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Epilepsy and Deletions at Chromosome 2q24

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To the Editor:

Chromosomal abnormalities are an important cause of epilepsy [Singh et al., 2002], which might be the presenting symptom in the context of a specific syndrome. A recent article by Langer et al. [2006] reports on a translocation t(2;15) with deletion at 2q24-q31 in a girl with epilepsy, dysmorphic features, and severe developmental delay. As this case adds to the growing list of severe epilepsy associated with deletions at chromosome 2q, it deserves complementary information and comments.

We would like to point out that we described a very similar case in a previous report on a girl carrying a deletion at chromosome 2q24 [Pereira et al., 2004]. In our patient as well as in the patient described by Langer et al. [2006], epileptic seizures first started early in life, at 2 and 3 months 1/2, respectively. Seizures were frequent in both cases and were accompanied by severe apnea. Both children had severe developmental delay and no speech development. In the two patients, additional common features were encountered, including microcephaly, downslanting and small palpebral fissures, and abnormal ears.

Despite the clear similarities existing between those two cases, other clinical manifestations were not shared in common by the two patients. Our patient had single palmar creases bilaterally and partial syndactyly between the 2nd and 3rd toes, and cardiac examination showed a small interventricular communication. In contrast, the patient in Langer et al. [2006] had micrognathia, blepharophimosis, hypertelorism, and coloboma of the iris and retina. This is reminiscent of the clinical features described in other cases of del(2)(q31q33) [Ramer et al., 1990] and del(2)(q24–q31) [Nixon et al., 1997].

The size and the boundaries of the respective deleted areas vary from one patient to another (Fig. 1) and this might well explain the clinical

differences described above. In the case of the patient described by Langer et al. [2006], the translocation breakpoint at 15q14 might also participate in the phenotype. In this latter patient, the deleted region on chromosome 2 spans about 13 Mb between markers rs198688 and rs1399959 and contains up to 76 genes including *SCN1A* and *SCN2A*, the mutations of which have already been associated with various epileptic syndromes [Meisler and Kearney, 2005]. Our critical region was of smaller size and spanned 3–7 Mb [Pereira et al., 2004] (Fig. 1). It is fully included within the 13 Mb-deleted area described by Langer et al. [2006] (Fig. 1) and ‘only’ contains 32 genes at most and 10 genes at least, including *SCN1A* and *SCN2A* as well as three other sodium channel genes (see the human genome sequence at UCSC web site: <http://genome.ucsc.edu>) [Pereira et al., 2004].

Epilepsy was not seen in the patient reported by Nixon et al. [1997]. The data reported by Langer et al. [2006] thus reinforce our previous hypothesis [Pereira et al., 2004], that the epileptic phenotype in these patients is specifically associated with the deletion of the genomic area comprised between marker D2S354 (marker d in Fig. 1) and marker D2S2345 (h) at most. This genomic region actually comprises the cluster of five sodium channel genes mentioned above. As already discussed [Pereira et al., 2004; Langer et al., 2006], the seizures in the affected children might well be due to loss or haploinsufficiency of one or several of these genes. Such deletion events might remain undetected and hence might be

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FIG. 1. Map of the deleted regions in the three patients with various del(2)(q24-q31) reported in (A) Nixon et al. [1997], (B) Pereira et al. [2004], and (C) Langer et al. [2006]. Markers are shown from centromere to telomere. **a:** rs198688, **(b)** rs719931, **(c)** D2S156, **(d)** D2S354, **(e)** D2S2157, **(f)** D2S382, **(g)** D2S111, **(h)** D2S2345, **(i)** D2S294, **(j)** D2S2284, **(k)** rs1362496, **(l)** D2S333, **(m)** rs1399959, **(n)** D2S2314, **(o)** D2S117. Squares represent the maximal size of the deleted regions. +, undetected markers; -, deleted marker; $\pm$, deletion status could neither be determined nor deduced. Gray symbols represent those markers with data available. Non-gray symbols represent the deletion status that was inferred assuming one single and contiguous deleted area in each patient. Physical distances between markers are based on the human genome sequence at UCSC web site (<http://genome.ucsc.edu>). Mb: Megabases.

underestimated in other patients with severe epilepsy and should thus probably be more systematically searched using the appropriate polymorphic markers (Fig. 1).

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