Restless Legs Syndrome/ Willis-Ekbom Disease and Growing Pains in Children and Adolescents

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KEYWORDS

• Pediatric restless legs syndrome (RLS) • Pediatric periodic limb movement disorder (PLMD) • Growing pains • ADHD • Iron therapy • Dopaminergic medication

KEY POINTS

- Recent epidemiologic studies have shown that restless legs syndrome (RLS) and periodic limb movement disorder (PLMD) are common but underrecognized disorders in children and adolescents.
- There is a significant overlap between RLS and growing pains in children.
- The diagnostic criteria for pediatric RLS have recently been updated to simplify and integrate with newly revised adult RLS criteria.
- In addition to typical RLS symptoms, other clinical features such as the presence of periodic limb movements in sleep (PLMS) and family history of RLS and PLMD are useful to support the diagnosis.
- Both pharmacologic and nonpharmacologic interventions are important in the management of RLS and PLMD in children.
- Children with low iron storage are likely to benefit from iron therapy.
- Although there is limited information on pharmacologic therapy, there is emerging literature showing the effectiveness of dopaminergic medications in the management of RLS and PLMD in children.

INTRODUCTION

RLS was first described in pediatric literature in 1994.[1] Recent epidemiologic studies have shown that RLS is common in children and adolescents with prevalence of 2% to 4%.[2–4] Such figures, if confirmed by additional studies, would indicate that approximately 1 million children are affected by RLS in the United States.

The cause of pediatric RLS and PLMD is not well understood. It remains unclear as to what specific roles are played by genetic factors, dopamine dysfunction, and low iron stores in the pathophysiology of RLS and PLMD. There is significant overlap between RLS and growing pains. The diagnosis of RLS in children can be quite challenging because of their inability to verbalize RLS symptoms. The International Restless Legs Study

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Group has recently revised the pediatric RLS diagnostic criteria, which were simplified and integrated with the newly revised adult RLS criteria.[5] Special consideration and supportive clinical features have been developed to guide the application of criteria in children. The management of RLS and PLMD involves both nonpharmacologic and pharmacologic approaches. Children with evidence of low iron storage would benefit from iron therapy. Overall, there is limited experience regarding the use of dopaminergic agents in children with RLS and PLMD; other medications including benzodiazepine, anticonvulsants, as well as α-adrenergic and opioid medications have not been adequately studied in children. This article covers clinical evaluation and management of RLS and PLMD in children and the relationship with growing pains.

EPIDEMIOLOGY

RLS is common in the adult population with an estimated prevalence of 4% to 10%.[6] Approximately 25% to 40% of adult patients with RLS reported early onset of symptoms before the age of 20 years.[7,8] Several studies have evaluated the prevalence of RLS and PLMD in children in various settings. RLS was noted in 17% of children in general pediatric clinics and 5.9% of children referred to sleep clinics.[9,10] PLMD was found in 8.4% of children who were referred to sleep clinics and 7.7% to 11.9% of children from community.[11] A large-scale population study has shown that RLS is common in children and adolescents with an estimated prevalence of 1.9% in school-aged children and 2% in adolescents.[4] Another recent study in high-school students confirmed the prevalence of 2% in adolescents.[2] There is no significant difference in the prevalence of RLS among boys and girls.[4] One study has suggested that PLMD is more common in Caucasian than African American children.[12]

PATHOPHYSIOLOGY

Several causes have been proposed to play a role in the pathophysiology of RLS and PLMD including genetic factors, dopamine dysfunction, and low iron stores. Many studies have shown genetic influences in the pathogenesis of RLS and PLMD. Large population studies have shown a significant association between RLS and PLMD and a common variant in an intron of BTBD9 on chromosome 6p21.1, emphasizing the potential for both genetic predisposition and genetic susceptibility to the occurrence of RLS and PLMD.[13,14] Other genetic variants such as the homeobox gene MEIS1 on chromosome 2p and the genes encoding MAP2K5 and the transcription factor LBXCOR1 on chromosome 15q have been reported in patients with RLS.[13] Interestingly, one study on childhood-onset RLS showed the association with MEIS1 and LBXCOR1, but not with BTBD9.[15] The role of dopamine dysfunction is discussed elsewhere.

There is emerging evidence of the role of iron in the pathophysiology of RLS and PLMD. Evidence of low iron storages have been found in cerebrospinal fluid, brain sonography, MRI, and autopsy report.[16–19] In children, low iron storage as evidenced by low ferritin and iron deficiency are found in children with RLS.[20,21] Low brain tissue iron concentration may lead to RLS and PLMD through alteration in dopaminergic system.[22]

CLINICAL MANIFESTATION

The clinical presentation of RLS and PLMD in children differs from that of RLS and PLMD in the adult population. Children with RLS and PLMD may present with nonspecific symptoms such as growing pains, restless sleep, sleep disturbances, insomnia, and daytime sleepiness.[23,24] These symptoms may go unnoticed by their parents.[4,23,25] A history of growing pains is noted in 78% to 85% of children and adolescents with RLS.[4] Sleep disturbances including sleep-onset and sleep-maintenance insomnia are common presentations in children with RLS and PLMD.[9,25] Young children may have difficulty describing symptoms of RLS and may describe these sensations with nonspecific but age-appropriate terms. Therefore, physicians and health care providers should be familiar with development-appropriate terms and descriptions. Some examples of description of sensory complaints in children are “oowies”; “boo-boos”; “tickle”; “legs need to stretch”; “ants crawling and aching feeling”; “legs hurt and feel funny”; “fidgety, restless, too much energy”; and “spider in the legs.”[4,25] A family history of RLS is common in children with RLS. In fact, a positive family history of RLS and PLMD is helpful as supportive evidence in making a diagnosis of RLS in children and to raise the possibility of developing RLS over time in children who do not meet criteria for RLS.[25]

DIAGNOSIS

The diagnosis of RLS in children is challenging, particularly because young children may not be able to describe typical RLS symptoms or because these symptoms may not manifest at very young ages. The interval between the initial