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Report of a patient with fragile X syndrome unexpectedly identified by karyotype analysis

Relato de um paciente com a síndrome do X frágil identificada de forma inesperada por meio do cariótipo

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ABSTRACT

Fragile X syndrome is considered the main known cause of inherited learning disabilities and it is characterized by mutations in the *FMR1* gene. Our aim was to report an unexpected detection of a patient with fragile X syndrome by GTG-Banding karyotype analysis (G-bands after trypsin and Giemsa). The karyotype analysis identified Xq27.3 fragility in 17% of the metaphases analyzed and in 54% when using TC 199, consistent with the cytogenetic diagnosis of the syndrome. This case was the sole one to present the fra(X) tests in the high-resolution karyotype analysis in our care service, contributing to future diagnoses of patients with history of developmental delay.

Key words: karyotype; fragile X syndrome; intellectual disability; chromosomal fragile sites.

INTRODUCTION

Fragile X syndrome is considered the main known cause of inherited learning disability and it is characterized by mutations in the *FMR1* gene[1]. Our aim was to report an unexpected detection of a patient with fragile X syndrome by GTG-Banding karyotype analysis (G-bands after trypsin and Giemsa). The patient was a 2-year-old boy with history of neuropsychomotor developmental delay. He was the second child of young parents, with no similar family history. His pregnancy was uneventful. The child was born by normal delivery at term, weighing 3,200 g and measuring 49 cm. He evolved with developmental and speech delay. Physical examination showed broad forehead, triangular face, epicanthal folds, and prominent ears. High resolution GTG-Banding karyotype analysis (≥ 550 bands) made from peripheral blood by the modified method of Yunis (1981)[2], using culture medium Roswell Park Memorial Institute medium (RPMI) 1640 (Invitrogen), identified spontaneous fragility of the region q27.3 of X chromosome in 17% of the 53 metaphases analyzed, which was consistent with the diagnosis of fragile X syndrome[3]. Further study using low folic acid culture medium (TC 199) showed the same fragile site in 54% of the metaphases analyzed, which confirmed the diagnosis (**Figure**)[3].

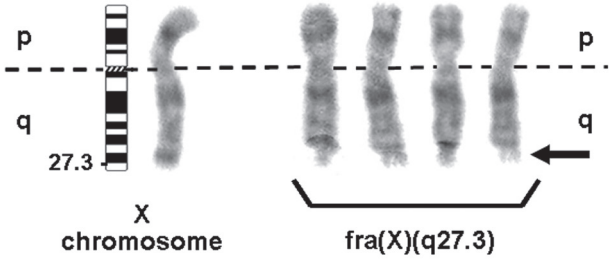

FIGURE – *Partial GTG-Banding karyotypes (≥ 550 bands) showing a normal X and fragile X [fra(X)(q27.3)] chromosomes*

GTG: G-bands after trypsin and Giemsa; p: short arm; q: long arm.

Lubs (1969) was the first to identify this chromosomal abnormality in individuals with fragile X syndrome, which he called "X chromosome marker"[4]. This alteration was more frequently verified when using the TC 199 medium[5]. Currently, the diagnosis of fragile X syndrome is more frequently performed by polymerase chain reaction (PCR) and southern blot, techniques

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that present a higher sensitivity and a lower cost[1]. Although we did not perform these molecular analyzes, the karyotype analysis using TC 199 medium, despite its lower sensitivity, when positive is also considered for diagnosis[4, 5].

In our case, TC 199 medium was used only after the high-resolution karyotype analysis result. It is noteworthy that methotrexate, a known folate antagonist, was utilized in the high-resolution karyotype analysis. Perhaps, this could help to explain our unexpected finding of X chromosome fragility. Currently, our service evaluated more than 11,000 patients, several of them due to developmental delay and/or intellectual disability. The current case was the only one to present a fragile X at high resolution karyotype analysis.

Therefore, despite rare, individuals with fragile X syndrome may be identified by high resolution karyotype analysis. This observation may be important in the karyotype analysis of patients with history of developmental delay and/or intellectual disability without a suspected diagnosis.

RESUMO

A síndrome do X frágil é a principal causa conhecida de deficiência de aprendizagem herdada, caracterizada por mutações no gene FMR1. *Relatamos a detecção inesperada de um paciente com síndrome do X frágil por meio de cariótipo de sangue periférico com bandamento GTG (bandamento G após tripsina e Giemsa). A análise cariotípica identificou fragilidade Xq27.3 em 17% das metáfases analisadas e em 54% quando utilizado TC 199, consistente com o diagnóstico citogenético da síndrome. Este caso foi o único a apresentar as provas de fra(X) no cariótipo de alta resolução em nosso serviço de atendimento, contribuindo para futuros diagnósticos de pacientes com história de atraso no desenvolvimento.*

Unitermos: *cariótipo; síndrome do cromossomo X frágil; deficiência intelectual; sítios frágeis do cromossomo.*

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