Peters Plus Syndrome: Another Way to See a Known Syndrome

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Abstract

Peters Plus Syndrome is a rare autosomal recessive disorder, clinically characterized by abnormal formation of various structures including anterior eye chamber, genitourinary tract, skeletal system and central nervous system anomalies are also commonly reported. PPS is due to defective B3GALTL gene encoding for a glycosyltransferase which plays a crucial role during embryogenesis. Here we report on a 12-year-old boy affected by Peters Plus Syndrome who showed peculiar additional features such as absence epilepsy and recurrent bacterial infections.

Keywords: Peters Plus syndrome; Absence epilepsy; B3GALTL

Introduction

Peters plus syndrome (PPS) is a rare autosomal recessive disorder mainly characterized by anterior chamber eye abnormalities (Peter’s anomaly) and rhizomelic limb shortening. Genitourinary tract and central nervous system (CNS) anomalies are also commonly reported. PPS is due to defective B3GALTL gene encoding for a glycosyltransferase which plays a crucial role during embryogenesis. Here we report a boy affected by PPS associated with peculiar additional features such as absence seizures and recurrent bacterial meningitis.

Clinical History

First son of a primigravida woman, he was born at 40 weeks. Intrauterine growth restriction was observed during pregnancy. At birth, Apgar indices were 8/10. Weight, length and head circumference were respectively at the 10th-25th centile, below the 3rd centile and at 25th-50th centile. Physical examination showed dysmorphic features and bilateral corneal leukemia. Genetic and metabolic testing, including karyotyping, urinary organic acids and mucopolisaccharides, were normal. Abdominal ultrasound (US) was normal except for the presence of testes in inguinal canals. Brain US showed a mild enlargement of lateral ventricles with calcifications of small thalamic arteries. Brain MRI imaging revealed widening of the 4th ventricle, enlarged cisterna magna, vermic hypoplasia, enlarged and dysmorphic lateral ventricles, increased signal intensity in the periventricular white matter and small bilateral areas of abnormal hyperintense signal at the level of the corona radiata.

Ophthalmological evaluation showed large bilateral central leukaemia associated with residuals of hyaloid artery, colobomatous appearance of right papilla and increased eye pressures.

In infancy, peculiar somatic traits became more evident. The child showed a round face, short upsloping palpebral fissures, thick eyebrows, small and low set ears, micrognathia, maxillary hypoplasia, and bilateral corneal leukaemia. Genetic and metabolic testing, including karyotyping, urinary organic acids and mucopolisaccharides, were normal. Abdominal ultrasound (US) was normal except for the presence of testes in inguinal canals. Brain US showed a mild enlargement of lateral ventricles with calcifications of small thalamic arteries. Brain MRI imaging revealed widening of the 4th ventricle, enlarged cisterna magna, vermic hypoplasia, enlarged and dysmorphic lateral ventricles, increased signal intensity in the periventricular white matter and small bilateral areas of abnormal hyperintense signal at the level of the corona radiata.

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Motor developmental milestones were reached timely while a mild language delay was observed.

On the basis of the physical appearance a diagnosis of Peters Plus Syndrome was formulated, subsequently confirmed by genetic analysis which detected a homozygous mutation c660+1G>A in B3GALTL gene. Both parents were found to be heterozygote for that mutation.

Figure 1: Facial appearance of the patient with round face, short up slanting palpebral fissures, thick eyebrows, small and low set ears, micrognathia and maxillary hypoplasia.

During childhood the patient developed three major infective episodes of CNS complicated by hearing loss with subsequent cochlear device implantation.

The first CNS infection episode occurred at the age of 4 years, when he presented pneumococcal meningitis. Immunological tests were normal. In that occasion an electroencephalogram (EEG) was performed which was proved normal. Three years later, he developed a second meningitis...
Figure 2: EEG during absence seizures. Ictal rhythm consisting with generalized spike-and-wave complexes of 3-3.5 Hz in both referential (A) and bipolar montages (B).
episode caused by non-capsulated haemophilus. Two years after this event, a new episode of meningitis occurred. The child was immediately placed under massive antibiotics therapy. Although cultural tests did not show bacterial growth, CSF was markedly turbid with increased protein concentration, very high cellularity, and reduced glucose levels.

The latest neuropsychiatric evaluation underlined a mild delay in performance subtests with better speech abilities, which could be considered within reference range.

At the age of 11 years he started to present with episodes characterized by abrupt loss of consciousness, with interruption of the ongoing activity and unresponsiveness, sometimes associated with mild clonic jerks of the eyelids, lasting 5-10 s and occurring several times per day.

A prolonged video-electroencephalogram recording was performed. Several episodes of typical absences were observed. Ictal EEG showed regular and symmetrical generalized discharges of 3-3.5 Hz spike-and-slow wave complexes which were congruent with a diagnosis of absence seizures (Figure 2). The interictal EEG demonstrated a substantially normal background with functional spikes and spike-and-slow waves in the frontal-central-temporal areas.

The patient was therefore placed under therapy with Valproate (VPA), which gave an incomplete control of absences. A combined therapy with Ethosuximide (ETS) resulted in a complete seizure control. The occurrence of side effects such as headache, gastritis and sleep disturbances led us to introduce Lamotrigine (LMT) in place of ETS. The patient is still seizure-free after two years of follow-up.

Discussion and Conclusion

PPS is a rare disease characterized by the association of Peters anomalies, represented by the triad of central corneal opacity, defects in the posterior layers of the cornea and lenticulo-corneal and/or irido-corneal adhesions, with systemic features such as short stature, short broad hands with fifth finger clinodactyly, distinctive facial features, cleft lip and/or cleft palate, hearing loss, abnormal ears, heart defects, genitourinary anomalies, mental retardation and CNS abnormalities [1-3].

PPS is a congenital disorder of glycosylation caused by a defect in a 1,3-glucosyltransferase whose function is to complete the synthesis of a normal background with functional spikes and spike-and-slow waves in the frontal-central-temporal areas.

The patient we report showed the classical clinical phenotype of PPS. Diagnosis was confirmed by molecular analysis which detected the most common mutation found in that disorder. However, he presented with additional findings such as absence seizures and recurrent bacterial meningitis.


References


