

SHORT COMMUNICATION:

A case of Cri-du-chat Syndrome with karyotype del (5) (p14), +mar

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ABSTRACT

The karyotype 47,XX, del(5) (p14), +mar, *de novo* was found in a girl with Cri-du-chat Syndrome. The phenotypic abnormalities appear to have no relationship with the marker chromosome.

INTRODUCTION

The Cri-du-chat syndrome (5p-) is one of the most frequent syndromes of chromosome deletion in man, with an incidence close to 1/50,000 (Niebuhr, 1978a). Analysis of different carriers of translocations involving 5p suggests that the DNA sequences at 5p15.2-5p15.3, when in hemizygous condition due to deletion, cause the phenotype associated with Cri-du-chat syndrome (Overhauser *et al.*, 1986).

The diversity of physical malformations and mental development is correlated with the cytogenetic diversity of this condition: terminal and interstitial deletions, rings and other structural rearrangements. The comparison between patients with isolated deletions and carriers of unbalanced translocations shows the latter to have a higher incidence of physical anomalies, hospitalization rate and mortality (Wilkins *et al.*, 1983). Reviewing 331 cases of Cri-du-chat syndrome, Niebuhr

(1978a) found more than 10% to be carriers of inherited translocations, while rare cytogenetic conditions (mosaicism, rings, and *de novo* translocations) together account for less than this rate.

The investigation of chromosomal variants in 35 Danish Cri-du-chat patients (Niebuhr, 1978b) revealed several cases of heteromorphisms in the pericentromeric regions of chromosomes 1, 9 and 16, distal fluorescent bands on the long arm of the Y chromosome, and two unusual variants of maternal origin: a bright band with orange acridine in 14p and an increase in the heterochromatin region in chromosome 19.

CASE REPORT

J.G.S., female, born in May 1986, when her mother was 31 and her father 46 years old, has been followed since she was three months. The girl was born at term, weighing 2740 g after a normal pregnancy, labour and prompt delivery. Length was 50 cm, head circumference 33 cm and thoracic circumference 36 cm. After 17 days she was hospitalized with severe asphyxia, inspiratory stridor and feeding difficulties. She is the last of four children, with no similar case in the

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+ Deceased

family. The uncommon craniofacial features associated with the weak crying and the failure to thrive, led to the clinical diagnosis of Cri-du-chat syndrome.

Physical examination

The observed anomalies included: deficit of stature and weight; hypotony; microcephaly; prominent ears; hypertelorism; left epicanthic folds; ogival palate; small maxillar; tachypnea; congenital heart defect; presence of IV/V grade cardiac murmur in tricuspid focus; umbilical hernia; rectum diastasis; typical transverse flexion creases; bilateral elevated t'-triradius axial distal; verticils in the first and second fingers, arch in the third finger, ulnar loops in the forth and fifth fingers; absence of patterns in the thenar and hypothernar regions; short distal loops in the hallucal region; camptodactyly in the third finger of the left hand; bilateral clinodactyly in the second and fourth toes.

Clinical evolution

During growth, changes were observed in the facial morphology: the face became relatively thinner, the small maxiliar more pronouced with prognatism and dental malocclusion (Figure 1). The hypertelorism became less remarkable. Later the patient slept regularly at night.

Psychomotor evaluation

The girl had generalized hypotony, severe retardation in sensoty-motor coordination, as well as. Psycomotor stimulation started when she was eight months old, but early treatment was frequently hampered by episodes of respiratory disease. There was slow and poor evolution in the motor, perceptive, affective, and intelectual areas. A recent examination showed no equilibrium in erect position, atypica locomotion (creeps, pushing ahead with the elbows), ataxia and difficulties with coordination, and with manual dexterity.

Psychological evaluation

There was not sufficient intelectual development for an evaluation: no language, no alternative way of communication except by occasional responses to visual or auditory stimuli. There was severe deficiency in general development.

Cytogenetic analysis

The GAG-banding chromosome analysis of the patient and her parents was performed with the usual peripheral lymphocyte culture. Limited material and posterior relocation of the patient precluded the use of other banding techniques. The nomenclature recom-

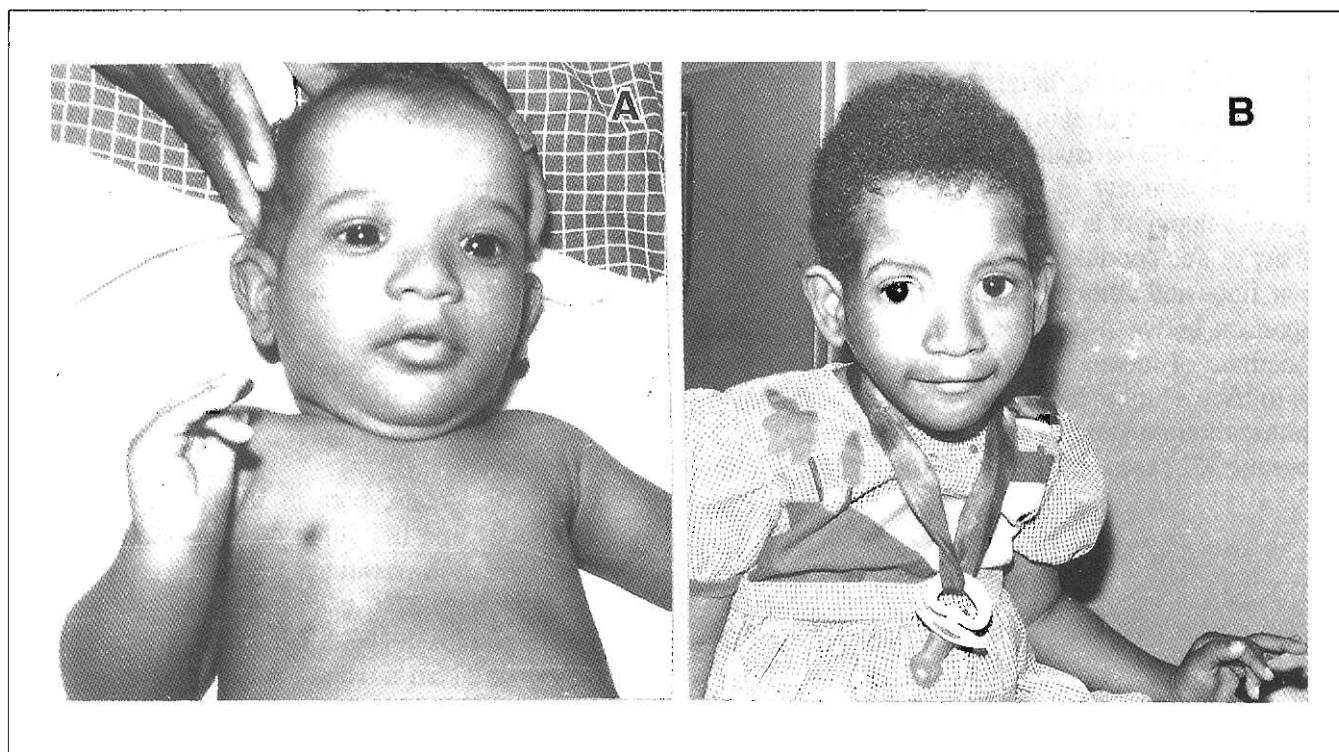


Figure 1 - Cri-du-chat patient, at age seven months (A) and four years (B).

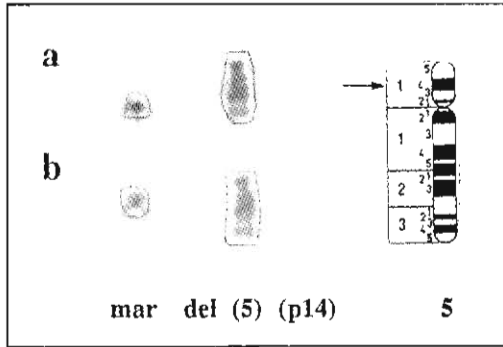


Figure 2 - Partial karyotypes showing the chromosome rearrangement and the diagrammatic representation of chromosome 5 from ISCN (1985).

mended by the International System of Cytogenetic Nomenclature (ISCN, 1985) was used for chromosome description. Thirty metaphases were analyzed for each individual.

Chromosome analysis of the patient showed karyotype 47,XX, del(5) (p14), +mar (Figure 2). The additional chromosome was present in all 30 cells scored. The appearance of the marker was similar in every cell. It presented a very short heterochromatic region, and was never observed in satellite association. Parental chromosomes were normal. No such association between del(5) (pter-p14:) and a marker chromosome has been previously reported the registration of this case was justified.

DISCUSSION

In the present case, the morphology and behavior of the small marker, suggested that it was generated by rearrangement of the heterocentromeric chromatin; thus probably it has no phenotypic effect.

Phenotypic abnormalities caused by marker chromosomes have varied among patients (Kosztolaky, 1987), therefore the prognosis has been generally propitious. In the cases examined by Callen *et al.* (1990) there was no phenotypic effect of the marker chromosome and the phenotypical disturbances were explained by the simultaneous occurrence of another chromosome aberration. The symptomatology of the patient herein described is characteristic of the 5p-syndrome and seems to have no relationship with the marker chromosome.

All observed symptoms, save the finger III camptodactyly are typical for Cri-du-chat syndrome. The dermatoglyphics and the flexion creases are characteristic, except for the absence of thenar pattern and hallucal loops. A severe mental handicap is observed in 99% of the cases (Niebuhr, 1978a), but apparently early psychomotor stimulation was beneficial for this patient, as already emphasized by Wilkins *et al.* (1980) for patients with Cri-du-chat syndrome.

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RESUMO

A síndrome do Cri-du-chat, uma das mais frequentes síndromes de deleção no homem, é determinada pela deficiência da região cromossômica situada entre 5p15.2-5p15.3. Diferentes rearranjos estruturais envolvendo 5p ocorrem associados ao fenótipo: deleções terminais e intersticiais, translocações e anéis. O presente relato refere-se ao cariótipo 47,XX, del(5) (p14) +mar *de novo*, em uma menina clinicamente diagnosticada como portadora da síndrome. A apresentação do caso é justificada pela ausência de registro na literatura de associação da del(5) (pter-p14:) com cromossomo marcador. A maioria dos relatos de pacientes com marcador extra não evidencia efeitos fenotípicos do rearranjo, o que parece também ocorrer no presente caso, onde a sintomatologia observada é típica de síndrome do 5p-.

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