

## Case Report

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# Management of attention-deficit/hyperactivity in a patient with fibular hemimelia

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## ABSTRACT

Fibular hemimelia (FH) is a rare condition defined by the partial or complete absence of the fibula, often accompanied by associated deformities and anomalies, with an estimated incidence of 1 in 40,000 live births. In parallel, attention-deficit/hyperactivity disorder (ADHD) is a prevalent neurodevelopmental disorder marked by patterns of inattention, hyperactivity, and impulsivity that disrupt daily functioning and quality of life. The ADHD medication may influence children with FH, given their shared developmental risk factors. Understanding the interplay between these conditions is vital for developing comprehensive care strategies that address both the physical and behavioral challenges faced by these individuals. This case describes an 8-year-old male with ADHD and anxiety linked to FH. The patient faced challenges in learning, reading and attention, along with disruptive behaviors and feelings of bullying from peers. Evaluation indicated appropriate hygiene, a linear thought process and mild anxiety, with the patient describing his mood as "okay." As a part of his treatment plan, the patient was prescribed 18 mg of methylphenidate HCl daily, 15 mg of L-methylfolate and referred for psychological testing. The intersection of FH and ADHD presents clinical challenges that require a nuanced understanding of both conditions. FH can result in significant limb discrepancies and may necessitate orthopedic interventions, while ADHD is often treated with stimulant medications that, while effective, can have side effects including potential impacts on growth. This highlights the importance of monitoring growth in children with both conditions, as stimulant use may influence physical health outcomes. Upon follow up, the patient demonstrated improved attention and behaviour, with no evidence of growth suppression.

**Keywords:** Fibular hemimelia, Visceral anomalies, ADHD

## INTRODUCTION

Fibular hemimelia (FH) is commonly defined as a partial or complete absence of the fibula, potentially accompanied by other fibular deformities, anomalies, foot deformities and absent rays.<sup>1</sup> This is typically considered a rare disorder that may be isolated or associated with visceral anomalies.<sup>1</sup> FH is an extremely rare condition associated with regular inconsistency regarding its true incidence rate; however, it is estimated to be approximately 1 in 40,000 live births.<sup>2</sup> FH, very rarely, may be concurrent

with non-skeletal formations such as cardiac anomalies, renal dysplasia, anophthalmia, thoracoabdominal schisis, spina bifida and thrombocytopenia.<sup>2</sup>

ADHD is known as a developmental disorder characterized by a continual pattern of inattention, such as staying on task or being organized, hyperactivity, such as excessive movement (often during inappropriate times) or talking and impulsivity, such as interrupting or intruding on others.<sup>3</sup> It is common for individuals to exhibit these behaviors, however those with ADHD, these behaviors

typically occur frequently across a variety of situations. ADHD is one of the most common disorders diagnosed in the younger population.<sup>3</sup> Symptoms may generally begin in childhood and progress throughout adolescence and adulthood. ADHD is frequently comorbid with other conditions such as learning disorders, sleep disorders, conduct issues, anxiety and/or depression, which can further complicate diagnoses.

ADHD symptoms can significantly affect daily functioning and quality of life. It is found that the inattentive subtypes of ADHD exhibit prevalence in about 18.3% of total patients, while hyperactive/impulsive subtypes and combined reflect 8.3% and 70% respectively.<sup>4</sup>

Impulsiveness often leads to hasty decisions, while disorganization and difficulty prioritizing tasks result in poor time management. Individuals may struggle to focus on tasks and feel overwhelmed by multitasking.<sup>5</sup> Restlessness and a low tolerance for frustration are common, alongside frequent mood swings.<sup>5</sup> Many face challenges in completing commitments, leading to feelings of inadequacy and coping with stress can be particularly hard, which may contribute to increased agitation.<sup>5</sup>

Although FH and ADHD originate from differing domains, the subjective experience of children with FH is associated with developmental risk factors that can co-occur and/or overlap with pathways linked to ADHD. Furthermore, these risk factors can increase in complexity depending on an individual's specific medication, lifestyle and other external factors. Previous research suggests that stimulant medications taken for ADHD can stunt growth, further affecting existing developmental complications.<sup>6</sup> While there are studies and research regarding this concept, there are still more questions than answers. The primary challenge that is posed to researchers is the ability to conduct long-term studies following children using stimulants to observe any developmental and/or growth effects.

Prevalence studies on FH and ADHD with potential implications by stimulant medications further affecting growth and development are limited. This condition, although widely recognised, is currently underrepresented in the database. We present a case of an 8-year-old male exhibiting ADHD behaviors concurrent with his condition of fibular hemimelia.

## CASE REPORT

An 8-year-old male presented to the clinic with ADHD and anxiety concerns regarding his condition of fibular hemimelia. The patient reported increasing difficulty with learning and reading, and noted prolonged periods of inattention. He acknowledged exhibiting disruptive and distracting behavior during class times. The patient expressed concerns about feeling bullied in school by his classmates, who claim he "is crazy." He reported feelings

of anxiety and nervousness, often interfering with his willingness to attend school and participate in academic events/extracurricular activities.

On the mental status examination (MSE), the patient appears to present with appropriate hygiene and is dressed in casual clothes. The patient exhibits a linear thought process, expressing some aspects of preservation. He describes his mood as "okay." The patient's behavior appears cooperative with some fidgeting, constricted and mildly anxious affect with normal speech. The patient reports no delusions or hallucinations and is alert and oriented to person, place and time. The patient demonstrates fair insight for his age and denies any suicidal or homicidal ideation.

The patient's past medical history is notable for his multiple surgical interventions regarding his fibular hemimelia. The patient underwent his first two surgeries at 1.5 years old under general anaesthesia, performed three weeks apart, each with an operative time of roughly four to five hours. At the age of 6, the patient required two additional surgeries, supplemented by shorter surgeries lasting about an hour. The patient was carried to full term and has no history of falls, trauma, seizures or infection.

The patient was initiated on methylphenidate HCl 18 mg orally, once daily, to supplement the 15 mg of L-methylfolate (folic acid). He was additionally recommended for psychological testing to gather more information regarding his condition.

Following initiation of methylphenidate HCl 18 mg daily with L-methylfolate, the patient was monitored for behavioral symptoms, academic functioning, anxiety, and physical growth. Caregivers reported noticeable improvements in attention, classroom participation, and task completion, with a decrease in disruptive behaviours. Mild anxiety related to school and peer interactions persisted but showed gradual improvement. The medication was well tolerated, with no significant adverse effects reported. Serial measurements of height and weight remained stable without deviation from the expected growth trajectory. The patient was referred for psychological and neuropsychological testing to further assess learning difficulties and support academic planning, with continued multidisciplinary follow up the recommended.

## DISCUSSION

During early embryonic development, the lower extremities can be sonographically viewed via a routine prenatal ultrasound, before the upper extremities.<sup>1,9</sup> However, the movement of the upper extremities can be seen before that of the lower extremities.<sup>1</sup> Thus, further aid in diagnosis can be carried out through other imaging tests such as X-rays, MRI or a CT scan.<sup>9</sup> As a partial or missing fibula is frequently accompanied by other abnormalities, it is important to evaluate the entirety of the leg.<sup>9</sup> The

etiology of fibular hemimelia remains uncertain, however, previous research and theories suggest an absent anterior tibial artery can progress to further defects in muscle development and complications in the apical ectodermal ridge.<sup>1</sup> Another proposed theory regards limb disruption during the embryogenesis process, such as a spontaneous genetic error during limb bud development at roughly 6 to 8 weeks after conception.<sup>1,2</sup>

The appearance of fibular hemimelia in a child depends on the severity of the deformity.<sup>8</sup> The aspect of limb length discrepancies can range in intensity from mild to distinctive shortening. The shortened tibia most frequently includes an anteromedial or anterior bow that is considered to arise via the tethering effect of the rudimentary fibular anlage, which can clinically express as a taut posterior band in the fibular area, with a potential skin dimple at the apex of the bow.<sup>8</sup> Treatment most commonly includes prosthetics and orthotics, with or without surgical intervention.<sup>8</sup> Other angular deformities in the fibular area and knee instability may also require surgical intervention. Symptoms of fibular hemimelia may present with physical indications such as asymmetrical lower limb lengths (shorter or longer), foot and ankle abnormalities, missing toes, knock-kneed on the affected side and less obvious indications such as weak or missing knee ligaments or a shallow hip joint.<sup>9</sup>

The pathophysiology of ADHD is associated with a wide variety of genetic and environmental factors.<sup>4</sup> In a psychiatric perspective, it is known to be one of the most heritable conditions with a greater concordance in monozygotic twins compared to dizygotic twins.<sup>4</sup> Furthermore, smoking during pregnancy, viral infections, alcohol exposure and nutritional deficiency in the fetus have been investigated as potential causes of the disorder.<sup>4</sup> Despite this, there have been no consistent findings or studies on the brain imaging of patients with ADHD. Additionally, the quantity of dopaminergic receptors has been implicated in the development of ADHD, as research has shown that the number of receptors is known to decrease in the frontal lobes of ADHD individuals.<sup>4</sup>

Current research suggests that the combination of behavioral therapy and pharmacotherapy may benefit the majority of individuals with ADHD.<sup>6</sup> Stimulant medications largely remain the primary medical treatment of choice for those with ADHD, exhibiting a significantly positive response rate.<sup>6</sup> These drugs are available in various formulations which may cause uncertainty and prospective errors in the prescription of these medications. Learning and understanding the advantages and disadvantages of these drugs can lead to better-informed individualized treatment. An individualized approach can aid in maximizing the therapeutic benefits while minimizing the potential risks, consequently being able to support more effective treatment for individuals with ADHD.

Although stimulants generally perform favorably with a pattern of a low risk profile, they do carry some risks for children on these medications, with the most common adverse effects being weight loss and suppression of appetite.<sup>6</sup> A recent systematic review and meta-analysis involving 18 studies (with the sample size ranging from 34 to 1,758) examined the long-term effects of methylphenidate. The findings showed that prolonged treatment with methylphenidate might be associated with a reduction in growth, especially height. However, effect sizes were found to be small (standardized mean difference=0.27, 95% CI=0.16-0.38), indicating that the clinical significance might be minimal.<sup>7</sup>

There are three main proposed mechanisms by which growth can potentially be affected in children taking stimulant medications. First, suppression of appetite is a commonly discussed feature of stimulant medications, which can lead to decreased caloric intake, negatively affecting potential growth in children.<sup>6</sup> The dopaminergic effects associated with stimulant medications may also be implicated via their role in growth hormone suppression, more directly affecting growth in children.<sup>6</sup> Lastly, previous studies suggest stimulants may slow the rate of cartilage tissue growth, affecting bone development.<sup>6</sup>

Taken together, these mechanisms propose the notion that stimulant medications may have a multifactorial impact on development and growth in the child population. While the effects can be minimal, it may prove to be clinically significant and relevant in children with genetically pre-existing growth complications or anatomic anomalies. Within the scope of this case, comprehensively investigating fibular hemimelia in the context of a patient with ADHD taking stimulant medication is critical in being able to understand further implications of growth/development. Careful monitoring of developmental parameters and individualized treatment plans are warranted for stimulant drug prescription in such populations.

## CONCLUSION

Fibular hemimelia is a serious condition presenting a range of challenges from embryonic development to clinical manifestations, emphasizing the need for tailored treatment, including the use of prosthetics and orthotics. The causes of ADHD involve a mix of genetic and environmental factors in which medications and behavioral therapies can be effective treatments. While stimulant medications are the main medications for ADHD, their potential impact on growth calls for careful consideration. Ultimately, an awareness of both conditions and how they affect each other is essential for providing the best care, guiding treatment decisions, and optimizing outcomes for affected individuals.

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