A constitutional 5q23 deletion

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Abstract

A 14 month old girl was found to have a deletion of the whole of band 5q23. By comparing 19 other cases monosomic for a part of the 5q13-q31 segment, the constitutional 5q interstitial deletions fall into two groups: adult patients with Gardner-like symptoms and mental retardation associated with deletion 5q21-q22, and patients (mostly children) with unspecific signs and symptoms and different deletions.

Nineteen patients (14 children and five adults) with constitutional deletions within the 5q13-q31 region have been reported.¹⁻⁵ We describe a further case and attempt an analysis of the karyotype-phenotype correlation.

Case report

This female patient was the first child of unrelated parents (mother aged 20 and father 25 years) and was born at term after an uncomplicated pregnancy. Birth weight was 3350 g and length 50 cm.

At 3 months, she could not control her head but the muscle tone and deep reflexes appeared normal. Her weight was 5730 g (around the 50th centile) and she had brachycephaly with an OFC of 40 cm (around the 40th centile), a flat forehead, antimongoloid slant of the palpebral fissures, flat nasal bridge, carp-like mouth, median cleft of the soft palate, and low set ears. At 7 months her development was at a 3 month level. Fundoscopy disclosed no abnormalities and an EEG showed slight disorganisation. When last seen at

A chromosome 5 pair of the patient showing the deletion of band 5q23.

14 months, she could sit alone but was unable to walk or speak; weight was 7 kg (<3rd centile), length was 75 cm (around the 25th centile), and OFC was 46 cm (>40th centile).

CYTOGENETIC STUDIES

Chromosome analysis of the patient and her parents, performed on GTG banded lymphocyte metaphases, showed a de novo 5q interstitial deletion. Subsequent high resolution banding⁶ at the 550 band level indicated the loss of band 5q23 (figure), the karyotype being 46,XX,del(5)(pter→q22::q31.1→qter). The parents had normal karyotypes.

Discussion

A definite karyotype-phenotype correlation in constitutional 5q interstitial deletion is complicated by the lack of discriminant clinical features, as well as by the difficulty in unambiguously distinguishing bands q14, q21, and q23. These limitations could be resolved if patients with distinctive phenotypes were studied and more refined techniques applied. Thus, a disorder similar or identical to Gardner's syndrome has been observed in three adult patients with constitutional deletions probably involving the segment 5q21-q22,^{5,7} where the gene for familial adenomatous polyposis maps.^{8,9} The lack of such a phenotype in other cases with similar deletions could be attributed to the young ages of the patients or to incomplete clinical examinations, or both. These factors could also explain the apparent absence of refractory anaemia in 5q constitutional deletions, even

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though in this case the mapping of the gene is still to be refined.¹⁰ The observation that the three adult patients with Gardner-like symptoms did not show refractory anaemia or other haematological problems suggests that there are two separate DNA segments responsible for the distinct phenotypic effects. As to the technical limitations mentioned above, the present case illustrates the effectiveness of high resolution banding in discriminating a deletion of the whole of band 5q23.

The variable size of constitutional 5q deletions, ranging from one to four bands, compares with that of the acquired 5q deletions observed in haematological disorders,¹⁰ but whether or not the breakpoints are the same remains unclear.

Among the previous cases, the most similar to our case was a 4 month old infant with loss of band q23.3 and of the proximal half of q31.1.² Their phenotypes, however, do not overlap more than those of all children with deletions within the q13→q31 region or even of a different 5q segment.¹¹ Therefore, we conclude that constitutional 5q interstitial deletions can currently be placed into two clinical groups: adult patients with a Gardner-like syndrome and mental retardation associated with deletion 5q21–q22, and patients (mostly children) with rather unspecific symptoms and different deletions.

These deletions of 5q usually result from simple two break deletions, but in three instances interchromosomal rearrangements occurred.^{1 3 4} A de novo origin was ascertained in all 15 cases where both

parents were karyotyped, whereas two brothers probably inherited the deletion from their mother.⁵ The mean maternal (27.1 years) and paternal (30.1 years) ages at the patients' birth in 15 informative families did not differ from the general population means.

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