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Terminal Deletion with Stable Acentric Fragment of 1q in a Child with Congenital Malformations

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SUMMARY

The terminal deletion with stable acentric fragment of 1q was found in a girl with multiple congenital malformations and severe mental retardation. The karyotype of both parents was normal, and the aberration appears de novo. The medium did not influence the expression of the aberration.

INTRODUCTION

Fragile sites of human chromosomes, first mentioned by Dekaban [1], are referred to from time to time in the literature [2–8]. In his detailed study of heritable sites of human chromosomes, Sutherland [4, 5] did not include the fragility of chromosome 1 among the most common events. In his opinion, only chromosomes 2, 10, 16, 20, and X have their "fragility-hot-spots," some of them more than one. Sutherland [4] demonstrated that some factors present in the medium during the lymphocyte cultivation enhance the expression of fragility and some of them suppress it.

We had an opportunity to karyotype a girl with multiple congenital malformations and severe mental retardation in whom we found the deletion of chromosome 1 (breakpoint 1q32), together with deleted terminal fragment, in each cell analyzed. This aberration remains to some extent the fragile site; however, it has a specific character and most probably cannot be included in the group of fragile sites.

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MATERIALS AND METHODS

Hungerford's culture method [9], medium F10, and medium M199, recommended by Sutherland [5] for enhancement of fragility expression, were used after the repeated blood collection in parallel. The culture time was 72 hrs. The G-band [10] and C-band techniques [11] were used for chromosomal analysis.

CASE REPORT

The proposita's parents are young and healthy; they are not married. The father has two healthy legitimate children. During the third month of pregnancy, the mother had a virus infection, and from the sixth month, she was treated for abortus imminens. The infant, born at the end of the eighth month of pregnancy, had a birth weight of 1,900 g and length of 43 cm. She showed signs of early respiratory distress and failed to thrive. At the age of 9 months, she is mentally retarded (at the level of 3 months). Her main abnormalities are: congenital hydrocephalus without progress, stridor, triangular shape of the face, congenital heart defect (ventricular septal defect), and abnormal immunoglobulins. Radial immunodiffusion detected IgG of 3.2 IU (normal 8 ± 2), IgA of 0.47 IU (normal 0.9 ± 0.2), and IgM of 0.20 IU (normal 0.9 ± 0.2).

CYTOGENETIC OBSERVATIONS

The karyotypes of both parents are normal (50 cells from the mother and 50 cells from the father were scored). The child's karyotype is: 46,XX,del(1)(pter to q32:), +f(1)(:q32 to qter) (fig. 1). The fragment was present in each of the 70 cells

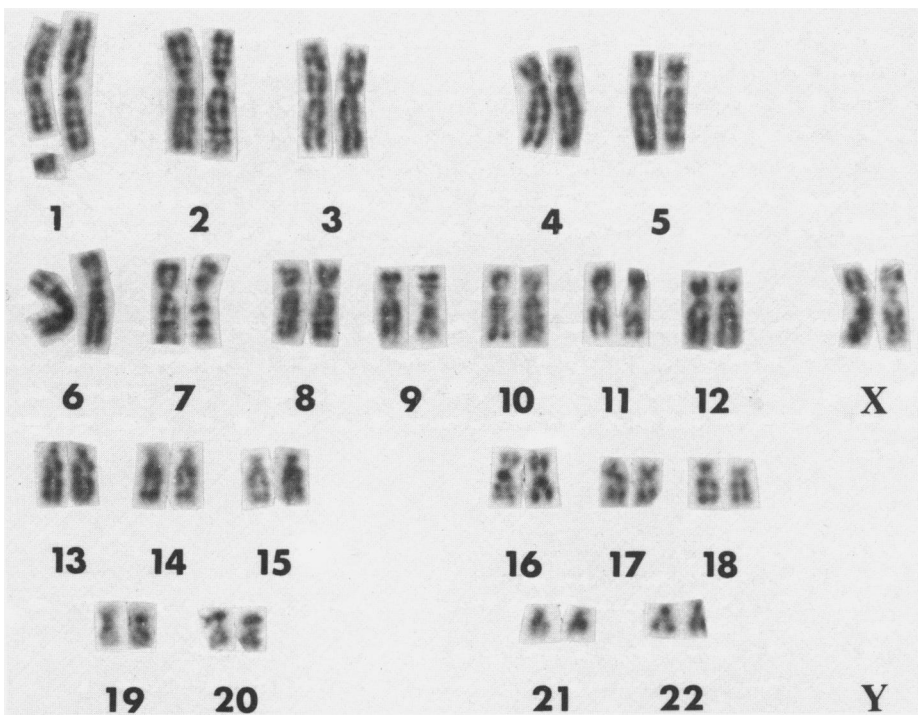
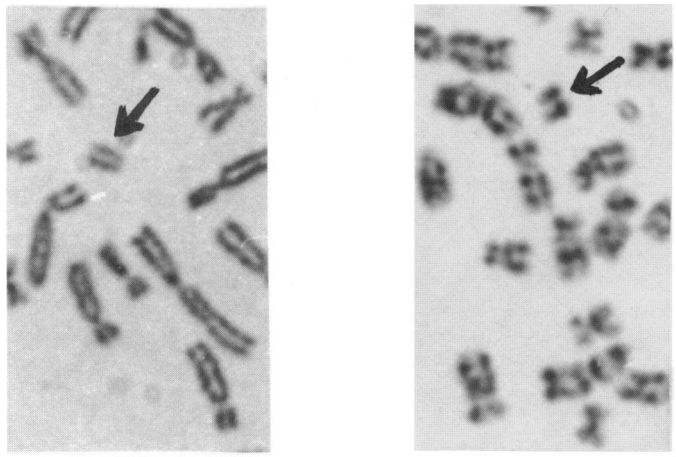


FIG. 1.—Karyotype of the child with stable acentric fragment of 1q G-bands



a b

FIG. 2.—Partial metaphases with random position of the deleted fragment of 1q (*a*, *b*)

scored. The position of the fragment in metaphases was random, and it was never attached to the chromosome 1, never duplicated, or never absent (fig. 2). Autosomal fragile sites are generally believed to be asymptomatic or (if associated with phenotypic abnormalities) possibly predisposing to simple mental retardation without congenital malformations.

Our patient's phenotype resembles the phenotype of children with partial trisomy 1q as table 1 shows (hydrocephalus, triangular face, severe mental retardation, and heart defect), which is quite opposite to our expectation of resemblance to the phenotype of children with partial deletion 1q.

TABLE 1

CLINICAL SIGNS IN CHILDREN WITH PARTIAL 1q TRISOMY AND IN A CHILD WITH FRAGILE SITE 1q32

	Partial 1q trisomy (six cases, summary [12])	Partial 1q trisomy (one case [13])	1q−, +f (one case [this study])
Head:			
Hydrocephalus	+	+	+
Triangular shape of the face	+	+	+
Big malformed ears	+	+	+
Sharp chin	+	+	+
Mongoloid shape of eyelids	+	−	−
Prominent upper lip	+	−	−
Chest:			
Congenital heart defect	+	+	+
Limbs:			
Long fingers	−	+	+
Clinodactyly	+	−	−
Urogenital:			
Malformations	+	+	−

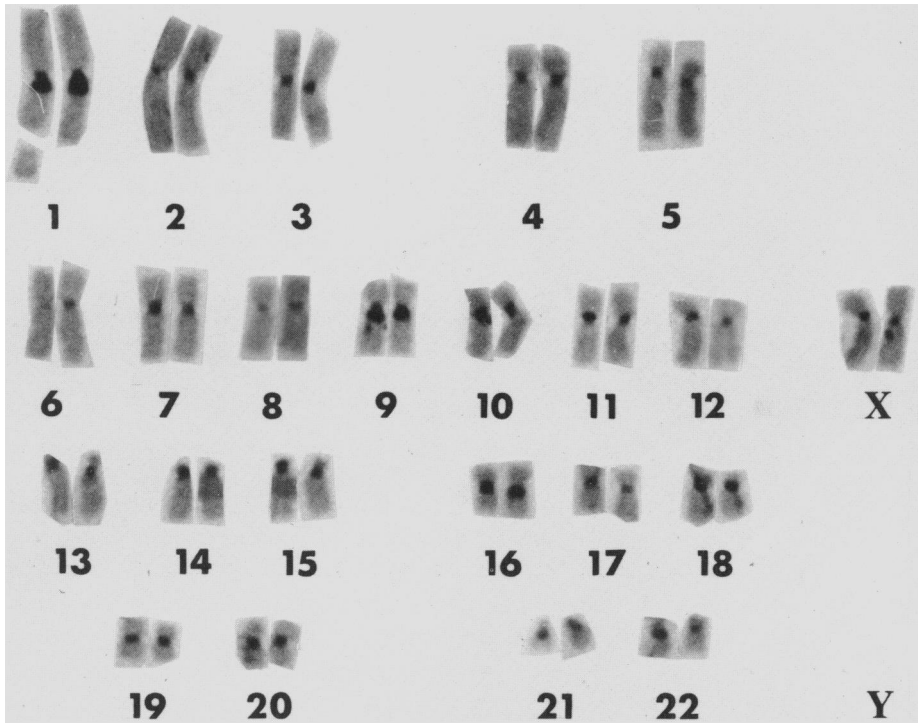


FIG. 3.—Karyotype of the child with stable acentric fragment of 1q C-bands

Why this terminal fragment without centromere and without connection with the original chromosome "survives" repeated mitoses and why it is not lost is open for discussion. We also used the C-banding technique, which demonstrated that the fragment has no centromeric heterochromatin, as we had supposed (fig. 3). Thus it is difficult to explain the stability of the fragment.

We once again repeated the culture of the patient's peripheral lymphocytes using medium M199 and F10 in parallel. We did not find any difference in the incidence of the cells with the fragment, and the fragment was present in all cells cultured in both media. We conclude that in our case the medium did not influence the aberration and its stability. It is possible that the fragile site of 1q is present in all the patient's cells in vivo, but the break with dislocation of the fragment appears after cytogenetic procedures in vitro. There is another possibility: that the aberration detected in the proposita's cells is not the real fragile site but is of some different unknown origin.

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