CASE REPORT

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Osteogenesis imperfecta and attention deficit hyperactivity disorder: A rare combination

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Abstract

Osteogenesis Imperfecta (OI) is a rare, autosomally inherited disorder of the connective tissue matrix that is characterized by bone fractures, deafness, and blue sclera. The impairment of Type 1 collagen production causes frequent fractures and increased bone fragility as well as reduced bone mass. Attention Deficit Hyperactivity Disorder (ADHD) is a chronic neurobehavioral disorder developed during childhood that is characterized by inattention, hyperactivity, impulsivity and, consequently, high risk for unintentional injury. This study will examine the case of a 6-year-old male admitted to the researchers’ clinic who has been diagnosed with OI and ADHD and has experienced recurrent traumatic injury. While in the clinic, the patient also expressed symptoms of anxiety such as insomnia, restlessness and irritability. This case has been presented since associations of both disorders is rare. Aside from the fact that these disorders are injury-related and, thus, require additional attention by clinicians, the simultaneous nature of these diseases is also important in that their interaction may provide opportunity for early diagnosis and necessary intervention.

Keywords: Attention deficit hyperactivity disorder, osteogenesis imperfecta, injuries

Introduction

Osteogenesis Imperfecta (OI) is a rare, autosomally inherited disorder of the connective tissue matrix that is characterized by bone fractures, deafness, and blue sclera. The impairment of Type 1 collagen production causes frequent fractures and increased bone fragility as well as reduced bone mass [1]. Type 1 collagen molecules consist of two α1 chains and one α2 chain. COL1A1 and COL1A2 genes on chromosome 17 and chromosome 7, respectively, are responsible for the synthesis of these chains, and mutations in these genes are play a significant role in the pathogenesis of OI [2]. Attention Deficit Hyperactivity Disorder (ADHD) is a chronic neurobehavioral disorder developed during childhood that is characterized by inattention, hyperactivity, impulsivity and, consequently, high risk for unintentional injury. In addition to the aforementioned behavioral characteristics, aggression and risk-taking behaviors are also present [3].

This study will examine the case of a 6-year-old male admitted to the researchers’ clinic who has been diagnosed with OI and ADHD and has experienced recurrent traumatic injury. This case has been chosen since it involves the rare situation of being diagnosed with ADHD and OI simultaneously.

Case Report

M.A., a six-year-old boy attending kindergarten, was referred to our clinic by the pediatric endocrinology department where he was followed up for having OI and expressing the inability to stand on his feet, restlessness and nervousness after an accidental lower extremity fracture that had healed. The patient was brought to our clinic by his father. His anamnesis revealed that he had suffered a lower extremity fracture three months prior, after which he became reluctant to stand on his feet and suffered easy irritability, restlessness, and difficulty sleeping. His father stated that since the boy had been physically hyperactive, able to play with his toys only for short periods, talkative and frequently interrupting others’ speech, he consequently experienced problems with peer relations and success in school. The family applied to a child psychiatry outpatient clinic upon the recommendation of his kindergarten school teacher one year prior to being admitted to our clinic. The child was diagnosed with ADHD, and pharmacotherapy was recommended; however, this treatment was refused by the family. The patient was born via a normal spontaneous vaginal route after a healthy pregnancy period and completed developmental milestones in a timely manner. He suffered his first fracture when he began walking and eventually was admitted to an orthopedic clinic for experiencing fractures on six occasions. He finally was diagnosed with OI seven months prior to this study. The Clinical Global Impression (CGI) Scale and Conners’ Parent Rating Scale (CPRS) were employed during this study’s interview with the client [4,5]. His CGI score was 6 “severe”, CPRS hyperactivity

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score was 8, CPRS attention deficit score was 6, CPRS oppositional defiant score was 3, and CPRS conduct disorder score was 4.

Mental examination of the patient revealed that he was anxious and irritable, his affect was consistent with his mood, and his thought processes were intact. Based on physical and mental examination via psychometric assessment scales and DSM-5 diagnostic criteria, he was diagnosed with ADHD and Generalized Anxiety Disorder [6]. Atomoxetine was selected for medical treatment since the patient expressed a combination of anxiety and ADHD symptoms [7]. The drug was initially administered at a dose of 0.5 mg/kg/day and titrated to 1 mg/kg/day a week later. The patient was regularly examined at bi-monthly intervals, and the maintenance treatment was continued with a 1 mg/kg/day dose of atomoxetine. His anxiety and ADHD symptoms markedly regressed, and he experienced no traumatic injury. A psychometric assessment conducted six months after his initial visit revealed a CGI score of 2 “borderline mentally”, a CPRS hyperactivity score of 4, attention deficit score of 2, oppositional defiant score of 2, and conduct disorder score of 3. The patient was followed up monthly in accordance with his maintenance drug therapy.

Discussion

This study involves a client diagnosed with ADHD and OI who was referred to our clinic due to his expression of anxiety symptoms following a lower extremity fracture. Our case was assessed for OI based on the Shapiro classification that categorizes OI into 4 groups based on the timing of the first fracture and radiological appearance [8]. According to this classification, our case is considered as Tarda B, which is the mildest form of OI. Shapiro classification is summarized in Table 1.

Table 1. Shapiro Classification

<table>
<thead>
<tr>
<th>Classification</th>
<th>Features</th>
</tr>
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<tbody>
<tr>
<td>Konjenita A</td>
<td>Fractures at birth, bones radiologically abnormal*</td>
</tr>
<tr>
<td>Konjenita B</td>
<td>Fractures at birth, bones radiologically normal*</td>
</tr>
<tr>
<td>Tarda A</td>
<td>First fracture before or at walking stage, bones narrow and osteopenic</td>
</tr>
<tr>
<td>Tarda B</td>
<td>First fracture after walking, bones radiologically normal</td>
</tr>
</tbody>
</table>

*As defined by Shapiro[8]

It should be acknowledged that children diagnosed with ADHD and OI simultaneously experience a higher risk of recurrent fractures since traumatic injuries are associated with greater incidence of bone fractures in children with OI and are more frequent as well as detrimental in children with ADHD [1,3]. It is therefore necessary in preventing bone fractures to consider ADHD and other behavioral risk factors in children with recurrent fractures unexplainable by the clinical severity of OI. Our client also experienced multiple recurrent fractures despite his clinically mild form of OI. Clinicians should also be vigilant when treating patients diagnosed with both OI and ADHD, regardless of reduced ADHD symptoms. This is because the mild phenotypes of OI and cases without complications may be easily overlooked [9]. According to DSM-5 criteria, our patient was diagnosed with Generalized Anxiety Disorder because he conveyed symptoms of anxiety after recurrent fractures. Psychiatric disorders including Generalized Anxiety Disorder, Major Depression and Posttraumatic Stress Disorder may induce traumatic injuries in children [6,10]. Clinicians should be aware of possible psychiatric disorders after such injuries and refer the patient to the appropriate medical departments. Our patient was first referred to our department for displaying symptoms of anxiety. We appropriately planned his medical treatment by considering anxiety symptoms in addition to ADHD symptoms. Although methylphenidate initially might have been a reasonable treatment choice for the patient’s ADHD symptoms, atomoxetine was selected because of the concurrent nature of his anxiety symptoms. Atomoxetine is an effective treatment option for both ADHD and anxiety symptoms when anxiety disorders interact with ADHD [7]. There is a growing view that pharmacotherapy in children with ADHD reduces the risk of unintentional injuries, and recent studies have supported this view [11,12]. Reducing the risk of injury via ADHD treatment has also illuminated the issue of whether ADHD treatment may be an option in such diseases as OI, in which severe physical activity is limited due to reduced bone mass. There has not yet been a study on this subject and, thus, it is an important issue for future research [13].

According to research, the most promising regions for the elucidation of the etiology of ADHD are 16p13 and 17p11 [14]. Moreover, the COL1A1 and COL1A2 genes, responsible for the α1 and α2 chains of Type 1 collagen and which play a role in OI, are located on chromosomes 17 and 7, respectively. More than 90% of patients have expressed mutations related to these two genes [2]. Despite these facts, no previous studies have examined their common role in both ADHD and OI genetics. Further studies on this subject would be beneficial for elucidating whether the comorbidity of these two disorders is causal or coincidental. Keeping in mind that ADHD and OI may coexist in patients with frequent traumatic injuries might aid clinicians in making the right diagnoses and planning appropriate treatment.

References


