CASE REPORT

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A Closer Look at Familial Dysautonomia from a Social Communication Perspective: A Case Report and Review of Literature

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ABSTRACT

Familial dysautonomia (Riley-Day syndrome) is a rare but fatal autosomal recessive peripheral neuropathy caused by a point mutation in I-κ-*B* kinase complex-associated protein gene. The disease, which affects primarily people of Ashkenazi Jewish origin, prejudices the development of primary sensory neurons determining the depletion of autonomic and sensory neurons. In this study, we report a 5-year-old girl with familial dysautonomia, and how her different psychiatric aspects may lead to genetic vulnerability. Obviously, the gene, the reason for this syndrome, and overreactions to different kinds of emotions, maybe a risk factor for having any mood disorders. From another perspective, this "genetic vulnerability" may be protective or related to the syndromes that affect social communication like autism.

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INTRODUCTION

Empathy can be defined as the experience of understanding another person's condition from their perspective. Although the definitions of empathy generally refer to difficulties in labeling others' emotions, recent neuroscientific findings have shown that empathy deficits may be related to a person's own emotions as well.[1] The relationship between emotion regulation and empathy is a recent research topic in the area of neurodevelopmental disorders, particularly in autism spectrum disorders, and there is still a lack of evidence of the neurobiological basis of this relationship.[2,3] Familial dysautonomia (FD) generally refers to a dysregulation of the autonomic nervous system (ANS) that involves the over- or underactivity of the sympathetic or parasympathetic components. As the dysautonomia may mostly be due to secondary causes, one of the primary etiologies appears to be familial, and it is known as hereditary sensory and autonomic neuropathy.[4] Many case reports show that there are also psychiatric problems in patients with FD and suggest that there may be emotion dysregulation as well.[5,6] To the best of our knowledge, there is no research on emotion and autonomic dysregulation together or research that refers to possible neuroimaging findings. In this study, we will provide a clinical picture and report on the neuroimaging findings of a child with Riley-Day syndrome who shows emotion regulation and overemphatic reactions in addition to FD symptoms.

CASE PRESENTATION

A 5-year-old Turkish girl had referred to us with an 8-month history of abnormal reactions, emotional dysregulation, sleep disturbances, restlessness, and hyperactivity. The case was first referred to the hospital for vomiting attacks, binge eating problems, weight gain, and convulsions when she was 2.5 years old. As a result of the genetic tests performed, she was diagnosed with Riley-Day syndrome and epilepsy after the findings of hyposensitivity, hyperacusis, exotropia, acrocyanosis, atrophic glossitis, vomiting attacks, and ulcerative esophagitis upon examination.

She was overweight with average height. At the time of examination, she was well-groomed and dressed. On appearance, there were no signs of restlessness; however, she showed signs of emotional dysregulation and hyperactivity consistent with Riley-Day syndrome. There

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was extreme sensitivity to social codes at assessment. She maintained eye contact, except when seeing another child cry in front of the outpatient clinic door, at which point she began to cry sobbingly. She was excessively overjoyed and laughed unstoppably over a simple toy. She developed psychiatric symptoms that included distraction, sometimes disobedience, and defiant behaviors. She did not articulate herself clearly and answered questions at high speed and often with a single word, also she could hardly use any new or creative words, particularly in emotionally dysregulated situations. Her developmental milestones had been reached on time. Denver II Developmental Screening Test was performed, and she was at an age-appropriate developmental level. During the crisis that is the "dysregulation crisis," it was very difficult to establish cooperation with her. She gave almost 1-word answers. This was observed on examination as well. However, outside of those crises, as her speech issue was just articulation problems, she was able to take the test, even if her emotional responses were still extreme. Her parents reported that she had a poor response to needle pricks during blood drawing, and her touching hot objects without any visible response indicated decreased sensitivity to pain; additionally, there were inappropriate laughs and quick relationships with strangers. These findings were seen both in the home and in the outdoor environment, such as at kindergarten. She could only continue for 1 month at kindergarten because of her extreme emotional reactions to the other children's emotions. There were signs of sub-threshold Attention Deficit Hyperactivity Disorder (ADHD) and Disinhibited Social Engagement Disorder based on DSM-5 (Table 1). Magnetic resonance imaging (MRI) findings showed that she had mega cisterna magna, bilateral hyperintense areas at posterior periventricular white matter, centrum semiovale, and inferior olivary nucleus. We learned through a telephone visit that she had passed away due to respiratory insufficiency 4 months after the referral to us. Informed consent was obtained from her parents.

DISCUSSION

One of the most important findings, which affects life and social functioning in individuals, is excessive sympathetic activation of any infection or emotional stress, known as a dysautonomic crisis, which may include vomiting attacks, crying crises, and irritability, sometimes accompanied by personality changes.[7] Although this syndrome has a genetic diagnosis and attachment pathologies in the family,[8] the fact that our case was extremely sensitive to emotional stimuli led us to think differently in terms of social communication in such patients. This "emotional depth," seen in our examination, may be explained by certain theories, and each emotion may be triggering the activation of the sympathetic system through different network systems among the forebrain, hypothalamus, and ventrolateral medulla. It can be clearly seen that patients with FD have severe and inconvenient responses to trivial emotions or stimuli.[6,9]

Table 1. Related Subthreshold Symptoms in the Child

Related Symptoms with ADHD	Related Symptoms with Disinhibited Social Engagement Disorder
Fidgeting with hands or feet	Absence of normal fear or discretion when approaching strangers.
Feelings of restlessness	Unusually comfortable touching and emotional expression with an adult stranger or peers
Difficulty engaging in quiet, leisurely activities	Awkward emotional and social expressions

Additionally, the cerebellum is known to play a role in schizophrenia and mood disorders. Cerebellar dysregulation may be associated with bipolar disorder.[10] In 2 case reports, the mega cisterna magna's associations with schizophrenia and bipolar disorder were discussed.[10,11] In our case, the MRI findings of mega cisterna magna and impaired mood regulation suggest that these may be a precursor to mood disorders in children with FD because mega cisterna magna may contribute to the activation of the cerebellum.[12] In addition, it has been stated that there are dysregulations in the cortico-sub-cortical and cerebellar regions in bipolar patients which may lead to the occurrence of symptoms.[10] There are also studies indicating that cerebellar vermis neurons may play a role in mood modulation.[13,14] Taken together, studies that show that the cerebellar region and related connections may be related to mood problems will shed light on this information. Also, the potential relationship of an individual with multiple system atrophy with pathological laughing or crying problems with neurodegenerative changes in the inferior olivary nucleus has been described.[15] Our case and these findings are consistent with the view that the cerebellum structures may be involved in emotional regulation. Considering the idea that such unexplored unusual social behaviors may be seen in hereditary syndromes (e.g., hyper socialization in Williams syndrome),[16] it is clear that there would be a need for further studies on individuals with familial dysautonomia.

Obviously, the gene responsible for this syndrome and for overreactions to different kinds of emotions may be a risk for any mood disorders. From another perspective, this "genetic vulnerability" may be protective or related to those syndromes that affect social communication, such as autism.

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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