SHORT REPORTS

Premature chromosome condensation in a child with trisomy 21

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Premature chromosome condensation (PCC), chromatid gaps, breaks, and interchromatid exchanges are characteristic findings in chromosomal instability syndromes like Fanconi's anaemia, Bloom's syndrome, and xeroderma pigmentosa.¹ They are also often observed in malignancies and haematological disorders, particularly leukaemia.² It is well known that Down's syndrome children are at increased risk of developing leukaemia, but the aetiological factors are not well understood. Here, we report a rare observation of spontaneous occurrence of PCC in a female child with trisomy 21. To our knowledge this is the first reported case of PCC associated with trisomy 21.

A 3 month old female infant with features of Down's syndrome was investigated. She was the product of the second pregnancy of healthy parents. The first pregnancy was a first trimester miscarriage. On clinical examination, the child had a flat facial profile, upward slanting eyes, flat nasal bridge, short neck, high arched palate, low hairline, bilateral clinodactyly and simian crease, increased space between the first and second toes, and hypotonia. Haematological investigation showed an increased differential leucocyte count (48%, normal 20 to 30%), but was otherwise normal. There was

no history of exposure to x rays or viral infection. Bone marrow biopsy could not be performed.

Cytogenetic analysis using trypsin-Giemsa banding showed trisomy 21 with a 47,XX,+21 karyotype. The parents were cytogenetically normal. Preliminary analysis of 30 metaphases from the proband showed trisomy 21 in all the cells and one cell with PCC was observed. Further analysis of 300 cells showed 14 cells with PCC (4.66%). All the cells with PCC were in G1 phase (figure). A cell line is not available from the patient.

PCC is characterised by unusual morphological changes in affected nuclei ranging from finely granulated masses of chromosomal material to greatly modified discernible chromatids. PCC is relatively common in malignant or mutagen treated cells and extremely rare in the lymphocytes of the general human population. It occurs through fusion of a chromosome in metaphase with a cell in interphase and is a well known phenomenon.³ Spontaneous fusion of normal untreated somatic cells resulting in PCC has been observed only in lymphocytes in Bloom's syndrome.⁴

G1 PCC observed in our patient was the result of fusion of two cells in different stages of cell cycle (G1 and M phase) (figure), making

Metaphase with prematurely condensed chromosomes. Arrows indicate chromosome 21.

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the total chromosome count 94. In our laboratory during the last 12 years, chromosome analysis has been carried out in more than 1500 persons with various pathological conditions including trisomy 21, and PCC has not been observed in any other patient with trisomy 21, in patients with other cytogenetic conditions, or in normal subjects. There have also been no published reports of trisomy 21 associated with spontaneous occurrence of PCC to our knowledge. Hence, it is difficult to explain the significance of this rare and unusual cytogenetic finding with regard to any particular pathogenesis. However, it could be that spontaneous occurrence of PCC associated with trisomy 21 may be a predisposing factor for leukaemia or

neoplasia, since PCC is a relatively common finding in neoplasia and other haematological disorders.

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