Prenatal Diagnosis Of Tay-Sachs Disease

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OBJECTIVE: To emphasize the efficacy and safety of the prenatal invasive procedures for prenatal diagnosis of Tay-Sachs disease.

STUDY DESIGN: In this case series, the results of the prenatal invasive procedures that were performed for diagnosing Tay-Sachs disease in 8 patients between 2000 and 2008 are reported. The samples were obtained by chorionic villus sampling or by cordocentesis. Total hexosaminidase level and the percentage of isoenzyme ß-Hexosaminidase A were measured in fetal samples.

RESULTS: There were 8 patients in diagnosed prenatatlly between 2000-2008. Sufficient material for enzyme analysis was obtained without any complications. Total hexosaminidase levels and the percentage of hexosaminidase were in normal limits in all fetal samples. All pregnancies ended up with uneventful term births.

CONCLUSION: Tay-Sachs disease can be diagnosed prenatally by measuring hexosaminidase enzyme activity in fetal tissue samples with an acceptable complication rate. Prenatal diagnosis should be offered to families who have affected siblings with Tay-Sachs disease.

Key Words: Prenatal diagnosis, Tay-sachs, Gangliosidosis

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Introduction

Tay-Sachs disease is an autosomal recessive, neurodegenerative disorder that results from a deficiency of the isoenzyme ß-Hexosaminidase A (Hex A).[1] Hex A deficiency causes accumulation of GM 2 gangliosides within the lysosomes of cells which results in severe progressive neurologic disease that causes death in early childhood.[2] The disease incidence is ~1/3600 in Ashkenazi Jews , ~1/360.000 in other populations and 1/433.333 in Turkish population.[1,3]

Tay-Sachs disease can be diagnosed prenatally by measuring hexosaminidase enzyme activity in samples obtained by amniocentesis, chorionic villus sampling or by cordocentesis.[3]

In this case series, we report the results of the prenatal invasive procedures that were performed for diagnosing Tay-Sachs disease antenatally in 8 patients.

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Material and Method

Patients

Between 2000 and 2008, 8 pregnant patients with a history of affected sibling(s) with Tay-Sachs disease were referred to our department. After consultation with pediatric neurology and genetics departments chorionic villus sampling(CVS) or cordosentesis were performed by experienced materno-fetal medicine unit fellows.

Enzyme Activity Determination

The samples obtained from the patients were sent to Biochemistry Department of Hacettepe University Faculty of Medicine which is the national main reference center for enzym analyses. Hexosaminidase enzyme activity and Hex A percentage were measured in fetal samples by flourometric and spectrophotometric methods.[4] The karyotypes of the fetuses were studied simultaneously after family approval.

Results

The patients' mean age was 30,1(±4.9), mean gestational age was 12 weeks and 5 days and the patients had a mean of 3.9 pregnancy per head. All patients had at least 1 affected sibling, and two of the patients were married to their relatives (Table 1). 7 patients were performed chorionic villus sampling and 1 patient underwent cordocentesis. Sufficient material for

enzyme analysis and genetic karyotyping were obtained with no complications. Total hexosaminidase levels and the percentage of Hex A were in normal limits in all fetal samples. Only one patient accepted karyotype analysis and found to be normal. All pregnancies ended up with term births uneventfully (Table 2).

Table 1: Demographic features and the obstetric history of the patients

CASE	Age	Gravida	Number of Affected Sibling(s)	Consanguinity
1	23	3	1	-
2	31	3	1	-
3	33	6	2	-
4	35	4	2	-
5	27	3	1	+
6	38	4	2	+
7	27	5	2	-
8	27	3	1	-

Table 2: The Prenatal Enzyme Analyses and the pregnancy outcomes

CASE	Gestational Age	Procedure	Total Hexosaminidase (600-2675 nmol/s/mgpr)	Hex A Percentage	Karyotype	Pregnancy Outcome
1	12 weeks	CVS	1567	62 %	Family Refusal	Birth at term
2	11 weeks	CVS	1743	59 %	Family Refusal	Birth at term
3	12[4] weeks	CVS	2732	70 %	46 XY	Birth at term
4	18[5] weeks	CORDO CENTESİS	1232	61 %	Family Refusal	Birth at term
5	12[3] weeks	CVS	1102	64 %	Family Refusal	Birth at term
6	10[6] weeks	CVS	1525	66 %	Family Refusal	Birth at term
7	12[3] weeks	CVS	2856	53 %	Family Refusal	Birth at term
8	11[4] weeks	CVS	2353	63 %	Family Refusal	Birth at term

Discussion

The aim of Prenatal diagnosis is to identify the structural or functional abnormalities in the fetus. Tay-Sachs disease is uniformly fatal and there is no effective treatment at present.[1] It is important to diagnose the diseased fetus prenatally for genetic counselling of the patients. In our study we performed prenatal invasive procedures to diagnose Tay-Sachs disease in fetuses whom parents had affected siblings. All of the fetal samples found to have normal enzyme activity and normal Hex A percentage; this result was not expected due to autosomal recessive heritage of the disease, at conception, each sib of an affected individual has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier, so the normal enzyme levels are associated with small sample size of our study.

There were 2 consanguineus marriages in our study population, this %25 rate is similar with the %22 frequency of consanguineus marriages in Türkiye.[5] In a study which the authors examine the incidences of lysosomal storage diseases including Tay-Sachs they found that %80 of the parents in the study were consanguineous,[3] according to that study we should have found a greater consanguineus marriage rate if we had adequate sample size.

No complications were observed during and after the invasive procedures but the procedure related fetal death cited to be 0.7 percent for CVS,[6] 0.6 percent for amniocentesis[6] and 1 percent for cordosentesis[7] should be kept in mind before counselling patients.

Tay-Sachs disease is uniformly fatal and there is no effective treatment at present. It is important to diagnose the diseased fetus prenatally for genetic counselling of the patients. The disease incidence in Turkish population is 1/433.333 and similar to other countries. The rareness of this disease renders it extravagant to screen whole population but prenatal diagnosis should be offered to families who have affected siblings with Tay-Sachs Disease.

Tay-Sachs Hastalığının Prenatal Tanısı

AMAÇ; Bu çalışmanın amacı, Tay-Sachs hastalığının prenatal tanısında invaziv prenatal işlemlerin güvenilirliğini ve etkinliğini ortaya koymak.

GEREÇ VE YÖNTEM Bu vaka serisi takdiminde, 2000 - 2008

yılları arasında tay-sachs hastalığı teşhisi için 8 hastaya uygulanan invaziv prenatal işlemlerin sonuçları rapor edilmiştir. Fetal örnekler koryonik villus biyopsisi veya kordosentez ile elde edilmişlerdir. Fetal örneklerde total heksozaminidaz miktarı ve izoenzim β-Heksozaminidaz A yüzdesi ölçülmüştür.

BULGULAR: Sonuçlar Enzim analizi için gerekli olan fetal örnekler komplikasyon olmadan elde edilmişlerdir. Hastalardan alınan tüm örneklerdeki total heksozaminidaz miktarı ve izoenzim β-Heksozaminidaz Ayüzdesi normal aralıkta bulunmuştur. İşlem yapılan gebeliklerin takibinde sorun yaşanmamış ve term doğumla sonlanmışlardır.

SONUÇ: Karar Kabul edilebilir komplikasyon oranıyla fetal doku örneklerinde heksozaminidaz enzim aktivitesi çalışılarak Tay-Sachs hastalığının prenatal tanısı koyulabilir. Tay-Sachs'lı çocuk öyküsü olan ailelere prenatal tanı önerilmelidir.

Anahtar Kelimeler: Prenatal tanı, Tay-Sachs hastalığı, Gangliosidozis

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