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Pituitary MRI Findings of Pediatric Patients with Growth-Hormone Deficiency and Biologically Inactive Growth-Hormone

Büyüme Hormonu Eksikliği ve Biyoinaktif Büyüme Hormonu Tanılı Çocuk Hastalarda Hipofiz MRI Bulguları

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ABSTRACT

Background: Growth hormone (GH)-related short stature is a rare but important problem during pediatric follow-up. The determination of pituitary anatomy via pituitary magnetic resonance imaging (MRI) is an important tool in the diagnosis of GH disorders and acquired pituitary diseases. Pituitary dimensions in children vary according to age, and clear limits are not known. In this study, we investigated the relationship between pituitary MRI findings and GH in patients with GH deficiency (GHD) and bioinactive GH.

Materials and Methods: A total of 306 pediatric patients with GHD and bioinactive GH were analyzed. Pituitary MRI was performed in all patients, and the diagnoses were divided into 3 groups: severe GHD, mild-moderate GHD, and bioinactive GH.

Results: According to pituitary size, 63.4% of patients had a normal pituitary MRI scan, 27.5% were hypoplastic, and 0.3% were hyperplastic. Pituitary height and volume were lower in patients with severe GHD than in the mild-moderate group ($p<0.05$). The most effective measurement of pituitary volume was the height of the pituitary gland. A significant correlation was observed between the height standard deviation score and pituitary height ($r=0.824$, $p<0.001$). The relationship between peak GH level and pathologic MRI was analyzed. Cut-off 14.5 area under the curve (AUC) (95%): 0.59 (0.52-0.67), sensitivity 97%, specificity 95% ($p=0.007$).

Conclusion: There was a strong correlation between GH and pituitary size measured by MRI for the estimation of pituitary volume. Pituitary height measurement alone is an important supportive finding for the diagnosis of isolated GHD in children with slow growth.

Keywords: Bioinactive growth hormone, growth hormone deficiency, magnetic resonance imaging

ÖZ

Amaç: Büyüme hormonu (BH) ilişkili boy kısalığı nadir olmakla beraber çocuk izleminde önemli bir sorundur. Hipofiz manyetik rezonans görüntülemesi (MRG) ile hipofiz anatomisinin belirlenmesi, BH bozuklukları ve edinsel hipofiz hastalıklarının tanısında önemli bir araçtır. Çocuklarda hipofiz boyutları yaşa göre değişkenlik göstermektedir ve net sınırları bilinmemektedir. Bu çalışmada, BH eksikliği (BHE) ve biyoinaktif BH tanılı hastalarda hipofiz MRG bulguları ile BH arasında ilişki olup olmadığı araştırıldı.

Gereç ve Yöntemler: BHE ve biyoinaktif BH tanılı 306 çocuk hasta incelendi. Tüm hastalara hipofiz MRG çekildi ve tanılar 3 gruba ayrıldı: Ağır BHE, hafif-orta BHE ve biyoinaktif BH.

Bulgular: Hipofiz büyüklüğüne göre hastaların %63,4'ünün hipofiz MRG taraması normal, %27,5'inin hipoplastik ve %0,3'ünün hiperplastikti. Ağır BHE olan hastalarda hipofiz yüksekliği ve hacmi, hafif-orta gruba göre daha düşüktü ($p<0,05$). Hipofiz hacmini

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ÖZ

tahmin etmede en etkili ölçümün, hipofiz boyu olduğu görüldü. Boy standard sapma skoru ile hipofiz yüksekliği arasında anlamlı bir korelasyon gözlendi (r=0,824, p<0,001). Pik BH düzeyi ile patolojik MRG ilişkisi incelendi. Cut-off 14,5 eğrinin altındaki alan (%95): 0,59 (0,52-0,67), sensitivite %97, spesifite %95 saptandı (p=0,007).

Sonuç: BH ve hipofiz hacminin tahmini için MRG ile ölçülen hipofiz boyu arasında güçlü bir ilişki vardır. Yavaş büyüyen çocuk hastalarda tek başına hipofiz yükseklik ölçümü izole BHE tanısı koymada önemli destekleyici bulgudur.

Anahtar Kelimeler: Biyoinaktif büyüme hormonu, büyüme hormonu eksikliği, manyetik rezonans görüntüleme

Introduction

Short stature is a common problem in the follow-up of children. A height below 2 standard deviations score (SDS) is defined as a short stature. Most variants are variants of normal. Growth hormone (GH)-related causes are rare (1). GH deficiency (GHD) is an important endocrine cause with a frequency of 1/3500-10000 (2). Unfortunately, there is no gold standard for the diagnosis of GHD. In addition to compatible auxologic findings, the issues of low growth rate, delayed bone age, and low insulin-like growth factor-1 (IGF-1) levels have continued to be discussed. Stimulated GH levels support the diagnosis. Drugs commonly used for stimulation include L-dopa, clonidine, glucagon, and insulin. For stimulated GH, values >10 ng/mL are considered normal (3). However, it is also believed that a reference value should be determined according to the stimulating agent used (4). Most cases of GH deficiency are idiopathic, and only 20% are due to organic causes, including congenital central nervous system abnormalities, tumors, and other acquired pathological conditions involving the pituitary-hypothalamic axis (5). Pituitary imaging is normal in 20-70% of patients with isolated GHD (IGHD) (6,7,8,9).

In a short child with a low serum IGF-1 level, if the stimulated GH level is normal, a decrease in GH effect is considered. The GH-IGF axis may be impaired. If classical GH insensitivity (Laron syndrome) is not observed, then Kowarski syndrome (bioinactive GH) is considered (10).

Neuroimaging, particularly magnetic resonance imaging (MRI) of the pituitary anatomy, is an important tool in GH disorders, congenital malformations, and acquired pituitary disease (11). Imaging of the pituitary gland anatomy is also important for monitoring multiple pituitary hormone deficiencies (MPHD). In the presence of an abnormal pituitary gland, other pituitary hormones are likely to be affected (12). Normal values are presented for each part of the pituitary gland in adults (11). However, in children, values vary with age, and no clear cutoff values are known (12). For the pituitary stalk, values 1 mm are considered thin (13).

In our study, we analyzed the MRI findings of the pituitary gland in pediatric patients with GHD and bioinactive GH who were initiated on GH therapy.

Material and Methods

Our study was a retrospective, single-center analysis of 306 pediatric patients diagnosed with GHD and bioinactive GH between May 2021 and February 2023. We obtained ethical approval from the Scientific Research Ethics Committee of Health Sciences University Türkiye, Başakşehir Çam and Sakura City Hospital (approval number: 2023-35, date: 25.01.2023) and recorded the patients' sociodemographic information. Patients with familial and structural short stature and syndromic patients were excluded. The body weight and height of all participants were measured, and the child metrics program was used to calculate the height and body weight SDSs based on published normal values (14,15). All patients underwent puberty staging using Tanner staging (16,17).

The study evaluated each patient using a GH provocation test, in which GH levels were measured at 30-60-90-120-150 minutes after the administration of L-dopa, clonidine, or glucagon. Patients who exhibited a peak GH value below 5 ng/mL were considered to have severe GHD, whereas those with a peak GH value of 5-9,99 ng/mL were considered to have moderate-mild GHD (18,19,20). Patients who had normal GH provocation test results but low IGF-1 levels (⩽2 standard deviation) were subjected to an IGF-1 generation test. Synthetic somatropin GH was administered subcutaneously for four consecutive days at a dose of 0.1 mg/kg/day. A significant increase in IGF-1 levels above 15 ng/mL compared to baseline was used to diagnose bioinactive GH (4,21). No molecular studies were conducted on the patients.

A total of 306 individuals underwent MRI using a 3T MRI machine (Ingenia; Philips Medical Systems; Best, Netherlands). The hypophysis MRI protocol was standard and encompassed sagittal T2-weighted (T2-W) turbo spin echo (TSE) [repetition time (TR): 3000 milliseconds (ms), echo time (TE): 80 ms, slice thickness (st): 2.5 mm, field of

view (FOV): 150 mm]. The brain imaging scans used included sagittal T1-weighted (T1-W) TSE (TR: 557 ms, TE: 7 ms, st: 2.5 mm, FOV: 150 mm, matrix: 216x156 mm, gap: 1), coronal T2-W TSE (TR: 3000 ms, TE: 80 ms, st: 2.5 mm, FOV: 130 mm, matrix: 188x163 mm, gap: 1), and coronal T1-W TSE (TR: 557 ms, TE: 7.5 ms, st: 2.5 mm, FOV: 120 mm, matrix: 200x146 mm, gap: 1). Post-contrast imaging included coronal dynamic T1-W TSE (TR: 12 ms, TE: 884 ms, st: 2.5 mm, FOV: 125 mm, matrix: 156x110 mm, gap: 1), and sagittal T1-W TSE (TR: 507 ms, TE: 7 ms, FOV: 150 mm, matrix size: 232x179, interslice gap: 1 mm), and coronal T1-W TSE (TR: 557 ms, TE: 7.5 ms, st: 2.5 mm, FOV: 120 mm, matrix size: 200x159, interslice gap: 1 mm) MRI images were retrospectively evaluated by a 9-year experienced pediatric radiologist.

The anterior pituitary dimensions were measured in three dimensions: height (mm), anteroposterior diameter (mm), and mediolateral width (mm). The height of the pituitary gland was measured at the midline in the coronal T2-W. The anteroposterior diameter of the adenohypophysis was measured in the sagittal T1-W sequence to avoid neurohypophysis measurement. The mediolateral width of the pituitary gland was measured in the delayed post-contrast coronal T1-W sequence to avoid measuring the cavernous sinuses (Figure 1).

The anterior pituitary height, coronal width, and volume were measured according to sex and age. Patients were classified as "normal pituitary", "hypoplasic pituitary", or "hyperplasic pituitary" using a reference range from a previous study (22). Pituitary volume was calculated according to the ellipsoid formula (pituitary height x pituitary anteroposterior diameter x pituitary width/2) using the values of pituitary height, pituitary anteroposterior diameter, and pituitary width (23). Anatomical anomalies, including pars intermedia cyst, Rathke's cleft cyst, and ectopic neurohypophysis, were recorded.

Statistical Analysis

The study data were analyzed using SPSS 24.0 (SPSS Inc., Chicago, Illinois). Descriptive statistics are presented as mean ± SD and frequency (%). The Kolmogorov-Smirnov test was used to assess the normal distribution of continuous variables between groups. Parameters that fit the normal distribution were compared using Student's t-test, and those that did not fit the normal distribution were compared using the Mann-Whitney U test. Categorical variables were compared between groups using the chi-squared test. Pearson's correlation analysis was performed according to the distribution of variables. p-value <0.05 was considered statistically significant. The diagnostic sensitivity of pituitary measurements was determined using receiver operating characteristic (ROC) curve. The cut-off point for the curve was set at the highest sensitivity and specificity. From there, the data were recoded and positive predictive values and negative predictive values were calculated. Confidence intervals for these values were obtained using the syntax in SPSS software. This study analyzed the correlations between pituitary height, anteroposterior diameter, width, and volume and puberty.

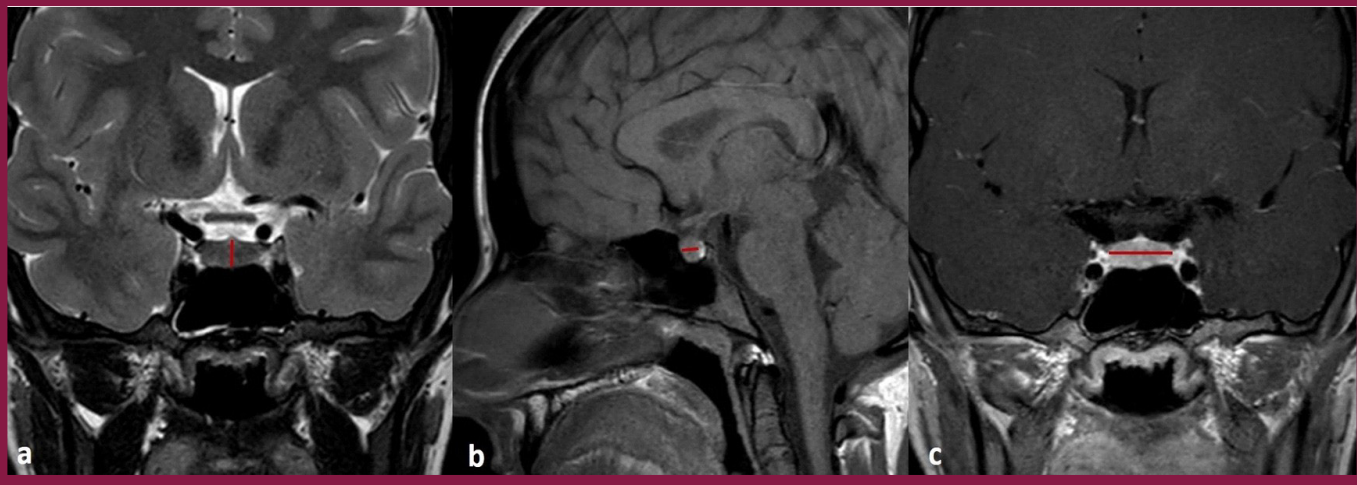

Figure 1. In a 14-year-old female patient with mild-moderate GHD, coronal T2-W (a), sagittal T1-W (b), and post-contrast coronal T1-W (c) sequences revealed a pituitary gland of normal size, with a measured height of 6.1 mm (a), anteroposterior diameter of 5.5 mm (b), and mediolateral diameter of 14.6 mm (c). Pituitary gland measurements were performed as follows: height was measured from the midline in the coronal T2-W sequence, anteroposterior diameter of the anterior pituitary was measured in the sagittal T1-W sequence, and mediolateral width was measured in the post-contrast coronal T1-W sequence (red lines)

GHD: Growth hormone deficiency, T2-W: T2-weighted, T1-W: T1-weighted

Results

One hundred and sixty-five (53.9%) male and 141 (46.1%) female patients were analyzed. The mean age was 9.96±3.25 years [minimum (min.)=0.7 years, maximum (max.)=16.9 years]. The mean height was 123.73±17.44 cm (min.=57 cm, max.=159 cm), height SDS value was -2.47±0.79 (min.=-6.8, max.=-0.43), body weight was 27.66±12.22 kg (min.=6.1 kg, max.=79 kg), body weight SDS value was -1.71±1.1 (min.=-5.9, max.=2.2), body mass index SDS value was -0.42±1.1 (min.=-3.9, max.=3.4). When puberty status was analyzed, 200 patients (65.4%) were prepubertal and 106 patients (34.6%) were pubertal. Fourteen patients (4.6%) had hypothyroidism (4 patients had central hypothyroidism). Three patients had panhypopituitarism and 1 patient had a history of brain gamma-knife treatment due to a congenital malformation.

All patients underwent GH stimulation tests. Those who had a peak GH level below 10 ng/mL during the initial test underwent a second stimulation test. Of the patients, 63.1% (n=193) were diagnosed with mild-moderate GHD and 27.1% (n=83) were diagnosed with severe GHD. Patients with a normal response to either of the two stimulation tests were subjected to an IGF-1 generation test. Nine point eight percent of all patients (n=30) were diagnosed with bioinactive GH by the IGF-1 generation test. GHD and bioinactive GH were diagnosed in 89.7% and 10.3% of the males, respectively. On the other hand, GHD and bioinactive GH were diagnosed in 90.8% and 9.8% of female patients, respectively. Notably, there was no significant difference between the genders in terms of diagnoses (p=0.75).

Pituitary MRI was performed in all patients, and the diagnoses were divided into three groups: severe GHD, mild-moderate GHD, and bioinactive GH. The MRI images were then compared. Based on pituitary size, 63.4% (n=194) of the patients exhibited normal pituitary MRI scans, 27.5% (n=84) were hypoplastic, and 0.3% (n=1) were hyperplastic. The table (Table 1) illustrates pituitary MRI and pathological findings in the examined regions. Thirty-two point seven percent (n=54) of boys and 22% (n=31) of girls had pathological MRI scans. MRI pathology was more prevalent in males than females (p=0.032). Patients with GHD had a higher incidence of pathologic MRI (29%) than those with bioinactive GH (16.7%). However, no significant difference was observed between the groups (p=0,15). The prevalence of pathologic MRI was 36,1% (n=30) in patients with severe GHD and 25.9% in those with mild-moderate GHD (p=0.059). Figure 2 presents an example of a patient's pathology.

There were no significant differences in pituitary volume and height between patients with and without GHD. In patients with severe GHD, pituitary height and volume were lower than those with mild-moderate GHD (p=0.04) (Table 2). Likewise, the width and anteroposterior diameter measurements did not differ significantly between the groups (Table 3). The pituitary volume increased significantly with the progression of puberty (Table 4).

The pituitary volume of individuals with pars intermedia cyst measured 139.85±62.9 mm^3, which was greater than that of other patients (p=0.045). Due to the limited number of patients, it is unclear whether this finding affected GHD or not.

Table 1. MRI findings of all patients

MRI finding	Severe GHD (n=83)	Mild-moderate GHD (n=193)	Bioinactive GH (n=30)	Total number of patients n (%)
Normal	48	125	21	194 (63.4%)
Hypoplasic pituitary	29	50	5	84 (27.5%)
Hyperplasic pituitary	0	1	0	1 (0.3%)
Ectopic neurohypophysis	2	0	0	2 (0.7%)
Arachnoid cyst	0	1	0	1 (0.3%)
Encephalomalacia	0	2	0	2 (0.7%)
Agenesis of the corpus callosum	0	0	1	1 (0.3%)
Microadenoma	0	2	0	2 (0.7%)
Pars intermedia cysts	4	7	2	13 (4.2%)
Rathke's kleft cyst	0	3	1	4 (1.3%)
The pituitary gland central region is thin		1	0	1 (0.3%)
Enlarged sella	0	1	0	1 (0.3%)

MRI: Magnetic resonance imaging, GHD: Growth hormone deficiency, GH: Growth hormone, n: Number of patients

The most effective measurement for estimating pituitary volume was determined to be height (r=0.824, p<0.001). Subsequent correlation analysis indicated that the factors with the greatest impact on volume were height, anteroposterior diameter, and width. When examining pituitary height, volume, and peak responses in the GH stimulation test, we found no correlation between volume and peak GH values (r=0.096, p=0.093). However, peak GH values increased with increasing height (r=0.133, p=0.02).

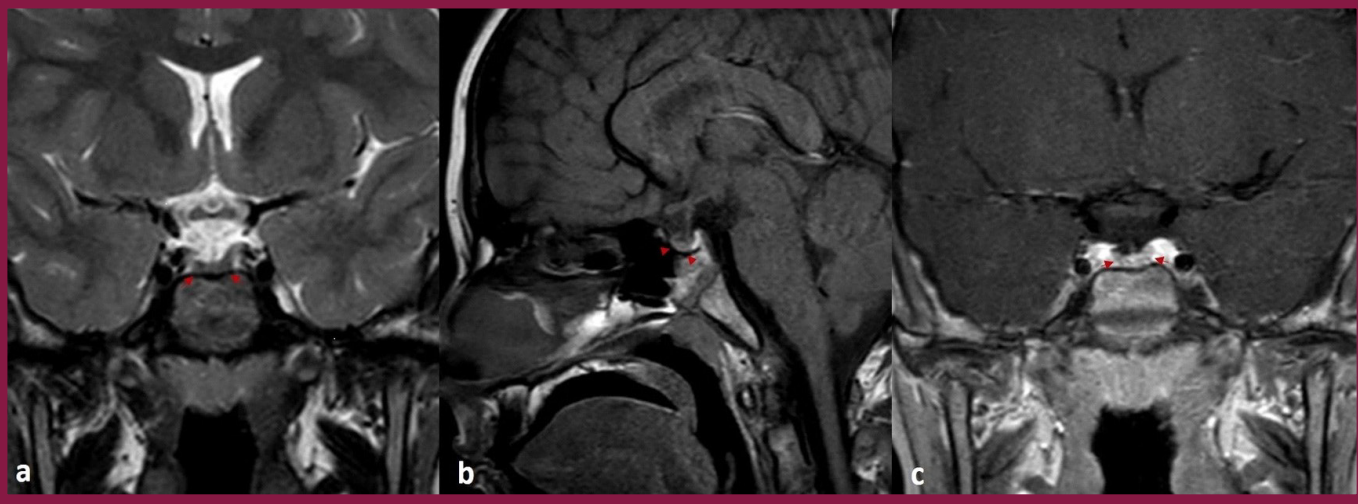

Figure 2. In an 11-year-old male patient with severe GHD, coronal T2-W (a), sagittal T1-W (b), and post-contrast coronal T1-W (c) sequences reveal a hypoplastic pituitary gland that is thinner than the normal gland for the age. The pituitary gland height was 1.8 mm, anteroposterior diameter was 4.7 mm, and mediolateral diameter was 10.8 mm. The pituitary gland, shown between red arrows, was measured in height from coronal T2-W, anteroposterior from sagittal, and width from coronal sequences

GHD: Growth hormone deficiency, T2-W: T2-weighted, T1-W: T1-weighted

Table 2. Relationship between pituitary volume, pituitary height, and diagnosis

Diagnosis	Pituitary volume (mm³)	Pituitary height (mm)	p (95% confidence interval)
GHD (severe and mild to moderate GHD) (n=276)	103.8±64.79	3.48±1.08	0.88 (volume) 0.57 (height)
Bioinactive GH (n=30)	102.42±47.21	3.36±1.26	0.19 (volume) 0.07 (height)
Severe GHD (n=83)	89.04±48.14	3.05±1.12	**0.004 (volume)** **0.004 (height)**
Mild-moderate GHD (n=193)	110.15±69.91	3.5±1.3	0.44 (volume) 0.94 (height)

GHD: Growth hormone deficiency; GH: Growth hormone; n: Number of patients

Table 3. Relationship between pituitary measurement and diagnosis

Diagnosis number of patients (n): SD standard error					
Pituitary height (mm)	Bioinactive GH	30	3.4867	1.08524	0.19814
	GHD	276	3.3678	1.26460	0.07612
Pituitary width (mm)	Bioinactive GH	30	11.4500	1.64940	0.30114
	GHD	276	11.5308	1.94438	0.11704
Pituitary anterior-posterior diameter (mm)	Bioinactive GH	30	5.0300	0.95381	0.17414
	GHD	276	5.1069	1.05905	0.06375
Pituitary volume (mm³)	Bioinactive GH	30	102.42580	47.217026	8.620610
	GHD	276	103.80915	64.791440	3.899986

GHD: Growth hormone deficiency, GH: Growth hormone, n: Number of patients, SD: Standard deviation

A significant correlation was observed between SDS and pituitary height (r=0.096, p=0.012), but no similar correlation was found between other pituitary measurements.

ROC analysis was conducted to examine the association between GHD and pituitary height, with a cut-off value of 3.55% area under the curve (AUC) (95% confidence interval: 0.46, 0.56), sensitivity of 40.6%, and specificity of 40% (p=0.51) (see Figure 3). Additionally, we investigated the relationship between peak GH levels and pathologic MRI using a cutoff of 14.5 AUC (95% confidence interval: 0.59, (0.52-0.67), sensitivity of 97%, and specificity of 95% (p=0.007) (see Figure 4).

Table 4. Relationship between stage of puberty and pituitary volume

Puberty stage	Number of patients	Pituitary volume (mm^3)		p
		Mean	SD	
1	200	83.45	37.18	
2	46	108.75	46.41	0.001
3	34	139.75	101.45	0.003
4	8	154.21	53.48	0.007
5	18	224.69	66.88	0.000

SD: Standard deviation

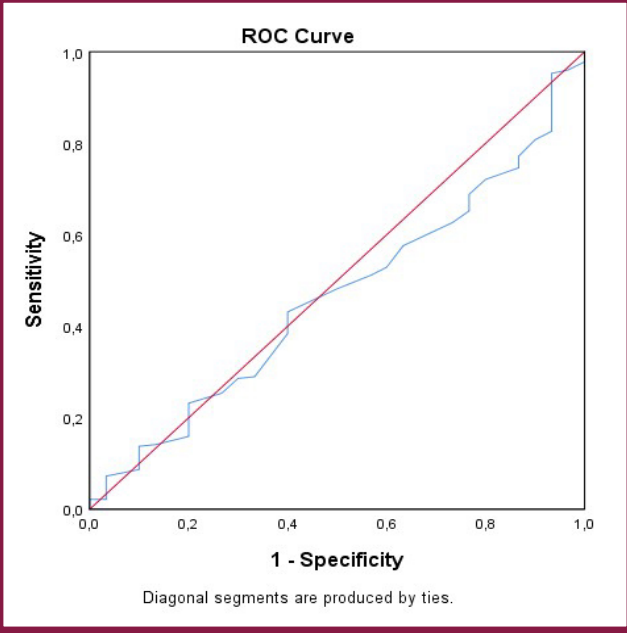

Figure 3. ROC curve analysis of GHD and pituitary height
ROC: Receiver operating characteristic, GHD: Growth hormone deficiency

DISCUSSION

GHD results in short stature during childhood, slow growth rate, and significantly reduced adult height. Diagnosis is based on auxologic data, detailed physical examination, and GH stimulation testing. The decision to perform stimulation testing is based on clinical findings and auxologic analysis. Our study involved the application of stimulation tests and pituitary MRI in all patients. The agents typically used in GH stimulation tests include clonidine, arginine, and glucagon (24). For our study, we used L-dopa, clonidine, and glucagon.

A correlation between peak GH levels obtained via GH stimulation testing and sagittal and coronal pituitary heights in children with GHD has been reported (25). In our study, an increase in pituitary height was observed with increasing peak GH, but there was no effect on volume.

MRI is the optimal method for identifying pituitary abnormalities. The radiologist's expertise is crucial in executing MRI evaluations. T1-W sequences reveal the brightness of the rear pituitary gland, which the radiologist must observe in terms of appearance and location. Our research focused on adenohypophysis. To avoid neurohypophysis measurement, we measured the anteroposterior diameter using sagittal T1-W sequences. In addition, the mediolateral width was measured using post-contrast coronal T1-W images, excluding the cavernous sinuses, which have similar intensity to the pituitary gland

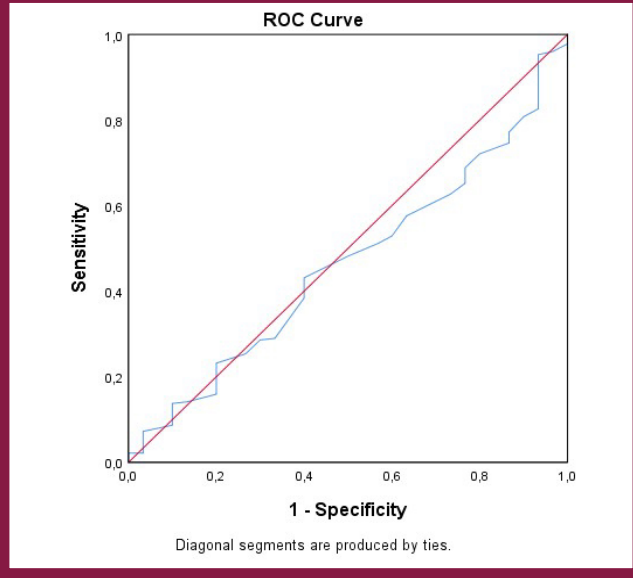

Figure 4. ROC analysis of peak GH and pathological MRI findings
ROC: Receiver operating characteristic, GHD: Growth hormone deficiency, MRI: Magnetic resonance imaging

in T2-W. The height of the pituitary gland was measured at the midline in the coronal T2-W. The width of the pituitary gland was measured in the delayed post-contrast coronal T1-W sequence to avoid measuring the cavernous sinuses.

A meta-analysis found sellar and parasellar abnormalities in 58% of patients with non-acquired GHD. Patients with MPHD were found to have a higher rate of pathology. Furthermore, patients with a peak stimulated GH level of 5 ng/mL had a higher frequency of severe MRI pathology (26). In a separate study, the incidence of abnormal MRI in patients with a peak GH level ⩽5 ng/mL was 36.9%, which was significantly higher than that in the other groups (groups with a peak GH level >5 ng/mL). The incidence of MRI pathology was also high in MPHD (27). In our study, the frequency of MRI pathology in patients with GHD was 29%. However, the rate was higher in patients with severe GHD (36.1%). The frequency of MRI abnormalities was higher in individuals with severe GHD than in the other groups, although not significantly.

Although the use of MRI for the diagnosis of IGDH is not recommended, current guidelines recommend pituitary MRI in all cases of GHD without discrimination. Tillmann et al. (11) reported that MRI is highly specific and predictive in the presence of sessile ectopic neurohypophysis and hypoplastic anterior pituitary in the diagnosis of GHD. Abnormal pituitary anatomy has been demonstrated at a rate of 50% in patients with idiopathic GHD (12). In congenital GHD, abnormal pituitary anatomy and concomitant pituitary hormone deficiency may be observed. Pituitary stalk interruption, thin pituitary stalk, ectopic neurohypophysis, and pituitary hypoplasia are important MRI findings of congenital GHD (28). Sharma et al. (29) reported pituitary hypoplasia as the most important MRI marker of disease severity in children with congenital GHD (66% IGHD, 34% MPHD). The finding that significantly predicted MPHD was pituitary hypoplasia (29).

Because most patients in our study had IGHD, we could not draw a definitive conclusion on this issue. However, 3 patients with MPHD had pituitary hypoplasia. One of these patients had congenital GHD.

A previous study revealed that ectopic neurohypophysis and interrupted pituitary stalk occurred in 48.6% of patients with IGHD and 93.5% of patients with MPHD (30). Another neuroimaging-oriented study showed that pituitary MRI was normal in 67% of patients with IGHD. Since no MPHD cases displayed isolated anterior pituitary hypoplasia, the conclusion reached was that IGHD should be considered in such cases (31). In the present study, 28.6% of patients with GHD exhibited anterior pituitary hypoplasia. Patients with severe GHD had a significantly lower pituitary volume than those in the other groups.

In this study, the average pituitary height of 49 patients with IGHD was significantly lower than that of the control group (70 patients). Additionally, in the same study, pituitary height was observed to be lower during the pre-pubertal period (32). Another study compared 69 pediatric patients with IGHD to those with idiopathic short stature and healthy controls, and the results revealed lower pituitary volume in the GHD group (33). There was no control group in this study, but we evaluated it based on a previous study that established the normal range for pituitary measurements (22). Comparing the severe GHD group with the other groups, we found significantly lower pituitary height and volume. Furthermore, we observed that pituitary volume increased as puberty progressed.

It is uncertain whether pituitary microadenoma contributes to the etiology of GHD. In our study, only 2 patients had microadenomas, a notably lower rate than in previous studies. It is important to consider the experience of the radiologist in such cases.

ROC analysis was performed to compare abnormal MRI findings with peak GH levels, and the results revealed AUCs of 0.614% and 0.728 for IGHD and MPHD, respectively (27). In our study, we found a cut-off value of 14.5 AUC (95%): 0.59 (0.52-0.67), a sensitivity of 97%, and a specificity of 95% for the relationship between peak GH level and pathological MRI. As previously reported in the literature, the frequency of pathology detection increased with decreasing GH levels. However, no relationship was observed between peak GH levels and pituitary height.

Pars intermedia cysts or Rathke cleft cysts are not expected to result in endocrine disorders unless they are exceptionally large and do not require special follow-up (34). Our study found that patients with pars intermedia cysts did not exhibit low pituitary volume. Additionally, 3.9% of patients with GHD had a pars intermedia cyst, although it was unclear whether it contributed to the etiology of GHD given the limited number of patients in our study.

Pituitary imaging is typically normal in patients with bioinactive GH, also known as Kowarski syndrome (35). However, our study found that 5 out of 30 patients with bioinactive GH (16.6%) had pituitary hypoplasia. In one patient, a rathke left cyst was present with a size of 11 mm, while the other pituitary hormones were in the normal range. This unexpected finding requires further support, as it contradicts the existing literature on the subject.

Study Limitations

This study has several limitations, including its retrospective nature, potential selection bias, and limited number of patients. The findings may be generalizable to

some populations, and more extensive prospective studies are needed to confirm these results. In addition, not having a control group is a limitation.

Conclusion

In patients with severe GHD, MRI is more effective in identifying pituitary pathology. Imaging of the pituitary gland is necessary for severe GHD and MPHD. In the diagnosis of a slowly growing child with IGHD, pituitary volume measurement via MRI can be beneficial. The most reliable measure of pituitary volume is the pituitary height. Height measurement alone is the most significant supportive finding for diagnosing GHD. Although current MRI technology has proven helpful in detecting large structural lesions, there is optimism that further improvements in imaging techniques will offer greater benefits to clinical practice.

Ethics

Ethics Committee Approval: This study obtained ethical approval from the Scientific Research Ethics Committee of Health Sciences University Türkiye, Başakşehir Çam and Sakura City Hospital (approval number: 2023-35, date: 25.01.2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.H.A.K., N.G.A., Z.K.S., A.Ö., H.Ö., Concept: E.H.A.K., Design: E.H.A.K., Data Collection or Processing: E.H.A.K., N.G.A., Z.K.S., A.Ö., H.Ö., Analysis or Interpretation: E.H.A.K., M.Ş., Literature Search: E.H.A.K., N.G.A., Z.K.S., A.Ö., H.Ö., M.Ş., Writing: E.H.A.K., N.G.A., Z.K.S., M.Ş.

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