Available online at www.sciencedirect.com
ScienceDirect
Taiwanese Journal of Obstetrics & Gynecology 50 (2011) 212–216
www.tjog-online.com

Case Report

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

Chih-Ping Chen [a,b,c,d,e,f,*], Shuan-Pei Lin [b,g], Yu-Peng Liu [h,i], Jeng-Daw Tsai [g], Chen-Yu Chen [a], Shin-Lin Shih [h], Fuu-Jen Tsai [d,j,k], Pei-Chen Wu [a], Wayseen Wang [b,l]

[a] *Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan*
[b] *Department of Medical Research, Mackay Memorial Hospital, Taipei, Taiwan*
[c] *Department of Biotechnology, Asia University, Taichung, Taiwan*
[d] *School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan*
[e] *Institute of Clinical and Community Health Nursing, National Yang-Ming University, Taipei, Taiwan*
[f] *Department of Obstetrics and Gynecology, School of Medicine, National Yang-Ming University, Taipei, Taiwan*
[g] *Department of Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan*
[h] *Department of Radiology, Mackay Memorial Hospital Hsinchu Branch, Hsinchu, Taiwan*
[i] *Mackay Medicine, Nursing and Management College, Taipei, Taiwan*
[j] *Department of Medical Genetics, China Medical University Hospital, Taichung, Taiwan*
[k] *Department of Medical Research, China Medical University Hospital, Taichung, Taiwan*
[l] *Department of Bioengineering, Tatung University, Taipei, Taiwan*

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 slopping 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.

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

* Corresponding author. Department of Obstetrics and Gynecology, Mackay Memorial Hospital, 92, Section 2, Chung-Shan North Road, Taipei, Taiwan.
E-mail address: cpc_mmh@yahoo.com (C.-P. Chen).

1028-4559/$ - see front matter
doi:10.1016/j.tjog.2011.04.005

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

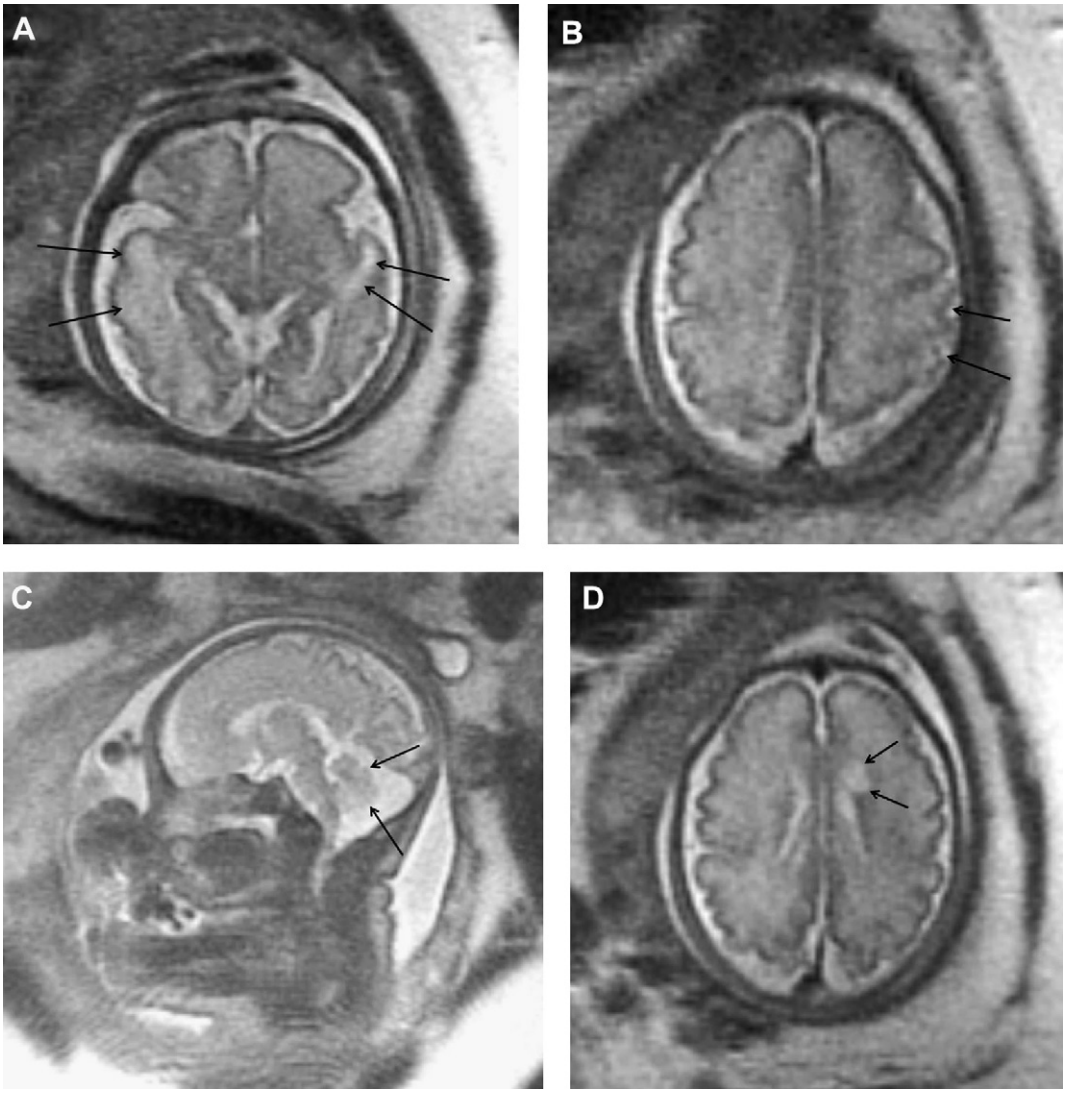

Fig. 1. Fetal ultrafast magnetic resonance imaging at 32 weeks of gestation shows (A) hypomyelination with increased T2 signal intensity over bilateral temporal white matter (arrows); (B) pachygyria with effacement of cortical gyri (arrows); (C) cerebellar atrophy (arrows); and (D) a cyst arising from 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 (3^{rd}–10^{th} centile); body length was 51 cm (50^{th} centile); and occipitofrontal circumference was 31 cm (less than third centile). The infant manifested microcephaly, a narrow slopping 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 prepontine and retrocerebellar cisterns because of cerebellar atrophy (Fig. 2). At the age of 2 weeks, she became edematous, developed nephrotic syndrome with proteinurea and hypoalbuminemia, and presented typical craniofacial appearance and digital abnormalities of Galloway-Mowat syndrome (Fig. 3).

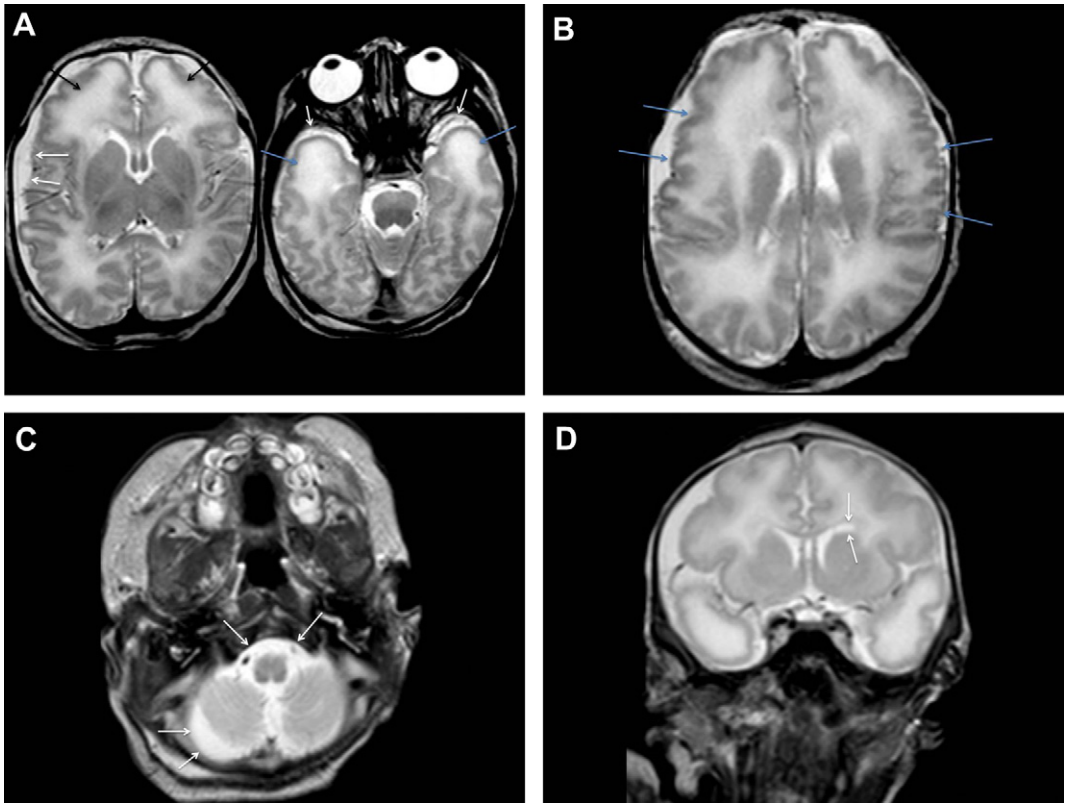

Fig. 2. Magnetic resonance imaging at the age of 6 days shows (A) poor hypomyelination over bilateral frontal white matter (black arrows) and temporal white matter (blue arrows), and subdural fluid collection over bilateral frontal and temporal areas (white arrows); (B) pachygyria with effacement of cortical gyri in bilateral frontal and temporal lobes (arrows); (C) prominence of prepontine and retrocerebellar cisterns (arrows) because of cerebellar atrophy; and (D) a cyst arising from the frontal horn of left lateral ventricle (arrows).

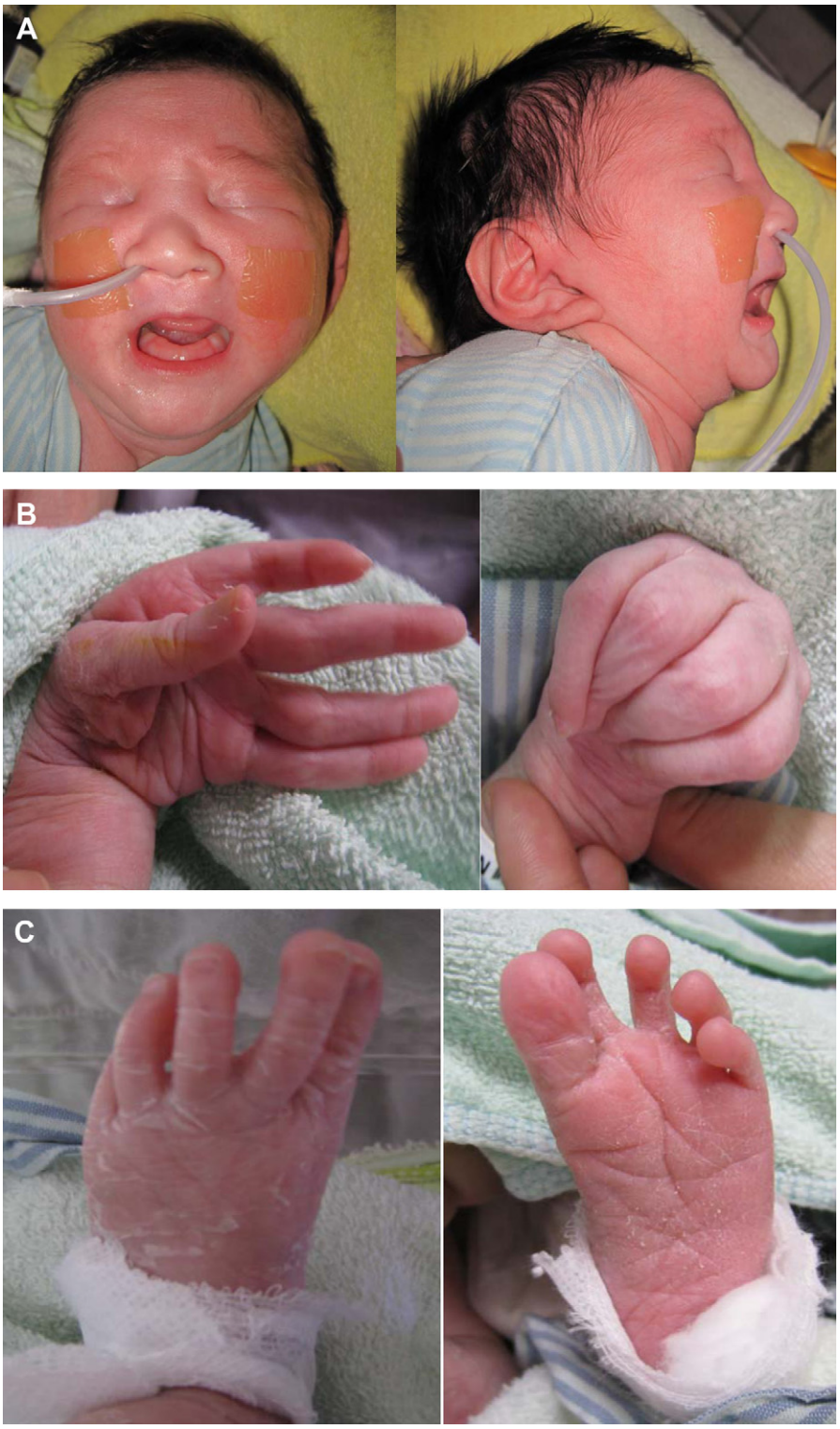

Fig. 3. (A) Craniofacial appearance of the infant at the age of 2 weeks. (B) Arachnodactyly of the hand and the clenched hand. (C) Arachnodactyly of the foot.

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

uncommon and were limited to those of recurrence. Hou and Wang [4] reported IUGR and polyhydramnios in a pregnancy with fetal Galloway-Mowat syndrome. Kang et al [8] reported late-onset IUGR and microcephaly in a pregnancy with fetal Galloway-Mowat syndrome. Microcephaly, oligohydramnios, and IUGR in late gestation have been reported in three separate cases of Galloway-Mowat syndrome [5,6,9]. Horton et al [7] reported microcephaly, oligohydramnios, and a mid-trimester thickened nuchal fold in a case of fetal Galloway-Mowat syndrome. Chen et al [5] first used fetal MRI at 34 weeks of gestation to detect the extent of brain involvement in fetal Galloway-Mowat syndrome. Horton et al [7] used fetal MRI at 25 weeks and 32 weeks of gestation to evaluate fetal cortical patterns in a case of Galloway-Mowat syndrome. The present case additionally shows that cerebellar atrophy can be a prominent fetal MRI finding in addition to abnormal gyri and sulci in the prenatal diagnosis of fetal Galloway-Mowat syndrome. Central nervous system abnormalities associated with Galloway-Mowat syndrome include defects of neuronal migration, hypomyelination, and cerebellar atrophy [10]. Keith et al [11] suggested that neuropathological findings in true Galloway-Mowat syndrome are abnormal gyral patterns, disordered cortical lamination, absent dentate gyri, and cerebellar hypoplasia with aplasia of the granular layer.

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.

References

[1] Galloway WH, Mowat AP. Congenital microcephaly with hiatus hernia and nephrotic syndrome in two sibs. J Med Genet 1968;5:319–21.
[2] Meyers KEC, Kaplan P, Kaplan BS. Nephrotic syndrome, microcephaly, and developmental delay: three separate syndromes. Am J Med Genet 1999;82:257–60.
[3] Srivastava T, Warady BA. Galloway-Mowat syndrome. In: The National Organization for Rare Disorders. NORD guide to rare disorders. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. p. 687–8.
[4] Hou J-W, Wang T-R. Galloway-Mowat syndrome in Taiwan. Am J Med Genet 1995;58:245–8.
[5] Chen C-P, Chang T-Y, Lin S-P, Huang J-K, Tsai J-D, Chiu N-C, et al. Prenatal magnetic resonance imaging of Galloway-Mowat syndrome. Prenat Diagn 2005;25:441–5.
[6] Chen C-P, Lin S-P, Tsai J-D, Huang J-K, Yen J-L, Tseng C-C, et al. Perinatal imaging findings of Galloway-Mowat syndrome. Genet Couns 2007;18:353–5.
[7] Horton AL, Smith JK, Strauss RA. Recurrence of Galloway Mowat syndrome and associated prenatal imaging findings. Prenat Diagn 2009; 29:280–2.
[8] Kang L, Kuo P-L, Lee K-H, Liu Y-C, Chang C-H, Chang F-M, et al. Late onset growth restriction in Galloway Mowat syndrome: a case report. Prenat Diagn 2005;25:159–62.
[9] Chen C-P, Lin S-P, Chang T-Y, Tsai J-D, Huang J-K, Wang W. Recurrent Galloway-Mowat syndrome associated with abnormal prenatal findings. Genet Couns 2006;17:87–9.
[10] Pezzella M, Yeghiazaryan NS, Veggiotti P, Bettinelli A, Giudizioso G, Zara F, et al. Galloway-Mowat syndrome: an early-onset progressive encephalopathy with intractable epilepsy associated to renal impairment. Two novel cases and review of literature. Seizure 2010;19:132–5.
[11] Keith J, Fabian VA, Walsh P, Sinniah R, Robitaille Y. Neuropathological homology in true Galloway-Mowat Syndrome. J Child Neurol 2011;26: 510–7.
[12] Kobayashi N, Mominoki K, Wakisaka H, Shimazaki Y, Matsuda S. Morphogenetic activity of extracellular matrices on cultured podocytes. Laminin accelerates podocyte process formation in vitro. Ital J Anat Embryol 2001;106:423–30.
[13] Kobayashi N. Mechanism of the process formation; podocytes vs. neurons. Microsc Res Tech 2002;57:217–23.
[14] Srivastava T, Whiting JM, Garola RE, Dasouki MJ, Ruotsalainen V, Tryggvason K, et al. Podocyte proteins in Galloway-Mowat syndrome. Pediatr Nephrol 2001;16:1022–9.
[15] Dietrich A, Matejas V, Bitzan M, Hashmi S, Kiraly-Borri C, Lin S-P, et al. Analysis of genes encoding laminin β2 and related proteins in patients with Galloway-Mowat syndrome. Pediatr Nephrol 2008;23: 1779–86.