CASE REPORT

Neurophysiological findings in a newborn with chromosome 10 trisomy

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SUMMARY

The trisomy of the short arm of chromosome 10 is a rare condition. The phenotypic expression of this genetic aberration is characterised by growth and mental retardation with several neurological signs. We report the neurophysiological findings in a newborn affected by 10p chromosome trisomy who developed seizures. Serial EEGs showed a progressive reduction in burst-suppression activity and a slow rhythmic basal activity. At 1 year of age the recording showed for the first time spikes of high amplitude (up to 800 μ V) in bilateral frontal regions. These findings could be related to an asymmetrical cerebral maturation in the context of perinatal suffering and brain malformation due to the genetic aberration.

BACKGROUND

Chromosome 10 trisomy is a rare genetic aberration. Such mutation can be caused by a duplication or a translocation of the short arm of chromosome 10. Since the first description by Schleiermacher *et al*,¹ 10p duplication has been observed in more than 60 patients, who subsequently developed trisomy 10p.² The 'phenotypic' expression of this aberrant condition depends on the size of the trisomic segment and/or the involvement of another chromosome. Typical features consist of mental retardation, a dysmorphic appearance, growth retardation and cardiac/renal/ocular abnormalities. Although the trisomy of short arm of chromosome 10 is well documented, the prognosis is poor. We report the clinical and neurophysiological findings of a newborn with chromosome 10p trisomy.

CASE PRESENTATION

A male neonate was delivered by caesarean section after 35 weeks of gestation due to a severe perinatal suffering. Apgar index was 1 at 1 min and 3 at 5 min. Birth weight was 3.15 lb and head circumference 11.22 inch (<3rd centile). Physical examination showed frontal bossing, wide cranial sutures, down-slanted short palpebral fissures, low nasal root with anteverted nares, thin lips and micrognathia. The newborn also presented with severe and diffuse hypotonia with reduced muscle mass, camptodactyly and severe hyperdistensibility of both hands and clubfeet. The neurological examination revealed a severe psychomotor retardation with difficult suction and deglutition. He was born to non-consanguineous parents, without history of repeated miscarriages, mental retardation or malformation syndromes. Chromosome analysis was carried out by banding on peripheral blood using multiprobe system octochrome

for fluorescence in situ hybridisation (FISH) (figure 1A). The results showed a trisomy of the short arm of chromosome 10 caused by an unbalanced translocation between chromosome 10 and chromosome 14: 46, XY, der(14) t(10;14) (p11;p11). The chromosomal rearrangement resulted from paternal translocation (figure 1B). A few days after birth, seizures caused by external stimuli occurred. Because of these clinical manifestations, an EEG was performed, showing a diffuse burst-suppression pattern with low voltage rhythm and sudden onset of bursts of δ activity (figure 2A). With the persistence of epileptic manifestations, a treatment with oral suspension of phenobarbital (20 mg/die) was introduced to control seizures. The following examination in polygraphy showed repeated and prolonged apnoeas with a diffuse low voltage rhythm with sudden bradycardiac activity, subdominant in δ range until 1–2 Hz. MRI was performed at 15 days of age and this neuroradiological study showed diffuse signs of hypoxic-ischaemic suffering with right lateral ventricle haemorrhage, periventricular multiple hypointensities, cerebral circonvolution reduction and Dandy-Walker type cerebellar atrophy. At 1 month of age the participant showed sporadic focal seizures characterised by right arm and leg clonic movements and the EEG showed a spike activity on left hemispheric derivations. For this reason clonazepam (0.4 mg/die per os) was added to the previous anticonvulsant drug. During the next few months, an intestinal haemorrhage occurred. Blood samples revealed piastrinopenia and alteration of the coagulation, involving factors V and X and C and S coagulative proteins. The baby also suffered from several episodes of vomiting and regurgitation and an investigation to detect oesophageal pH diagnosed a disease related to gastro-oesophageal reflux. A treatment with ranitidine was then introduced which showed an improvement of symptoms. At 6 months the baby was hospitalised because of the persistence of seizures, manifesting as clonus in the face with significant desaturation and bradycardia that required the administration of oxygen and intravenous phenobarbital. Then vigabatrin (500 mg/die per os) was added to the other two drugs. The EEG showed a fundamental activity in θ range at 6 Hz with intervals of slower activity in δ waves up to 2 Hz and isolated spikes. During hospitalisation, brainstem auditory evoked potentials (BAEPs) were performed without any reproducible response. At 11 months of age, the baby presented a retardation in mental and motor development with a difficulty in trunk and arms coordination. He still presented downslanted short palpebral fissures, epicanthal folds, low nasal root with anteverted

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Figure 1 (A) Fluorescence in situ hybridisation multiprobe system octochrome banding on peripheral blood; (B) trisomy of chromosome 10 by an unbalanced translocation between chromosomes 10 and 14 (arrows).

nostrils. The polygram trace revealed an irregular fundamental rhythm of 5–6 Hz, with sporadic paroxysmal irritative activity corresponding to clinical focal seizures manifesting with apnoeas and oral movements. The last EEG registered at 1 year of age showed spikes of high amplitude in bifrontal regions (up to 800 μ V)—never observed before—without any clinical manifestation (figure 2B). The baby died of respiratory failure at 16 months of age.

DISCUSSION

In this report we describe a new case of trisomy of the short arm of chromosome 10 caused by an unbalanced translocation. To date, over 60 patients with trisomy 10p have been reported. While the majority of trisomy 10p are familial, *de novo* trisomy has been described in only eight patients.^{2–3} As reported in past reviews and clinical reports, most common clinical features include severe mental retardation, proportionate growth retardation, hypotonia, microcephalia, bossing of forehead, dysplastic ears, arched or cleft palate, nose abnormalities and clubfoot. Only one third of patients affected by this chromosome abnormality present with heart or renal abnormalities.^{2–4} Only few reports in the literature describe the clinical course of these patients, because most of them died early. However, growth and

mental retardation with previously described clinical characteristics have been reported in two children at 2 and 16 years of age.^{5–6}

The participant of this report showed all the main and most frequent clinical characteristics described by other reports, such as psychomotor retardation, head and arm abnormalities. Diffuse growth retardation also includes the maturation of brain, as confirmed by MRI and clinical picture. No previous reports in the literature described patients with seizures and chromosome 10p trisomy. In the mapping and sequencing genes of this chromosome, the specific alterations in the short arm were related to several diseases, such as hyperparathyroidism, renal dysplasia, glaucoma, diabetes mellitus, immunodeficiency disease and Refsum disease, while seizures were associated to a locus of the long arm (10q23–q24: autosomal dominant lateral temporal epilepsy).^{7–8} In this case the occurrence of epileptic manifestations could be directly related to pathological lesions and maturation of the brain—two consequences of malformation due to genetic aberration. As the clinical improvement of seizures confirms, the serial EEGs showed a progressive organisation of the activity with reduction of irritative aspects that could be related to brain maturation. Paroxysmal high-voltage

Figure 2 (A) Diffuse burst-suppression pattern with a low voltage rhythm and with sudden onset of bursts of δ activity at the first EEG; (B) spikes of high amplitude in bifrontal regions (up to 800 μ V) registered at the last EEG.

figures that were registered only in frontal derivations in the last EEG may be a consequence of an abnormal and asymmetrical cerebral maturation with a reduced development of frontal lobes. The severe grade of cerebral impairment can also be supported by the absence of response of brainstem potentials at brainstem evoked potentials.

In conclusion, according to the literature, trisomy 10p syndrome seems to be an aggregation of multiple syndromes rather than a single one. In order to better correlate phenotype with karyotype, patients with trisomy 10p should be divided into distinct groups based on the corresponding implicated region. The brain maturation in very young patients could be monitored also by means of serial EEGs.

Learning points

- ▶ Trisomy of the short arm of chromosome 10 is quite a rare condition.
- ▶ Clinical features of this genetic aberration are varied, configuring syndromic clusters of pathology by the corresponding implicated regions of the chromosome.
- ▶ Neurophysiological findings derived from serial EEGs could help to monitor the brain maturation of newborns affected by this genetic aberration.

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Competing interests None.

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