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# A CASE OF PRADER WILLI SYNDROME WITH DEL 15 (q11 → q13)*

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**SUMMARY: Tunçman G, Tükün A, Yalaz K, Bökesoy I. (Department of Medical Biology, Ankara University Faculty of Medicine, Ankara, Turkey). A case of Prader Willi syndrome with del15 (q11 → q13). Turk J Pediatr 1993; 35: 333-336.**

**Prader Willi syndrome is a sporadically seen genetic disease with an incidence of 1:25.000. In 56% of cases there is an interstitial deletion (q11 → q13) on chromosome 15.**

**Cytogenetic analysis was performed on a four-year-old girl with obesity, mental retardation, recurrent febrile convulsions and a provisional diagnosis of Prader Willi syndrome. High-resolution banding was done to observe the subchromosomal deletion. An interstitial deletion (q11 → q13) on one of the 15th chromosomes was observed in all metaphases.** *Key words: PWS, clinical manifestations, cytogenetic findings, chromosome 15.*

Prader-Willi Syndrome (PWS) was first defined by Prader and his colleagues in 1956[1], and hundreds of cases have been reported since then. It is generally seen sporadically with an incidence of 1:25,000. Major clinical features include: infantile hypotonia (94%), an early-childhood manifestation of obesity (94%), mental retardation with an IQ average of 65 (97%), short stature (76%), small hands and feet (83%), hypogenitalism (95%), and a typical facial expression[2].

In 1980, Ledbetter et al[3] were the first to assert that a deletion at 15q could be a cause of PWS. In 56% of cases there is an interstitial deletion (q11 → q13) on chromosome 15[2]. Cytogenetic translocations, inversions and duplications have been reported[2]. Since there is no karyotypical anomaly in 40% of cases, a mutation at the molecular level is also considered to be a possible cause of the PWS[2,4,5].

Variety in the clinical findings of PWS, as in some other autosomal dominant syndromes, has raised questions about the influence of more than one gene expression, and since 1988, it has been placed in a category of "contiguous gene syndrome"[6].

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The other fact that affects the clinical expression is the parental origin of the chromosome, and this encouraged scientists to define some models to explain the diversity of inheritance, including imprinting[2,5]. Since 1989 PWS has been considered to be a result of the phenomenon of imprinting[7].

## Case Report

The patient is a four-year-old girl who was admitted to the Medical Faculty of Hacettepe University Pediatric Neurology Department because of her recurrent febrile convulsions. She was sent to our laboratory for cytogenetic analysis with a provisional diagnosis of PWS. She was born by vacuum extraction, with a birth weight of 2,500 g, and her gross motor development was as follows: she lifted her head at approximately the fifth or sixth month of age, she sat without support at the sixth month, she walked holding on to furniture at the age of fifteen months and walked well at the age of three. Despite being on a diet, she progressively gained weight.

The pedigree analysis revealed a parental age of 25 at her birth and no consanguinity. She had a healthy brother.

At the time of admission, the patient was 99 cm tall ($10^{th}$-$20^{th}$ percentile), weighed 21 kg ($90^{th}$ percentile), and had a head circumference of 47 cm ($< 5^{th}$ percentile). She was obese and hypotonic. On physical examination, she was found to have low-set ears, plain occiput, simian line at the right hand, pes equinus, small labia majora and hirsutism on the legs. T3, T4, lactic acid, and pyruvic acid levels were found to be within normal limits. Bilateral calcifications at the basal ganglia on cranial computed tomography (CT), dysrhythmia at the mid-portions of the left hemisphere on EEG, and myopathy on EMG were depicted, while the muscle biopsy was found to be normal. Because of the patient's age, hypogonadism could not be evaluated.

For cytogenetic analysis, high-resolution chromosomes of the cultured lymphocytes from the patient's peripheral blood were used with Methotrexate synchronisation at the $48^{th}$ hour and addition of Thymidine for the last five hours[8] (Fig. 1a). An interstitial deletion (q11 → q13) on one of the $15^{th}$ chromosomes was observed (Fig. 1b) in all metaphases. Parental cytogenetic analysis is planned for the near future.

## Discussion

Early-onset obesity, hypotonia and hypogenitalism/hypogonadism are the major findings observed in nearly all cases of PWS[2,9,10]. Obesity and hypotonicity were remarkable in our patient. Investigations of hypopigmentation and small hands/feet have led researchers to name a "contiguous gene syndrome"[2,5,11-13]. Whether there is a correlation between the 15 (q11 → q13) deletion, hypopigmen-

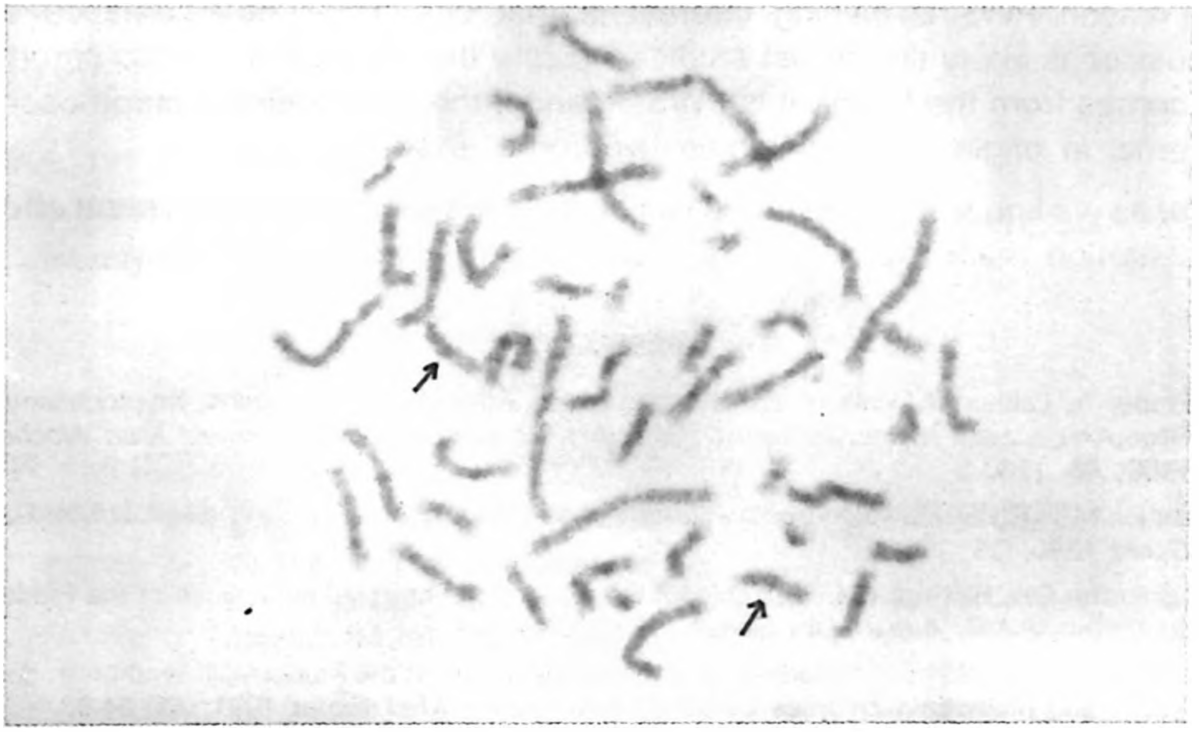

Fig. 1a: The metaphase of the patient.

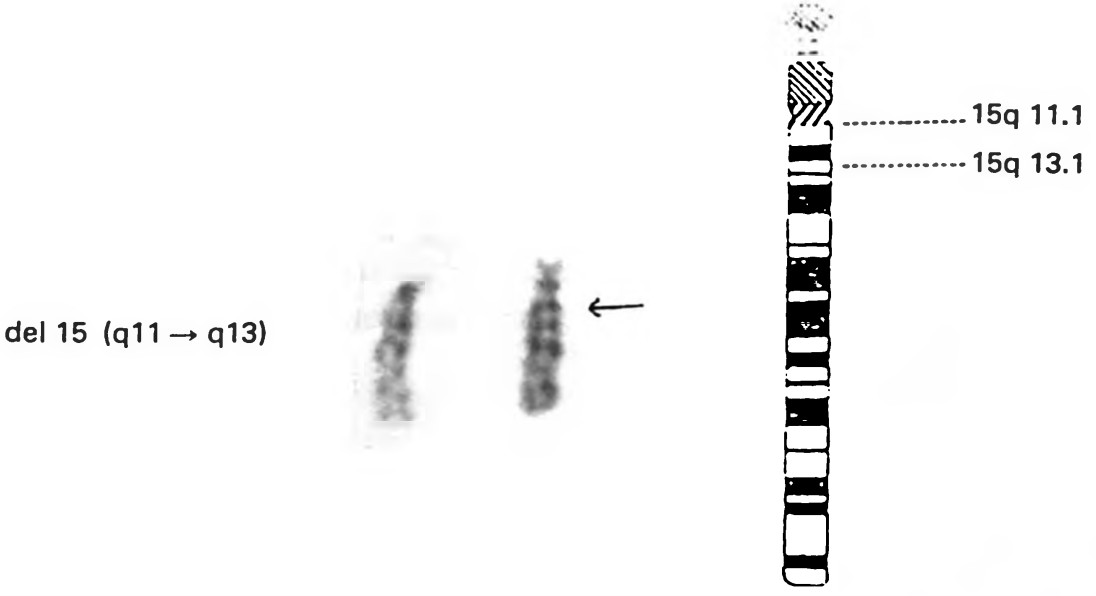


Fig. 1b: Del15 (q11 → q13) is shown at the left side with the ideogram of no 15 on which the deleted region is shown.

tation and small hands/feet is still a matter some controversy, at least at the cytogenetic level. Molecular research suggests that the genes responsible for these characteristics should be separate from the critical PWS locus. And our case supports this theory in that none of these findings was present except deletion.

The reason PWS is gaining interest is that one mode of inheritance under discussion is imprinting. Most studies indicate that when the deleted chromosome comes from the father, it is PWS[2,5], and if the same deleted chromosome is maternal in origin then Angelman syndrome is seen.

As far as we know, this presented case is the first published PWS patient after the presentation made by Kılıç et al[14] with typical deletion in Turkey.

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