İSTANBUL ÜNİVERSİTESİ YAYINEVİ

CASE REPORT / OLGU SUNUMU
DOI: 10.26650/IUITFD.2018.0008
İst Tıp Fak Derg 2019 / J Ist Faculty Med 2019

FETAL BRAIN SHRINKAGE: A RARE, MYSTIFYING ANOMALY

FETAL BEYİN BÜZÜŞMESİ: NADİR, İLGİ ÇEKİCİ BİR ANOMALİ

Gürcan TÜRKYILMAZ[1], Şahin AVCI[2], Umut ALTUNOĞLU[2], Emircan ERTÜRK[1], Melis CANTÜRK[1], Tuğba SİVRİKOZ[1], İbrahim KALELİOĞLU[1], Recep HAS[1], Atıl YÜKSEL[1]

İstanbul Üniversitesi, İstanbul Tıp Fakültesi, [1]Kadın Hastalıkları ve Doğum Anabilim Dalı, [2]Tıbbi Genetik Anabilim Dalı, İstanbul, Türkiye

ORCID IDs of the authors: G.T. 0000-0002-5514-0233; Ş.A. 0000-0001-9545-6657; U.A. 0000-0002-3172-5368; E.E. 0000-0003-0169-6903; M.C. 0000-0003-1114-4678; T.S. 0000-0001-5482-9429; İ.K. 0000-0002-5504-2166; R.H. 0000-0002-1372-8506; A.Y. 0000-0002-6487-0860

Cite this article as: Turkyilmaz G, Avci S, Altunoglu U, Erturk E, Canturk M, Sivrikoz T, et al. Fetal brain shrinkage: a rare, mystifying anomaly. J Ist Faculty Med 2019;82(2):123-6. doi: 10.26650/IUITFD.2018.0008

ABSTRACT

Objective: Brain shrinkage in fetal life is a dismal, misunderstood anomaly. In this report, we described a rare case of severe brain shrinkage diagnosed in the 25th weeks of gestation complicated with fetal anemia and ascites.

Case Report: We detected polyhydramnios, ascites and severe brain anomaly in the fetus. Although the head circumference was normal; the brain tissue was atrophic and positioned in the center of the skull. The two cerebral hemispheres were adequately developed. Subarachnoid space was much extended, and the surface of the brain was smooth. Also, we detected severe fetal anemia. Perinatal infectious diseases were excluded. Fetal cranial MRI confirmed the brain shrinkage and TOP were performed.

Conclusion: We showed a unique fetal brain malformation which comprises intracranial shrinkage and extreme subarachnoid space wideness without microcephaly. It is not well recognized in the literature, and the etiology is unclear.

Keywords: Brain, fetus, MRI, prenatal diagnosis, ultrasonography

ÖZET

Amaç: Fetal hayatta gerçekleşen beyin büzüşmesi iyi anlaşılamamış, kötü bir anomalidir. Bu vaka sunumunda fetal anemi ve asitle komplike olmuş ve 25. haftada tanı almış ciddi bir beyin büzüşmesi anomalisini tanımladık.

Vaka Sunumu: Fetüste polihidramniyos, asit ve ağır bir beyin anomalisi saptadık. Kafa çevresi normal sınırlarda olmasına rağmen; beyin dokusu atrofikti ve kafatasının ortasında yerleşmişti. Her iki hemisfer yeterli ölçüde gelişmişti. Subaraknoid mesafe oldukça genişti ve beyin yüzeyi düzleşmişti. Ayrıca fetüste ağır anemi saptadık. Perinatal enfeksiyonlar dışlandı. Fetal MRI beyin büzüşmesini doğruladı ve aileye gebeliğin terminasyon seçeneği sunuldu.

Sonuç: Mikrosefali eşlik etmeksizin beyin büzüşmesi ve aşırı genişlemiş subaraknoid mesafe ile tanımlanan nadir bir beyin malformasyonunu gösterdik. Bu anomali literatürde yeteri kadar tanımlanmamıştır ve etiyolojisi henüz aydınlatılamamıştır.

Anahtar Kelimeler: Beyin, fetüs, MRI, prenatal tanı, ultrasonografi

INTRODUCTION

Fetal brain shrinkage or atrophy is a rare anomaly which describes reducing the brain volume without small skull size. It is characterized by the positioning of well-developed cerebral hemispheres in the central of the skull and most of the space of cranium fulfill with cerebrospinal fluid. The cause of the pathology is unknown in the majority of cases; however, determined risk factors are maternal alcohol consumption, intrauterine infections, particularly cytomegalovirus (CMV) and vascular insults (1). It is different from microcephaly or micrencephaly which is defined as low brain weight accompany decreased skull circumference. The other differential diagnoses are perinatal Zika virus (ZIKV) and cytomegalovirus (CMV) infections, hydranencephaly and fetal brain disruption sequence. This report shows a rare case of severe brain shrinkage diagnosed in the 25th weeks of gestation complicated with fetal anemia and ascites and review of the literature.

Corresponding author/İletişim kurulacak yazar: gurcanturkyilmaz@gmail.com

Received Date/Geliş tarihi: 14.09.2018 • **Accepted Date/Kabul tarihi:** 08.03.2019

CASE REPORT

A 22-year-old woman, gravida five paras 2, 25th-week gestation referred to our center for hydrocephaly, ascites, and polyhydramnios. She was healthy, and there was no familial disease. There was no history of medication or drug abuse. She had two healthy children and first-trimester aneuploidy screening test was negative. Ultrasonographic examination revealed polyhydramnios (amniotic fluid index: 24 cm) and ascites. There was no pleural or pericardial effusion, ascites or skin edema. The biparietal diameter and head circumferences were 36 and 58 percentiles respectively, and the cranial sutures were visualized. The brain appeared highly abnormal. Entire brain tissue was atrophic. In the axial plan, the cerebral hemispheres were positioned in the center of the skull and most of the space of cranium occupied by anechoic cerebrospinal fluid. The subarachnoid space was very extended (Figure 1). Cavum septum pellucidium and cerebellum were absent. The surface of the brain was smooth, and sulcus and gyri pattern vanished. Falx cerebri was preserved, and lateral ventricles were containing the choroid plexus could be demonstrated but markedly diminished. The circle of Willis could not be visualized. In the coronal plane, thalamic nuclei and falx cerebri were demonstrated (Figure 2). After counseling the patient, cordocentesis was performed, and fetal karyotype and microarray results were normal. Fetal hemoglobin was 3.1 gr/dl, and thrombocyte count was 112.000, fetal blood group was A Rh negative and direct Coombs was negative. For the investigation of fetal anemia, hemoglobin electrophoresis was performed and demonstrated normal values (HbF %87, HbA2 %5.7, and HbA %6.6). Indirect Coombs, Parvovirus IgM, and IgG results were negative. Glucose-6-phosphate dehydrogenase deficiency was ruled out by genetic testing. Toxoplasma and CMV polymerase chain reaction (PCR) analysis in amniotic fluid were negative. Also, maternal Zika virus (ZIKV) IgM and IgG antibodies were negative. Fetal cranial MRI suggested, and it demonstrated central display of atrophic brain with the wideness of subarachnoid space and confirmed our findings (Figure 3). After counseling with the pediatric neurologist, poor outcome was declared and termination of pregnancy was offered. The family decided to continue the pregnancy. One week later, fetal death and 1280 gr male fetus were delivered. A medical genetic specialist performed the morphologic examination of the fetus and revealed normal morphology. A fetal autopsy was suggested, but it was rejected by the family.

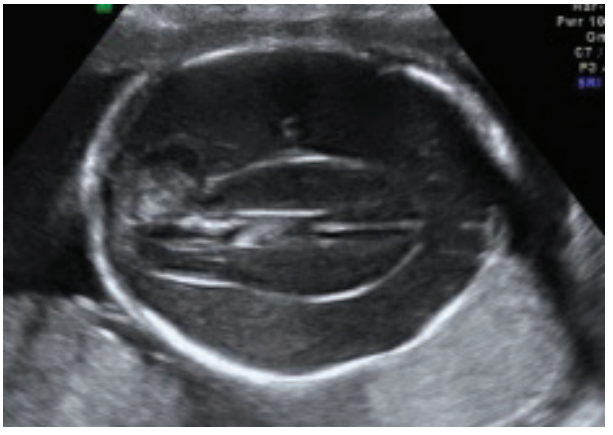

Figure 1: An axial ultrasound image of the fetal brain shows shrunken cerebral hemispheres and wide distance between the brain surface and calvarium bones

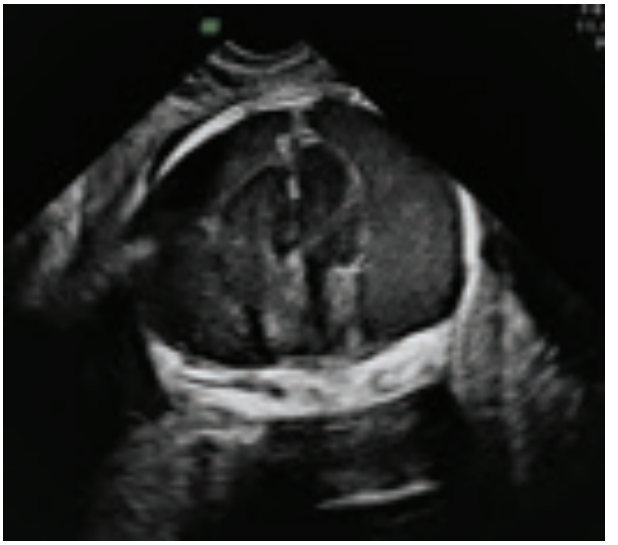

Figure 2: A coronal view of extenden subarachnoid space of the brain in ultrasonography

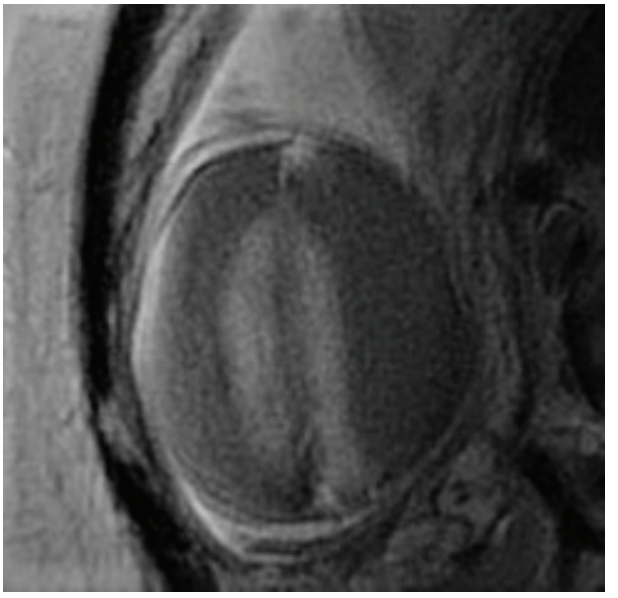

Figure 3: Fetal MRI demonstrates atrophic brain hemispheres

DISCUSSION

Fetal brain shrinkage or atrophy is a rare anomaly, and its incidence is unknown. The diagnosis is based on the presence of very small brain hemispheres in the centrum of the cranium and extreme subarachnoid space wideness. Paradoxically, the skull circumference is in the normal range. Only one case report was presented during the prenatal period which was published by Tongsong et al. (2). They demonstrated a fetus at 34 weeks of gestation which was diagnosed with severe brain shrinkage. The cerebral hemispheres were very small but were developed clearly and displayed to the center of the skull. A wide range between the surface of the brain and calvarium bones was present. They elucidated the pathogenesis with heavy maternal alcohol consumption. Possible hazardous effects of alcohol consumption during pregnancy has been interpreted in the literature. Unfortunately, alcohol abuse is common among many populations. Alcohol exposure during the prenatal period is responsible for devastating consequences, which are broadly termed fetal alcohol syndrome (FAS). The diagnosis of FAS is based on individual facial dysmorphologies, growth retardation and central nervous system (CNS) malformations (3). Alcohol alters fetal development by multiple mechanisms. Ethanol (the metabolite of alcohol) disrupt neuronal cell-cell adhesion also, cause apoptosis of neurons (4). Microcephaly and structural CNS defects are findings of FAS. Global loss of volume accompanied by measurement of head circumference (HC) below -2 SD is a strong determination for the diagnosis of microcephaly. A spectrum of structural anomalies; listed as corpus callosum anomalies; dysgenesis, agenesis, or partial agenesis, and posterior fossa anomalies which include cerebellar hypoplasia and Dandy-Walker malformation is present (5, 6). Reduced brain volume; most prominent in basal ganglia and diencephalon; has been implied (7). Our case was similar to the consequence of FAS, but there was no alcohol consumption history of the patient.

Maternal red cell alloimmunization is the leading cause of fetal anemia. The other etiologies are Parvovirus B19 infection, alpha thalassemia, glucose 6-phosphate dehydrogenase deficiency, etc. Fetal anemia can be diagnosed with noninvasive or invasive methods. The noninvasive method is the first line method for assessment of anemia. Investigation of MCA (Middle Cerebral Artery) with Doppler is a suggested tool because of its relative easily measurement and strict measuring conditions (8). Fetal anemia can be indirectly evaluated by fetal blood sampling which is the gold standard for diagnosis; however, 1-2% of the risk of loss is present due to the procedure. Severe anemia leads to hyperdynamic cardiac failure and hydrops fetalis. It can cause edema in the fetal brain, but there is no evidence that it can be related to intracranial shrinkage. We could not evaluate the MCA Doppler due to severe brain damage and detected the fetal anemia by fetal blood sampling. However we examined the fetal anemia reasons, we could not identify the underlying cause.

We determined Zika virus and CMV infection, Hydranencephaly and fetal brain disruption sequence (FBDS) in the differential diagnosis

Zika virus (ZIKV); member of Flaviviridae; transmitted by Aedes mosquitoes, infections are mostly asymptomatic (9). In pregnancy, it is associated with severe congenital anomalies mainly if infection occurs in the first trimester. Microcephaly and ZIKV relation were demonstrated in several reports, but microcephaly was not the only cranial anomaly observed, and other malformations were reported. Ventriculomegaly, cerebral and cerebellar calcifications, vermian agenesis, mega cisterna magna, abnormal cortical development, and severe brain atrophy were demonstrated in ultrasonography or MRI (10). We performed ZIKV IgM and IgG in maternal blood and resulted negative.

Congenital CMV accounts for common reasons of congenital malformations; such as developmental delay, sensorineural hearing loss, and fetal death; in developed countries (11). Though the frequency is strongly related to the gestational age of primary infection, the rate of congenital CMV infection is reckoned as 0.3-0.7% in all live births worldwide. CMV can cause a wide range of malformations in CNS. Ventriculomegaly and increased periventricular echogenicity are frequently present in periventriculitis. Microcephaly and intracranial calcifications can be seen as the consequence of encephalitis. Periventricular pseudocyst and intraventricular synechiae are specific findings of CMV infection. Also, it can lead to cortical development disorders and agenesis of corpus callosum. Although it is associated with severe cranial destructive lesions, intracranial shrinkage was not reported related to CMV in literature. We performed CMV PCR analysis in amniotic fluid, but it resulted negative.

Hydranencephaly; defined as replacement of cerebral neural tissue by large volumes of fluid accumulation in sacs around brain stem and supratentorial area (12). The definitive cause of hydrocephaly is not explicit; however the mostly accepted theory supports sudden occlusion of bilateral internal carotid arteries; which leads to necrosis of evolving cerebral structures. Ultrasonography reveals large volumes of anechoic fluid accumulation rather than the presence of cerebral hemispheres. We demonstrated atrophic but developed brain hemispheres in our patient.

Partial necrosis of brain tissue leads sequela of several malformations, which is called Fetal Brain Disruption Sequence, such as the failure of proper skull formation, severe microcephaly, overlying sutures along with protrud-

ing occipital bone and scalp rugae (13). Hyperthermia, viral infections, and vascular disruption have been suggested for possible etiologies. Severe microcephaly and marked destruction of cerebral hemispheres are cardinal findings in the prenatal period.

However brain volume was markedly decreased, cranium circumference was within normal range, and relatively well developed cerebral hemispheres existed. Based on this findings, we hypothesized that the brain malformation has occurred after the basic brain structures were fully formed. Most likely a vascular disruption may have damaged the brain and caused globally necrosis. Unfortunately, we could not perform a fetal autopsy to reveal the exact reason.

CONCLUSION

We described a unique fetal brain malformation which comprises of intracranial shrinkage and extreme subarachnoid space wideness without microcephaly. We could not determine the exact etiology, however it is most likely a consequence of vascular insult.

Ethics Committee Approval: Ethics committee approval was received for this study from the local ethics committee.

Informed Consent: Written consent was obtained from the participants.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- G.T., E.E., M.C., R.H.; Data Acquisition- G.T., E.E., T.S.; Data Analysis/Interpretation- G.T., E.E., A.Y.; Drafting Manuscript- İ.K., R.H., A.Y.; Critical Revision of Manuscript- G.T., M.C.; Final Approval and Accountability- G.T., Ş.A., U.A., E.E., M.C., T.S., İ.K., R.H., A.Y.; Technical or Material Support- G.T., E.E.; Supervision- G.T., R.H.

Conflict of Interest: Author declared no conflict of interest.

Financial Disclosure: Author declared no financial support.

Etik Komite Onayı: Etik komite onayı bu çalışma için, yerel etik komiteden alınmıştır.

Bilgilendirilmiş Onam: Katılımcılardan bilgilendirilmiş onam alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Çalışma Konsepti/Tasarım- G.T., E.E., M.C., R.H.; Veri Toplama- G.T., E.E., T.S.; Veri Analizi/Yorumlama- G.T., E.E., A.Y.; Yazı Taslağı- İ.K., R.H., A.Y.; İçeriğin Eleştirel İncelemesi- G.T., M.C.; Son Onay ve Sorumluluk- G.T., Ş.A., U.A., E.E., M.C., T.S., İ.K., R.H., A.Y.; Malzeme ve Teknik Destek- G.T., E.E.; Süpervizyon- G.T., R.H.

Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.

Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

REFERENCES

1. Maiser SE, Chen WJ, Miller JA, West JR. Fetal alcohol exposure and temporal vulnerability regional differences in alcohol-induced microencephaly as a function of the timing of binge-like alcohol exposure during rat brain development. Alcohol Clin Exp Res 1997;21:1418-28. [CrossRef]
2. Tongsong T, Puntachhai M, Mekjarasnapha M, Traisrisilp K. Severe fetal brain shrinkage following heavy maternal alcohol consumption. Ultrasound Obstet Gynecol 2014;44:245-47. [CrossRef]
3. Jones KL, Smith DW. Recognition of the fetal alcohol syndrome in early infancy. Lancet 1973;302:999-1001. [CrossRef]
4. Charness ME, Safran RM, Perides G. Ethanol inhibits neural cell-cell adhesion. J Biol Chem 1994;269:9304-9.
5. Mattson SN, Jernigan TL, Riley EP. MRI and prenatal alcohol exposure: images provide insight into FAS. Alcohol Health Res. World 1994;18:49-52.
6. Astley S, Aylward EH, Olson HC, et al. Magnetic resonance imaging outcomes from a comprehensive magnetic resonance study of children with fetal alcohol syndrome spectrum disorders. Alcohol Clin Exp Res 2009;33:1671-89. [CrossRef]
7. Roussotte F, Sulik K, Mattson S, et al. Regional brain volume reductions relate to facial dysmorphology and neurocognitive function in fetal alcohol spectrum disorders. Hum. Brain Mapp 2012;33:920-37. [CrossRef]
8. Bhide A, Acharya G, Bilardo CM, Brezinka C, Cafici C, Hernandez-Andrade E. ISUOG practice guidelines: use of Doppler ultrasonography in obstetrics. Ultrasound Obstet Gynecol 2013;41:233-9. [CrossRef]
9. Lindenbach BD, Rice CM. Molecular biology of flaviviruses. Adv Virus Res 2003;59:23-61. [CrossRef]
10. Junior E, Carvalho FH, Tonni G, Werner H. Prenatal imaging findings in fetal Zika virus infection Curr Opin Obstet Gynecol 2017;29:95-105. [CrossRef]
11. Kagan K, Hamprecht K. Cytomegalovirus infection in pregnancy. Arch Gynecol Obstet 2017;296:15-26. [CrossRef]
12. Bianchi DW, Crombleholme TM, D'Alton ME, Malone FD. Hydranencephaly. In: Fetology: Diagnosis and Management of the Fetal Patent. New York NY: McGraw-Hill; 2010:130-3.
13. Russell LJ, Weaver DD, Bull MJ, Weinbaum M. In utero brain destruction resulting in collapse of the fetal skull, microcephaly, scalp rugae, and neurologic impairment: the fetal brain disruption sequence. Am J Med Genet 1984;17(2):509-21. [CrossRef]