A Case of Galloway–Mowat Syndrome with Classic Clinical Triad in the Neonatal Period

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Galloway-Mowat syndrome (GMS) is a rare malformation syndrome characterized by intrauterine growth retardation (IUGR), early-onset nephrotic syndrome, hiatal hernias and central nervous system involvement such as microcephaly, cerebellar atrophy and developmental delay. In the original description, GMS was reported as a clinical triad of nephrotic syndrome, neurological manifestations, and hiatal hernia. However, hiatal hernia is no longer considered essential findings for diagnosis. In our knowledge, the patients with classic clinical triad in neonatal period have not been reported in Korean population.

Key Words: Galloway-Mowat syndrome, Nephrotic syndrome, Newborn

Galloway–Mowat syndrome (GMS) is a rare malformation syndrome characterized by intrauterine growth retardation (IUGR), early-onset nephrotic syndrome, hiatal hernias and central nervous system involvement such as microcephaly, cerebellar atrophy and developmental delay. Therefore, the authors herein describe an infant showing hiatal hernia, neurologic abnormalities such as microcephaly and nephrotic syndrome in neonatal period.

A 31-year-old woman was referred to our hospital at 39 weeks of gestation because of congenital diaphragmatic hernia and intrauterine growth restriction, which were suspected by ultrasonography at 36 weeks of gestation. A male infant weighing 2,250 g was born at gestational week 39\(^{\text{+3}}\) by cesarean section. The patient revealed mild dysmorphic facial features and microcephaly. On day 7, Nissen fundoplication was done because of hiatal hernia with gastric volvulus. At the age of 2 weeks he developed nephrotic syndrome with proteinuria and hypoalbuminemia. This is the first case of GMS that three classic findings were present in neonatal period in Korea.
Chest radiography and upper gastrointestinal series revealed hiatal hernia with gastric volvulus (Fig. 1). On day 7, Nissen fundoplication was done. A feeding problem was apparent and a nasogastric tube was required for nutrition. At the age of 2 weeks, he became edematous and developed nephrotic syndrome with proteinuria and hypoalbuminemia. The 24 hour excretion of urinary protein was 2.871 g. Fundus in optic evaluation was normal without microcoria. On day 28, open renal biopsy was done. Renal biopsy showed focal segmental glomerulosclerosis (Fig. 2). Magnetic resonance imaging (MRI) of brain was suggestive of lissencephaly (Fig. 3). The patient’s karyotype indicated 46, XY. Screening for metabolic disease was unremarkable. The patient was discharged while keeping tubal feeding at 43-days-of-age.

The patient was readmitted because of afebrile convulsion at 4 month of age. The interictal electroencephalogram during sleep was moderately abnor-

![Fig. 1. Upper gastrointestinal series show esophagogastric junction above diaphragm and folded stomach with anteriorly high located duodenal bulb.](image1)

![Fig. 2. Hematoxylin and eosin stained section showing high power view of glomeruli with increased and hypercellular mesangium (A, X100) and segmental lobular collapse and sclerosis (B, X200).](image2)

![Fig. 3. Magnetic resonance image of brain T1 weighted axial images showing thickened and flattened cortical gyri predominantly involves bilateral frontal and parietal region.](image3)
mal due to poorly organized sleep feature with diffuse voltage attenuation and intermittent focal epileptiform discharges. Medication of phenytoin was started. The neurologic examination revealed axial hypotonia with poor neck control. After discharge, the patient was followed up in outpatient clinics. His seizures subsequently increased within few months and were refractory to treatment of phenytoin, levetiracetam, oxcarbazepine, valproic acid and clobazam. At age of 9 months the patient developed generalized edema, poor urination and electrolyte imbalance due to nephrotic syndrome. The patient was treated with corticosteroids and cyclophosphamide but revealed no response. At age of 10 months he died from renal insufficiency.

### Discussion

Approximately 60 cases have been reported since two siblings with central nervous system anomaly, hiatal hernia and nephrotic syndrome were described in 1968. In our knowledge, two cases have been reported since 2001 in Korean population. The first case reported on two siblings with microcephaly, gyral abnormality, minor facial anomalies, and congenital nephrotic syndrome. Although two siblings developed nephrotic syndrome in neonatal period, they did not present neurologic abnormalities and hiatal hernia respectively in neonatal period. The second report described a girl with microcephaly, seizures, and psychomotor retardation who developed nephrotic syndrome at 17 months of age.

In the original description, GMS was reported as a clinical triad of nephrotic syndrome, neurological manifestations, and hiatal hernia. Although hiatal hernia is no longer considered essential findings for diagnosis, this is the first case of GMS that three classic findings were present in neonatal period in Korea.

It appears that nephrotic syndrome usually manifests within the first 3 years of life and is refractory to treatment in GMS patients. The nephrotic syndrome also occurs in the first months of life and is typically steroid–resistant. As death usually occurs within few years from the onset of nephrotic syndrome, neonatal manifestation of nephrotic syndrome was suspected to have poor prognosis in GMS. Actually we experienced that GMS patient with refractory epilepsy and steroid resistant nephrotic syndrome which occurs in neonatal period had very poor prognosis.

GMS is postulated to have an autosomal recessive inheritance pattern. The genetics of GMS remains unknown, despite the defective roles of several proteins of glomerular basement membrane such as the family of laminins and integrons were assumed as a candidate pathogenesis for GMS. Although Dietrich et al. studied whether GMS is associated with mutations of LAMB2 or genes encoding proteins that interact with laminin β2, they failed to find causative mutations in these genes. Further research is required to clarify the pathogenesis of GMS for genetic counseling and family planning.

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### References

신생아 시기에 전형적인 특징을 보인 Galloway-Mowat syndrome 1례

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Galloway-Mowat syndrome은 태내 성장지연, 조기발현 신증후군, 소두증이나 뇌이랑 병변과 같은 신경계 이상, 식도열공 탈장과 함께 나타나는 증후군으로 현재는 식도열공 탈장이 진단에 필수 요건이 아니지만 이전에는 신증후군, 신경계 이상, 식도열공 탈장의 clinical triad라고 명명하였다. 상염생체 열성으로 유전되는 것으로 알려져 있으며 신증후군의 발생 시기는 대부분 3세 이전이다. 식도열공 탈장 소견, 소두증, 뇌이랑 병변, 신증후군 등의 병리소견을 보이는 주된 진단 기준이다. 현재까지 국내에서는 두 개의 증례가 보고되었는데 이들 모두 신생아기에 발생한 증례들이다. 이에 저자들은 신생아기에 신증후군, 신경계 이상, 식도열공 탈장의 clinical triad를 보이는 증례들을 경험한 바 있다.

= 국 문 초 록 =

신생아 시기에 전형적인 특징을 보인 Galloway-Mowat syndrome 1례

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Galloway-Mowat syndrome은 태내 성장지연, 조기발현 신증후군, 소두증이나 뇌이랑 병변과 같은 신경계 이상, 식도열공 탈장과 함께 나타나는 증후군으로 현재는 식도열공 탈장이 진단에 필수 요건이 아니지만 이전에는 신증후군, 신경계 이상, 식도열공 탈장의 clinical triad라고 명명하였다. 상염생체 열성으로 유전되는 것으로 알려져 있으며 신증후군의 발생 시기는 대부분 3세 이전이다. 식도열공 탈장 소견, 소두증, 뇌이랑 병변, 신증후군 등의 병리소견을 보이는 주된 진단 기준이다. 현재까지 국내에서는 두 개의 증례가 보고되었는데 이들 모두 신생아기에 발생한 증례들이다. 이에 저자들은 신생아기에 신증후군, 신경계 이상, 식도열공 탈장의 clinical triad를 보이는 증례들을 경험한 바 있다.

중심 단어: Galloway-Mowat 증후군, 신증후군, 신생아