification; trunk and extremity bones develop from the hyaline cartilage model, while flat bones develop directly from the mesenchyme in intramembranous ossification. Upper extremity buds begin to form a few days before the lower extremity buds at 5-6 weeks of gestation during the embryonic period. Fetal ossification begins in the clavicle at the 8th gestational week. Frontal bones and long bones are ossified at 11th gestational week, metacarpal and metatarsal bones are ossified between 12th and 16th gestational weeks and can be visualized ultrasonographically. Carpal bones are ossified after birth[2].

Damages occurring during the organogenesis period, in which the tissues rapidly differentiate from day to day, become irreversible and result in major anomalies. Teratogens, trauma and genetic mutations that the mother is exposed to are also factors in the development of anomalies.

[1] Şadan Tutuş, MD Kayseri City Hospital Radiology Clinic, sadantutus35@yahoo.com.tr

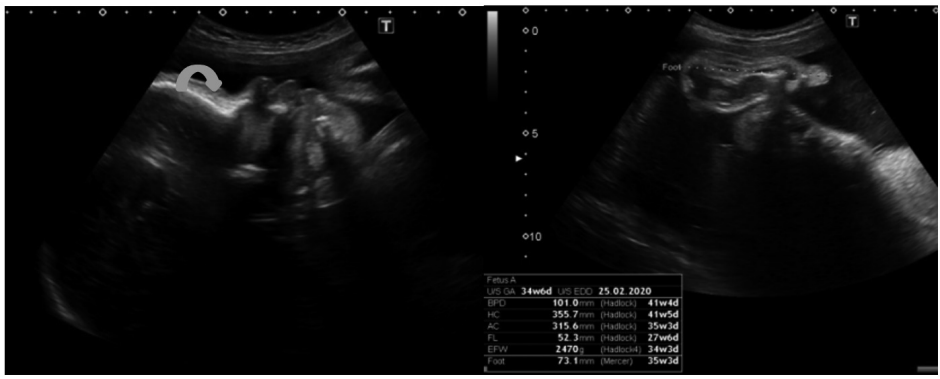

Figure 14: (A) Macrocephaly incompatible with the last menstrual period, frontal bossing (arrow) and (B) according to fetal measurements, while the foot is compatible with the last menstrual period, the femur length is observed short (risomelia Short Rib Polydactyly Syndrome

It is an extremely rare skeletal dysplasia characterized by small thorax secondary to short ribs. There are four subtypes. It is accompanied by micromelia, polydactyly, congenital heart disease, cleft lip, polycystic kidney and brain malformations. It is incompatible with life.

Camptomelic Dysplasia

Its incidence is 1 in 20,000 live births (Camptos: means bowing). Various degrees of abnormal bowing are observed in the femur, tibia and humerus. Thorax is narrow, scapulae are hypoplasic. There is a disproportionately small face versus a large head. It has micrognathia. 30% cardiac defects and 30% hydronephrosis accompany. Polyhydramnios is common. Male fetuses have gender development problems. Mortality occurs due to pulmonary problems secondary to thoracic hypoplasia[38].

REFERENCES

1. Coady AM, Bower S. *Twinning's Textbook of Fetal Abnormalities*. Third ed2015
2. Mahony BS, Filly RA. High-resolution sonographic assessment of the fetal extremities. *J Ultrasound Med 1984;3*:489 - 498. doi.org/10.7863/jum.1984.3.11.489
3. Bonafe L, Cormier-Daire V, Hall C et al. Nosology and classification of genetic skeletal disorders: 2015 revision. *Am J Med Genet A. 2015;167A(12)*:2869-2892. doi.org/10.1002/ajmg.a.37365
4. Froster-Iskenius, U. G., & Baird, P. A. Limb reduction defects in over one million consecutive livebirths. *Teratology*, *1989;39(2),* 127–135. doi.org/10.1002/tera.1420390205
5. Goncalves LF, De Luca GR, Vitorello DA, et al. Prenatal diagnosis of bilateral proximal femoral hypoplasia. *Ultrasound Obstet Gynecol. 1996;8*:127-130. doi.org/10.1046/

j.1469-0705.1996.08020127.x
6. Daentl DL, Smith DW, Scott CI, et al. Femoral hypoplasia–unusual facies syndrome. *JPediatr1975; 86*: 107–111.
7. Paladini D, Maruotti GM, Sglavo G et al Diagnosis of femoral hypoplasia-unusual facies syndrome in the fetus.*Ultrasound Obstet Gynecol. 2007;30(3)*:354-358. doi.org/10.1002/uog.4080
8. Pakkasjarvi N, Koskimies E, Ritvanen A, et al. Characteristics and associated anomalies in radial ray deficiencies in Finland--a population- based study. *Am J Med Genet Part A 2013;161A*:261-267. doi.org/10.1002/ajmg.a.35707
9. Bromley B, Shipp TD, Benacerraf B. Isolated polydactyly: prenatal diagnosis and perinatal outcome. *Prenat Diagn. 2000;20(11)*:905-908. doi.org/10.1002/1097-0223(200011)20:11<905::AID-PD934>3.0.CO;2-N
10. Seok HH, Park JU, Kwon ST. New classification of polydactyly of the foot on the basis of syndactylism, axis deviation, and metatarsal extent of extra digit. *Arc Plast Surg. 2013;40*:232-237. doi: 10.5999/aps.2013.40.3.232
11. Hall B: Mongolism in newborn infants. Clin Pediatr 5:4, 1966.
12. Hatipoğlu N, Kurtoğlu S, Büyükayhan D, et al. Hypothalamo-pituitary insufficiency associated with ectrodactyly-ectodermal dysplasia-clefting syndrome. *J Clin Res Pediatr Endocrinol 2009;1(5)*:252-255. doi: 10.4274/jcrpe.v1i5.252
13. Dobbs MB, Purcell DB, Nunley R, et al. Early results of a new method of treatment for idiopathic congenital vertical talus. *J Bone Joint Surg [Am] 2006; 88(6)*: 1192-1200. doi: 10.2106/JBJS.E.00402
14. Z. Miedzybrodzka, Congenital talipes equinovarus (clubfoot): a disorder of the foot but not the hand, *J. Anat 2003; 202 (1)*:37–42. doi.org/10.1046/j.1469-7580.2003.00147.x
15. Magriples U. Prenatal Diagnosis of Talipes Equinovarus (Clubfoot). Post TW eUW, MA: UpToDate Inc. http://www.uptodate.com (Accessed on October 12, 2018).
16. B. Viaris de le Segno, N. Gruchy, C. Bronfen, et al., Prenatal diagnosis of clubfoot: chromosomal abnormalities associated with fetal defects and outcome in a tertiary center, *Journal of Clinical Ultrasound: JCU 2016*;44 (2):100–105. doi.org/10.1002/jcu.22275
17. Takagi T, Seki A, Takayama S, et al. Current Concepts in Radial Clubhand *Open Orthop J. 2017; 11*: 369–377. doi: 10.2174/1874325001711010369
18. McDaniel LD, Prueitt R, Probst LC et al. Novel assay for Roberts syndrome assigns variable phenotypes to one complementation group. *Am J Med Genet 2000; 93*:223-229. doi.org/10.1002/1096-8628(20000731)93:3<223::AID-AJMG13>3.0.CO;2-J
19. Sabry MA, Farag TI. Hand anomalies in fetal-hydantoin syndrome: from nail/phalangeal hypoplasia to unilateral acheiria. *Am. J. Med. Genet. 1996;62 (4)*: 410-412. DOI: 10.1002/ajmg.1320620403
20. Witters I, Moerman P, Fryns JP. Fetal akinesia deformation sequence: a study of 30 consecutive in utero diagnoses. *Am J Med Genet. 2002 ;113*:23-28. doi.org/10.1002/ajmg.10698
21. Higginbottom MC, Jones KL, Hall BD, et al. The amniotic band disruption complex: timing of amniotic rupture and variable spectra of consequent defects. *J Pediatr. 1979;95(4)*:544-549. doi.org/10.1016/S0022-3476(79)80759-3
22. Bodamer OAF, Popek EJ, Bacino C. Atypical presentation of amniotic band sequence. *Am J Med Genet. 2001;100(2)*:100-102. doi.org/10.1002/1096-8628(20010422)100:2<100::AID-AJMG1234>3.0.CO;2-E
23. Warman ML, Cormier-Daire V, Hall C et al Nosology and classification of genetic

skeletal disorders: 2010 revision. *Am J Med Genet A* ;*155*:943–968. doi.org/10.1002/ajmg.a.33909
24. Orioli IM, Castilla EE, Barbosa-Netos. The birth prevalance rates for the skeletal dysplasias. *J Med Genet 1986*; *23*: 328–32. dx.doi.org/10.1136/jmg.23.4.328
25. Parilla BV, Leeth EA, KambichMP et al. Antenatal detection of skeletal dysplasias. *J Ultrasound Med 2003; 22*:255–258. doi.org/10.7863/jum.2003.22.3.255
26. Romero R, Athanassiadis D, Jeanty P. Fetal skeletal Anomalies. *The Radiologic Clinics of North America 1990*; 28:75.
27. Goncalves LF, Espinoza J, Mazor M, et al. Newer imaging modalities in the prenatal diagnosis of skeletal dysplasias. *Ultrasound Obstet Gynecol. 2004;24(2):*115–120. doi.org/10.1002/uog.1712
28. Nelson DB, Dashe JS, McIntire DD et al Fetal skeletal dysplasias: sonographic indices associated with adverse outcomes. *J Ultrasound Med 2014; 33*:1085–1090. doi.org/10.7863/ultra.33.6.1085
29. Bonafe L, Cormier-Daire V, Hall C, et al. Nosology and classification of genetic skeletal disorders. *Am J Med Genet Part A 2015;9999A*:1–24. doi.org/10.1002/ajmg.a.37365
30. Schild RL, Hunt GH, Moore J et al Antenatal sonographic diagnosis of thanatophoric dysplasia: a report of three cases and a review of the literature with special emphasis on the differential diagnosis. *Ultrasound Obstet Gynecol 1996; 8*:62–67. doi.org/10.1046/j.1469-0705.1996.08010062.x
31. Rasmussen SA, Bieber FR, Benacerraf BR, et al. Epidemiology of osteochondrodysplasias: changing trends due to advances in prenatal diagnosis. *Am J Med Genet 1996;61(1):*49-58. Doi.org/10.1002/(SICI)1096-8628(19960102)61:1<49::AID-AJMG10>3.0.CO;2-W
32. Özeren S., Yüksel A., Tükel T. Prenatal sonographic diagnosis of type I achondrogenesis with a large cystic hygroma. *Ultrasound in Obstetrics & Gynecology. 1999;13(1)*:75–76. Doi.org/10.1046/j.1469-0705.1999.13010075.x
33. Lee H.S., Doh J.W., Kim C.J., et al. Achondrogenesis type II (Langer-Saldino achondrogenesis): a case report. Journal of Korean Medical Science. *2000;15(5)*:604–608.
34. Lyn S Chitty and David Griffin. Prenatal diagnosis of skeletal dysplasias. *Fetal and Maternal Medicine 2008;19(2):* 135-164. DOI:10.1017/S096553950800212X
35. Mornet E. Hypophosphatasia. Orphanet J Rare Dis 2007; 2: 40. doi: 10.1186/1750-1172-2-40.
36. Lemyre E, Azouz EM, Teebi AS et al. Bone dysplasia series. Achondroplasia, hypochondroplasia and thanatophoric dysplasia: review and update Can Assoc Radiol J. 1999 Jun;50(3):185-97.
37. Elçioglu, N. H., & Hall, C. M. Diagnostic dilemmas in the short rib-polydactyly syndrome group. *American Journal of Medical Genetics, 2002; 111(4)*, 392–400. doi.org/10.1002/ajmg.10562
38. Mansour S,Offiah AC, McDowall S, et al. The phenotype of survivors of campomelic dysplasia. J MedGenet 2002; **39**: 597–602. doi.org/10.1136/jmg.39.8.597.