Detection of Chromosome 15 Deletion in Prader-Willi Syndrome Patients Using Fluorescence In Situ Hybridization (FISH)

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INTRODUCTION
The Prader-Willi (PWS) and Angelman (AS) syndromes are two distinct mental retardation syndromes that are caused by either deletions (approximately 70 %) or uniparental disomy of the same chromosomal region. The deletions responsible for PWS and AS have been localized to band 15q11-q13 of chromosome 15.

PWS is characterized by infantile hypotonia with feeding problems, short stature, small hands and feet (acromicria), almond-shaped eyes, hypogonadism, psychomotor retardation, hypopigmentation, and development of obesity (Fig. 1).

AS is characterized by severe mental retardation, seizures, inappropriate laughter, ataxic gait, puppet-like upper limb movements, lack of speech, large mandible, hypopigmentation, an open mouth with protruding tongue, and microcephaly.

Presented here are the results of molecular cytogenetic and clinical studies on a total of 30 patients: 27 patients suspected of PWS and 3 patients suspected of AS. The incidence of 15q11-q13 deletions using fluorescence in situ hybridization, or FISH, was investigated.

PATIENTS AND METHODS
Patients:
Thirty patients, 10 males and 20 females ranging in age from 1 to 27 years, were included in this study. The clinical data were ascertained by a clinical geneticist and included these major diagnostic criteria: weight, presence of hypotonia, obesity, hypogonadism, mental retardation (except for the newborns), short stature, and acromicria.

Methods:
Peripheral blood samples were cultured and fixed according to a standard technique. The karyotypes were examined using GTG-banding and analysed by an image analysis system.

For FISH analyses on metaphase chromosome spreads, the Vysis LSI SNRPN and D15S10 Prader-Willi/Angelman Region Probes were used (Fig. 3, 4). The LSI D15S10 Probe identifies deletion of the locus D15S10 and the UBE3A gene located within the 15q11-q13 region of chromosome 15. The LSI SNRPN Probe identifies deletion of the SNRPN locus, also located within the 15q-11q13. In situ hybridizations were performed as described in detail at http://www.vysis.com.
RESULTS

Chromosome analysis using G-banding did not reveal the deletion in 30 patients with the suspected diagnosis of PWS and AS (Fig. 2). However, FISH confirmed the deletion of chromosome 15 in 5 out of 27 PW suspected patients, or 19%. The clinical comparisons indicated that all deletion patients fulfilled the main clinical criteria for PWS (Tab. 1). In most of the non-deletion patients, some typical PWS features were missing. In patients without molecular cytogenetic findings, the detection of uniparental disomy (UPD) by microsatellite studies is being performed.

CONCLUSIONS

It would appear that FISH analysis is an effective diagnostic test for the detection of chromosome 15 deletion. FISH is an efficient first step for stepwise diagnostic testing and mutation-type analysis of patients suspected of having PWS or AS.

REFERENCES


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