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Case Report

A Case of Neurofibromatosis Type 1 with Severe Mood and Behavioral Symptoms

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ABSTRACT

INTRODUCTION: Neurofibromatosis type 1 (NF1) is a genetic disorder caused by a mutation in the NF1 gene. In addition to physical manifestations, complications such as cognitive and behavioral deficits have been described.

CLINICAL FINDINGS: We describe a case of a 14-year-old male with a past psychiatric history of obsessive-compulsive disorder (OCD), attention deficit hyperactivity disorder (ADHD), and multiple suicide attempts, who presented with suicidal ideation and command hallucinations. The patient became aggressive, physically assaulting hospital staff, and required sedative medication and physical restraints for several days. He required inpatient hospital admission due to rhabdomyolysis. Throughout his admission, the patient was intermittently verbally and physically abusive to people around him. They described his outbursts as impulsive and thought to be out of motivation to get what he wants. He preferred to keep to himself and did not have relationships with people at his home.

CONCLUSION: This case report provides insight into the behavioral characterization of children diagnosed with NF1. While the mechanism of how NF1 relates to behavioral issues is unknown, the association between NF1 and behavioral issues should be carefully considered in NF1 patients presenting with aggression.

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INTRODUCTION

Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder caused by a loss of function mutation in the NF1 gene on chromosome 17 that encodes the protein neurofibromin.[1] The function of neurofibromin is as a tumor suppressor protein by stimulating RAS expression through GTPase activity.[2] NF1 is a multi-system disease that has a variable phenotypic presentation. Dermatologic manifestations of NF1 include multiple cafe-au-lait spots, Lisch nodules, neurofibromas, and skinfold freckling. Optic gliomas are also common, leading to vision loss.[1,3] The most common complications of NF1 are cognitive and behavioral deficits, such as attention-deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD).[1] Children with NF1 have been described as having autistic traits and symptoms, highlighting a deficit in social functioning.[4] Furthermore, specific learning disorders in reading, writing, and mathematics, as well as deficits in cognitive domains, such as visual-spatial performance and executive functioning, have been noted in children with NF1.[5]

Our patient with a confirmed diagnosis of NF1 initially presented to the Emergency Department (ED) with the complaint of suicidal and homicidal ideation after a conflict with a peer. During subsequent hospital admission, he was intermittently agitated and defiant, cursing and physically assaulting hospital staff. He has a long psychiatric history and multiple prior psychiatric hospitalizations as well as suicide attempts. The patient also has a

strong family history of NF1, including a parent and grandparent. He was diagnosed with NF with optic gliomas that have been monitored with annual ophthalmologic visits.

Research on NF1 patients has produced evidence that these patients have poor social functioning and cognitive impairment.[6] While the focus has been placed on cognitive and physical manifestations of NF1, in this article, we present a case of an adolescent with NF1 and severe behavioral abnormalities.

CASE PRESENTATION

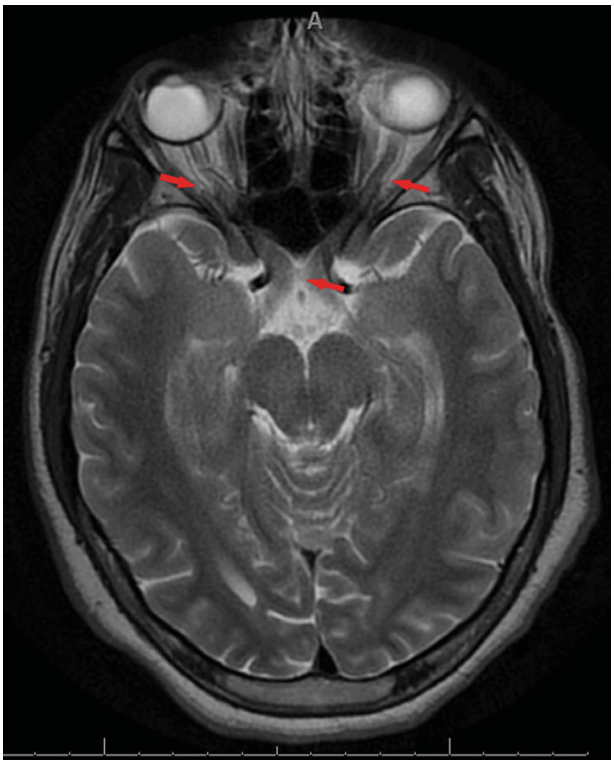
History of Present Illness

A 14-year-old male with a past psychiatric history of obsessive-compulsive disorder (OCD), ADHD, and multiple suicide attempts presented himself after running away from a care home due to a conflict with his peers. On presentation to the ED, he reported suicidal and homicidal thoughts and was subsequently transferred to the emergency room. He reported that he sat in the street trying to get hit by a car because his peers hit and bullied him. During the psychiatric evaluation, he reported auditory command hallucinations telling him to jump in front of a car and lay on train tracks. He also endorsed a history of self-injurious behaviors that involved intermittently scratching his body.

He had two prior ED evaluation after running away from his care home and sitting in the street with the plan of being hit by a car. He was ultimately discharged back to the care home after a mental health evaluation. At the time, it was thought that the patient's actions were motivated by him not liking his living situation and having conflicts with his peers.

The patient's past psychiatric history includes numerous inpatient psychiatric hospital visits in the past few years. Specifically, a month prior to this visit, he was brought to the ED for agitation and suicidal ideation. He was placed in an inpatient psychiatric hospital twice in the past months to address his suicidal ideation and behavioral problem. He has physically assaulted other people by hitting, biting, and spitting when he does not get what he wants or does not agree with what he is being asked to do. During the most recent ED visit, the patient was heard threatening to kill anyone he sees. He continued his outburst by throwing things and hitting people around him. His outbursts have been described as impulsive and as reactions to not having his way. Although he stated he has a good relationship with his immediate family members, he prefers to keep to himself and has not made relationships with people around him. He is currently in school with good grades but still requires special education.

Figure 1: Magnetic resonance imaging of the brain. Diffuse thickening of the bilateral pre-chiasmatic optic nerves extending into the optic chiasm and continuing into the bilateral optic tracts (red arrows), most likely related to an optic nerve glioma given the history of neurofibromatosis[1].



EXAMINATION

On exam, the patient was well-groomed, cooperative, and well-dressed. His behavior was guarded, withdrawn, and he avoided eye contact. His speech was brief, with a normal rate and tone. He described his mood as "okay". His affect was constricted, and his mood is congruent. His thought process was linear and goal directed. He reported command auditory hallucinations telling him to sit in front of cars, active suicidality with a plan to cut himself, and endorsed homicidal ideation. He had poor insight and poor judgment. He had been self-harming by scratching his arm. He denied changes in sleep, appetite, energy levels, focus, and concentration. On physical exam, there was evidence of a neurofibroma (subcutaneous forehead mass), axillary freckling bilaterally, and cafe au lait spots on the trunk and back.

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INVESTIGATION

An MRI obtained during this admission revealed thickening of the pre-chiasmatic optic nerves, chiasm, and optic tracts likely related to the optic glioma, as well as nonspecific T2 hyperintensities within the right putamen and left centrum semi-ovale (*Figure 1*).

He required restraints for several days intermittently that prompted a check of creatine phosphokinase (CPK) which was elevated at 1879 IU/L (reference range 38-258 IU/L). He was subsequently admitted to a medical-surgical floor for management of his rhabdomyolysis.

The patient was started on IV normal saline for treatment of rhabdomyolysis with an initial CPK of 1879 IU/L, after which CPK returned to normal limits within five days. A urinalysis was also performed and was negative for myoglobinuria. Basic metabolic workup was non-contributory.

TREATMENT

Throughout the hospital admission, the patient was intermittently aggressive. He consistently voiced his wishes to be placed into an inpatient psychiatric facility and not discharged to his former residence. While he was awaiting admission to placement in mental health emergency department, he was intermittently agitated and defiant, cursing and physically assaulting people around him requiring administration of as needed (PRN) dosing of intramuscular haloperidol 2mg and lorazepam 1mg.

All home medications (Chlorpromazine, Clonidine, Dexmethylphenidate, and Divalproex sodium) were restarted during his admission. Due to his symptoms, the chlorpromazine dose was increased from 150mg to 300 mg twice daily. In addition, intramuscular haloperidol 2mg PRN was discontinued, and he was instead started on intramuscular olanzapine 5 mg PRN for agitation. After completion of his treatment for rhabdomyolysis, he was discharged to inpatient psychiatric care.

DIFFERENTIAL DIAGNOSIS

Other conditions were considered in the differential diagnoses. The patient has a past psychiatric history of obsessive-compulsive disorder (ODD), which is supported by his continued loss of temper, disobedience to authority, emotions of anger and resentment, and the deliberate annoyance of others; however, OCD does not manifest as physical aggression. Bipolar disorder was ruled out due to the lack of manic or hypomanic symptoms.

DISCUSSION

This case study demonstrates insight into the behavioral characterization of children diagnosed with NF1. Most research available has been focused on cognitive or physical manifestations of NF1, not the emotional-psychological impact NF1 has on children. Evidence shows that there are extensive neurobehavioral disorders among NF1 patients, including alterations in memory, language, cognitive skill, intelligence, and academic performance.[1,7] Our patient has a comorbid diagnosis of ADHD, and reported good grades at school, but receives special education as well. Combined, children with NF1 and ADHD have been shown to have intermittent reactive and aggressive behavior due to poor inhibitory control rather than maladjustment of social functioning in relation to reading facial expressions and voices.[8] Using Social Skills Rating Systems, NF1 patients have been shown to have poorer social skills than normal children.[7] This detriment regarding social skills leads to a decrease in social outcomes. Children with a comorbid diagnosis of ADHD and NF1 have the poorest outcomes in regard to social functioning.[9] In our patient, he did not see his responses to violence as an issue. There was little to no remorse about his actions when asked to reflect on his behavior. Research has suggested brain abnormalities, such as reduced white matter integrity, macrocephaly, and abnormal gamma-aminobutyric acid (GABA)-activity, may be responsible for the social and behavioral difficulties in patients diagnosed with NF1.[10] Behavioral difficulties reported include poor social skills, and both internalizing and externalizing behavior problems.[11] This is shown through our patient's intermittent agitation before and during his hospital admission. It has been noted that children with NF1 have difficulty engaging in successful peer relationships; in addition, these children are more likely to be victims of teasing because of weak interpersonal skills and ADHD-like behaviors rather than physical manifestations of NF1.[12] Interestingly, it has been shown that children with NF1 have also been found to be targets of bullying behavior.[13] It is unclear whether our patient was a victim of bullying at school or in his peer home, though he did admit to frequent disagreements with his peers and a lack of positive social relationships. Perhaps bullying behavior may be contributing to the behavioral issues with patient with NF1. Future research needs to be performed to determine the impact of neurobehavioral symptoms in patients with NF1. Additionally, future research should seek to determine the underlying mechanism explaining the occurrence of agitated behavior in patients with NF1.

CONCLUSIONS

Although much of the current research explores the physical and cognitive manifestations of Neurofibromatosis Type 1 in children, there are behavioral issues that should be explored, specifically, aggression and difficulties with social interactions. This patient with NF1 displays significant behavioral difficulties in the form of intensely aggressive behavior towards the people around him. It is not yet known what the underlying mechanism is to explain this relationship between NF1 and behavioral issues, but it should be carefully considered in this patient population and investigated further.

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