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Urticaria pigmentosa in a child with Prader-Labhart-Willi syndrome

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A 7-year-old girl with Prader-Labhart-Willi syndrome¹ was found to have urticaria pigmentosa. Prader-Labhart-Willi syndrome has not previously been associated with any specific skin disorder, although many patients are reported to have fair skin.² The affected child has two siblings with urticaria pigmentosa. Familial urticaria pigmentosa may be either autosomal recessive or autosomal dominant,³ whereas Prader-Labhart-Willi syndrome is generally sporadic. The occurrence of the two conditions may be coincidental but should alert the clinician to look for cutaneous lesions of urticaria pigmentosa in patients with Prader-Labhart-Willi syndrome.

Case report.

Our patient was a white girl born at 42 weeks gestation to a 21-year-old gravida 2, para 2 mother and a 23-year-old father. She was delivered by cesarean section because of a breech presentation. Her birth weight, length, and head circumference were 2.31 kg (5th percentile), 48.3 cm (25th percentile) and 34 cm (4th percentile), respectively.

Except for a decrease in fetal movement, the pregnancy was free from complications. The family medical history was unremarkable. Severe hypotonia, a weak cry, and an absent suck reflex were noted at birth. Tube feedings were required during the neonatal period. Seizures were noted in the patient at 5 months of age, and she was treated for dislocated hips during her first year of life. Thermal lability was also noted during infancy.

On physical examination of the patient at 2 years of age, the weight, height, and weight-height measurements were at or below the 5th percentile with a head circumference of 47.5 cm (10th percentile). The following features were also noted: dolichocephaly with a narrow bifrontal diameter, almond-shaped eyes with strabismus, scoliosis, small hands and feet, decreased muscle mass with a normal muscle biopsy specimen and electromyogram, hypotonia improving with age, early onset of hyperphagia, and psychomotor retardation. The results of routine laboratory and x-ray studies were normal. Results of high resolution chromosome studies were also normal.

At 7 years of age the patient was found to have 10 to 15 slightly raised, light brown, oval lesions on her back, neck, and chest. The lesions developed typical wheals and pruritus after scratching (Darier's sign). There was no history of flushing, diarrhea, or headaches. The patient's 9-year-old sister and 4-year-old brother had similar lesions. A skin biopsy specimen of the older sister showed the usual findings of cutaneous mastocytosis. Skin biopsy was not performed in the patient because of the older sister's classic clinical presentation and positive biopsy specimen. The child has been treated with topical steroid creams and systemic antihistamines on a symptomatic basis only. Gradual fading of a few of the lesions has occurred over time.

Although there was no history of consanguinity in the family, human leukocyte antigen (HLA) studies of the patient's mother, who was clinically unaffected with urticaria pigmentosa, indicated that she was homozygous A2,B13,DR7. We were unable to perform HLA typing on our patient. The HLA findings of other family members were as follows: A2-B13-DR7/A28-B44-DR6 (older affected sister of patient), A2-B13-DR7/A3-B35-DR4 or 8 (younger affected brother of patient).

Discussion.

Prader-Labhart-Willi syndrome features hypotonia at birth, hypogonadism, early childhood obesity, and mental deficiency. Other features such as small hands and feet, short stature, hypopigmentation, behavioral problems, and a deletion of the proximal long arm of chromosome 15 may also be present.^{1,2,4} To our knowledge, our patient is the first patient reported to have urticaria pigmentosa with Prader-Labhart-Willi syndrome.

Previous HLA studies in another family that has members affected with urticaria pigmentosa has been reported, but no apparent linkage or association was found. Fowler et al.³ reported identical HLA haplotypes in an affected boy and his unaffected brother, but other affected relatives had different HLA phenotypes. Results of the HLA studies in the family members we observed also do not correlate with expression of the disease. These data suggest that genes located on chromosome 6, which code for HLA haplotypes, are not linked to the gene or genes responsible for hereditary transmission of urticaria pigmentosa.

Both dominant and recessive inheritance patterns have been postulated for urticaria pigmentosa.⁵ In our case, the mother and father were clinically unaffected, but urticaria pigmentosa was diagnosed in their three children. The rest of the family history was normal. Therefore it appears that the most likely mode of inheritance in this family would be autosomal recessive, although autosomal dominant with nonpenetrance cannot be ruled out. Although the occurrence of both Prader-Labhart-Willi syndrome and urticaria pigmentosa may be coincidental, the clinician should look for cutaneous lesions of urticaria pigmentosa in patients with Prader-Labhart-Willi syndrome. The risk for Prader-Labhart-Willi syndrome in children born subsequently would be less than 1% in view of normal chromosomes; the risk for urticaria pigmentosa would be 25% if the gene in this family is segregating in an autosomal recessive way.

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Table I.

Clinical and genetic findings in Prader-Labhart-Willi syndrome

Finding	Patients (%)
Infantile hypotonia	100
Mental deficiency	99
Hypogonadism	98
Early childhood obesity	93
Short stature (<-1 SD)	78
Small hands, feet	76
Chromosome 15 deletion	50-70

SD, Standard deviation.