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A Case Report of Wolf-Hirschhorn Syndrome (WHS) The Importance of a MLPA test confirmation

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A boy, 17 years old, was cytogenetically investigated because of a moderate mental retardation, short stature, hypotonia and several dysmorphisms including microcephaly, a Greek helmet appearance, telecanthus, strabismus, a broad base of the nose with a pointed nasal tip, a wide mouth, thick lips, micrognathia, unusual palmar creases and flat feet. He is the only child of healthy, non-consanguineous Javanese parents from Indonesia. This case was found in the course of our screening program at a special school.

In the initial cytogenetic analysis using a GTG-banding technique, a terminal deletion of the short arm of one of his chromosomes 4 was seen, revealing the following karyotype: 46,XY,del(4)(p16). Subsequently, Multiplex Ligation-dependent Probe Amplification (MLPA) using subtelomeric probe sets (p070 and p036D; MRC-Holland) demonstrated a deletion of chromosome 4pter and a duplication of 8pter. Fluorescence *in-situ* hybridization (FISH) using probes for the subtelomeric regions of chromosome 4p and 8p (Vysis) confirmed this finding, showing only one signal for 4pter and 3 signals for 8pter (of which one on the aberrant chromosome 4p). Therefore, the aberration should be designated as: 46,XY,der(4)t(4:8)(p16;p23)dn. It appeared to be a *de novo* unbalanced translocation since both parents showed normal karyotypes. More detailed MLPA analysis using a specific probe set for several MR syndromes (p096; MRC-Holland) showed a deletion of the whole Wolf-Hischhorn Syndrome Critical Region (WHSCR).

Further characterization of the deleted and duplicated regions using SNP array analysis is currently in progress. To the best of our knowledge this is the first reported Wolf-Hirschhorn Syndrome patient, confirmed by cytogenetic and molecular analysis in Indonesia.

Keywords: *Wolf-Hirschhorn Syndrome (WHS), der(4)t(4:8), Multiplex Ligation-dependent Probe Amplification (MLPA)*