

Early Diagnosed Meckel-Gruber Syndrome

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Abstract

Objective: The Meckel-Gruber syndrome is a rare autosomal recessive disorder that is characterised by typical sonographical findings: encephalocele, polydactyly and cystic dysplastic kidneys. Consecutive loss of pregnancies, appearing in the family history, emphasises the importance of early prenatal diagnoses in such cases.

Case: A 23-year-old woman, gravida 6, abortion 5, and having a consanguineous marriage was admitted to our clinic at 12th weeks of gestation according to the date of her last menstrual date. Obstetric history revealed that two of the previous pregnancies were affected with meningomyelocele and neural tube defects. In the sonographic evaluation, CRL was measured as 45 mm and NT 4.5 mm. The detailed sonographical examination of the fetus revealed encephalocele, and bilateral enlargement of the kidneys was noticed. Meckel-Gruber syndrome was suspected. After fetal karyotyping, termination of pregnancy is performed by the decision of perinatology council of our hospital. In the histopathological examination, encephalocele, polydactyly and bilateral dysplastic kidneys were diagnosed and Meckel-Gruber syndrome was established.

Conclusion: Meckel-Gruber syndrome is a syndrome which displays an autosomal recessive inheritance and is mostly confused with trisomy 13. In the cases with consecutive losses of pregnancy first trimester diagnosis is important. In countries with high rates of consanguineous marriage, as it is in our country, one should be careful and genetic counselling should be advised.

Keywords: Meckel-Gruber syndrome, encephalocele, dysplastic kidneys, polydactyly.

Erken tanı almış Meckel-Gruber sendromu

Amaç: Meckel-Gruber sendromu otozomal resesif geçiş gösteren, major triadı ensefalosel, polidaktili ve kistik displastik böbrekler olan bir sendromdur. Bu olgu tekrarlayan gebelik kaybı olan vakalarda erken tanının önemini vurgulamak için sunulmuştur.

Olgu: 23 yaşında G6P0A5 olan akraba evliliği mevcut hasta son adet tarihine göre 12. haftasının içinde kliniğimize başvurdu. Daha önceki gebelik kayıplarından ikisinde meningomyelosel ve nöral tüp defekti öyküsü mevcuttu. Yapılan ilk ultrasonografik değerlendirmesinde CRL ölçümü 45 mm (11 hafta), NT 4 mm olarak ölçüldü. Hastanın yapılan ayrıntılı ultrasonografisinde ensefalosel ve böbreklerde bilateral büyüklük dikkati çekti. Meckel-Gruber sendromu ön tanısı konulan olguda hastanemiz perinatoloji konseyinin kararı ile karyotip analizi sonrası gebelik sonlandırıldı. Yapılan histopatolojik incelemede ensefalosel, polidaktili ve bilateral olarak büyümüş böbreklerle Meckel-Gruber sendromu tanısı doğrulandı.

Sonuç: Meckel-Gruber sendromu otozomal resesif geçiş gösteren ve en çok trisomi 13 ile karışan bir sendromdur. Tekrarlayan gebelik kayıpları ve bu kayıplarda nöral tüp defekti öyküsü olan olgularda erken haftalarda tanı önemlidir. Akraba evliliği oranı yüksek olan ülkemizde bu açıdan dikkatli olunmalı ve genetik danışmanlık önerilmelidir.

Anahtar Sözcükler: Meckel-Gruber sendromu, ensefalosel, displastik böbrek, polidaktili.

Introduction

Some diagnoses of Meckel-Gruber Syndrome were first described by Meckel in 1898. Gruber defined it as a syndrome where posterior encephalocele, polydactyly and cystic dysplastic kidneys were together. Other anomalies that they may be together are heart, genital, facial and extremity defects.¹ It shows autosomal recessive transition. The recurrence risk is 25% if there is any affected child in family. In families affected before, it should be careful in terms of early prenatal diagnosis.

In this case presentation, it is aimed to emphasize the importance that Meckel-Gruber syndrome can be diagnosed early by transvaginal ultrasonography, and to review the literature accordingly.

Case

The case G6P0A5 was 23 years old and had been married for 6.5 years, and it was reported that there was a second degree of kinship with her husband (the son of her aunt). It was learnt that her first pregnancy was ended with encephalocele, second pregnancy was ended with missed abortus, third pregnancy was ended with meningocele, and fourth and fifth pregnancies were ended with missed abortus. The result of amniocentesis performed at her third pregnancy was found as normal karyo-

otype. No characteristic was observed in the history and family background of the patient. In the ultrasonography of patient when applied in her 12th gestational week according to her last period date, CRL was found as 45 mm (11 weeks and 3 days) and NT was found as 4.5 mm. Also encephalocele and kidneys were observed as big bilaterally and clearly (Fig. 1).

The patient was discussed in Weekly Council of Perinatology Department of Health Ministry Maternity Hospital. The decision was to end pregnancy and to give genetic consultancy to the family. To make clear the diagnoses, the pregnancy was ended by determining the fetal karyotype in the case observed up to 14th gestational week. Fetal karyotype was found as 46 XY. Encephalocele and polydactyly were found in macroscopic view of the fetus.

Six fingers were seen in hands and feet of fetus in the pathological examination. The face was observed as a cystic structure covered by encephalocele skin in occipital region in frog view. When abdomen was opened, both kidneys were 2-3 times bigger than their normal shapes and they were filling the whole abdomen. Many cystic structures were observed in cortex and medulla. Other organs were in regular condition macroscopically (Fig. 2). The diagnosis was expressed as histopathological diagnoses consistent with Meckel-Gruber Syndrome for male fetus at 14th week



Figure 1. Encephalocele.



Figure 2. Kidney view.



Figure 3. USG view of the fetus.

including encephalocele, polydactyly and polycystic kidneys.

Discussion

Meckel Gruber syndrome can be with neural tube defects (NTD), encephalocele (80%), polydactyly (75%), cystic and dysplastic kidney (95%).^{1,2} Other anomalies displaying association in USG are reported as micrognathia, cardiac anomalies, syndactylia, clinodactylia and pes equinovarus.¹ For certain diagnosis of the disease, at least two diagnoses forming the typical triad should be found among cystic kidney dysplasia, occipital encephalocele, postaxial polydactyly diagnoses.³ In the presented case, encephalocele and cystic growth in bilateral kidneys were detected in the ultrasonography performed in the first trimester. Meckel Gruber syndrome is one of the well known central nervous system syndromes with autosomal recessive transition accompanied by renal dysplasia.⁴

It was reported that Meckel-Gruber syndrome is observed as one 12,000th–140,000th in the general population.⁵ While NTD recurrence risk is 1-3%, it is 25% in Meckel-Gruber syndrome due to displaying autosomal recessive transition and therefore, perinatal follow-ups and early diagnosis are important in next pregnancies.⁶

		10:46:32	21-01-2006				
Institution		Diag. Physician					
Ref. Physician		Sonographer					
ID		Heart Rate	bpm				
Name		Birthday	23-04-1982				
Gender	Female	Age	23y 8m				
Height	158.00cm	Weight	56.00kg				
BSA	1.56m ²	Indication					
Description		Custom Field1					
Custom Field2							
LMP	23-10-2005	Estab. Due Date					
GA(LMP)	12w6d	Average US GA	11w3d				
EDD(LMP)	30-07-2006	EDD(Average US GA)	09-08-2006				
EFW Hadlock3		GA(EFW)					
Percentile(EFW)		SD(EFW)					
Fetal Biometry							
		1	2	3	Last	G.A.	Percentil
CRL	Hadlock	4.65			4.65	cm	11w3d
Fetal Cranium							
		1	2	3	Last	G.A.	Percentil
NT		0.45			0.45	cm	

Figure 4. USG readings of the fetus.



Figure 5. Fetus.



Figure 6. Fetus kidneys.

Meckel-Gruber syndrome is seen only in 5% of all NTDs.^{1,7} Early diagnosis is important due to the high recurrence risk of the syndrome (25%) and the loss of those born with Meckel-Gruber syndrome at or after delivery. Sonographical examination can be performed towards the end of first trimester. In a study performed in England, Meckel-Gruber syndrome could be shown in high and low risk groups at 11th-14th gestational weeks by routine ultrasonographical examination.^{8,9} In a mother in Bulgaria of whom previous pregnancy was ended at second trimester due to Meckel-Gruber syndrome, Meckel-Gruber syndrome could be detected at 13th gestational week by transvaginal ultrasonography.¹⁰

Definitive diagnosis of Meckel-Gruber syndrome should be performed by trisomia 13 and Smith-Lemli-Opitz syndrome. Its definitive diag-

nosis sometimes may be hard since it has similar pathologies with trisomia 13. Because cystic kidneys accompany trisomia 13 at a rate of 15-30%. While mid-line central nervous system anomalies or holoprosencephaly are diagnostics for trisomia 13, bigger kidneys, oligohydramnios and the existence of occipital encephalocele are diagnostics for Meckel-Gruber syndrome.¹¹ Karyotyping should be done when these findings are found.^{1,2} Karyotyping was also done in the presented case. 46 xy was found as normal karyotype as a result of karyotyping. In addition, holoprosencephaly, korpus kallozum agenezisi, heart defects, renal anomalies, meningomyelocele, polydactyly, cystic hygromata are frequently seen in trisomia and they are sporadic. Meckel-Gruber syndrome is autosomal recessive transitive. In this regard, recurrence rates are differ-

Table 1. Comparison of Meckel-Gruber syndromes diagnosed at first trimester.

Case Presentation	Diagnosis Tool	GA	Fetal Anomaly	Familial	Sporadic
Pachi et al. 1989 ¹⁴	USG	13	OE, PB, HD	1	-
Quintero et al. 1993 ¹⁵	EF	11	OE, PB*, HD, BD	1	-
Dumez et al. 1994 ¹⁶	E	E 10+4	OE, HD, AN	1	-
Braithwaite et al. 1995 ¹⁷	USG	12+2	OE, PB, HD*	-	1
Sepulveda et al. 1997 ¹⁸	USG	11-14	OE, PB, HD	4	1
Den Hollander et al. 2002 ¹⁹	USG	13+4	OE, PB	1	-
Liu et al. 2006 ²⁰	USG	13	OE, PB	-	1
Our case	USG	11+3	OE, PB, HD	1	-

GA: Gestational age week/day; USG: Ultrasonography; E: Embryoscopy; EF: Embryofetoscapy; OE: Occipital encephalocele; PK: Polycystic kidney; HD: Hexadactyly; BD: Biliary disgenesis (found in pathological examination); AN: Abnormal nephrogenesis (found in pathological examination); HD*: Hexadactyly (found during delivery); PK*: Polycystic kidney (found in pathological examination).

ent. Family should be given genetic consultancy in terms of next pregnancies.^{1,2}

In Meckel-Gruber syndrome, renal cystic dysplasia exists in almost all cases.¹² Kidneys sometimes may be 10-20 times bigger than their normal dimensions. Cysts are seen macroscopically in autopsy examination. Other renal anomalies such as renal agenesis, renal hypoplasia and ureteral duplication may also accompany this syndrome.¹³

When encephalocele is found in the prenatal follow-up of pregnant, a wide examination including extremities and kidneys should certainly be performed. As it can be seen in this case who was diagnosed by the examination of nuchal opacity increase, the increase of nuchal opacity does not only inform us about trisomies but also enables to know other syndromes. Not only nuchal opacity increase but also whole fetus should be examined during 11th-14th week scanning (Table 1).

Conclusion

In conclusion, fetal anomalies can be diagnosed by ultrasonography and some invasive methods, and affected fetuses can be eliminated. Meckel-Gruber Syndrome which is fatal and autosomal recessive transitive can be detected even before 20th gestational week by ultrasonographic scannings. After informing such families with the risk of this syndrome, pregnancies can be ended by performing early prenatal diagnosis at 11th-14th weeks in perinatology clinics.

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