Concomitant Craniorachischisis and Omphalocele in a Male Fetus: Prenatal Magnetic Resonance Imaging Findings and Literature Review

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SUMMARY

Objective: To present the prenatal magnetic resonance imaging (MRI) findings of concomitant craniorachischisis and omphalocele, review the literature, and discuss the pathogenesis.

Case Report: A 20-year-old, gravida 2, para 0, woman was referred to genetic counseling at 17 weeks of gestation because of multiple congenital malformations in the fetus. Level II ultrasound revealed acrania, a ventricular septal defect, an upward-turned face, and omphalocele containing the intestines. MRI revealed normal extremities, exencephaly, hyperextension of the fetal head, significant shortening of the spinal column, marked lordosis and hyperextension of the malformed spine, an upward-turned face, and absence of a neck. A diagnosis of iniencephaly associated with anencephaly, rachischisis and omphalocele was made. Amniocentesis revealed a karyotype of 46,XY. Postnatal X-ray showed anencephaly with total spina bifida of the cervical and thoracic spine.

Conclusion: Prenatal MRI is able to provide a clear whole-body image of the fetus and its relationship with the placenta. Prenatal MRI is very useful in the differential diagnosis of concomitant craniorachischisis and omphalocele from amniotic band sequence, limb body–wall complex with craniofacial defect and *Disorganization* human homologue. [*Taiwan J Obstet Gynecol* 2009;48(3):286–291]

Key Words: craniorachischisis, iniencephaly, magnetic resonance imaging, neural tube defect, omphalocele, prenatal diagnosis

Introduction

Iniencephaly is a neural tube defect (NTD) involving a bony defect at the occiput and rachischisis of the cervical and thoracic spine with retroflexion of the head [1]. Iniencephaly is characterized by: (1) a variable deficit of the occipital bones resulting in an enlarged foramen magnum; (2) partial or total absence of cervical and thoracic vertebrae with an irregular fusion of those present, accompanied by incomplete closure of the vertebral arches and/or bodies; (3) significant shortening of the spinal column as a result of marked lordosis and hyperextension of the malformed cervicothoracic spine; and (4) an upward-turned face and mandibular skin directly continuous with that of the chest because of the absence of a neck [2]. The incidence of iniencephaly is about 1:1,000–1:2,000 births [3,4]. There is a tendency for iniencephaly in females. Iniencephaly may be associated with other anomalies

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such as anencephaly, encephalocele, meningomyelocele, hydrocephalus, Dandy-Walker malformation, holoprosencephaly, omphalocele, congenital diaphragmatic hernia, hydronephrosis, polycystic kidneys, cardiac defects, caudal regression sequence, arthrogryposis, club foot, single umbilical artery, and gastrointestinal atresia [1,5]. Craniorachischisis, an example of defective neural groove closure combining anencephaly and total spina bifida with meningomyelocele, is often associated with iniencephaly and may be associated with omphalocele. Here, we present such a case.

Case Report

A 20-year-old, gravida 2, para 0, woman was referred to genetic counseling at 17 weeks of gestation because of multiple congenital malformations in the fetus. Level II ultrasound revealed acrania, a ventricular septal defect, an upward-turned face, and omphalocele containing the intestines. The parents involved in this pregnancy were unrelated, and there was no family history of malformations, maternal diabetes, or teratogenic medication. The fetal biometry was consistent with 17 gestational weeks, and the amniotic fluid was normal. The fetal head was anencephalic and persistently hyperextended. Magnetic resonance imaging (MRI) revealed normal extremities, exencephaly, hyperextension of the fetal head, significant shortening of the spinal column, marked lordosis and hyperextension of the malformed spine, an upward-turned face, and absence of the neck (Figure 1). A diagnosis of iniencephaly associated with anencephaly, rachischisis and omphalocele was made. Amniocentesis revealed a karyotype of 46,*XY*. The pregnancy was subsequently terminated. A 120-g male fetus was delivered with iniencephaly, craniorachischisis, and omphalocele (Figure 2). Postnatal X-ray showed anencephaly with total spina bifida of the cervical and thoracic spine.

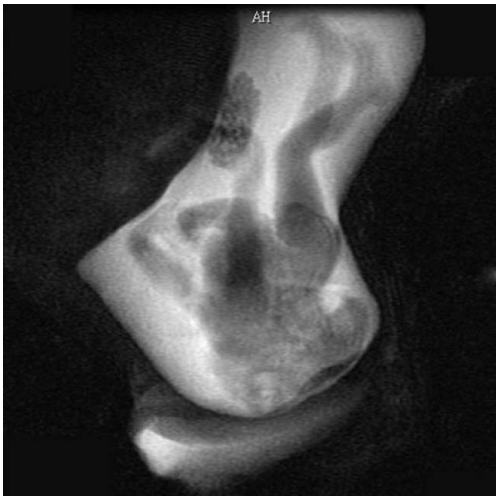

Figure 1. Prenatal magnetic resonance imaging at 17 weeks of gestation shows normal extremities, exencephaly, hyperextension of the fetal head, significant shortening of the spinal column, marked lordosis and hyperextension of the malformed spine, an upward-turned face, and absence of the neck.

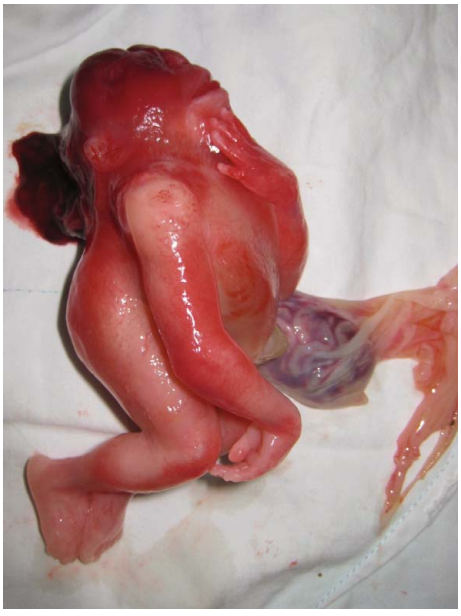

Figure 2. Image of the fetus at birth.

Discussion

We have presented a rare occurrence of concomitant iniencephaly, craniorachischisis, and omphalocele in a male fetus. To date, at least 17 cases of prenatally diagnosed iniencephaly associated with omphalocele have been reported (Table) [2,6–13]. The Table indicates a female tendency in the cases with concomitant iniencephaly and omphalocele.

In a review of 63 cases with iniencephaly, Chen [1] found that 20.6% of the cases had omphalocele. In a study of 60 cases with omphalocele, Forrester and Merz [14] found that 15% of the cases had NTDs, including 5% with anencephaly and 10% with spina bifida. Omphalocele and NTDs are related disorders [1,15–17]. Calzolari et al [18] proposed that omphalocele and NTDs are related congenital anomalies by the findings of a tendency for omphalocele to be associated with anencephaly and/or spina bifida. Chen et al [19] reported exencephaly and limb defects in a fetus with pentalogy of Cantrell. Central nervous system abnormalities such as anencephaly, meningocele, encephalocele, hydrocephalus, exencephaly, craniorachischisis and

Table. Reported cases of prenatally diagnosed iniencephaly associated with omphalocele

Reference	Gender	Cytogenetic analysis	Gestational age at diagnosis (wk)	Prenatal sonographic findings	Associated anomalies at birth
Mórocz et al [2]					
Case 1	F	NA	33	Anencephaly, iniencephaly, omphalocele	Omphalocele containing the liver and small and large intestines, anencephaly
Case 3	F	NA	32	Iniencephaly, microcephaly, omphalocele	Encephalocele, omphalocele containing the liver, single umbilical artery, uterus unicornis, right renal agenesis, agenesis of right ovary and fallopian tube
Meizner and Bar-Ziv [6]	F	NA	26	Polyhydramnios, iniencephaly, anencephaly, omphalocele, bilateral club feet	Omphalocele, anencephaly, thoracic rachischisis, club foot, bilateral cleft lip and palate
Meizner et al [7]	F	NA	21	Polyhydramnios, iniencephaly, occipital encephalocele, omphalocele	Omphalocele, occipital encephalocele
Doğan et al [8]					
Case 6	M	NA	21	Polyhydramnios, iniencephaly, anencephaly, spina bifida, omphalocele, bilateral cleft lip	Omphalocele, bilateral cleft lip, cervicothoracic rachischisis, anencephaly
Case 11	M	NA	26	Polyhydramnios, iniencephaly, anencephaly, omphalocele	Omphalocele, rachischisis, anencephaly
Case 12	F	NA	25	Polyhydramnios, iniencephaly, omphalocele, anencephaly, single umbilical artery, cervical spina bifida, left club foot	Omphalocele, left club foot, single umbilical artery, anencephaly
Case 15	F	NA	25	Polyhydramnios, iniencephaly, omphalocele, anencephaly, single umbilical artery, cervical spina bifida	Omphalocele, single umbilical artery, anencephaly
Donaldson et al [9]	M	47,XY, + 18	25	Craniorachischisis, thoraco-abdominoschisis	Anencephaly, thoraco-abdominoschisis

Jeanne-Pasquier et al [10]					
Case 4	F	NA	12	Iniencephaly, omphalocele, congenital diaphragmatic hernia	Omphalocele, congenital diaphragmatic hernia, anomalous pulmonary lobulation, encephalocele
Jeanne-Pasquier et al [11]	F	NA	13	Iniencephaly, exencephaly, anencephaly, omphalocele	Omphalocele, anencephaly
Polat et al [12]					
Case 1	F	NA	18	Polyhydramnios, craniorachischisis, omphalocele containing liver, stomach and intestines, ectopia cordis, pentalogy of Cantrell, club foot	Pentalogy of Cantrell, anencephaly, craniorachischisis, club foot
Case 2	F	NA	26	Polyhydramnios, craniorachischisis, omphalocele containing liver, stomach and intestines, ectopia cordis, pentalogy of Cantrell, bilateral club hands and feet	Pentalogy of Cantrell, anencephaly, omphalocele, club hands and feet
Joó et al [13]					
Case 2	?	Normal	?	Polyhydramnios, iniencephaly, occipital encephalocele, omphalocele	Iniencephaly apertus, occipital encephalocele, microcephaly, omphalocele
Case 14	?	Normal	?	Polyhydramnios, iniencephaly, anencephaly, omphalocele	Iniencephaly clauses, anencephaly, cervicothoracic spina bifida, omphalocele, cleft lip and palate
Case 16	?	Normal	?	Polyhydramnios, iniencephaly, anencephaly, rachischisis, gastroschisis	Iniencephaly clauses, anencephaly, rachischisis, omphalocele, cleft lip and palate, macroglossia
Present case	M	46,XY	17	Omphalocele, acrania, ventricular septal defect, iniencephaly	Craniorachischisis, omphalocele, anencephaly, ventricular septal defect, iniencephaly

F = female; NA = not available; M = male; ? = unknown.

spina bifida can be associated with pentalogy of Cantrell (Table).

Various hypotheses, such as polymorphisms of the folate-related genes, schisis association, insult of the midline developmental field and leucine zipper protein (LUZP) deficiency, have been suggested to explain the concurrence of NTDs and omphalocele. Folate-related genes play an important part in the susceptibility to NTDs. In particular, the thermolabile variant of methylenetetrafolate reductase *MTHFR* 677C → T has been shown to be a risk factor for NTDs. Mills et al [20] found a significant association between *MTHFR* 677C → T and omphalocele. The authors hypothesized that folate-related genes play a role in the etiology of omphalocele and suggested that folic acid containing multivitamins may prevent omphalocele. Czeizel [21] first proposed the schisis association of a combination of two or more schisis defects such as NTDs (anencephaly, encephalocele, and spina bifida), omphalocele, diaphragmatic defects (diaphragmatic hernia or agenesis of diaphragm), and cleft lip and/or cleft palate. Czeizel [21] observed that 0.29% (130/44,608) of malformed infants had two or more schisis defects without other major congenital malformations, and the most frequent combination of the schisis defects was anencephaly with cleft lip and/or cleft palate (33 of 130 cases). Martínez-Frías et al [22] observed that 0.09% (20/22,264) of live and stillborn malformed infants identified by the Spanish Collaborative Study of Congenital Malformations had two or more schisis defects not known to have other major or minor defects, and the most frequent associations were omphalocele with cleft palate and/or cleft lip, and omphalocele with diaphragmatic defects. Martínez-Frías et al [22] suggested that combinations of two schisis defects may represent blastogenetic sequences. Opitz and Gilber [23] suggested a "midline developmental field" concept by which anything that adversely impacts the midline field may disrupt the midline structures, causing midline defects such as central nervous system defects, cardiac defects, anal defects, genitourinary defects, and congenital diaphragmatic hernia. Recently, Hsu et al [24] found that deficiency of LUZP, a leucine zipper-containing protein, affected neural tube closure during mouse brain development. LUZP deficiency may cause congenital heart defects, facial cleft and omphalocele, in addition to NTDs (A. C. Chang, PhD, oral communication, June 2009).

As shown in this presentation, prenatal MRI is able to provide a clear whole-body image of the fetus and its relationship with the placenta. Prenatal MRI is very useful in the differential diagnosis of concomitant craniorachischisis and omphalocele from amniotic band sequence (ABS), limb body–wall complex (LBWC) with craniofacial defect and *Disorganization* (*Ds*) human homologue. ABS consists of a group of sporadic abnormalities characterized by congenital ring constrictions or amputation of digits and limbs, terminal digital fusion (pseudosyndactyly), talipes, and multiple craniofacial, visceral and body wall defects. Cranial defects associated with ABS include hydrocephalus, microcephaly, asymmetric encephalocele, meningocele, exencephaly, acrania, acalvaria, and anencephaly. Facial anomalies include cleft lip (usually bilateral), bizarre mid-facial clefts, nasal deformity, bony orbital clefts, hypertelorism, eye-lid colobomas, ptosis, ectropion, lacrimal outflow obstruction, and corneal opacities. LBWC describes a heterogenic group of fetal malformations including lateral body–wall defects and limb reduction anomalies [25,26]. Cases of LBWC with craniofacial defects frequently show severe anomalies of the upper limbs, craniofacial defects, constrictive amniotic bands, and cranioplacental attachment; cases of LBWC without craniofacial defects usually present with major anomalies of the lower limbs, abnormal genitalia, anal atresia, renal defects, abdominoplacental attachment, and umbilical cord abnormalities [27]. Birth defects resembling those of the mouse mutant gene *Disorganization* (*Ds*) or *Ds*-like human malformations include both common human birth defects (NTDs, orofacial clefting, gastroschisis and limb defects) and rare ones (anophthalmia and duplicated rectum) [28].

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