CASE REPORT

Mesangioproliferative glomerulonephritis in an infant with Prader-Willi syndrome

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Abstract
Prader - Willi syndrome (PWS) is a neurobehavioral disorder characterized mainly by neonatal hypotonia, dysmorphic features, hypogonadism, mental retardation and behavioral problems. The PWS has not been associated with renal complications. We report the case of an infant with Prader-Willi syndrome due to loss of the paternal copy of chromosome 15q11.2-13, who presented with severe proteinuria and microscopic hematuria. Renal biopsy revealed mesangioproliferative glomerulonephritis (MPGN). The early onset of the primary MPGN in this infant make us consider a possible association between the deficiency of the paternally expressed genes from the 15q11-q13 region and the renal disease. Hippokratia 2009; 13 (2): 125-126

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Prader-Willi syndrome (PWS) is the first human disorder attributed to genomic imprinting[1]. The most common molecular defect found in PWS patients is a ~6-Mb chromosomal deletion of the 15q11-q13 region on the paternal chromosome[2]. Characteristics which have commonly been associated with PWS are diminished fetal activity, hypotonia, dysmorphic features, obesity, mental retardation, short stature and hypogonadotropic hypogonadism[3-5]. Most clinical manifestations are evident by the age of 3 to 5 years. Renal problems have only sporadically been mentioned in these patients. We report a case of an infant with PWS who developed proteinuria and microscopic hematuria. Renal biopsy revealed findings consistent with mesangioproliferative glomerulonephritis (MPGN).

Case Report

A 13-month old girl, delivered at 40 weeks gestation by a cesarean section, was suspected to be a case of PWS due to her profound hypotonia and poor suck reflex. Methylation specific polymerase chain reaction (MSPCR) documented an abnormal methylation pattern of 15q11.2-13 chromosome, characteristic of PWS. The deletion of the paternal copy of 15q11.2-13 was proved by fluorescent in situ hybridization (FISH), confirming the diagnosis of PWS at the age of 2 months. Pending the results of the genetic testing, a thorough metabolic screening was performed with unremarkable findings.

At the age of 6 months the patient presented microscopic hematuria as a random finding in the course of a respiratory tract infection. Four months later the hematuria was complicated persistent, progressive proteinuria. Her protein excretion, mainly albumin, increased gradually up to 1.3 gr/m²/24hour. The infant was normotensive, without edema and her renal function tests as well as serum total cholesterol, protein and albumin levels were normal. No serologic or other evidence of streptococcal, mycoplasmatic, human immunodeficiency virus, hepatitis B and C virus infections were noted. Her immunologic evaluation was also unremarkable. Renal ultrasonography demonstrated a mild increase in the echogenecity and the length of both kidneys (left 7.0 cm-right 7.4 cm).

At the age of 13 months, as the proteinuria persisted, we performed a renal biopsy. The findings of the histologic examination by light microscopy and immunohistochemistry were consistent with mild mesangioproliferative glomerulonephritis (Figure 1). In detail, the glomerular capillaries were patent. Mild mesangial hypercellularity (3-4 cells per mesangial region) and segmental mild podocyte hyperplasia were noted in 2 glomeruli, without segmental sclerotic lesions. Only few IgM granular deposits of low intensity, localized to the mesangium, were found by direct immunofluorescence technique. The IgG, IgA, C3, C4 and C1q or C9 stains were negative.

Discussion

A case of PWS with early presentation of primary MPGN at the infantile period is reported. Prader-Willi syndrome, with deletion of the paternal copy of 15q11.2-13 was diagnosed in our patient in early infancy due to neurologic manifestations. The renal complications presented at the age of 6 months initially with microscopic hematuria followed by persistent heavy

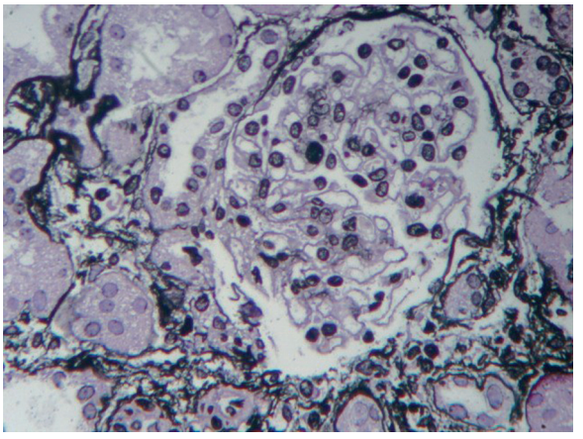

Figure1: Light micrograph of glomerulus stained with PASM, showing thin and delicate capillary walls and mild mesangial hypercellularity, without matrix increase (x450).

Treatment with a converting enzyme inhibitor (captopril 0.5mg/kg/d) was initiated. Follow-up is continued on an out-patient basis.

proteinuria. Renal biopsy revealed findings consistent with MPGN.

The classification of MPGN is complicated due to the existence of primary forms, such as resolving post-infectious glomerulonephritis and IgA nephropathy and multiple secondary subcategories, including autoimmune diseases, Henoch-Schönlein purpura and infective endocarditis[6]. In our patient there were no findings suggestive of secondary nephropathy.

Renal problems in PWS are uncommon. Mochizuki et al reported a case a 16 year-old girl with PWS complicated with focal segmental glomerulosclerosis[7]. The authors attributed the glomerulonehritis to coexistent renal agenesis and to glomerular adaptive hemodynamic changes due to the patient's extreme obesity. This speculation is excluded in our patient as neither a renal anatomical problem nor obesity, that could affect glomerular structure and function, were present. Other renal problems, which have been reported in cases of children with PWS, included renal tubular acidosis[8], unilateral renal malmigration and hydronephrosis combined with hydroureter and vesicoureteral reflux[9]. In the latter case an association between renal diseases and structural anomalies of bands q13-15 of chromosome 15 was postulated for the first time. This association was considered again by Lane et al in 1992 in a case of PWS complicated with membranoproliferative glomerulonephritis[10]. No other cause of renal disease was identified in our patient; therefore the kidney damage is likely to represent an idiopathic form of mesangioproliferative glomerulonephritis.

In our case we can not rule out the possibility of simple co-incidence of the two entities. Chromosome 15 is one of the seven human chromosomes with a high rate of segmental duplication[11]. The clinical significance of these duplications has not been clarified. Further researche of new mutations leading to familial forms of nephropathy could elucidate the possible association between renal diseases and genetic disorders such as Prader-Willi syndrome.

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