



Neuroimaging Findings in Patients with Idiopathic Intracranial Hypertension after Treatment

İdiyopatik İntrakraniyal Hipertansiyon Olgularında Tedavi Sonrası Nörogörüntüleme Bulguları

© Eylem Özaydın Göksu¹, © Şennur Delibaş Katı¹, © Ayşe Eda Parlak²

¹University of Health Sciences Turkey, Antalya Training and Research Hospital, Clinic of Neurology, Antalya, Turkey

²University of Health Sciences Turkey, Antalya Training and Research Hospital, Clinic of Radiology, Antalya, Turkey

Abstract

Objective: Few reports have investigated the reversal of neuroimaging findings of idiopathic intracranial hypertension (IIH). Our study aimed to show to what extent these findings are reversible after treatment.

Materials and Methods: Eight patients with magnetic resonance imaging (MRI) findings who were followed-up in the University of Health Sciences Turkey, Antalya Training and Research Hospital Headache Outpatient Clinic and diagnosed as having IIH between 2017 and 2019 were included in the study. Demographic characteristics of the patients, body mass indexes (BMI), duration of treatment, the timing of MRI taken after treatment, and MRI before and after treatment were recorded.

The sellar configurations were measured on midsagittal T1 images and the height of the midsagittal pituitary gland was measured on T1 or T2 sagittal images. Optic nerve (ON) thickness was measured from T2 axial sections in brain MRI. The Globus configuration was evaluated using diffusion-weighted imaging (DWI) for ON hyperintensity using axial FLAIR images. ON tortuosity was evaluated in T2 images of horizontal sections.

Results: The mean age was 36 [minimum (min): 22, maximum (max): 45] years, the average BMI was 31.8±2.8. All patients were women. Post-treatment MRI was performed after an average of 5.5 (min: 3, max: 10) months later. After the treatment, a partial sella image was detected in one patient with empty sella, and empty sella was observed in one patient with partial sella. The mid sagittal pituitary gland height decreased after treatment in all patients except one. ON thickness improved for both eyes (right eye p=0.041, left eye p=0.012). The Globus configuration before and after treatment was the same in all patients. The ON tortuosity improved in one patient, and became clear in one patient. The ON hyperintensity observed in DWI persisted in all patients.

Conclusion: Despite the small sample size, this study showed that many of these MRI findings are somewhat reversible after treatment.

Keywords: Idiopathic intracranial hypertension, pseudotumor cerebri, neuroimaging findings

Öz

Amaç: İdiyopatik intrakraniyal hipertansiyonunun (İİH) nörogörüntüleme bulgularının geri dönüşümünü araştıran az sayıda çalışma vardır. Çalışmamız, bu bulguların tedavi sonrasında ne derece geri dönüşlü olduğunu göstermeyi amaçlamıştır.

Gereç ve Yöntem: Sağlık Bilimleri Üniversitesi, Antalya Eğitim ve Araştırma Hastanesi Baş Ağrısı Polikliniği'nde takipli, 2017-2019 yılları arasından İİH tanısı konmuş ve manyetik rezonans görüntüleme (MRG) bulguları olan 8 hasta çalışmaya dahil edildi. Hastaların demografik özellikleri, vücut kitle indeksleri (VKİ), tedavi süresi, tedaviden ne kadar sonra MRG çekildiği, tedavi öncesi ve sonrası MRG'leri kayıt edildi.

Sellar konfigürasyonlar midsagittal T1 görüntülerde ve midsagittal hipofiz bezinin yüksekliği T1 veya T2 sagittal görüntülerde ölçüldü. Optik sinir (OS) kalınlığı beyin MRG'de T2 aksiyel kesitlerden ölçüldü. Globus konfigürasyonu, aksiyal FLAIR görüntüleri kullanılarak ve OS hiperintensitesi diffüzyon ağırlıklı görüntüleme (DAG) ile değerlendirildi. OS tortiozitesi horizontal kesitlerin T2 görüntülerinde değerlendirildi.

Bulgular: Ortalama yaş 36 [minimum (min): 22, maksimum (maks): 45] ve ortalama VKİ 31,8±2,8 idi. Tüm hastalar kadındı. Tedavi sonrası MRG ortalama 5,5 ay sonra çekildi (min: 3, maks:10 ay sonra). Boş sellası olan 1 hastada tedavi sonrası parsiyel sella görüntüsü tespit edilirken parsiyel sellası olan 1 hastada

Address for Correspondence/Yazışma Adresi: Eylem Özaydın Göksu MD, University of Health Sciences Turkey, Antalya Training and Research Hospital, Clinic of Neurology, Antalya, Turkey

Phone: +90 505 469 17 58 E-mail: eylemozaydin@hotmail.com ORCID: orcid.org/0000-0001-8851-3094

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tedavi sonrası boş sella gözlemlendi. Midsagittal hipofiz bezi yüksekliği 1 hasta hariç tüm hastalarda tedavi sonrası azalmıştı. OS kalınlığı her iki göz için düzelme gösterdi (sağ göz p=0,041, sol göz p=0,012). Tüm hastalarda globus konfigürasyonu tedavi öncesi ve sonrası aynı idi. OS tortiozitesi açısından 1 hastada düzelme gözlenirken 1 hastada belirginleşme gözlemlendi. Tüm hastalarda DAG'de gözlenen OS hiperintensitesi devam etmekteydi.

Sonuç: Hasta sayımız az olsa da, çalışmamız bu MRG bulgularının birçoğunun tedaviden sonra bir dereceye kadar geri dönüşümlü olduğunu göstermiştir.

Anahtar Kelimeler: İdiyopatik intrakraniyal hipertansiyon, psödötümör serebri, nörogörüntüleme bulguları

Introduction

Idiopathic intracranial hypertension (IIH), which is also called benign intracranial hypertension or pseudotumor cerebri, is characterized by high intracranial pressure occurring without any identifiable causal factor. The exact cause is still unclear. IIH often affects young, obese women of childbearing age. The incidence in overweight young adult women is 15-19 cases per 100,000 people in the United States. Its incidence has tended to increase with increasing obesity in the world because IIH is associated with obesity (1,2,3,4,5). The clinical syndrome was initially established with the Dandy criteria. It has undergone various modifications to include imaging findings such as computed tomography and magnetic resonance imaging (MRI) and is now defined in the Headache Classification of the International Headache Association (6,7). The most common symptoms of IIH include headache (94%), transient blurred vision (68%), pulse-related tinnitus (58%), photopsia (54%), and retrobulbar pain (44%) (8). Diagnosis includes neuroimaging techniques to exclude secondary causes of high intracranial pressure and to show increased intracranial pressure. In these patients, the diagnosis may be largely dependent on MRI. Reported MRI findings that may aid the diagnosis of IIH include empty sella, posterior globe flattening, optic nerve (ON) tortuosity, ON sheath distension, and transverse sinus stenosis (9,10).

Although the neuroimaging findings showing IIH are well established, few reports have investigated the reversibility of these features. Our study aimed to show how reversible such MRI findings were after treatment.

Materials and Methods

Eight patients who were followed up in the University of Health Sciences Turkey, Antalya Training and Research Hospital Headache Outpatient Clinic, diagnosed as having IIH according to modified Dandy criteria between 2017 and 2019, had MRI findings before and after treatment, and whose clinical treatment was discontinued due to improvement, were included in the study. Approval was obtained from the Ethics Committee of University of Health Sciences Turkey, Antalya Training and Research Hospital (date: 2.3.2020, decision no: 4/12). Informed consent was obtained from all patients. Demographic characteristics of patients, pre- and post-treatment MRIs, body mass index (BMI), cerebrospinal fluid (CSF) opening pressure, duration of treatment, and time of MRI performed after treatment were recorded. Routine brain MRI, pituitary MRI, and orbital MRI were evaluated comprehensively by a single experienced neuroradiologist.

Sellar configuration, one of the MRI findings, was evaluated on midsagittal T1 images and classified as normal, partially empty sella, and empty sella (Figure 1). The height of the midsagittal pituitary gland was measured on T1 or T2 sagittal images (Figure 2). ON thickness was measured on T2 axial sections in brain MRI.

Globus configuration was classified as normal, flattened sclera, and prominent ON head protrusion, using the axial FLAIR images. ON hyperintensity was evaluated using diffusion-weighted imaging (DWI). ON tortuosity were evaluated on T2 images, horizontally (Figure 3).

Statistical Analysis

Statistical analysis was performed using the SPSS version 23 software. The normal distribution of the variables was examined using visual (histogram and probability graphics) and analytical methods (Kolmogorov-Smirnov). Descriptive analyses are given using the median and interquartile for variables that were not

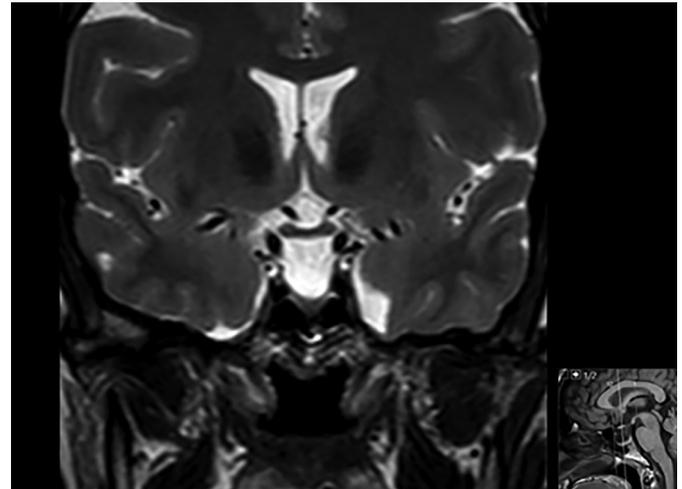


Figure 1. Empty sella

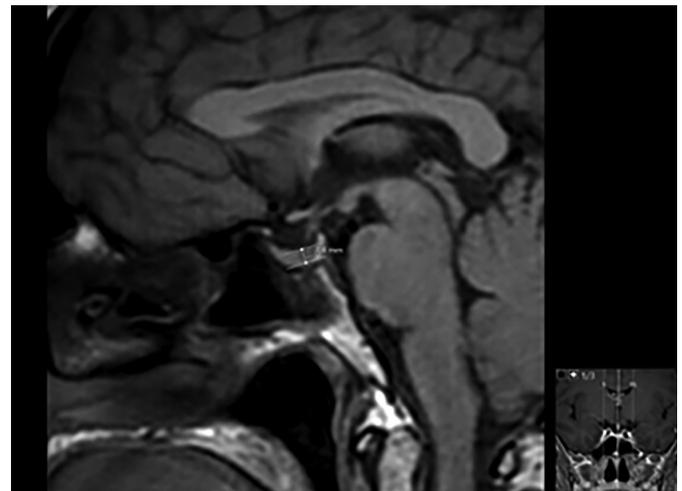


Figure 2. Measurement of pituitary gland height

normally distributed. Variables were compared using the Wilcoxon test because they did not show normal distribution, and $p < 0.05$ was considered statistically significant.

Results

The average age of the eight patients included in the study was 36 [(minimum (min): 22, maximum (max): 45] years and all patients were female. All of the patients, with a mean BMI of $31.8 \pm 2.8 \text{ kg/m}^2$ were overweight. The treatment period was 17.5 months on average, the dose range of acetazolamide used was 750-1,500 mg, and the mean time to perform MRI after treatment was 5.5 (min: 3, max: 10) months later. Before treatment, the sellar configuration was normal in four patients, partial empty sella in three patients, and empty sella in one patient. Partial empty

sella was detected after treatment in the patient who had empty sella before, and empty sella was observed after treatment in a patient who had partial empty sella before. Midsagittal pituitary gland height decreased after treatment in all patients except one ($p=0.16$). ON thickness improved after treatment in both eyes (4.5 ± 0.94 before treatment and 3.5 ± 0.93 after treatment for the right eye, $p=0.041$), and 5 ± 0.58 before treatment and 3.6 ± 0.67 after treatment for the left eye, $p=0.012$).

In terms of globus configuration, pre-treatment and post-treatment MRI characteristics of all patients were the same. ON tortuosity improved in one patient after treatment and worsened in one patient after treatment. No change was observed in other patients. Hyperintensity in DWI-weighted imaging was observed in all patients before treatment and persisted after treatment. The MRI findings of the patients are shown in Table 1.

In subsequent follow-ups, it was found that symptoms recurred in three of the patients after 3, 4, and 12 months of the treatment. The patients could not be evaluated in terms of previous MRI findings because they did not undergo repeat MRIs.

Discussion

In our study, in patients with IIH whose drug treatment was discontinued because of the improvement of clinical symptoms and papillary edema, ON thickness significantly reduced. Although an improvement was observed in the height of the midsagittal pituitary gland, it was not statistically significant.

Although empty sella is the oldest and most frequently reported neuroimaging finding in patients with IIH, it is a non-specific finding, and it has been hypothesized that cumulative CSF pressure causes sellar restructuring starting from the subclinical stages of IIH (11,12). In a study conducted by Chang et al. (13) in 2016, similar to our study, although they showed a possible

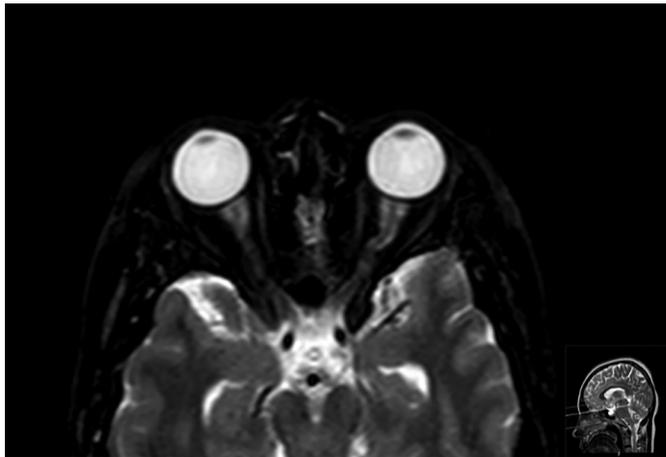


Figure 3. Optic nerve tortuosity

Table 1. Magnetic resonance imaging findings													
Patients	Age	Optic nerve tortuosity				Optic nerve thickness (mm)				Sellar configuration		Midsagittal pituitary gland height (mm)	
		BT L eye	AT R eye	BT L eye	AT L eye	BT R eye	AT R eye	BT L eye	AT L eye	BT	AT	BT	AT
1. SC	36	-	-	+	+	4.5	3.5	5.0	3.6	Empty sella	Partial empty sella	1	1.5
2. EK	42	+	-	+	+	5.4	5.6	5.1	4.6	Normal	Normal	2.8	2.9
3. SE	36	-	-	-	-	4.6	4.3	4.3	4.1	Normal	Normal	4.8	5.2
4. SA	22	-	-	-	+	4.3	4.3	4.9	4.7	Normal	Normal	3.0	3.1
5. SÇ	45	-	-	+	+	4.5	3.5	5.0	3.6	Partial empty sella	Partial empty sella	2.8	3.0
6. FG	38	-	-	+	+	3.5	3.3	4.2	3.6	Normal	Normal	3.3	4.6
7. SS	32	+	-	+	-	4.2	3.1	5.0	3.2	Partial empty sella	Partial empty sella	2.0	2.3
8. MD	31	-	-	+	+	6.4	2.5	6.2	2.7	Partial empty sella	Empty sella	2.5	1.0

BT: Before treatment, AT: After treatment, L: Left, R: Right

improvement tendency in the sellar configuration, no statistical significance was found. In our study, an improvement was observed in one patient and worsening was observed in one patient, no change was detected in the others.

Hoffmann et al. (14) accepted the cut-off value of the pituitary height of patients with IIH as 4.80 mm (sensitivity 88.0%, specificity 69.57%, accuracy 82.0%) and found that it was significantly reduced in the patient group compared with controls. Ranganathan et al. (15) found that the area and height of the pituitary gland increased in patients with IIH after treatment, and based on this, they suggested that the pituitary gland was not compressed, but rather deformed, and that filling of the suprasellar cistern created an empty sella. In the study conducted by Batur Caglayan et al. (16) in 2019, the height of the pituitary gland in patients before and after treatment was found to be significantly lower than in healthy controls, but even though an improvement was observed after months of treatment, they still found it lower than in the control group. In our study, midsagittal pituitary gland height increased in all patients except one after treatment, but there was no statistically significant difference.

The normal convexity of the posterior sphere reflects the balance between intracranial and intraocular pressure (16,17). Previous studies reported that this MRI finding was highly specific but not sensitive to IIH. Nevertheless, Agid et al. (18,19) found that flattening of the sclera was the only sign that definitively reflected IIH. In another study designed as a before and after treatment study, the high specificity of the globus configuration was confirmed and also it was shown that it improved after treatment (16). In our study, similar to the study of Chang et al. (13), no change was observed in the patients in terms of the globus configuration before and after treatment. This might be due to the low number of patients and the absence of orbital MRI in all our patients.

The ON sheath is relatively flexible, so it responds to changes as expansion in the presence of increased pressure. The diameter of the ON sheath decreased in cerebral hypovolemia, but it increased in patients with IIH. Increased cerebral pressure and ON sheath diameter were found to be strongly associated with IIH in adults (20). Increase in ON sheath thickness is among the most common MRI findings in IIH (21). In previous studies, it was shown that the mean ON sheath diameter decreased after IIH treatment, but remained higher than in healthy controls (13,16). Although we could not measure the ON sheath diameter clearly in our study because not all patients had orbital MRIs before and after treatment, ON thickness measurement performed on brain MRIs increased before treatment in all our patients, and it decreased significantly after treatment in both eyes.

ON hyperintensity assessed by DWI-weighted imaging is a reliable and highly specific marker of papilledema (22). However, Salvay et al. (23) found no relationship between lower-grade papilledema and ON hyperintensity. In our study, ON hyperintensity in DWI-weighted imaging, which was detected in all patients, persisted after treatment in all patients.

Twisting of the ON observed in the sagittal and axial planes is defined as the tortuosity of ON. Horizontal or vertical bending is associated with stretching of the ON sheath between the proximal and distal fixation points. Although the sensitivity of this MRI finding is not high, it has been reported that horizontal tortuosity is more specific to IIH than vertical tortuosity (17,24,25). In the

study of Batur Caglayan et al. (16), the frequency of horizontal tortuosity was found to be significantly higher in the pre-treatment IIH group compared with the control group; however, no difference was found between the post-treatment IIH group and control group. This finding suggested that horizontal tortuosity was an indicator of IIH in the pre-treatment group, but it was not a valuable follow-up indicator. In our study, although ON tortuosity improved in one patient after treatment and became apparent in one patient after treatment, no change was observed in the other patients.

Study Limitations

Not all patients had orbital MRI and MR venography in this retrospectively designed study, which is a limitation of the study.

Conclusion

Despite the small sample size, this study showed that MRI findings, especially midsagittal pituitary gland height and ON sheath thickness measurements, were to some extent reversible after treatment. The limited reversal of MRI findings in post-treatment patients with IIH may be due to possible bone erosion and loss of flexibility of anatomic structures over time. To detect changes in neuroimaging findings before and after treatment, prospective studies with larger sample sizes are needed.

Ethics

Ethics Committee Approval: Ethics Committee of University of Health Sciences Turkey, Antalya Training and Research Hospital (date: 2.3.2020, decision no: 4/12).

Informed Consent: Informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.Ö.G., Design: E.Ö.G., A.E.P., Data Collection or Processing: E.Ö.G., Ş.D.K., A.E.P., Analysis or Interpretation: E.Ö.G., Ş.D.K., A.E.P., Literature Search: E.Ö.G., Ş.D.K., Writing: E.Ö.G.

Conflict of Interest: The authors have not declared any conflict of interest related to this article.

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