CASE REPORT

Galloway-Mowat Syndrome

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ABSTRACT

Galloway-Mowat syndrome is a rare multisystem genetic disorder with constellation of neurological, skeletal, growth, facial, gastrointestinal and renal abnormalities. This case report describes Galloway-Mowat syndrome in a young boy suffering from congenital microcephaly, developmental delay, seizures and various dysmorphic features in whom nephrotic syndrome became apparent at 5 years of age.

Key words: *Microcephaly. Seizures. Developmental delay. Dysmorphism. Nephrotic syndrome. Galloway-Mowat syndrome.*

INTRODUCTION

Galloway–Mowat syndrome, also known as Microcephaly-Hiatal hernia nephrotic syndrome, is a rare genetic disorder inherited as an autosomal recessive trait usually presenting before 2 years of life. It is mostly resistant to steroid therapy.

A variety of physical and developmental abnormalities occur in addition to nephrosis which include short stature/intrauterine growth retardation, microcephaly, developmental delay, distinct facial dysmorphism, gut and brain malformations in addition to skeletal deformities comprising arachnodactyly, camptodactyly and/or clasp thumb. The craniofacial anomalies particularly an extremely small-sized head with flat vertex and occiput are obvious at birth. The characteristic facies include an abnormally high but narrow forehead, ocular hypertelorism, almond-shaped eyes, pinched nose, large and low-set ears with or without ear cartilage deficiency, micrognathia, high-arched palate and abnormal dentition. Hiatal hernia and megaesophagus are the commonly exhibited gut abnormalities. Neuropathological findings include abnormal gyral pattern (microgyria or pachygyria), lissencephaly,encephalomalacia/poren-cephaly, cortical atrophy, leukomalacia, paraparesis, quadriparesis, stenosis of the aqueduct of Sylvius and hypomyelination in cerebrum, spinal cord/ and brain-stem. The latter results in seizures, mental retardation and developmental inability to perform certain motor skills normal for the chronological age, particularly skills requiring co-ordination of muscular and mental activity (psychomotor retardation).[1] As nephrosis fails to respond to any form of therapy and progresses to end-stage of renal disease, the prognosis of this condition is poor as death almost inevitably supervenes during the first decade of life. A few cases have been reported with late-onset proteinuria and a more protracted course.[2,3]

CASE REPORT

A 5-year-old developmentally delayed boy presented through outpatient department with complaints of generalized body swelling for one month and seizures for two days prior to admission. He was born full term but was small-for-gestational age to consanguineous parents who had two other healthy siblings and a stillbirth. Although ante- and perinatal events were unremarkable, he had achieved his developmental milestones at a late stage with respect to chronological age.

Physical examination revealed an edematous, short-statured child (height=72 cm - < 5th percentile) with obvious microcephaly (OFC=41 cm - < 3 SD) and stable vital signs. Blood pressure was normal initially but later became more than 95th percentile for age (140/95 mmHg). He had facial dysmorphism with high narrow forehead, almond-shaped eyes, large, low-set ears, micrognathia, high arched palate and malocclusion of teeth. On neurological examination, there was generalized hypotonia and the reflexes were difficult to elicit, while later on the boy developed hemiplegia. Fundoscopy was performed for exclusion of chorioretinitis, which is a manifestation of TORCH infections that was considered the closest differential of this condition. The rest of general as well as systemic examination was unremarkable except anasarca along with scrotal swelling.

The biochemical workup revealed nephrotic range proteinuria (spot urinary protein : creatinine ratio=9.6) with hypoalbuminemia (serum albumin=1.6 g/dl) and hypercholesterolemia (serum cholesterol=565 mg/dl). The initial evaluation also included determination of

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renal function, serum electrolytes and blood calcium levels as well as cerebrospinal fluid analysis all of which were normal. Barium swallow and CT scan of brain were carried out for detection of associated esophageal and brain malformations respectively but none was found. The electroencephalogram, skeletal survey and TORCH screening were also found to be unremarkable. Renal biopsy was planned to confirm the presence of Focal Segmental Glomerulosclerosis (FSGS) or Diffuse Mesangial Sclerosis (DMS), the two most common renal pathologies occurring in this syndrome. As the child developed fulminant septicemia, refractory convulsions and hemiplegia during stay in the hospital, the biopsy was postponed. He was offered multiple antibiotics and steroids (oral as well as methylprednisolone pulses) for treatment of infection and nephrosis respectively. He received supportive/ symptomatic treatment in the form of anticonvulsants and antihypertensive agents in addition to counseling of parents regarding the prognosis of the disease.

DISCUSSION

Since the first description by Galloway and Mowat in 1968,[4] about 40 further patients with Galloway-Mowat syndrome have been reported. This inherited disorder is believed to be transmitted in an autosomal recessive pattern. The genetic defect is still unknown, although mutations in podocyte proteins and reduced expression of synaptopodin, GLEPPI and nephrin have been seen in these patients.[5] Mutation analysis was not done in this case due to the lack of the facility.

The onset of nephrotic syndrome is usually evident in the first 2 years of life but a later onset has also been recorded as in this patient in whom it became apparent at 5 years of age. There is a wide variation of renal histological patterns seen in such a syndrome, which comprise of Focal Segmental Glomerulosclerosis (FSGS) and Diffuse Mesangial Sclerosis (DMS) with alterations in glomerular basement membrane ultrastructure, which is the most common cause of mortality in these patients due to therapy-resistant renal failure.[6-8] The decision of renal replacement therapy (dialysis/transplantation) in case renal failure develops is entirely on parents' discretion. Nephromegaly, microcystic renal dysplasia and mesangial hypercellularity are other features seen in this condition.[9]

A variety of brain malformations are found in majority of patients as described earlier. The gyral abnormalities are essential for the diagnosis of Galloway-Mowat syndrome. Some children may lack structural changes of brain as reported by Meyers *et al.*[10] as seen in this case. The child did not have any esophageal abnormality.

Although microcephaly and nephrotic syndrome with or without Hiatal hernia has been equated with Galloway-Mowat syndrome in the literature, the brain and renal pathology in these reported cases have been very variable. It is likely that this group as a whole is etiologically heterogenous.

There is no specific treatment for this condition except genetic counseling and supportive or symptomatic care along with a multidisciplinary approach involving co-ordinated efforts of a team of general practitioners, nephrologists, gastroenterologists, neurologists and physical therapists to ensure a systematic and comprehensive approach to treatment.

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