Severe low growth and 2q37 syndrome

Hipocrecimiento severo y síndrome 2q37

Dear Editor:

Ring chromosome 2 was first described in 1981, encompassing a set of common phenotypic characteristics such as short stature, nonspecific dysmorphic features and varying degrees of psychomotor retardation. Ninety-nine percent of cases are sporadic. Ring chromosome 2 is a rare chromosomal abnormality, with few cases described in the medical literature.

We present the case of a male patient aged 12 months. Symmetrical intrauterine growth restriction (IUGR) had been detected at 22 weeks’ gestation. The patient was born by elective caesarean section at 35.5 weeks’ gestation with a birth weight of 1750 g (−2.46 SD), length of 42 cm (−2.78 SD) and head circumference (HC) of 28.5 cm (−2.64 SD). The following characteristics were observed at birth: small palpebral fissures, epicanthus, microphthalmia, wide nasal root, teletelia, mild axial hypotonia, arachnodactyly, a wider-than-normal gap between the first and second toes (“sandal gap”) in both feet, and two café-au-lait spots in the dorsal region and lower right limb less than 0.5 cm in diameter. Central nervous system involvement was suspected, so a transfontanelle ultrasound examination was performed that revealed no malformations. Echocardiographic examination detected a patent foramen ovale, and abdominal ultrasonography a right pelvic kidney. Cytomegalovirus was not detected in the blood or urine. Karyotyping evinced the presence of ring chromosome 2. A 60K oligonucleotide array comparative genomic hybridization (CGH; KayroArray® v3.0, Agilent) found a 6.45Mb deletion in the 2q37.1−2q37.3 region. The parents were healthy and nonconsanguineous, and had normal karyotypes. The physical examination found a weight of 6300 kg (−3.55 SD), length of 67 cm (−3.55 SD) and HC of 38.4 cm (−5.51 SD for age and length). At 12 months of age, the dysmorphic features present at birth remained and were accompanied by a prominent forehead with a low-set hairline, arched eyebrows, a long philtrum, thin upper lip, low-set and rotated ears, prominent antihelix, short neck, 12 café-au-lait spots scattered through the left upper limb, right lower limb and posterior side of the thorax (the largest one 2 cm and the rest 0.5 cm in diameter), hypoplastic scrotum with presence of both testes, 2 mL in volume, and accumulation of fatty tissue in the dorsum of hands and feet. The patient showed mild psychomotor retardation, predominantly motor, with hypotonia.

Figure 1 Phenotype of patient with ring chromosome 2. Note the small palpebral fissures, epicanthus, microphthalmia and broad nasal root.

Chromosome 2 is the second largest human chromosome, accounting for 8% of the genetic material. The ring fusion takes place after the break of the chromosome arms at the telomeric regions, with or without loss of genetic material. Deletions occur most commonly in the 2q37 and 2p25 regions, as they are at the distal ends of the chromosome. Cote et al. defined “ring syndrome” as a set of phenotypic manifestations observed in many patients with different ring chromosomes that were caused by mitotic instability and tissue-specific mosaicism, with possible loss of genetic material. The most common clinical manifestations found in patients with ring chromosome 2 are: intrauterine growth restriction, microcephaly, failure to thrive, psychomotor retardation and minor dysmorphic features, all of which were found in our patient. Cases in which there is loss of genetic material from the 2q37 region may also present with additional phenotypic characteristics, such as brachydactyly, obesity, hypotonia, dysmorphic facial features such as those found in our patient and joint hypermobility, and there is a higher incidence of autism spectrum disorders in these cases. Other and less frequent manifestations include congenital heart malformations such as septal defects or patent ductus arteriosus, congenital hearing loss, tracheomalacia, urogenital malformations, situs anomalies and osteopaenia. The phenotypic variability found in these patients suggests that there are various cryptogenic and environmental factors at play in the individual development of the disease. The diagnosis is confirmed by genetic testing. The diagnosis was performed prenatally in one case reported in the literature by means of CGH arrays of amniotic fluid samples performed after detection of IUGR and lissencephaly in prenatal ultrasound examination. If mosaicism is ruled out in both parents, the recurrence risk is less than 1%. Although changes in fertility have been reported in the literature, especially in males,
50% of the offspring may inherit the ring chromosome, so genetic counselling is recommended. These patients require followup by an interdisciplinary team with periodic evaluations.

References


Meningoencephalitis as a presentation form of Behçet

Meningoencefalitis de tronco como presentación de Behçet

Dear Editor:

Behçet’s disease (BD) is a disease of unknown aetiology that is rare in the paediatric population. Its typical features are recurrent oral and genital ulcers associated with other systemic ocular, cutaneous, neurologic, vascular and articular manifestations. In exceptional cases, the onset occurs with central nervous system manifestations. We describe the case of a female patient aged 10 years with brainstem meningoencephalitis as the initial presentation of BD that responded well to immunosuppressive therapy.

The patient, born to consanguineous Maghrebi parents, sought care for fever of four days’ duration, oral ulcers, headache and sleepiness. The parents reported that in the past 18 months she had experienced recurrent, but not periodic, four-day episodes of fever (maximum temperature, 39.5 °C) and oral ulcers that had not been investigated. The physical examination revealed fever, three ulcers in the oral mucosa, leathery, nuchal rigidity and upbeat nystagmus with no other apparent neurological abnormalities. The following diagnostic tests were performed: complete blood count and blood chemistry panel (normal [N]); erythrocyte sedimentation rate (18 mm/h; N <20); C-reactive protein (89 mg/L; N <15), eye fundus examination (N), lumbar puncture (predominantly mononuclear pleocytosis with 950 white blood cells/mL; N <10), cerebrospinal fluid protein (mildly elevated at 68 mg/mL; N, 15–40) and glucose (N).

Meningoencephalitis was suspected and empirical treatment with intravenous acyclovir initiated while awaiting the results of PCR tests for herpes simplex virus 1 and 2, which turned out negative. The patient was tested for infectious agents (Mantoux test, antibody testing for HIV, Borrelia, Listeria and syphilis) and cancer (chest radiograph, blood differential test and LDH), and no abnormalities were found. Faecal calprotectin was measured to rule out intestinal inflammatory disease, and was found to be normal.

During hospitalisation, she experienced palsy of the VI cranial nerves with ongoing fluctuations in the level of consciousness, leading to performance of a head CT scan with contrast that showed no abnormalities. Forty-eight hours later, the patient underwent a cranial MRI scan that showed a hyperintense T2 signal at the level of the brainstem, centred at the midbrain and extending towards the cerebral peduncles and the pons, with leptomeningeal enhancement and an uptaking punctiform focus at the level of the right cerebellar peduncle (Fig. 1A and B). Given the presence of a brain lesion probably caused by inflammation, the patient was screened for autoimmune diseases, and the antinuclear antibodies, complement and antineutrophil cytoplasmic antibodies tests were all negative. The patient underwent genetic testing for hereditary autoinflammatory diseases (familial Mediterranean fever, periodic fever syndrome due to mevalonate kinase deficiency, TRAPS, BLAU syndrome/early-onset sarcoidosis) that found no mutation associated with her disease. The test for HLA-B51 was negative.

Behçet’s disease was suspected based on the clinical presentation and imaging findings, leading to initiation of empirical immunosuppressive therapy with corticosteroids (first with intravenous methylprednisolone bolus injection at 30 mg/kg/day for 3 days, and then by the oral route at 2 mg/kg/day), colchicine (0.5 mg every 12 h by the

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