

Rare *de novo* inversion-duplication case with pure 3qter duplication syndrome including an overlap of the dup(3q) critical region: A case report

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Abstract. We report here a very rare case of *de novo* inversion-duplication chromosomal abnormality with a pure 3qter duplication syndrome. Interestingly, the 3q duplication includes an overlap of the syndrome's critical region. Although there have only been 9 cases of this syndrome reported in the past, our patient had more severe neurological abnormalities than anticipated. In this regard, we have gathered the 3q chromosomal duplication abnormalities known to cause pure 3q duplication syndrome to date as a reference for comparisons and we discuss the particulars of our case.

Introduction

Pure chromosome 3q duplications are very rare. Most of the reported cases with a 3q duplication syndrome are thought to occur from parental unbalanced translocations (1). Here we report the case of a little girl with a very rare chromosomal abnormality consisting of pure duplication of 3qter due to a mechanism of *de novo* inversion(3)-duplication and its associated clinical syndrome.

Case report

The mother of the unborn baby had been hospitalized since the middle of her pregnancy due to premature labor risk signs. The fetus was diagnosed with ventricular enlargement by ultrasonic examination. The female neonate was born through vaginal delivery at 31 weeks and 2 days of the maternal pregnancy. Her birth weight was 1,308 g. Asphyxia was noted at birth.

Also, multiple anomalies were recognized at birth including hypertelorism, wide nasal bridge, micrognathia, cleft palate and lips, low-set ears and dysmorphic fingers. A large soft hemangioma was localized on the occipital region of the head. Cardiac ultrasonography confirmed a ventricular septal defect muscular region of 2 mm in diameter. The baby also presented congenital hearing loss confirmed by tests. Oral feeding with milk was difficult due to stenosis of the throat and the tongue settlement, and it became necessary to provide the infant with a feeding tube. Unfortunately, aspiration pneumonia associated with gastro-esophageal reflux occurred and the infant had to be placed under long term-artificial ventilation therapy.

At the time, the parents were provided genetic counseling; after which chromosomal examination revealed the infant's karyotype as 46 XX, dup(3)(q29q22) (Fig. 1). Motor and intellectual developments were delayed and at 6-months of age, the infant was still unable to stabilize her head and neck in the upright position. Brain magnetic resonance imaging (MRI) showed evidence of delayed myelination and agenesis of the corpus callosum (Fig. 2). No further abnormalities were noted until the little girl became two years old, then a diagnosis of developmental retardation was given and a gastrostomy line had to be established for her daily nutrition.

Discussion

There are three types of mechanisms by which 3q partial trisomy occurs. In one, an inversion(3) in a parent's chromosome 3q becomes the recombinant chromosome. In another, the defect is caused by a parental unbalanced translocation. And finally, a last possible mechanism involves partial chromosome duplication with *de novo*-inversion. In recombinant chromosomes with translocations, there are many cases where partial monosomy by a chromosome different from that involved in the partial trisomy chromosome is also present. Many of the papers previously reported on 3q trisomy syndrome included partial monosomies in chromosomes other than the 3q chromosome involved in the partial trisomy (1).

Our case is special in that the 3q partial trisomy is caused only by *de novo* 3q inversion-duplication. The chromosomal

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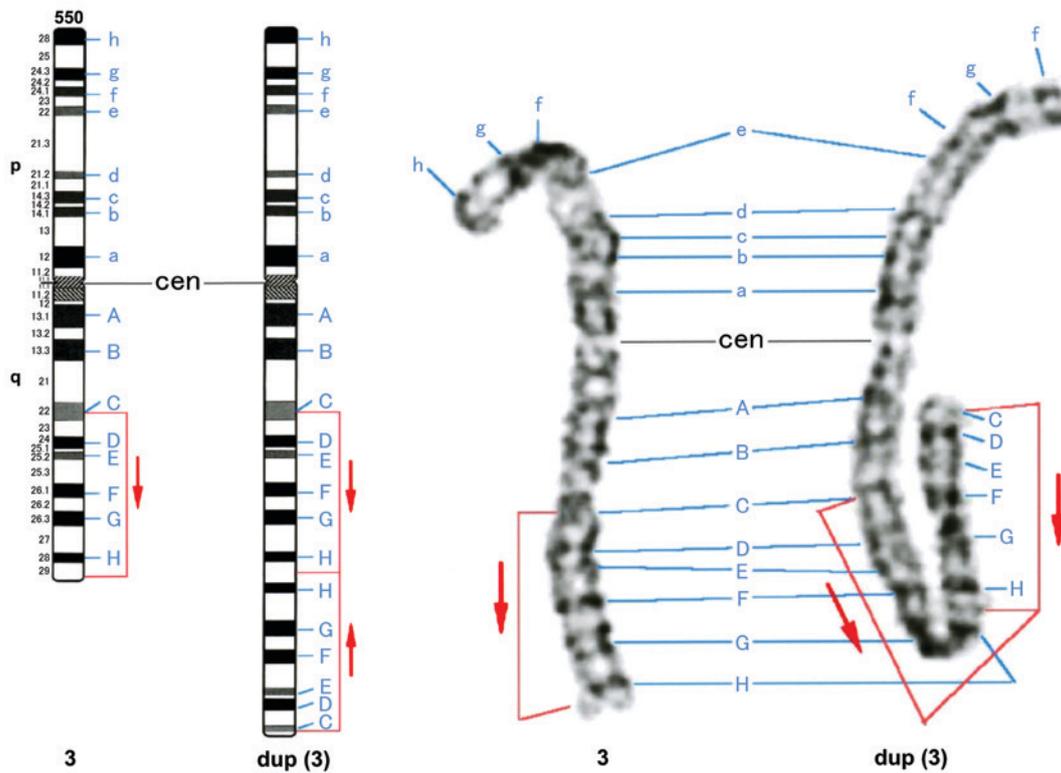


Figure 1. Chromosomal analysis with high resolution band stain, employing fifteen cells. Stain band level is 550. The karyotype of the patient revealed dup(3)(q29q22).

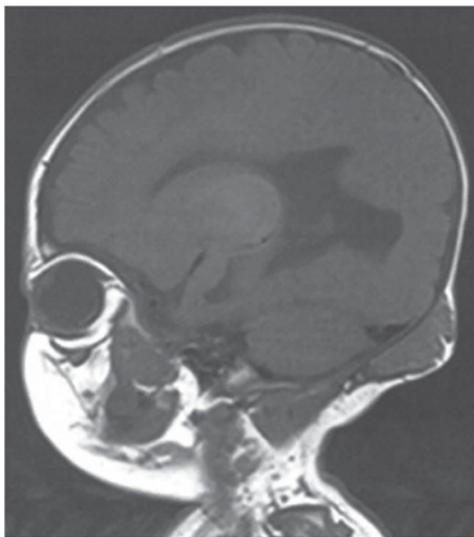


Figure 2. Sagittal MRI image of the 6-month-old patient showing delayed myelination, agenesis of the corpus callosum and non-involuting congenital posterior hemangioma. Spin echo method (echo time, 13.00 msec; repetition time, 700.00 msec) T1-weighted sagittal brain MRI. MRI, magnetic resonance imaging.

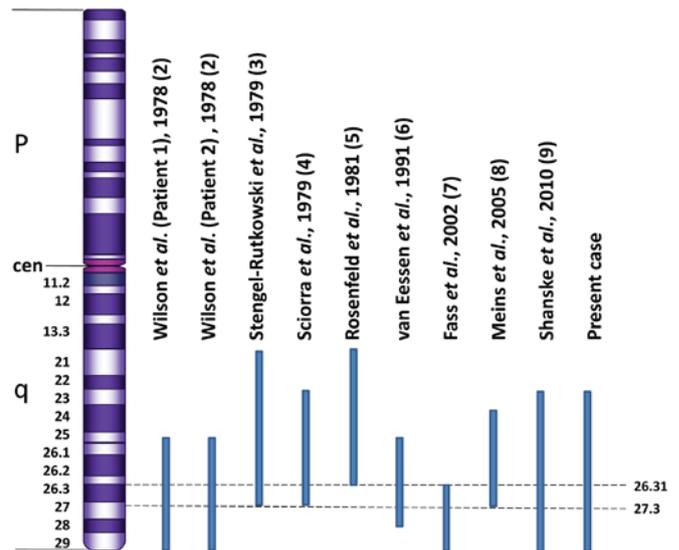


Figure 3. Overview of the chromosomal abnormalities in all the reported pure 3q duplication syndrome cases found. A critical region of 3q duplication at the chromosomal 3q26.31-q27.3 region is essential for the characteristic clinical phenotype.

karyotype of our patient is 46 XX, dup(3)(q29q22), which can be classified as a pure 3q duplication (since it does not involve excess or deficiency of other chromosomal fragments). Our report is a very valuable source of information for the clinical syndrome resulting from pure 3q duplication, given the scarcity of such cases. Furthermore, the etiology of many of the reported 3q duplication syndromes is duplication of

3q21→qter, and to the best of our knowledge only 9 individuals with pure 3q duplication syndrome have been reported in the literature (2-9). Our case represents the 10th case; Fig. 3 for a graphic comparison of the partial 3q trisomy in our case with the others available. In pure 3q duplication syndrome, it is not necessary to consider the monosomy of another chromosomal fragment when analyzing the etiology of phenotypic clinical

features. Thus, careful comparison of the clinical features described in other pure 3q duplications can help elucidate the influence of specific gene critical regions on the phenotype. Faas *et al* reported a *de novo* 3q duplication syndrome with descriptions of 6 other previous cases and concluded that a critical region responsible for the 3q duplication phenotype could be assigned to 3q26.31-q27.3 (7). In this study, our case was analyzed in view of the previous reports; our 3q partial trisomy overlaps with the described critical region on chromosome 3. Moreover, the severity of the motor and intellectual deficiencies in our case is uncommon. This may be due to the specific chromosomal fragments involved in the inversion-duplication in our case when compared to the syndromes described in past reported cases (2-8). More cases should be examined in the future in order to fully understand the characteristics of pure 3q duplication syndrome.

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