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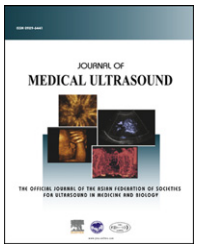

REVIEW ARTICLE

Prenatal Sonographic Features of Miller-Dieker Syndrome

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Miller-Dieker syndrome (MDS) is a contiguous gene deletion disorder involving genes on chromosome 17p13.3. Clinical manifestations include central nervous system (CNS) anomalies (mainly Type I lissencephaly), facial dysmorphism, growth restriction, profound mental retardation, seizure, and extracranial anomalies. The affected individuals often die in infancy or early childhood. Owing to the poor prognosis of MDS, early diagnosis of fetuses with MDS is important. Currently, ultrasound is regarded as a useful tool in prenatal detection of MDS, in addition to fetal magnetic resonance imaging. This article provides an overview of the reported prenatal sonographic features of MDS, including CNS anomalies (ventriculomegaly, agyria or lissencephaly, abnormal sylvian fissures, agenesis or dysgenesis of corpus callosum, and microcephaly), intrauterine growth restriction, polyhydramnios, cardiac anomalies, omphalocele, facial anomalies, and rare anomalies. Several diseases may have phenotypic overlaps with MDS, including Type I lissencephaly (Lissencephaly 1, Lissencephaly 2, and X-linked lissencephaly) and Type II lissencephaly. Increasing the awareness and knowledge of fetal structural anomalies associated with MDS on prenatal ultrasound will be helpful in the early detection, thus allowing appropriate genetic counseling and optimize clinical management.

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Introduction

Miller-Dieker syndrome (MDS, OMIM 247200), described by Miller [1] and Dieker et al [2], is a contiguous gene deletion syndrome characterized by central nervous system (CNS) anomalies, facial dysmorphism, growth restriction, profound mental retardation, and extracranial anomalies. The CNS anomalies include cerebral agyria or Type I lissencephaly, ventriculomegaly, absent or hypoplastic corpus callosum, and microcephaly. The facial features may present prominent forehead with bitemporal narrowing, furrowed brow, small nose with anteverted nostrils, low set ears, prominent upper lip, and micrognathia. Seizure is often developed in early childhood. Life expectancy is significantly shortened and patients usually die during early childhood [3]. Associated extracranial anomalies may be present, such as cardiac anomalies, omphalocele, and genitourinary anomalies [4,5].

The normal six-layered brain cortex is formed by neuronal migration beginning at 8 weeks of gestation. Impairment or arrest of neuronal migration at about 3—4 months of gestation can result in lissencephaly. On the basis of clinicopathological classification, two types of lissencephaly have been proposed. Type I lissencephaly seen in MDS is often associated with a microdeletion of chromosome 17p13.3. Three genes, *LIS1* (*PAFAH1B1*; OMIM 601545), *14-3-3ϵ* (*YWHAE*; OMIM 605066), and *CRK* (OMIM 164762), are mapped to this locus [6,7]. Deletion or mutations in these genes can cause the lissencephaly. Lissencephaly is also present in several other diseases such as Norman-Roberts syndrome and Walker-Warburg syndrome. Therefore, differential diagnosis including Type I and Type II lissencephaly is discussed here.

Prenatal diagnosis is important due to the poor outcome in MDS-affected cases. Magnetic resonance imaging is considered to be a useful tool in the diagnosis of CNS anomalies in fetuses of MDS. However, it is more expensive and sedation of the fetus may be required during examination. At present, ultrasound is thought to be another possible tool in the prenatal detection of characteristic findings associated with MDS. To date, there have been approximately 25 reported cases of MDS having prenatal sonographic findings. Here, we review the sonographic features in these fetuses of MDS. Early diagnosis of MDS is significantly beneficial for prenatal counseling and obstetric management.

Prenatal Sonographic Features

The prenatal sonographic features of published MDS cases are summarized in Table 1 [5,8—23]. They include CNS anomalies (ventriculomegaly, agyria or lissencephaly, abnormal sylvian fissures, agenesis or dysgenesis of corpus callosum, and microcephaly), intrauterine growth restriction (IUGR), polyhydramnios, cardiac anomalies, omphalocele, facial anomalies, and rare anomalies.

Table 1. Prenatal sonographic features of reported cases with Miller-Dieker Syndrome [8—23]

Cases	Microdeletion	CNS anomalies			
		Ventriculomegaly	Lissencephaly (agyria)	Abnormal sylvian fissure	Agenesis of corpus callosum
Sermer et al [8]	del(17p)				
Greenberg et al [9]	del(17)(p13)				
Saltzman et al [10]	del(17)(p13.3)mat		(+)		
	del(17)(p13.3)		(+)		
Blass et al [11]	del(17)(p13.2)	(+)	(+)		(+)
Okamura et al [12]	(−)	(+)	(+)	(+)	
	(−)	(+)	(+)	(+)	
Alvarado et al [13]	del(17)(p13.3)pat				
Holzgreve et al [14]	(−)	(+)			
McGahan et al [15]	del(17)(p13.3)	(+)			
Chitayat et al [5]	del(17)(p13.3)	(+)	(+)		
Greco et al [16]	(−)	(+)	(+)		
Fong et al [17]	del(17)(p13.3)	(+)	(+)	(+)	
	del(17)(p13.3)	(+)	(+)	(+)	
	del(17)(p13.3)mat	(+)		(+)	
	del(17)(p13.3)	(+)	(+)	(+)	(+)
	del(17)(p13.3)pat	(+)	(+)	(+)	
	del(17)(p13.3)		(+)	(+)	
	del(17)(p13.3)	(+)	(+)	(+)	
Pastorino et al [18]	(−)	(+)	(+)		
Lenzini et al [19]	del(17)(p13.3)	(+)	(+)		(+)
Herman and Siegel [20]	distal 17p deletion				
Aslan et al [21]	(−)		(+)	(+)	
Lin et al [22]	del(17)(p13.3)	(+)	(+)		
Chen et al [23]	del(17)(p13.2)	(+)			

(*continued*)