PALLISTER-KILLIAN SYNDROME: CYTOGENETIC AND BIOCHEMICAL STUDIES

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Summary  Pallister-Killian syndrome is characterized by specific dysmorphologic features and tissue-limited mosaicism for tetrasomy 12p. We describe an additional case of a stillborn neonate, who had not only the specific craniofacial features seen in the syndrome but also various internal malformations. Cytogenetic study showed that an extra F-like chromosome was found in 43% of lymphocytes and in 90% of fibroblasts. The high resolution G-banded pattern of the extra chromosome was consistent with an interpretation of an i(12p). The diagnosis of tetrasomy 12p was further confirmed by four-fold gene dosage effects in fibroblasts for GAPD and LDH-B, whose locus was both assigned to the 12p. The proportion of tetrasomic cells in fibroblasts decreased remarkably during long-term cultures. These results suggest that the tissue specific mosaicism in the syndrome is not simply a result of preferential selection against lymphocytes carrying the marker but may be related to the time of mosaic formation as well as the somatic selection of different intensity in different tissues.

INTRODUCTION

Pallister-Killian syndrome is an eponymous designation honoring the initial discoverers (Pallister et al., 1977; Teschler-Nicola and Killian, 1981). It is a rare clinical entity based on a tissue-limited mosaicism for tetrasomy 12p: an isochromosome of chromosome 12p [i(12p)] is found in a high percentage of skin fibroblasts but virtually absent from blood lymphocytes. The similarity of banding patterns between the 12p and 21q has sometimes led to a misinterpretation of i(12p) as i(21q).
(Fryns et al., 1982; Hunter et al., 1982; Kwee et al., 1984; Lopes et al., 1985). More than two dozen of cases have so far been reported (Reynolds et al., 1987). Patients with Pallister-Killian syndrome invariably show characteristic clinical features, including normal intrauterine growth, severe mental retardation, pigmentary dysplasia, aberrant scalp hair pattern in infancy and coarse face (Buyse and Korf, 1983). The occurrence of serious internal malformations is rare, and the life prognosis is usually excellent. We describe here another case of a stillborn neonate associated with various internal malformations, where tetrasomy 12p mosaicism were confirmed by cytogenetic and gene dosage studies. The observation of i(12p) in a hitherto unreportedly high proportion of lymphocytes and the substantial reduction in percentages of tetrasomic cells during long-term cultures of fibroblasts provides an important insight into the cytogenetic mechanism of the distinctive pattern of chromosome abnormality in the syndrome.

CASE REPORT

The patient, a male infant with 32 weeks' gestational age, was a product of the fourth pregnancy of unrelated 34-year-old parents, which was complicated by polyhydramnios (ca. 5,000 ml of amniotic fluid) and premature onset of labor. The death had occurred during the delivery. There was no family history of mental

Fig. 1. The patient at autopsy.