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Evaluation of cerebrospinal fluid opening pressure and protein levels in relation to clinical profile and recovery in idiopathic intracranial hypertension

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ABSTRACT

Aims: Idiopathic intracranial hypertension (IIH) is an increase in CSF pressure without any other primary cause such as hydrocephalus, mass lesion, or meningeal abnormality. Evaluation of the severity of the disease and management of the treatment in patients are important for clinicians, and different parameters such as blood biomarkers and cerebrospinal fluid (CSF) opening pressure or protein levels are investigated. This study aimed to review the cases with IIH and evaluate the relationship between CSF opening pressure and protein levels obtained at the first presentation and the patient's clinical findings.

Methods: The data of patients diagnosed with IIH between 2012 and 2024 were retrospectively reviewed in the hospital electronic database, and demographic, clinical findings, neuroimaging results, and CSF analysis results were documented. The association between CSF opening pressure and protein levels obtained at the first presentation and the patient's clinical profile was analyzed. SPSS version 25 program was used in the statistical analysis of the data. p<0.05 was found to be statistically significant.

Results: Among 56 cases, 47 patients (83.9%) were female. The median age was 35 years. Visual impairment was the most common symptom (n=42, 75.0%). The mean of the CSF opening pressure was 332.68 mm H_2O , and patients had protein levels with a median of 27.05 mg/dl. Median CSF protein levels were found to be statistically significantly higher in patients presenting with decreased vision compared to those without (p=0.031). The number of patients with severe papilledema and decreased visual acuity was found to be significantly higher in the high CSF pressure group (p=0.041, p=0.042). Also, the number of patients with recurrent symptoms during the follow-up period was found to be significantly higher in high-pressure group (p=0.045).

Conclusion: In this retrospective study, clinical, laboratory, and radiological profiles of IIH patients were examined. Elevated CSF opening pressure in patients was found to be associated with visual impairment, increased symptom recurrence during follow-up, and severe papilledema; however, no association was observed with overall clinical recovery. CSF protein level was found to be associated only with improvement in visual acuity during follow-up. These findings underscore the need for multicenter studies to be conducted on this subject with a larger patient population to define the parameters and associations with the clinical course and prognosis.

Keywords: Idiopathic intracranial hypertension, headache, cerebrospinal fluid, protein, opening pressure

INTRODUCTION

Idiopathic intracranial hypertension (IIH), which was previously named benign intracranial hypertension or pseudotumor cerebral syndrome, is a disorder characterized by isolated increased intracranial pressure without any other primary cause. ¹⁻³ Therefore, other primary causes of increased intracranial pressure, such as intracranial mass, cerebral venous thrombosis, or obstructive hydrocephalus,

must be ruled out in patients with IIH.³ Patients can have favorable outcomes with early diagnosis and management but permanent visual loss can be seen in patients, especially with anemia, obesity, high-grade papilledema, or rapid onset of disease and patients with severe symptoms can need invasive procedures.^{1,2} Evaluating the severity of the disease and managing the treatment in patients is important



for clinicians as the prevalence of the disease increases worldwide.¹ However, differences in characteristics of the patients at presentation can vary between patients and make it hard to predict prognosis or plan the treatment and follow-up strategies.¹ Therefore, considering different parameters such as blood biomarkers, cerebrospinal fluid (CSF) opening pressure, or protein levels, is investigating.

There are only a few studies evaluating the associations between these parameters and symptoms or signs in patients with IIH. The aim of this study was to review the cases investigated in the neurology department with a diagnosis of IIH and evaluate the relationship between clinical symptoms and the profile of patients with CSF opening pressure and protein levels.

METHODS

The study was conducted with the permission of the Ethics Committee of Başkent University Faculty of Medicine and Health Sciences (Date: 04.06.2025, Decision No: KA25/218). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients evaluated with IIH in the neurology department in Başkent University Hospital between 2012 and 2024 were retrospectively investigated. The diagnosis of IIH was made according to the modified Dandy criteria (Table 1).⁴ Patients who have cerebral venous thrombosis, intracranial mass, central nervous system inflammatory diseases, other diseases including optic nerve, or other primary causes that can cause increased intracranial pressure were excluded. Patients with results of CSF and imaging evaluated in other centers were not included in the study. Patients with inadequate information about the diagnosis or incomplete imaging or laboratory test results were also excluded.

Table 1. Modified Dandy criteria

- 1. Awake and alert patients
- 2. Symptoms and signs of increased intracranial pressure
- 3. Absence of focal signs on neurologic examination (6^{th} and 7^{th} cranial nerve palsies are permitted)
- ${\it 4. Normal\ diagnostic\ studies\ (neuroimaging\ and\ CSF\ analysis)\ except\ evidence\ for\ increased\ intracranial\ pressure}$
- 5.No other etiology for increased intracranial pressure identified

CSF: Cerebrospinal fluid

Baseline demographic data of the patients, including patients' sex, age at onset, and body-mass index (BMI), were recorded. Past medical history, presence of endocrine diseases, migraine, polycystic ovarian syndrome, and drugs that are used, such as levothyroxine, tetracycline, steroids, or vitamin A derivatives, were listed. Duration and characteristics of the symptoms, clinical presentation of the disease at onset, and clinical examination findings were retrospectively evaluated, and papilledema grade, severity, visual acuity, and visual field test results were recorded. Papilledema was classified according to the Frisén Scale,⁵ and papilledema grade ≥2 was determined as severe papilledema.

Brain magnetic resonance (MR) images and cerebral MR venography images of patients were examined. Baseline hematological and biochemical blood test results were

recorded. All patients underwent lumbar puncture (LP). CSF opening pressure which was measured during LP in lateral decubitis position with a manometer was recorded. CSF protein concentrations were measured using a standardized turbidimetric method, which is routinely employed in this center. The analysis was performed with an automated biochemistry analyzer (Abbott Alinity c-Series) and compatible reagent kits were used. All measurements were conducted in accordance with the laboratory's internal quality control protocols. The laboratory reference range for CSF protein was 15-45 mg/dl.

In this study, patients were further divided into two subgroups according to CSF opening pressure. A data-driven approach was adopted, using the median CSF opening pressure value of 340 mm $\rm H_2O$ within this population as the cut-off point. Accordingly, patients with CSF opening pressures $\leq\!340$ mm $\rm H_2O$ were classified as low-pressure group, while those with pressures above $>\!340$ mm $\rm H_2O$ were classified as the high-pressure group.

Medical and surgical treatment procedures were reviewed. Dosage and types of medical treatments were listed. The duration of follow-up period and advancements, and course of the disease during the follow-up period were investigated.

Outcome during the follow-up period with treatment modalities was reviewed and divided into four groups: "total regression", "partial regression", "unchanged", and "progressed" according to the course of headache, visual field defects, papilledema or visual acuity. For the visual outcome, the worst eye of the patients was chosen.

Statistical Analysis

The data analyses were performed using SPSS (Version 25.0). Numerical data with normal distribution were presented as mean±standard deviation, while data with skewed distribution were reported as median (interquartile range (IQR)). Categorical variables were presented as numbers and percentage values. For the comparison of categorical data, Pearson's Chi-square test and Fisher's exact test were performed. The Mann-Whitney U, Kruskal-Wallis, and independent samples t-test were used for the comparison of numerical data. p values <0.05 were considered statistically significant.

RESULTS

After exclusion criteria, data of 56 patients were analyzed. The majority of patients were female (n=47, 83.9%), and patients had a median age of 35 (IQR: 15) years. Nineteen patients (33.9%) had increased BMI (overweight or obese), and 6 patients (10.7%) had thyroid dysfunction and were using levothyroxine. Only 1 patient (1.8%) was using oral contraceptive drugs. No patient was using tetracycline, steroids, or vitamin A derivatives. One patient was pregnant at the time of diagnosis, and one patient was in the postpartum period. Median duration of the symptoms was 2 (IQR: 4.50) months in patients, and visual impairment was the most common symptom in patients (n=42, 75.0%). Headache was observed in 36 patients (64.3%) at admission. Demographic data of the patients and symptoms at admission were listed in Table 2.

| Table 2. Demographic and clinical data of the pa | tients |
|---|-----------------------------------|
| | n=56 |
| Age, years, median (IQR) | 35 (15) |
| Female gender, n (%) | 47 (83.9%) |
| Comorbid diseases, n (%) Thyroid dysfunction Hypertension Diabetes mellitus | 6 (10.7%) 5 (8.9%) 3 (5.4%) |
| Migraine history, n (%) | 4 (7.1%) |
| Patients with increased BMI, n (%) | 19 (33.9%) |
| Symptoms of the patients | |
| Headache, n (%) | 36 (64.3%) |
| Visual impairment, n (%) | 42 (75.0%) |
| Tinnitus, n (%) | 12 (21.4%) |
| Diplopia, n (%) | 4 (7.1%) |
| Nausea, n (%) | 8 (14.3%) |
| Dizziness, n (%) | 3 (5.4%) |
| Duration of symptoms, months, median (IQR) | 2 (4.50) |
| Features of headache, n(%) | |
| Unilateral | 13 (23.2%) |
| Bilateral | 23 (41.1%) |
| Throbbing | 16 (28.6%) |
| Pressing or tightening Daily headache | 20 (35.7%) 25 (44.6%) |
| IQR: Interquartile range, n: Number, BMI: Body-mass index | |

Papilledema was the most common examination finding and was found in 96.4% of the patients, mostly as bilateral. Nineteen patients had severe papilledema. Thirty-three patients (58.9%) had visual field defects. Signs and types of ocular examination findings of the patients were shown in Table 3.

| Table 3. Frequency of ocular findings in patients with IIH | | | |
|--|------------|--|--|
| | n=56 | | |
| Decreased visual acuity, n (%) | 13 (23.2%) | | |
| Papilledema, n (%) | | | |
| Bilateral symmetrical | 35 (62.5%) | | |
| Bilateral asymmetrical | 15 (26.8%) | | |
| Unilateral | 4 (7.1%) | | |
| Friesen scale, n (%) | | | |
| Grade 0 | 2 (3.6%) | | |
| Grade 1 | 35(62.5%) | | |
| Grade 2 | 11 (19.6%) | | |
| Grade 3 | 6(10.7%) | | |
| Grade 4 | 1(1.8%) | | |
| Grade 5 | 1(1.8%) | | |
| Visual field defect, n (%) | 33 (58.9%) | | |
| Central scotoma | 20 (35.7%) | | |
| Constriction of peripheral fields | 10 (17.9%) | | |
| Arcuate field defect | 3 (5.4%) | | |
| Abducens nerve palsy, (%) | 2 (3.6%) | | |
| IIH: Idiopathic intracranial hypertension | | | |

All patients had cranial MR imaging, and 42 patients (75.0%) had cerebral MR venography. The major cranial MR imaging finding was perioptic subarachnoid space distension (POSD) with or without optic nerve tortuosity. According to the MR

imaging findings: fifteen patients (26.8%) had POSD with or without optic nerve tortuosity, 14 patients (25.0%) had transverse sinus stenosis (TSS), 6 patients (10.7%) had POSD and partial empty sella sign (PES), 4 patients (7.1%) had TSS and POSD, and 1 patient (1.8%) had PES.

All patients underwent the LP procedure. The mean of the CSF opening pressure was 332.68 $\rm mmH_2O$ and patients had protein levels with a median of 27.05 (16.03) $\rm mg/dl$. CSF cell counts were within normal limits, and CSF culture results were negative in all patients.

All patients were given medical treatment. Acetazolamide and topiramate were the most common options for medical treatment, either used alone or as multiple therapy. Thirty-seven patients (66.1%) were given acetazolamide as a monotherapy, 2 patients (3.6%) were given only topiramate, and 17 patients (30.4 %) were using both. The dose of diazomide was changing between 250 -1500 mg/day (median: 750 mg/day (IQR: 375)) in patients and topiramate was used in a range of 25-200 mg/day (median: 100 mg/day (IQR: 13)). Invasive procedures were suggested to 5 patients. Two patients had undergone ventriculoperitoneal shunt surgery, and one patient had optic nerve fenestration.

The median of the duration for the follow-up period was 9 months (IQR: 32). During the follow up period, 19 patients had repetitive LP. The median of the CSF pressure of the second LP was 250 mmH₂O (IQR: 90). During the followup no change was observed in the papilledema of 9 patients. While progression was observed in the papilledema findings of 3 patients (5.4%), total regression was observed in 17 patients (30.4%), and partial regression was observed in 25 patients (44.6%), respectively. When the change in headaches of the patients was evaluated during the follow-up period, partial improvement was observed in 21 patients (37.5%), total improvement was observed in 14 patients (25%), while no change was observed in the frequency or type of pain in 1 patient (1.8%). Improvement in visual acuity was observed at a lower rate during follow-up. While the decrease in visual acuity was completely resolved in only 3 patients (5.4%), partial improvement was observed in 2 patients (3.6%). No change was detected in visual acuity in 6 patients (10.7%). Progression and a decrease in visual acuity levels were observed during follow-up in 2 patients (3.6%).

The median CSF protein values were found to be significantly higher in men than in women (p=0.004). There was no significant difference in CSF protein levels with comorbid conditions, migraine history, or increased BMI. When the symptoms were evaluated, median CSF protein levels were only found to be statistically significantly higher in patients presenting with decreased vision compared to those without (p=0.031). No significant difference was observed between the groups in terms of decreased visual acuity, visual field defect, papilledema, or severity of papilledema in examination findings. No significant difference was observed between the groups in terms of median CSF protein values between treatment options or recurrence of complaints under treatment. When the clinical findings of the patients were evaluated during the follow-up period, no significant difference was observed in patients with headache and papilledema change, while CSF protein median

values were found to be significantly higher in patients with complete visual acuity recovery compared to those with no or partial recovery (p=0.022). Also in correlation analyses, no correlation was observed between CSF protein levels and age, duration of symptoms, and number of days with pain in patients with headache.

The CSF pressure was investigated in two groups as: the highpressure group (>340 mmH₂O) and low-pressure group (≤340 mmH₂O). No difference was observed between the groups in terms of gender, age, and comorbid conditions. Only the number of patients presenting with visual impairment was found to be significantly higher in the high-pressure group (p=0.044). No difference was observed between the groups in terms of other symptoms at admission. In the examination findings, the number of patients with a decrease in visual acuity was found to be statistically significantly higher in the high-pressure group (p=0.042). No significant relationship was found between the presence of visual field defect, type of visual field defect, or the type of papilledema, but the number of patients with severe papilledema was found to be significantly higher in the high-pressure group (p=0.041). No difference was observed between the groups in cranial MRI findings or treatment options. The number of patients who underwent repeated LP and the number of patients who were recommended to have invasive procedures were found to be similar between the groups. The number of patients whose papilledema or headache improved during the follow-up period was higher in the first group, although the difference was not found to be statistically significant. Also, the number of patients with recurrent symptoms during the follow-up period was found to be significantly higher in high-pressure group (p=0.045) (Table 4).

Table 4. Comparison of patient characteristics and outcomes in low vs. high CSF opening pressure groups

| Cor opening pressure groups | | | |
|---|-------------|-------------|---------|
| | <340 (n=31) | >340 (n=25) | p value |
| Age, years, median (IQR) | 32(14) | 37(20) | 0.282 |
| Female, n (%) | 27 (87.1%) | 20 (80.0%) | 0.472 |
| Headache, n (%) | 19 (61.3%) | 17 (68.0%) | 0.602 |
| Visual impairment, n (%) | 20 (64.5%) | 22 (88%) | 0.044 |
| Decreased visual acuity, n (%) | 4 (12.9%) | 9 (36.0%) | 0.042 |
| Visual field defect, n (%) | 17 (54.8%) | 16(64.0%) | 0.488 |
| Bilateral papilledema, n (%) | 23 (74.2%) | 12 (48.0%) | 0.073 |
| Severe papilledema, n (%) | 7 (23.3%) | 12 (50.0%) | 0.041 |
| Regression of papilledema, n (%) | 26 (86.7%) | 16 (66.7%) | 0.079 |
| Total relief of headache, n (%) | 9 (47.4%) | 5 (29.4%) | 0.352 |
| Recurrence of symptoms, n (%) | 5 (16.1%) | 10 (40.0%) | 0.045 |
| CSF: Cerebrospinal fluid. IOR: Interquartile ra | ange | | |

DISCUSSION

IIH is a rare disease with unknown etiology, and the disease is important for clinicians, as delayed access to care, diagnosis, and management can cause severe disability with permanent visual impairment and chronic headache. Therefore, correct diagnosis and evaluation of the patients and early management are essential in patients.

The recognition of the disorder has increased in recent years.⁷ Both the increased recognition and increasing prevalence

of obesity lead to an increase in the prevalence of IIH worldwide.⁶ The incidence of IIH varies between regions across the world, with 0.5-2 per 100.000 people in the general population.⁷ Western countries usually have higher incidence than Asian countries.⁷ The disease is generally seen in young adults and is rare in patients with an age of >50 years.³ Similarly, in this study, only 12.5% of the patients were older than 50 years. Most of the patients were found to be female, and the median age was found to be 35 years in this study, in accordance with the literature data from both Turkey and other countries.^{6,8-10}

The pathogenesis of IIH remains poorly understood, and different mechanisms for the disease have been proposed.^{3,11} One of the mechanisms is blockage of CSF absorption at arachnoid villi, which is caused by cerebral venous hypertension secondary to venous sinus stenosis.³ The hyperemic hydrocephalus hypothesis, which is characterized by cerebral blood flow fluctuations, is another theory.¹¹ In addition, hormones and adipose tissue were suggested to play a role as a result of the increased incidence of disease in obese women.³ The pathogenesis was also suggested to differ according to age or gender.⁸ Since obesity is less common in Turkish and Asian populations compared to patients in Western countries.⁸

Thyroid dysfunction was the most common comorbid condition in this study. Similarly, Keskin et al.⁸ reported that diabetes or thyroidopathy were the most frequent comorbid diseases (18.6%) in IIH patients in a study from Turkiye. However, Tian et al.⁷ found anemia as the most common comorbid condition in patients.

Transient visual obscuration, visual impairment, or double vision are the visual symptoms that can be seen in IIH patients. Blurred vision or visual impairment was observed as the most common symptom of the patients in this study. In different studies approximately half of the patients were reported to have visual impairment, 2,10 however, in this study the symptom was detected more commonly, and 75% of the patients were observed to be admitted to the hospital with visual symptoms.

Headache is the second most common symptom in IIH in this study, with 64.3%. In the IIH Treatment trial, it was reported that 84% of the patients had headaches, 12 and in a study from Turkiye, Keskin et al.8 reported that 78% of the patients had headache. Nausea and vomiting can accompany headache.3 Generally, pain is aggravated with positions that increase intracranial pressure and increases in severity in the morning, however, different headache features can also be seen in IIH patients.^{2,3} Most patients have bilateral headaches, although patients with unilateral headaches were also observed in this study (23.2%) which is consistent with other studies reported previously.¹³ The frequency of the days with headache can vary between patients, but in this study, 44.6% of the patients were found to have daily headaches. However, in two different studies, it was more commonly reported as 75% and 78.95% of the patients. 10,13

Pulsatile tinnitus is another common symptom of IIH and is observed in approximately 52-60% of the patients.³ Both unilateral and bilateral tinnitus can be seen.³ In this

study, 21.4% of the patients were found to have tinnitus, and in another study %8.5 of the patients were reported.⁸ The frequency of occurrence can be different between studies since the patients do not report spontaneously or underestimate the symptom in mild cases.

The most common and important sign of IIH is papilledema.^{3,14} Mostly it is bilateral symmetric, although rare cases with unilateral papilledema can be seen.^{3,10,14} Only four patients were observed to have unilateral papilledema in this study. Also, in some cases, papilledema might not be observed, and this is suggested to be as a result of anatomical divisions of the subarachnoid space and prevention of the CSF pressure from reaching the retrolaminar part of the optic nerve.³ In a study by Cho et al.² fundus examinations were found normal in 37.3% of the patients, and Sharma et al.¹⁰ reported 5.74% of the patients had no papilledema. The severity of papilledema can be changed in patients. In this study most of the patients had grade 1 papilledema according to the Frisén Scale. However, in other studies, papilledema grade ≥2 was more commonly detected.^{10,14}

Empty sella sign, posterior globe flattening, POSD with or without optic nerve tortuosity, and TSS are different MR imaging signs that are seen in IIH patients. The presence of at least three signs could be sensitive for IIH, but the absence of MR imaging signs does not rule out IIH, and 71.4% of the patients were observed to have MR changes in this study. Also, Bsteh et al. found that at least one MRI sign is present in 78.6% of the patients. No significant association was found between MRI features and symptoms at initial presentation or examination findings in this study, similar to literature data. Is

The mean opening CSF pressure was calculated as 332.68 mmH₂O in this study. There was no significant difference between male and female patients in terms of CSF opening pressure, consistent with other studies.8 The data about CSF opening pressure and clinical evaluation or outcomes of patients with IIH are limited and vary between studies. Kattah et al. 16 reported a mild correlation between baseline CSF pressure and papilledema grade. Opening CSF pressure was not found to be associated with headache frequency, severity of headache, visual acuity, or presence of tinnitus. In this study severity of papilledema was found associated with CSF opening pressure similar to data reported previously. 10,16 Also, CSF opening pressure was found to be associated with decreased visual acuity in examinations of the patients. Only visual impairment was found significantly associated with increased opening CSF pressure. Similarly, Sharma et al.¹⁰ also found an association between CSF opening pressure and visual impairment in literature data. Moreover, no other association was observed between CSF pressure and the presence and frequency of headache or other symptoms at admission in this study. In a different study comparing lower (200-250 mm) and higher (>250 mm) CSF opening pressure, patients with higher levels were observed to have more bilateral headaches, TVO, and horizontal diplopia with abducens palsy.¹⁷ However, BMI, headache frequency, and other clinical features were not different.¹⁷ Data about CSF opening pressure and MR imaging features are controversial. Sharma et al.10 reported a significant correlation between CSF opening pressure and MR imaging signs except empty

sella but in this study CSF opening pressure was not found to be associated with MR imaging signs or the number of MR imaging features, which is consistent with a study by Bsteh et al.¹⁵

In a study 64% of the patients were found to be stable or improved during the follow-up period. Delay in treatment and generalized constriction in the visual field were observed to be associated with poor prognosis. Cho et al. reported that 61.5% of the patients who had 3-6 months of follow-up showed remission or improvement in over 50% of the headache status.

Age was not found associated with the visual prognosis;⁹ similarly, in this study, no association was found between outcomes and age or gender. Although CSF total protein and increased opening pressure were independently associated with Humphrey visual field mean deviation in the worst eye on follow-up in a study, no significant association was observed between visual field defects or course of the defect and CSF protein or opening pressure in this study.¹⁸

For the follow-up period, CSF protein median values were only found to be significantly associated with complete visual acuity recovery compared to those with no or partial recovery. Also for the outcomes, no relationship was shown between regression of papilledema or headache and opening CSF pressure or CSF protein levels. Similarly, Takkar et al. 14 reported opening CSF pressure showed significant association with visual outcomes, but after adjusting for the vision at admission, no association was observed.

There are different data in the literature regarding the association between CSF protein levels and CSF opening pressure values. In a study it was found that CSF total protein and CSF opening pressure have a negative linear association regardless of age, sex, and BMI in both pediatric and adult patients but no significant correlation was found in this study.

Limitations

This study has several limitations that should be acknowledged. First, due to its retrospective design, the study relied on previously recorded data. Additionally, the study was conducted in a single center and sample size was relatively small that could potentially limit the generalizability of the findings to large populations. Also, the criteria for diagnosis of IIH have been revised over years, and cut-off values for opening CSF pressure can change between different classifications. This can cause discrepancies between studies. Moreover the variability in follow-up durations among patients may have influenced the assessment of clinical outcomes. Future prospective studies with larger cohorts and standardized follow-up periods are needed to elucidate the relationships between CSF characteristics and clinical features in IIH.

CONCLUSION

In this study, IIH patients who applied to a tertiary health institution were evaluated retrospectively and their clinical, laboratory, and radiological profiles were examined. Data on CSF pressure and clinical findings in the literature

show differences between regions. CSF opening pressure in patients was found to be associated with decreased vision clinically and increased frequency of symptom recurrence during follow-up and severe papilledema as a finding. While no relationship was observed between clinical recovery rates and opening CSF pressure, CSF protein level was found to be associated only with improvement in visual acuity during follow-up. The lack of a significant relationship between clinical recovery parameters and other examination parameters emphasizes the importance of individualized treatment and follow-up strategies. In order for CSF protein and opening pressure levels in IIH patients to be a guiding parameter for the clinician regarding the clinical course during the follow-up process, multicenter studies should be conducted on this subject with a larger patient population.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of the Ethics Committee of Başkent University Faculty of Medicine and Health Sciences (Date: 04.06.2025, Decision No: KA25/218).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The author has no conflicts of interest to declare.

Financial Disclosure

The author declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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