

## The butterfly pattern in a patient with chromosome 7 deletion

Sir,

Deletions in the *Forkhead-box P2(FOXP2)* gene are characteristically associated with language impairment. We report a 3-year-old girl with global developmental delay who had a deletion in the long arm of chromosome 7 involving the *FOXP2* gene. She also had a characteristic butterfly-shaped appearance of the ventricular

atria with decreased volume in the splenium of corpus callosum and delayed myelination of the parietal centum semiovale. Our patient was born to healthy, non-consanguineous parents. Mother was an 18-year-old primigravida and father was 33 years old. Father had two children from a previous partner. One child was normal and the other child was said to have “something wrong” but the details were not clearly known. Our patient was born at full term by cesarean section done for face presentation after an uncomplicated pregnancy. At birth, she was hypotonic and admitted to the neonatal intensive care unit for observation. Birth weight was 2.5 kg (5<sup>th</sup> percentile) and length was 45.7 cm (5<sup>th</sup> percentile). Physical examination was otherwise unremarkable except for hypotonia. She failed the initial hearing test. In the first few days of life, she had frequent apneas requiring stimulation. All the investigations for etiology of apnea were negative. She was discharged at 3 weeks on home apnea monitor. The home apnea monitor was discontinued at 4 months of age. Work-up included a karyotype which revealed 46XX with deletion involving chromosome-7.

At 7 months of age, social smile was the only milestone met. Further genetic evaluation with an oligonucleotide array revealed 19.1 Mb deletion in chromosome 7 spanning 7q22.1-q31.31. Mother was evaluated for this deletion by fluorescent *in-situ* hybridization and was found to be negative. Unfortunately, we could not do genetic testing in the father. Echocardiogram of the patient was within normal limits and her renal ultrasound was also normal. Repeat hearing test (tympanogram) showed type B pattern bilaterally.

In the first year of life, growth was consistently below 5<sup>th</sup> percentile despite increasing calorie density of the formula. Developmental milestones across all domains were severely delayed. Eye examination was done at 15 months for esotropia and daily patching was recommended. At 21 months of life, she was admitted to the pediatric intensive care unit for status epilepticus. Seizures were controlled with multiple medications and levetiracetam was continued for maintenance. Initial electroencephalogram (EEG) was consistent with mild to moderate diffuse global neuronal dysfunction. Magnetic resonance imaging (MRI) of the brain showed delayed myelination seen mostly in the region of posterior horns of the lateral ventricles [Figure 1a]. Additionally, the white matter of the Sylvian fissure was also attenuated and the fissure appeared to extend up to the lateral ventricles [Figure 1b]. This pattern resembled the shape of a butterfly [Figure 1b]. Another finding observed was attenuation of the posterior third of the body of corpus callosum [Figure 1c].



**Figure 1:** Magnetic resonance imaging of the brain. (a) FLAIR sequence. Axial slice. Unmyelinated white matter represented as hyperintensity in centrum semiovale. (b) Coronal T1W image—“butterfly”- shaped ventricles. Deep Sylvian fissure (arrow). Decreased white matter volume between cortex and ventricular cavity. (c) Sagittal T1W image—hypoplastic corpus callosum without the typical splenium knob

Currently, our patient is 3 year old and does not have any dysmorphic features. Her current weight is 9 kg and height is 78 cm (both below 5<sup>th</sup> percentiles). Her development is severely delayed in all domains. She is hypotonic and does not sit, stand or walk. She does not say a single word and also does not communicate non-verbally. She is under multidisciplinary care.

Language development has been partly localized to chromosome 7q31 which includes the *FOXP2* gene (SPCH1; OMIM#602081).<sup>[1]</sup> *FOXP2* gene defects are well known to cause speech and language deficits (developmental verbal dyspraxia), articulation problems and significantly limited oral vocabulary.<sup>[1-7]</sup> At least two dozen cases of interstitial deletions involving 7q31 have been reported so far.<sup>[2]</sup> Additionally, majority of these patients also have significant delay in cognition and motor development.<sup>[2,7]</sup> Imaging abnormalities of the brain were rarely reported in these children. Mild brain atrophy and bilateral hyperintensities in the white matter were reported by Zilina *et al.*<sup>[2]</sup> Cranial imaging was reportedly normal in some patients.<sup>[2,4,8]</sup> In our patient, the lateral ventricles appeared butterfly-shaped on the coronal images at the level of the atria with irregular walls. To the best of our knowledge, this butterfly pattern has so far not been reported in cases of chromosome 7q deletion. In view of no prior reports, the exact mechanism of pathogenicity of deletion (chromosome 7q22.1-q31.31) observed in our patient contributing to this butterfly imaging pattern is currently unknown and precise role in normal development is unclear.

Gonzalez-Toledo *et al.* presented butterfly pattern in eight patients with severe psychomotor retardation.<sup>[9]</sup> All

these patients were all reported from Argentina and they were aged 8 months, 17 months, 2 years, 3 years, 6 years, 6 years, 9 years and 22 years. The male:female (M:F) ratio was 6:2. In all cases, the lateral ventricles appeared butterfly-shaped on coronal views at the level of the atria, very similar to the present case. The features consistently observed were non-myelination in the juxtaventricular white matter, decreased volume of the posterior third of the corpus callosum, squaring of the posterior cap of the lateral ventricles and irregular contour of the ventricular walls. Additionally, the Sylvian fissures were deep and almost extended to the lateral ventricles. All these eight children had severe psychomotor retardation. However, unfortunately genetic studies could not be done in these patients due to financial constraints. The specific genetic associations underlying this neuroimaging pattern may be further elucidated by future case reports.

In conclusion, we report an unusual neuroimaging pattern in a patient with a 19.1 Mb deletion in chromosome 7 spanning 7q22.1-q31.31 who has severe developmental delay.

The exact prevalence and significance of this observed genetic and neuroimaging association is still unclear but can be further clarified with future similar observation and reports.

Suji Velayuthan, Amber Dawson<sup>1</sup>,  
Rosario Maria S. Riel-Romero<sup>2</sup>,  
Eduardo Gonzalez-Toledo<sup>3</sup>

Departments of <sup>1</sup>Pediatrics, Neurology and <sup>2</sup>Pediatrics and Neurology, <sup>3</sup>Pediatrics, Radiology, and <sup>3</sup>Anesthesiology, Louisiana State University Health Sciences Center-Shreveport, Shreveport, Louisiana, United States

**Address for correspondence:**

Dr. Rosario Maria S. Riel-Romero,  
Department of Neurology and Pediatrics,  
School of Medicine, Louisiana State University  
Health Sciences Center,  
1501 Kings Highway Boulevard,  
PO Box 3932, Shreveport,  
Louisiana - 71130 3932, United States.  
E-mail: rrielr@lsuhsc.edu

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