Neurology Asia 2021; 26(1) : 113 – 116

Evaluation of the relationship between pineal cyst and childhood headache with MR Imaging

[1]Saliha Ciraci, [2]Sevinç Kalın, [3]Hülya Maraş Genç, [3]Büşra Kutlubay, [2]Aslıhan Oysu, [2]Yaşar Bükte

[1]Department of Radiology, Sakarya University Trainig and Research Hospital, Sakarya; [2]Department of Radiology and [3]Department of Pediatrics, Umraniye Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

Abstract

This study was aimed to investigate the relationship between pineal cyst and headache in children. MR imaging was performed in 65 pediatric patients with headache and in a control group of 65 children with a 1.5 T Siemens MR device. The presence of pineal cysts and cyst sizes were noted. True pineal cysts and cystic transformations were evaluated separately. True pineal cysts were detected in 15 (23%) patients in the headache group and in 1 (1.5%) patient in the control group. True pineal cysts were detected in 5 (15.6%) migraine patients and in 10 (30.3%) patients with non-migraine headaches. A significant correlation was found between non-migraine headaches and pineal cysts ($p < 0.05$) on the chi-square testing. However, no significant relationship was found between migraine and pineal cyst on the Fisher's exact chi-square test. Pineal cystic transformations were detected in 13 (20%) patients in the headache group, in 13 (20%) patients in the control group. Pineal cystic transformations were detected in 5 (15.6%) migraine patients and in 8 (24.2%) non-migraine headache patients. There was no significant relationship between non-migraine headache and pineal cystic transformation and between migraine and pineal cystic transformation on chi-square testing.
In *conclusion*, disruption of the circadian release of melatonin may be causally related to headaches. The knowledge of clinicians that pineal cysts may play a role in headache development, may be of therapeutic relevance.

Keywords: Pineal gland, pineal cyst, headache, migraine, magnetic resonance

INTRODUCTION

The pineal gland is located in the diencephalon, behind the third ventricle, and is responsible for melatonin production.[1] Melatonin is a hormone that has important functions such as regulating circadian rhythm, immune function and blood pressure.[2] In addition to these, melatonin has effects on pain threshold and endorphin levels. A significant correlation has been found between low melatonin levels and migraine/cluster headache.[3-5]

Headache is one of the most common neurological problems in children. Patients who present to the neurology outpatient clinic with headaches are frequently referred to radiology to exclude possible underlying space-occupying lesions.[6] One of the most common pathologies encountered in MR examinations is pineal cysts, also known as benign glial cysts, which are considered as an incidental finding. In children, the incidence of true pineal cysts was found to be 10-11% when cysts between 2-5 mm are considered as cystic transformation of the gland and a value of 5 mm is considered as the lower limit of true cysts.[7]

There are studies demonstrating the relationship between headache and pineal cysts in adults. In these studies, the impaired circadian release of melatonin is postulated to be the reason that headaches are more common in patients with pineal cysts.[8,9] In this study, we aimed to investigate the relationship between pineal cyst and headache in children, since we have not encountered published research in the pediatric age group in the literature.

METHOD

Patients, imaging procedures and analysis of data

This prospective study was approved by the ethics committee of our hospital. MRI was

Address correspondence to: Saliha Ciraci, M.D., Department of Radiology, Sakarya University Training and Research Hospital, Sakarya, Turkey. Tel: (+90) 5063672436, E-mail: atasaliha@hotmail.com

Date of Submission: 5 October 2020; Date of Acceptance: 30 October 2020

performed in 65 pediatric patients who presented to the neurology outpatient clinic with headache and in a control group of 65 children without neurological complaints between November 2018 and February 2020. The control group consisted of patients free of any neurological/oncological disease who presented to the general pediatrics and endocrinology outpatient clinics and were sent to have an MRI for screening purposes. The patient and the control groups had a similar female/male ratio and a similar mean age. Patients who presented with headache complaints were classified as migraine and tension/other headaches.[10] The children in the control group had no headache or any other neurological symptoms. MR imaging was performed in our hospital with a 1.5 T Siemens MR device (Magnetom Aera, Siemens, Erlangen, Germany). The MR examination included the following sequences:

a. Coronal and axial T2-weighted fast spin echo (FSE) pulse sequence (TR / TE, 8380 ms / 87 ms; matrix, 150 × 320; slice thickness, 3 mm),
b. Axial fluid-attenuated inversion recovery (FLAIR) pulse sequence (TR/TE, 7640 ms/ 87 ms; matrix, 132×256; slice thickness, 3 mm),
c. Coronal, axial ve sagittal three dimension (3D) T1- weighted magnetization-prepared rapid gradient-echo (MP-RAGE) pulse sequence (TR/TE, 1500 ms/ 2.58 ms; matrix, 179×224; slice thickness, 1 mm),
d. Axial diffusion-weighted imaging (DWI) pulse sequence (TR/TE, 7800 ms/ 86 ms; matrix, 136×136; slice thickness, 3 mm),
e. Axial gradient-echo (GRE) T2* pulse sequence (TR/TE, 700 ms/25 ms; matrix, 92×256; slice thickness, 3 mm).

Images were evaluated by a pediatric radiologist with 12 years of radiology experience. The presence of pineal cysts and cyst sizes were noted. Size measurements were made on 3D T1-weighted MP-RAGE sequences. True pineal cysts (having a diameter exceeding 5 mm) and cystic transformations (having a diameter between 2-5 mm) were evaluated separately.

Statistical analyzes were performed using SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Numerical values were given as mean and standard deviation (SD), and categorical values were given as frequency and percentage. The relationship between headache/migraine and pineal cysts was investigated using the Chi-square test. $P < 0.05$ value was considered as a significant statistical threshold.

RESULTS

Sixty-five pediatric patients with headaches and 65 children without neurological complaints were included in the study. The Female/Male ratio was 33/32 in both patient and control groups. The mean age was 10.75±3.38 (SD), the median age was 10 (range, 5-16 years) in the patient group and the mean age was 10.96±2.98 (SD), the median age was 11 (range, 5-16 years) in the control group. In the patient group, headache types and number of patients were listed as following; migraine (32), tension headache (14) and other headache (19).

True pineal cysts (Figure 1) were detected in 15 (23%) patients in the headache group and in 1 (1.5%) patient in the control group. There was a significant correlation between headaches and pineal cysts ($p < 0.05$) on chi-square testing. True pineal cysts were detected in 5 (15.6%) migraine patients and in 10 (30.3%) patients with non-migraine headaches. A significant correlation was found between non-migraine headaches and pineal cysts ($p < 0.05$) on the chi-square testing. However, no significant relationship was found between migraine and pineal cyst on the Fisher's exact chi-square test.

Pineal cystic transformations (Figure 2) were detected in 13 (20%) patients in the headache group and in 13 (20%) patients in the control group. There was no significant relationship between headache and pineal cystic transformation on chi-square testing ($p < 0.5$). Pineal cystic transformations were detected in 5 (15.6%) migraine patients and in 8 (24.2%) non-migraine headache patients. There was no significant relationship between non-migraine headache and pineal cystic transformation on chi-square testing. Similarly, no significant relationship was found between migraine and pineal cystic transformation.

DISCUSSION

Headache is one of the most common neurological problems in children, and imaging studies are often used to detect brain masses.[6] Pineal cysts are frequently encountered in MRI examinations and are usually considered incidental findings.[7] However, there are studies in the literature which have shown a significant relationship between pineal cysts and headaches in adults.[8,9] Despite this, there are no studies examining the relationship between headache and pineal cysts in children. In this study, we demonstrate that, as with adults, there is a significant relationship between pineal cysts and headache in children.

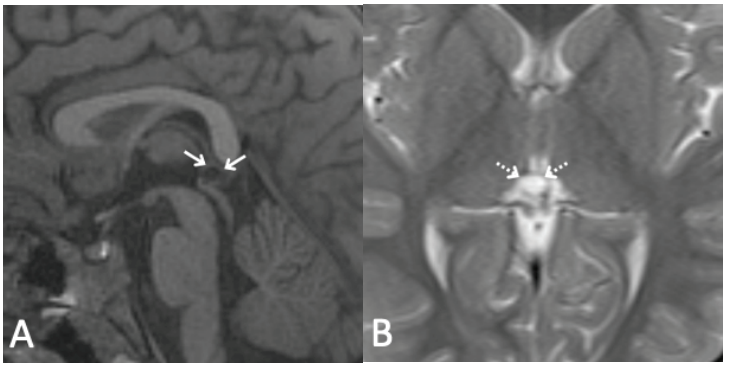

Figure 1. On MRI, a cystic lesion consistent with true pineal cyst (A) which appears hypointense in T1-weighted sagittal sequences and (B) hyperintense in T2-weighted axial sequences.

Melatonin, which is secreted from the pineal gland, can be involved in headache pathophysiology through various mechanisms. The main mechanisms are direct anti-inflammatory activity, inhibition of nitric oxide synthase activity, deactivation of dopamine release, modulation of GABA/glutamate neurotransmission, and the melatonin-immune-opioid network.[11] It has been shown that melatonin can increase the pain threshold by affecting opioid receptor expression and B-endorphin levels.[12] Disorders affecting the pineal gland may have a role in the development of headache by disrupting melatonin release. It has been postulated that patients with pineal cyst, may have headaches because of reduced melatonin secretion rather than mass effect.[8,9] Our results also strongly support this hypothesis.

Many studies have shown benefit of melatonin treatment in migraine, tension headache, cluster headache, hemicrania continua, and hypnic headache in children and adults. In these studies, the efficacy of melatonin treatment for migraine and cluster headache was evident, but studies conducted with other types of headaches have been mostly limited to case series and case reports.[13] In a study, performed by Seifert *et al*. with adult patients, headache was detected in 51% of patients with pineal cysts, and it was stated that half of the headache patients had migraine. In this study, the authors found a significant relationship between pineal cysts and migraine as well as headaches in general.[8] In our study, a substantial relationship was found between non-migranous headache and pineal cysts, but not between pineal cyst and migraines. Differences in the migraine diagnostic criteria for children and adults and the difficulty of diagnosing migraine in children may explain this finding. Our study also had a relatively small number of subjects.

In the study conducted by Lacroix-Boudhrioua *et al*., 5 mm was accepted as lower limit for true pineal cysts. The incidence of pineal cysts was found to be 10-11% in children. Cysts of 2-5 mm in diameter were regarded as cystic transformation of the pineal gland.[7] In our study, we divided the pineal abnormalities similarly into cystic

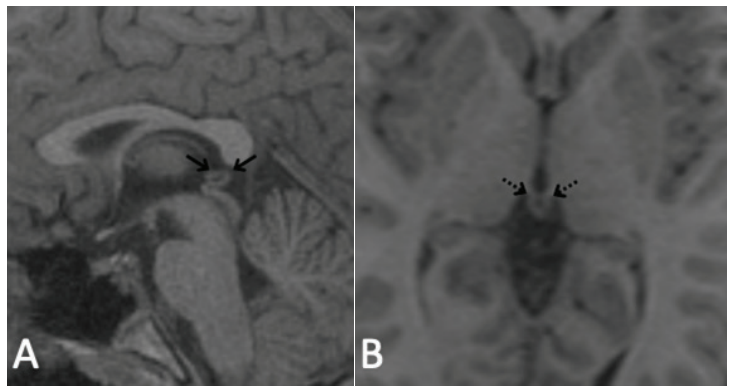

Figure 2. On MRI, a pineal cystic transformation consistent with true pineal cyst which appears hypointense (A) in T1-weighted sagittal sequences and (B) in T1-weighted axial sequences.

transformation and true cysts, and investigated the relationship between headache and each group. We noted that there was not a significant relationship between cystic transformations and headaches unlike the association between true pineal cysts and headaches. These results indicate that the hypothesis suggesting pineal cystic lesions may impair melatonin release from the pineal gland could only be asserted by considering cyst size.

There are studies showing reduced melatonin levels in patients with migraine and cluster headache.[3-5] In addition, disruption of the circadian release of melatonin has also been thought to be causally related to headaches.[8,9] However, we have not measured melatonin levels in our patients, and this is one of the limitations of this study.

In conclusion, headache is one of the most common neurological problems in children and it constitutes a substantial portion of presenting symptoms in a neurology outpatient clinic. The knowledge of clinicians that pineal cysts may play a role in headache development, may be of therapeutic relevance. Further studies on this subject can clarify headache etiology and enable a more targeted approach to treatment.

REFERENCES

1. Erlich SS, Apuzzo ML. The pineal gland: anatomy, physiology, and clinical significance. *J Neurosurg* 1985; 63: 321-41.
2. Altun A, Ugur-Altun B. Melatonin:Therapeutic and clinical utilization. *Int J Clin Pract* 2007; 61: 835-45.
3. Leone M, Lucini V, D'Amico D, et al. Abnormal 24-hour urinary excretory pattern of 6-sulphatoxymelatonin in both phases of cluster headache. *Cephalalgia* 1998; 18: 664-7.
4. Waldenlind E, Gustafsson SA, Ekbom K, Wetterberg L. Circadian secretion of cortisol and melatonin in cluster headache during active cluster periods and remission. *J Neurol Neurosurg Psychiatry* 1987; 50: 207-13.
5. Claustrat B, Loisy C, Brun J, Beorchia S, Arnaud JL, Chazot G. Nocturnal plasma melatonin levels in migraine: A preliminary report. *Headache* 1989; 29: 242-5.
6. Alehan FK. Value of neuroimaging in the evaluation of neurologically normal children with recurrent headache. *J Child Neurol* 2002; 17: 807-9.
7. Lacroix-Boudhrioua V, Linglart A, Ancel PY, Falip C, Bougneres PF, Adamsbaum C. Pineal cysts in children. *Insights Imaging* 2011; 2: 671-8.
8. Seifert CL, Woeller A, Valet M, Zimmer C, Berthele A, Tölle T, Sprenger T. Headaches and pineal cyst: a case-control study. *Headache* 2008; 48: 448-52.
9. Peres MF, Zukerman E, Porto PP, Brandt RA. Headaches and pineal cyst: A (more than) coincidental relationship? *Headache* 2004; 44: 929-30.
10. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders. 3rd Edition. *Cephalalgia* 2018; 38: 1-211.
11. Peres MF, Masruha MR, Zukerman E, Moreira-Filho CA, Cavalheiro EA. Potential therapeutic use of melatonin in migraine and other headache disorders. *Expert Opin Investig Drugs* 2006; 15: 367-75.
12. Barrett T, Kent S, Voudouris N. Does melatonin modulate beta-endorphin, corticosterone, and pain threshold? *Life Sci* 2000; 66: 467-76.
13. Gelfand AA, Peter J Goadsby PJ. The role of melatonin in the treatment of primary headache disorders. *Headache* 2016; 56: 1257-66.