Quality of Life in Children with Narcolepsy and Cataplexy

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KEYWORDS

• Sleep • Narcolepsy • Child • Quality of life • Cataplexy

KEY POINTS

- Narcolepsy is a chronic and disabling neurologic disorder that affects sleep and wakefulness and is characterized by excessive daytime sleepiness (EDS), sudden sleep episodes, and attacks of muscle atonia mostly triggered by emotions (cataplexy).
- Narcolepsy is a lifelong nonprogressive disorder, the onset of which occurs not infrequently during childhood. However, narcolepsy in children is frequently underdiagnosed or misdiagnosed.
- Since a signal regarding the potential association between H1N1 vaccination and narcolepsy was raised in Sweden and Finland, additional cases have been reported in different countries across Europe and particularly in France.
- Young patients affected by the disorder often show dramatic and abrupt impairment in their social skills and academic performance because of excessive daytime sleepiness, fatigue, and lack of energy.
- Underrecognition and undertreatment of narcolepsy represents a significant unmet medical need in childhood.

INTRODUCTION

As in adults, pediatric narcolepsy may show a great deal of variability in its presentation. Symptoms may start abruptly and sometimes dramatically with the sudden occurrence of extreme sleepiness and complete cataplexy, or progressively and insidiously, with excessive daytime sleepiness (EDS) or weight gain being the only symptoms over weeks or months. Although cataplexy is the most specific symptom of the disorder, it is usually not the first symptom to appear and may not be manifested for some 1 to 5 years after EDS occurs. This variability in presentation often leads to difficulties in recognizing the condition or making the diagnosis at an early stage.

Narcolepsy in children, therefore, is frequently underdiagnosed or mistaken for other diseases, and may not even be considered in the differential diagnosis of the presenting complaint.[1] Young patients affected by the disorder often show dramatic and abrupt impairments in many domains because of EDS, fatigue, and lack of energy, including social skills and academic performance.[2] This situation thus represents a significant unmet medical need in childhood.

PREVALENCE OF PEDIATRIC NARCOLEPSY

The incidence of narcolepsy in adults (<1 per 100,000 new cases per year) suggests that it is a rare condition; however, given that it is also a

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chronic disorder, the prevalence is much greater at 20 to 60 per 100,000 in Western countries. The prevalence of the disorder in children remains unknown. Based on a study conducted in the United States, the disorder could affect some 20 to 50 per 100,000 children.[3] Although narcolepsy has traditionally been considered to be a disease of adulthood, most cases have their onset in childhood or adolescence.[4,5]

Recently, systematic approaches have been established to study narcolepsy in childhood and adolescence. A French national database was created in 2007 (research program Narcobank, French Grant PHRC AOM07-138 from the French Health Ministry, Assistance Publique-Hôpitaux de Paris) that has thus far gathered clinical data on more than 100 children and adolescents aged 5 to 16 years with narcolepsy. The cohort was composed of 117 children (65 boys) with a mean age of 11.6 $\pm$ 3.1 years at time of diagnosis. The gender ratio was 0.56 in favor of males versus females. The children were followed up in different French expert orphan disease sleep centers for narcolepsy management, including the Robert Debré Children's Hospital in Paris, the Mother-Children's Hospital in Lyon, the Gui-de-Chauliac Adult's Hospital in Montpellier, and the Pitié-Salpétrière Adult's Hospital in Paris. The considerable number of patients enrolled in this database demonstrates that narcolepsy is far from exceptional in children and adolescents and should always be suspected when a youngster presents with abnormal daytime sleepiness or partial or complete loss of muscle tone triggered by emotions.

Primary care pediatricians can play a significant role in the care of patients with narcolepsy in regards to appropriate diagnosis and optimal management. Available treatments have been shown to be effective in clinical settings; however, lack of treatment can result in an increased risk of poor outcomes. For example, the tendency for increased weight gain is intrinsic to childhood narcolepsy and is manifested relatively early in the course of the disorder. Early identification and management of weight gain could thus prevent such significant consequences as morbid obesity[6] and even potentially precocious puberty.[7]

DEMOGRAPHICS OF CHILDHOOD NARCOLEPSY

Narcolepsy in children has been reported in a wide variety of ethnic groups, including white Americans and Europeans, Japanese, Korean, Mexican, and Chinese populations. For example, recent narcolepsy-cataplexy (NC) case studies have included reports on disease characteristics in both white children and Chinese children younger than 13 years of age.[8] Another study reported on the presentation of cataplexy in 23 young Italian patients.[9] Although this finding should be interpreted in light of recent immigration rates, in our own database we found a high proportion of patients (representing some 26% of the cohort) originating from Sub-Saharan Africa, especially Mali, Cameroon, or Benin. White patients represented 33% of our cohort, with the remaining originating from the French Indies (24%), North African Maghreb countries (10%), and Comoro Islands (3%).

NARCOLEPSY AND AGE OF ONSET

Early observations in the United States[10] and Japan[11] reported that approximately 50% of patients with narcolepsy had an onset before 15 years of age, with less than 10% with an onset before 5 years of age. Similarly, in a database of 1219 cases reported by Aran and colleagues,[12] although less than 10% were children (<18 years) at evaluation, 40% reported an onset before 15 years of age and 2.1% had an onset before 5 years of age (1.1% with cataplexy onset before age 5 years). In our own database of 117 children and adolescents affected by narcolepsy with or without cataplexy, the age range was 5.4 to 16.6 years and the mean age at disease onset was 9.2 years ($\pm$6.2).

Although the occurrence of narcolepsy has been reported in children during the first year of life, very early onset cases are anecdotal and most often secondary to comorbid brain disorders, including tumors or abnormalities localized most frequently to the diencephalon or to the brainstem. Niemann-Pick disease type C is often associated with early onset cataplexy.[13] Another cause of very early onset of secondary cataplexy is craniopharyngioma, which accounts for 9% of all pediatric intracranial tumors overall.

Importantly, it seems that the delay between the onset of narcolepsy symptoms and diagnosis is lower in childhood than in adulthood. Early adult studies in the 1980s to 1990s reported a median delay between onset of symptoms and diagnosis of more than 10 years[14]; a similar delay was also reported in the French Harmony study.[15] However, in the Narcobank cohort, we found a mean duration of symptoms before diagnosis of 31 months, and in three children the diagnosis had been made within 5 months after the first occurrence of narcoleptic symptoms (ie, abrupt cataplexy or sleep attack but excluding possible weight gain).

This is potentially very important because children diagnosed shortly after symptom onset may be preferential candidates for immunotherapy