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Brief Communication

Sleep disorders in children with incidental pineal cyst on MRI: a pilot study☆,☆☆

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ABSTRACT

Introduction: For several years, pineal cysts have been considered an incidental finding on brain MRI's even though research and case reports have shown a possible association of pineal cysts with headaches and sleep disturbances. This pilot study aims to evaluate sleep disorders in school-age children with an incidental pineal cyst in an otherwise normal brain MRI.

Method: Children aged 6–12 years, who were referred for evaluation of headaches, tics, or syncope, and had an incidental pineal cyst on an otherwise normal brain MRI were included and compared to a control group of children with the same referral reasons but with a normal MRI and to a cohort of normal controls. The Sleep Disturbance Scale for Children (SDSC) was administered to the parents. Exclusion criteria included use of medications that affect sleep, seizures, brain abnormalities, tumors, or comorbid medical conditions that affect sleep.

Results: Eighteen children (11 females) with pineal cysts, 19 children with normal MRI, and 100 age- and sex-matched controls were included in our study. There were statistically significant differences in the total SDSC score (with a difference of 10 between the median scores) and in two of the six domains of this scale. Children with pineal cysts scored significantly higher in the domains of disorders of excessive sleepiness and disorders of initiating and maintaining sleep than the two control groups. The scores in these two domains correlated significantly with the size of the cyst.

Conclusion: School-age children with pineal cysts have significantly increased levels of sleepiness and difficulty with sleep initiation and maintenance.

1. Introduction

The pineal gland is a neuroendocrine structure located between both hemispheres in the epithalamus. Its main function is to participate in circadian regulation by producing melatonin from serotonin. The normal pineal gland is ovoid and with a length of less than one cm. Pineal cysts are fluid filled, well-defined, smooth edge structures within the gland [1]. Pineal cysts are considered to be an incidental finding in the brain magnetic resonance imaging (MRI) of both adults and children, with an incidence in children of up to 57% [2]. Studies in adults and children have found a higher prevalence in females than in males [3] and that the majority of pineal cysts do not change much in size with age; repeated MRI studies are rarely ordered [3].

Although pineal cysts are mostly considered to be asymptomatic, there are medical literature reports associating pineal cysts with headaches [4]. The pathophysiology of headaches in patients with pineal cysts has been postulated to be secondary to aqueductal compression in large cysts, obstruction of the vein of Galen, or disturbances in melatonin production [5].

Headaches are a common complaint in school-age children with an incidence of up to 50% [6]. Headaches can have a bidirectional relationship with sleep: ie, lack of sleep can worsen headaches and lower the headache threshold and conversely, headaches can disrupt sleep. For example, children with migraine, have an increased disruption in sleep, and children with sleep disorders have an increased prevalence of headaches [7]. The International

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☆☆ The manuscript does not report on a clinical trial.
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Classification of Sleep Disorders third edition (ICSD-3) has included a category called “sleep-related headaches”; under this category, headaches occur during sleep or upon awakening. This type of headache is rare in children [8].

The Sleep Disturbances Scale for Children (SDSC) is a questionnaire validated for children and adolescents, which uses 26 questions with a Likert-type answer scale to categorize sleep disturbances under six domains: disorders of initiating and maintaining sleep (DIMS); sleep breathing disorders (SBD); disorders of arousal (DOA); sleep–wake transition disorders (SWTD); disorders of excessive somnolence (DOES); and sleep hyperhidrosis (SHY) [9].

Based on previous clinical observations [10,11], in this study we aim to identify the sleep patterns of children with incidental pineal cyst found in brain MRI and compare them to a group of children referred for brain MRI for similar clinical reasons, as well as compare to a group of normal controls. We hypothesize that children with pineal cysts will have more sleep problems, particularly circadian disruption and daytime sleepiness, than the other two groups.

2. Methods

2.1. Subjects

Our study consisted of two parts. The first consisted of a retrospective chart review of children who had undergone brain MRI. Inclusion criteria were as follows: MRI performed between July 2016 and December 2016 in children of age 6–12 years who were referred for brain MRI for evaluation of headaches, tics, syncope, toe walking, or hearing loss and who had an incidental pineal cyst on an otherwise normal brain MRI. The size of the cysts was evaluated by measuring their longer axis. Exclusion criteria were as follows: children with neurodevelopmental disorders or syndromes, traumatic brain injury, seizures, brain tumors, post brain surgery, comorbid medical conditions that affect sleep, and taking medications that affect or alter sleep. Children who fit the criteria were included consecutively. A clinical control group consisting of children with the same referral reasons who were then found to have a completely normal brain MRI was also included during the same process. Another normal control group was composed of children randomly selected in a public school. The control group did not undergo brain MRI. All children who underwent brain MRI were initially evaluated by a neurologist and a sleep disorder was not initially identified. None of the children had been referred to a sleep center for evaluation.

The study was performed at the Benioff Children's Hospital Oakland with the approval of the hospital's institutional review board.

2.2. Questionnaire

The second part of the study consisted of administration of the SDSC to the parents of children included in the cohort by a board-certified sleep physician by a telephone call or the SDSC was directly collected in a public school by the same physician after the approval of the school director and the consent of the parents.

Data collected included age, sex, diagnosis, medications, pineal cyst size, and SDSC parameters.

2.3. Statistical analysis

Data were analyzed using descriptive statistics, followed by between-group comparisons using nonparametric Kruskal–Wallis analysis of variance (ANOVA), followed by the Mann–Whitney test, used as a post-hoc analysis. Frequencies were analyzed using the chi-square or Fisher exact tests, as appropriate for the expected cell values. Correlations were evaluated with the Pearson's correlation coefficient r. P value was set at <0.05.

3. Results

Eighteen children (11 females) with pineal cysts (median age 10 years), 19 children (12 females) with normal brain MRI (median age 10 years), and 100 normal controls (median age 9.5 years, 52 females) were included in the study. Among children with pineal cysts, 10 were Caucasian, four were Hispanic, three were black, and one was Asian. Among children with normal brain MRI, eight were Caucasian, seven were Hispanic, three were black, and one was Asian. The normal reference controls were mainly Caucasian children.

The indications for MRI in the group with pineal cyst/clinical control group were as follows: headaches (6/6), migraines (5/5), hearing loss (3/4), toe walking (1/0), optic edema (1/1), neuropathy (1/1), syncope (1/1), and short stature (0/1). The indications for MRI were not statistically different between the two groups (chi-square or Fisher exact tests). None of the subjects had nocturnal headaches or morning headaches. Pineal cyst size varied from 4 to 21 mm in length (eight children had cyst <10 mm).

In terms of SDSC scale, there were statistically significant differences in the total SDSC score in children with pineal cysts vs. both control groups; in particular, children with pineal cyst scored significantly higher in the domains of DOES (Table 1). There was an increase in DIMS in children with pineal cyst compared to that in normal controls. This was not different from children with a normal brain MRI.

Fig. 1 shows the correlation between cyst size and total SDSC score, DOES score, and DIMS score, which is positive in all cases and reaches statistical significance for the two DOES and DIMS domains.

4. Discussion

Our study shows that school-age children with pineal cysts are sleepier than normal age-matched controls and children referred for MRI for similar reasons. We selected a group of school-age children to avoid the natural circadian delay changes associated with adolescence [12] and the confounding combination of sleep disturbances seen in toddlers and preschool children [13]. Our clinical control group was comparable in age, sex, race distribution, and presenting diagnosis. The association between headaches and sleep disturbances is well known; therefore, in the group with pineal cyst and the group with normal brain MRI, our cohort included an equal number of children with headache, migraine, and nonheadache indications for brain MRI. Furthermore, none of our patients complained of nocturnal headaches or morning headaches, and none of them were on medications that affect sleep.

Our findings suggest that the presence of a pineal cyst in these children could affect sleep patterns particularly regarding daytime sleepiness. The authors postulate that abnormal melatonin production may be responsible for these findings. However, these findings need to be confirmed by larger studies. Our results also showed an overall difference in SDSC scores in children with pineal cysts. Although we found a general difference in DIMS, the difference was not statistically significant between children with pineal cyst and children with normal brain MRI. These may be due to other factors or confounders not included, such as race or developmental stage among others.

Despite the important role played by the pineal gland in circadian regulation and melatonin production, there is scarcity of studies on pineal size, pineal abnormalities (calcifications and cysts), and sleep disorders. Bumb et al. [14], studied pineal volume in adult patients with insomnia and age-matched controls; they