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A Case of Prenatally Diagnosed Arthrogryposis Multiplex Congenita

Prenatal Tanı Alan Artrogripozis Multipleks Konjenita Olgusu

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ABSTRACT

Arthrogryposis multiplex congenita (AMC) is a clinical entity characterized by reduced fetal movements (fetal akinesia), fetal growth restriction (FGR), joint contractures (arthrogryposis), facial anomalies, lung developmental delay (pulmonary hypoplasia), and other developmental abnormalities. It is accepted that this condition is a description of a group of abnormalities resulting from reduced fetal movements rather than a true diagnosis or a specific syndrome. In many arthrogryposis cases, the etiology has not yet been determined. Prenatal diagnosis of AMC is critical for providing adequate counseling to families. When a fetus with multiple congenital contractures is detected on prenatal ultrasound (US), management of the pregnant woman should be undertaken by a multidisciplinary team. In this report, a case of AMC detected in the prenatal period, together with US and fetal magnetic resonance imaging (MRI) findings, was presented.
Keywords: Fetal akinesia; arthrogryposis multiplex congenita; prenatal ultrasound; fetal magnetic resonance imaging.

ÖZ

Artrogripozis multipleks konjenita (AMK), fetal hareketlerde azalma (fetal akinezi), fetal büyüme kısıtlaması (FBK), çoklu eklem kontraktürleri (artrogripozis), yüz anomalileri, akciğerlerde gelişimsel bozukluklar (pulmoner hipoplazi) ve diğer gelişimsel anormalliklerle karakterize bir klinik tablodur. Bu durumun gerçek bir tanı veya spesifik bir sendrom olmadığı, daha ziyade fetal hareketlerde azalma sonucu oluşan bir grup anormalliğin tanımı olduğu genel olarak kabul edilmektedir. Birçok artrogripozis vakasında etiyoloji henüz belirlenememiştir. Ailelere yeterli danışmanlık sağlamak için AMC'nin prenatal tanısı kritik öneme sahiptir. Prenatal ultrasonda (US) multipl konjenital kontraktürleri olan bir fetüs tespit edildiğinde, gebe kadının yönetimi multidisipliner bir ekip tarafından yapılmalıdır. Bu yazıda, prenatal dönemde tespit edilen bir AMK vakası, US ve fetal manyetik rezonans görüntüleme (MRG) bulgularıyla birlikte sunulmuştur.
Anahtar kelimeler: Fetal akinezi; artrogripozis multipleks konjenita; doğum öncesi ultrason; fetal manyetik rezonans görüntüleme.

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INTRODUCTION

For normal fetal functional development, intrauterine fetal movements are necessary (1). Normal fetal breathing, swallowing, facial muscle movements, and amniotic fluid volume are necessary for normal lung development, extremities, and facial configuration. The absence or reduction of these movements is responsible for lung hypoplasia, polyhydramnios, limb contractures, and facial abnormalities (2).

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The severity and prognosis of fetal joint contractures may vary depending on the degree of involvement and underlying cause (3,4). Of these, talipes equinovarus (TEV) is the most common and mildest. Adduction, supination, and varus deformities were observed in the ankle. Unilateral or bilateral, TEV is usually an isolated anomaly and has a good outcome with orthopedic treatment (5,6). The second most common and severe form, arthrogryposis multiplex congenita (AMC), is observed with joint contractures in more than one body region. The lower and upper extremities are most commonly involved, while contractures are less frequently observed only in the upper extremities. The least common but most severe form is the fetal akinesia deformity sequence (FADS), also known as the Pena-Shokeir syndrome. This is the lethal form of AMC, often accompanied by lung hypoplasia, polyhydramnios, flattened facial features, and fetal growth restriction (7).

It is accepted that this condition describes a group of abnormalities resulting from reduced fetal movements rather than a true diagnosis or a specific syndrome (8). This report aimed to present a case of AMC detected during the second-trimester screening ultrasound (US), together with ultrasound and fetal magnetic resonance imaging (MRI) findings.

CASE REPORT

A 27-year-old primigravida woman, 23 +4 gestational weeks, was referred to our clinic for a second-trimester screening US. She had no known disease in her history, no consanguinity with her husband, and antenatal screening test results were normal. In the US, mild ventriculomegaly in the cranium (atrial diameter approximately 11 mm), increased thickness in the nuchal fold (approximately 0.77 mm), open mouth on the fetal face, flexion contractures in the bilateral elbow joints (Figure 1a), extension contractures in the bilateral knee joints (Figure 1b), and dorsiflexion contractures in the ankle joints (Figure 1c) were observed.

No fetal swallowing or movement of the fetal extremities was observed during the examination. The amniotic fluid index (AFI) was 26 cm (polyhydramnios). However, a gastric pouch was also observed. No micrognathia or thoracic hypoplasia was observed. Due to the multiple anomalies observed in the US, fetal MRI was performed. Fetal MRI confirmed the US findings, but did not provide any additional findings (Figure 2).

Perinatology evaluation, genetic examination, and family counseling were recommended for the case with suspected AMC.

After perinatology evaluation, the patient was diagnosed with AMC and did not want to continue the pregnancy, and the pregnancy was terminated (Figure 3).

No genetic mutation was detected in the L1CAM whole gene sequence analysis performed on fetal material. Informed consent was taken from the patient's relatives.

DISCUSSION

Decreased intrauterine fetal movement is thought to lead to AMC (9,10). An alternative hypothesis is that atypical tissue modeling causes muscle hypercontractility during development, leading to restricted movement and joint

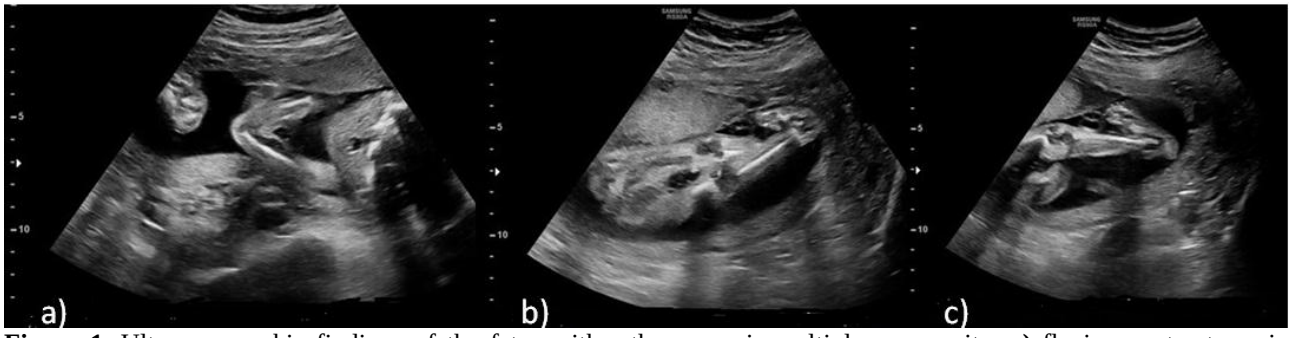


Figure 1. Ultrasonographic findings of the fetus with arthrogryposis multiplex congenita; **a)** flexion contractures in bilateral elbow joints, **b)** extension contractures in knee joints, and **c)** dorsiflexion contractures in ankle joints



Figure 2. Findings of fetal magnetic resonance imaging; **a)** Axial 2D FIESTA weighted image shows flexion contractures in bilateral elbow joints, **b)** Coronal 2D FIESTA weighted image shows extension contractures in bilateral knee joints and dorsiflexion contractures in ankle joints (white arrow), open mouth (white open arrow) and polyhydramnios, **c)** Axial T2 weighted image shows normal gastric pouch, **d)** Axial T2 weighted image shows normal thorax

contraction (11). Arthrogryposis may be accompanied by a number of syndromes (Pena-Shokeir syndrome, multiple pterygium syndrome, Fowler syndrome, and Freeman-Sheldon syndrome). It has also been observed as a clinical feature in more than 400 specific disorders, such as genetic disorders affecting fetal neurological and musculoskeletal development (12). Although chromosomal abnormalities, mitochondrial diseases, and more than 320 single-gene diseases have been described as etiologies in many arthrogryposis cases in the literature, the exact etiology has not yet been determined (13). As reported in the literature, no specific disorder was detected in our case to explain the exact cause.

Prenatal first and second trimester US, fetal MRI, and genetic tests are used for diagnosis.

Arthrogryposis multiplex congenita can be detected using US in the first trimester (14,15). Decreased movements, increased nuchal translucency, cystic hygroma, and hydrops fetalis are the first-trimester findings (16). However, it is usually diagnosed in the early second trimester (17). The majority of prenatally diagnosed AMC cases are detected by US in the second or third trimester. Common findings include decreased fetal movement, clenched hands, joint contractures, abnormal extension or flexion of the extremities, and polyhydramnios. Other findings include fetal growth retardation (FGR), brain malformations, cleft lip palate, retrognathia/micrognathia, cardiomegaly, diaphragmatic hernia, absent fetal gastric pouch, gastroschisis, short umbilical cord, fetal hydrops, and fetal musculoskeletal disorders. In some cases, intrauterine fetal death may occur (3). We performed a second-trimester screening US in our case. Mild ventriculomegaly, increased nuchal fold thickness, open mouth on the face, flexion contractures in the bilateral elbow joints, extension contractures in the bilateral knee joints, dorsiflexion contractures in the ankle joints, and polyhydramnios. We also did not observe fetal swallowing or movement of the fetal extremities during the examination.

Fetal MRI has been used as an adjunct to US imaging since 1983 (18). Magnetic resonance imaging is particularly useful for the evaluation of brain malformations and thoracic hypoplasia (19). However, fetal MRI is not as widely available as US, is more expensive, and requires specialized expertise for interpretation, limiting its use in prenatal diagnosis of AMC (3). In our case, we performed fetal MRI. Fetal MRI confirmed the US findings, but did not provide any additional findings.

Genetic testing is one of the most important steps in the prenatal diagnosis of AMC and decision-making for families. For this purpose, invasive tests such as chorionic villus sampling or amniocentesis should be offered (3).

Genetic analysis is not always performed before birth; sometimes, it can be postponed until after birth at the request of the families (3). Whole-exome sequencing (WES) and whole-genome sequencing (WGS) are the most comprehensive testing options (3). In our case, L1CAM WGS was performed on fetal material after the termination of pregnancy. However, no genetic mutations have been identified.

Despite advanced imaging, AMC remains a complex prenatal diagnosis without a single etiology in many instances. When AMC is detected on prenatal US, families should receive comprehensive support from a multidisciplinary team. This team typically includes specialists in perinatology, radiology, genetics, neonatology, pediatric neurology, pediatric orthopedics, and mental health counseling. Clear communication regarding findings, prognosis, and options is essential during this process (3). We recommend perinatology evaluation, genetic examination, and family counseling for this case.



Figure 3. Image of the fetus after termination

CONCLUSION

Prenatal diagnosis of AMC is critical for providing adequate counseling to families. Prenatal first and second trimester US, fetal MRI, and genetic testing are used for diagnosis. When a fetus with multiple congenital contractures is detected on prenatal US, management of the pregnant woman should be undertaken by a multidisciplinary team.

Informed Consent: Written informed consent was obtained from the patient for publication and accompanying images.

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