Galloway-Mowat syndrome: Prenatal ultrasound and perinatal magnetic resonance imaging findings

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Accepted 6 April 2011

Abstract

Objective: To present prenatal ultrasound and perinatal magnetic resonance imaging (MRI) findings of Galloway-Mowat syndrome.

Case Report: A 31-year-old woman, gravida 3, para 2, was referred for genetic counseling at 29 weeks of gestation because of abnormal ultrasound findings and a previous child with Galloway-Mowat syndrome. During this pregnancy, microcephaly, intrauterine growth restriction (IUGR), and oligohydramnios were first noted at 27 weeks of gestation. Repeated ultrasounds showed microcephaly, IUGR, and oligohydramnios. MRI performed at 32 weeks of gestation showed reduced sulcation of the brain, pachygyria, poor myelination of the white matter, and cerebellar atrophy. A diagnosis of recurrent Galloway-Mowat syndrome was made. At 40 weeks of gestation, a 2,496-g female baby was delivered with microcephaly, a narrow sloping forehead, epicanthic folds, microphthalmos, a highly arched palate, a small midface, a beaked nose, thin lips, large low-set floppy ears, clenched hands, and arachnodactyly. Postnatal MRI findings were consistent with the prenatal diagnosis. Renal ultrasound showed enlarged bilateral kidneys with increased echogenicity. At the age of 2 weeks, the infant became edematous and developed nephrotic syndrome.

Conclusion: Microcephaly, IUGR, and oligohydramnios are significant ultrasound triad of fetal Galloway-Mowat syndrome. Prenatal ultrasound diagnosis of microcephaly, IUGR, and oligohydramnios in late second trimester or in early third trimester should alert clinicians to the possibility of Galloway-Mowat syndrome and prompt a detailed search of abnormal sulcation, cortical gyral maldevelopment, and cerebellar atrophy by fetal ultrafast MRI.

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Keywords: Cerebellar atrophy; Galloway-Mowat syndrome; Magnetic resonance imaging; Prenatal diagnosis; Ultrasound
Introduction

Galloway-Mowat syndrome (online Mendelian inheritance in man 251300), or microcephaly, hiatus hernia and nephrotic syndrome, or nephrosis—neuronal dysmigration syndrome, or nephrosis—microcephaly syndrome, is a rare autosomal recessive disorder. This syndrome was first described by Galloway and Mowat in 1968 [1] in a brother and a sister with microcephaly, hiatal hernia, and nephrotic syndrome. Patients with Galloway-Mowat syndrome will develop early-onset intractable seizures and nephrotic syndrome, psychomotor delay, mental retardation, and death in early childhood because of renal failure [2]. Galloway-Mowat syndrome is characterized by microcephaly; early-onset corticosteroid-resistant nephrotic syndrome; developmental delay; and central nervous system abnormalities, such as defects of neuronal migration, hypomyelination, and cerebellar atrophy [3]. Other additional findings include a slopping forehead, flat occiput, hypertelorism, ptosis, corneal opacity, cataract, microphthalmos, hypoplastic iris, optic atrophy, large low-set floppy ears, a small midface, a beaked nose, high-arched palate, micrognathia, club feet, camptodactyly, flexion contractures of joints, hypoplastic nails, hiatal hernia, eventration of diaphragm, ovarian agenesis, atrophic thymus, calcification of the intervertebral discs, platybasia, Dandy-Walker malformation, aqueductal stenosis with hydrocephalus, and central canal malformation [3]. Arachnodactyly has been observed in some Taiwanese patients affected with Galloway-Mowat syndrome [4—6]. Here, we present prenatal ultrasound and perinatal magnetic resonance imaging (MRI) findings of recurrent Galloway-Mowat syndrome in a fetus.

Case report

A 31-year-old woman, gravida 3, para 2, was referred for genetic counseling at 29 weeks of gestation because of

Fig. 1. Fetal ultrafast magnetic resonance imaging at 32 weeks of gestation shows (A) hypomyelination with increased T2 signal intensity over bilateral temporal white matter (arrows); (B) pachygyria with effacement of cortical gyri (arrows); (C) cerebellar atrophy (arrows); and (D) a cyst arising from the frontal horn of left lateral ventricle (arrows).
recurrent fetal microcephaly, intrauterine growth restriction (IUGR) and oligohydramnios. She and her husband were nonconsanguineous. Six years previously, she had delivered a small-for-gestational-age male baby with microcephaly and abnormal brain MRI findings consistent with the diagnosis of Galloway-Mowat syndrome [5]. The infant suffered from nephrotic syndrome and psychomotor retardation, and died at the age of 5 months. Three years previously, she delivered a healthy male baby without any abnormality. During this pregnancy, the prenatal ultrasound findings were unremarkable until 27 weeks of gestation when microcephaly, IUGR, and oligohydramnios were first noted. Detailed sonographic examination at 29 weeks of gestation revealed decreased amount of amniotic fluid; a head circumference (HC) of 24.6 cm (26 weeks); a biparietal diameter (BPD) of 6.52 cm (27 weeks); an abdominal circumference (AC) of 22.2 cm (28 weeks); and a femur length (FL) of 5.6 cm (29 weeks). Fetal ultrafast MRI performed at 32 weeks of gestation showed hypomyelination with increased T2 signal intensity over bilateral temporal white matter, pachygyria with effacement of cortical gyri, cerebellar atrophy, and a cyst arising from the frontal horn of left lateral ventricle (Fig. 1). A diagnosis of recurrent Galloway-Mowat syndrome was made. At 33 weeks of gestation, ultrasound revealed an HC of 26.5 cm (28 weeks); a BPD of 7.4 cm (28 weeks); an AC of 23.8 cm (28 weeks); and an FL of 6.3 cm (35 weeks). At 39 weeks of gestation, ultrasound revealed an HC of 30.1 cm (33 weeks); a BPD of 8.75 cm (34 weeks); an AC of 28.76 cm (34 weeks); and an FL of 7.7 cm (41 weeks). At 40 weeks of gestation, a female baby was delivered uneventfully. Her body weight was 2,496 g (3rd—10th centile); body length was 51 cm (50th centile); and occipitofrontal circumference was 31 cm (less than third centile). The infant manifested microcephaly, a narrow sloping forehead, epicanthic folds, microphthalmos, a highly arched palate, a small midface, a beaked nose, thin lips, large low-set floppy ears, clenched hands, and arachnodactyly. Renal ultrasound showed enlarged bilateral kidneys with increased echogenicity. MRI scans at the age of 6 days documented a small head, reduced sulcation, and hypomyelination with T2 high signal intensity in bilateral white matter, particularly in both temporal and frontal lobes, subdural fluid collection over bilateral frontal and temporal areas, pachygyria with effacement of cortical gyri in bilateral temporal lobes, and prominence of preopticine and retrocerebellar cisterns because of cerebellar atrophy (Fig. 2). At the age of 2 weeks, she became edematous, developed nephrotic syndrome with proteinuria and hypalbuminemia, and presented typical craniofacial appearance and digital abnormalities of Galloway-Mowat syndrome (Fig. 3).
Discussion

We have demonstrated the perinatal MRI findings of Galloway-Mowat syndrome. Fetal ultrafast MRI has been shown to be a useful tool to determine the extent of central nervous system involvement in fetuses affected with Galloway-Mowat syndrome [5,7]. As presented in this case, a fetal MRI performed at 32 weeks of gestation manifested the characteristic findings of Galloway-Mowat syndrome, namely, reduced sulcation of the brain, gyral abnormalities, pachygyria, poor myelination of the white matter, and cerebellar atrophy.

Most reported cases of Galloway-Mowat syndrome were diagnosed postnatally, and prenatally detected cases were

There is a 25% recurrence risk in Galloway-Mowat syndrome. Prenatal diagnosis of Galloway-Mowat syndrome in early pregnancy, currently, is not possible and will require our understanding of the molecular genetics of Galloway-Mowat syndrome. The gene responsible for Galloway-Mowat syndrome remains unknown. It has been shown that glomerular podocytes and neurons share many molecular cell biological features, especially the process formation [12,13]. Accordingly, various hypotheses concerning the pathogenesis of Galloway-Mowat syndrome have been raised, such as genetic disorders of glomerular podocyte proteins (epithelial protein 1, synaptopodin, and nephrin) [14] and glomerular basement membrane proteins (laminins and integrins) [15]. However, a search of candidate genes is still unsuccessful at the present time.

The present case provides evidence that microcephaly, IUGR, and oligohydramnios are a significant ultrasound triad of fetal Galloway-Mowat syndrome. Prenatal ultrasound diagnosis of microcephaly, IUGR, and oligohydramnios in late second trimester or in early third trimester should alert clinicians to the possibility of Galloway-Mowat syndrome and prompt a detailed search of abnormal sulcation, cortical gyral maldevelopment, and cerebellar atrophy by fetal ultrafast MRI.

Acknowledgments

This work was supported by research grants NSC-96-2314-B-195-008-MY3, NSC-97-2314-B-195-006-MY3, and NSC-99-2628-B-195-001-MY3 from the National Science Council, and MMH-E-100-04 from Mackay Memorial Hospital, Taipei, Taiwan.

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