ORIGINAL ARTICLE

Fragile X Chromosome in Institutionalized Male Adults with Mental Retardation

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Abstract

A clinical and cytogenetical study of mentally retarded male adults with an IQ of below 35 has been carried out in the Ranzan Colony for Mental Retardates, Saitama, Japan. The study showed one fragile X-positive retardate with IQ 23 in the 53 residential retarded patients, giving a hemizygote prevalence of 1.9% (1/53). Macroorchidism and elongated ears, practical markers for the clinical diagnosis of fragile X-linked mental retardation, were also detected in this 43-year-old subject with fra(X)(q27.3). He is amiable and no autistic behavior has been observed. The subject, however, has been suffering from epilepsy since childhood and has cataract in both eyes.

Key words: fragile X, fra(X)(q27.3), institutionalized mental retardate, X chromosome, X-linked mental retardation

Introduction

Fragile sites on human chromosomes are rare heritable hot-spots which are liable to breakages under certain culture conditions.1,2 Currently 23 rare fragile sites have been found on autosomes and one rare fragile site has been located on the distal portion of the X chromosome. Such fragile sites are thought to be involved in the etiology of certain genetic diseases.
of the X chromosome (band q27.3).

The fragile site on X chromosome has attracted much interest in recent years, because it is associated with a common familial form of X-linked mental retardation and its transmission can occur through phenotypically normal male carriers.

The frequency of fragile X-linked mental retardation in Caucasians is estimated to be approximately 1 in 2,300 males and 1 in 2,400 females. The highest incidence of the fragile X was observed in special schools where 4.8% of the males and 3.5% of the females had it. Here in Japan, however, little is known about the prevalence of the fragile X, not only in the general population, but also in the population of retarded individuals except one report. This is a preliminary survey study on the prevalence of the fragile X-positive male adults with severe mental retardation in Japan.

Materials and Methods

A clinico-cytogenetical study was performed on the mentally retarded males with an IQ of below 35 in the Ranzan Colony, Saitama, Japan. For chromosome analysis, the lymphocytes of venous blood obtained from the patients were grown in two different culture media: (1) folic acid- and thymidine-deficient M-F10 medium (GIBCO) supplemented with 5% fetal calf serum (GIBCO) and PHA-M (Wellcome) and (2) RPMI-1640 medium (Nissui) containing 10% FCS and 2% PHA-M, to which 300 μg/ml of thymidine (Wako) was added 24 hr before harvesting. After culturing for 72 hr in 5% CO₂ at 37°C, the blood cells were collected by low-speed centrifugation, and metaphase chromosome preparations were made as previously described. More than 50 Giemsa-stained metaphase cells from every patient were scored for each assay. The fragile X was determined from unbanded karyotypes with subsequent chromosome identification by G-banding.

Results and Discussion

So far 53 institutionalized mentally retarded males with their ages ranging from 24 to 53 years (average 36) in the Ranzan Colony, Saitama, have been cytogenetically examined for the presence or absence of the fragile X chromosome. Of the 53 retardates, one patient was found to carry a fragile X chromosome in metaphase preparations obtained from a folate-free culture. The fragile X was detected in 4% of the cells examined. The subject carrying the fragile X is a 43-year-old male with IQ 23 and having a normal karyotype, 46, XY in cells grown in the control culture.

As shown in Fig. 1, the G-banded karyotype revealed a fragile site on the long arm of the X chromosome at band q27.3. The physical features associated with the fragile X syndrome in this individual are listed in Table 1. Birth weight and height were much lower than the average values for his age, whereas head circumference,
Fig. 1  G-banded partial metaphase chromosome of a lymphocyte in the folate-free culture medium obtained from a 43-year-old mentally retarded male with macroorchidism and enlarged ears. Arrow indicates the fragile site at Xq27.3.

Table 1  Physical Features of a 43-year-old Mentally Retarded Male with fra(X)(q27.3) in the Ranzan Colony for Mental Retardates, Saitama

<table>
<thead>
<tr>
<th>Case Age(y)</th>
<th>Sex</th>
<th>(IQ)</th>
<th>Birth weight (g)</th>
<th>Height (cm)</th>
<th>Ears</th>
<th>Eyes</th>
<th>Testes</th>
<th>Epilepsy</th>
<th>Autism</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td>M</td>
<td>23</td>
<td>2,625</td>
<td>147</td>
<td>large</td>
<td>cataract</td>
<td>large</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

* Mental retardation.

forehead, jaw and nose were within normal range. Macroorchidism, an associated trait first pointed out by Escalente et al., was also observed in the subject, in addition to enlarged ears, another useful marker for the clinical diagnosis of fragile X-linked mental retardation. He is amiable and hearing is normal. As suggested by his friendly manner, no autistic behavior was detected in this case, though some affiliation of autism with the fragile X has been noted by others. He has been suffering from epilepsy since
childhood, which is well controlled by antiepileptic drugs. He has also cataract in both eyes and now his left sight has been completely lost. Mother of the subject, a possible obligate carrier of the fragile X died 11 years ago for unknown reason. Father is alive and his only elder brother has three children.

The prevalence of mental retardation due to fragile X varies with investigators, depending on populations selected or culture techniques. The most reliable estimate of its prevalence is probably that by Sherman et al.,4 who calculated 4.4 in 10,000 males. Institutionalized retarded patients, however, have a higher frequency of about 1–5% in males.5,6,11 According to our study, though it is a preliminary one, the incidence of fragile X-linked mental retardation in the institutionalized severe retardates is 1.9% (1/53) in males, which does not significantly differ from the data previously reported.4–6,11

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