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Short Communication

2q13 deletion in a young boy with developmental delay, short stature and failure to thrive

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ABSTRACT

A. T. is a Caucasian male, former 27 week gestational age premature infant, with a history significant for respiratory distress and patent ductus arteriosus. He was discharged from the Neonatal Intensive Care Unit (NICU) at 3 months of age with no significant medical problems. His growth and stature had always been under the 5th percentile corrected for gestational age but remained parallel to the curve. After 12 months of age, his growth rate declined. Diagnosed with failure to thrive, he underwent a work-up which identified a 0.8 Mb deletion at band 13 in the long arm of one chromosome 2. Despite this imbalanced genomic alteration, his phenotype did not correlate to Joubert syndrome, as suggested by the array comparative genomic hybridization assay interpretation. His phenotype (failure to thrive, short stature, speech delay, and mild head and face dysmorphisms) and genotype do not match any published case report criteria for a recognized pattern of human malformation.

KEYWORDS: 2q13 deletion, chromosome abnormality, failure to thrive

INTRODUCTION

The 2q13 deletion has previously been reported in the medical literature. A deletion at 2q13 is associated with a deficiency in the interleukin-1 receptor antagonist (DIRA). As a result of DIRA, these patients are unable to secrete receptor antagonist protein which inhibits proinflammatory cytokines, thus producing an auto inflammatory syndrome [1]. Susceptibility loci within 2q13 for chronic lymphocytic leukemia have been found. It is unclear if a deletion of the area would be protective or deleterious in this regard [2]. 2q13 deletions have been associated with the loss of proapoptopic gene (BIM) which is a new candidate tumor suppressor gene in mantle cell lymphoma [3]. Another patient with this deletion had a phenotypically unusual craniosynostosis [4]. Another had a characteristic hindbrain malformation associated with the 2q13 deletion [5]. Deletions in the 2q13 area also have been associated with 80 percent of the familial and 65 percent of the sporadic cases in familial juvenile nephronophthisis (NPH) [6, 7]. Intellectual disability with transmitted genetic anomalies, including 2q13 deletion, has been reported as well [8].

CASE REPORT

A. T., a Caucasian male, was delivered at 27 weeks of gestational age. His course was complicated by premature labor and delivery with Apgar scores of 3, 3 and 4 at 1, 5 and 10 minutes respectively. He required intensive resuscitation and one dose of surfactant but was weaned to nasal Continuous Positive Airway Pressure (CPAP) at 3 days of life. Respiratory Syncytial Virus (RSV) immunoglobulin was provided in the NICU and then once monthly until one year of age. He also had a patent

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ductus arteriosus requiring indomethacin for medical closure at 5 days of life. His head ultrasounds at days 7 and 30 of life were normal. He passed his newborn hearing screen and had an unremarkable newborn metabolic screen. He was discharged at 86 days of life. At 4 months of life he was re-hospitalized for treatment of his first and only urinary tract infection. His renal sonogram and vesicocystourethrogram were both within normal limits. The remainder of his past medical history is significant for one episode of otitis media at 8 months and reactive airway disease beginning at 9 months of age. After his second exacerbation, at 12 months of age, he started inhaling corticosteroids.

His growth curves, even when corrected for gestational age, were always below the 5th percentile, but remained on their same curve. In comparison, his mother is 5 feet 1 inches (10th percentile) and his father is 5 feet 7 inches in height (between 10th and 25th percentile). After 12 months of age, his height and weight velocity decreased, necessitating a hospital admission and work-up for failure to thrive. Complete Blood Count (CBC), Complete Metabolic Profile (CMP), free T-4, Thyroid Stimulating Hormone (TSH), pre-albumin, urine analysis, sweat test and karyotype were all within normal limits. During his hospital stay he surpassed his weight gain and intake requirements, suggesting that his failure to thrive was likely social in origin. He was discharged on a high caloric diet with high caloric formula supplementation. Despite this intervention his growth continued to be poor. He was then evaluated by a gastroenterologist who checked his IgA and tissue transglutaminase levels - both were normal.

His developmental milestones were delayed but eventually appropriate for his corrected age, with the exception of a mild expressive speech delay. He is receiving speech therapy with good progress noted.

A genetic consultation was ordered due to the above problems plus some mild, non-specific dysmorphic features in his physical examination: a broad forehead, posterior hair whorls, relative macrocephaly, small nose, and a short philtrum. An array comparative genomic hybridization assay (aCGH) was performed and revealed a deletion of at least 0.8 Mb at band 13 in the long arm of one chromosome 2. The interpretation included a note specifying that this genomic alteration was expected to cause phenotypic and/or developmental abnormalities, which may include Joubert syndrome. A.T.'s parents underwent microarray analysis as well and the father carries the same deletion. Of note, the father does not have any major medical issues, but he also received speech therapy as a child. The geneticist concluded that the 2q13 deletion is likely a familial variant.

DISCUSSION

Despite the geneticist evaluation, A. T.'s phenotype does not match previously described findings in the 2q13 deletion. This alteration has been associated with an auto inflammatory condition, but this patient has never developed any inflammatory signs or symptoms and has been relatively free of serious infections. Despite craniosynostosis being associated with 2q13, A. T. has relative macrocephaly for his weight and height, not craniosynostosis. Hindbrain anomalies were not noted in his two head ultrasounds as a neonate. The NPH report was of particular interest due to the presence of a UTI in our patient, but two renal sonograms so far have been reported as normal, with no indication of NPH.

In chromosome rearrangement analysis studies, the 2q13 deletion is now being encountered with the new microarray procedures and has been noted in normal individuals [9]. This agrees with our geneticist's assessment, and who, like Bisgaard [8] also ponders whether the anomaly was incidental or just a variant.

Due to the microarray suggestion of Joubert syndrome, the diagnosis was entertained in our patient. Joubert patients have a distinctive brainstem malformation [5], hypotonia, developmental delays, hyperpnea or apnea, and atypical eye movements [10]. Our patient does have an expressive speech delay, but none of the other signs or symptoms. Therefore, our patient does not appear to have Joubert syndrome but either a new previously unreported phenotype, or perhaps a familial variant.

DISCLOSURES

The authors have no financial relationships relevant to this article.

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