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ORIGINAL RESEARCH

Evaluation of Medical Treatment Results in Patients with Giant Prolactinoma Who Previously Underwent Surgery or Not

Filiz MERCAN SARIDAŞ, Erhan HOCAOĞLU, Müge YAŞAR, Kadircan KARATOPRAK, Özen ÖZ GÜL, Soner CANDER

Bursa Uludağ University Tıp Fakültesi, Department of Endocrinology ve Metabolism, Bursa, Türkiye.

ABSTRACT

In this single-center retrospective study, we aimed to evaluate the results of medical therapy as primary or secondary treatment following surgery and compare follow-up outcomes between the two approaches. Patients were grouped as medical therapy alone (Group M) and surgery plus medical therapy (Group S+M). Patients' demographics, such as age and gender, and age at the diagnosis were recorded. Differences between the pre-and post-treatment tumor size, prolactin (PRL) levels, Knosp grades, tumor response to treatment, improvement in hypofunctions, visual field, and biochemical control were recorded and compared between the two groups. A total of 41 patients diagnosed with giant prolactinomas were included in the study. Hypopituitarism was found in 82.93%, hypogonadism in 80.59%, GH deficiency in 51.22%, ACTH deficiency in 36.59%, and TSH deficiency in 41.46% of the patients. Visual field defects were found by 60.53%. Tumor volume at diagnosis was significantly higher in Group M ($p<0.001$). A mean tumor volume reduction of 75.22% was observed with medical therapy alone, compared to 60.20% achieved with surgical intervention and medical therapy ($p=0.36$). The comparison of PRL levels at the last visit revealed no statistically significant difference between the groups ($p > 0.05$). This study's results demonstrate no statistically significant difference between medical therapy alone and surgery plus medical therapy regarding the reduction of tumor volume and normalization of PRL values in patients with giant prolactinomas. Surgery should be reserved for severe compression conditions, and potentially unnecessary surgical approaches should be avoided.

Keywords: Giant prolactinoma. Tumor volume. Prolactin. Decompression. Medical therapy.

Operasyon Öyküsü Olan ve Olmayan Dev Prolaktinomalı Hastalarda Medikal Tedavi Sonuçlarının Değerlendirilmesi

ÖZET

Bu tek merkezli retrospektif çalışmada, primer tedavi veya cerrahi sonrası sekonder tedavi olarak medikal tedavinin sonuçlarını değerlendirmeyi ve iki yaklaşım arasındaki takip sonuçlarını karşılaştırmayı amaçladık. Hastalar tek başına medikal tedavi (Grup M) ve cerrahi + medikal tedavi (Grup S+M) olarak gruplandırıldı. Hastaların yaş ve cinsiyet gibi demografik özellikleri ve tanı anındaki yaşları kaydedildi. Tedavi öncesi ve sonrası tümör boyutu, prolaktin (PRL) düzeyleri, Knosp dereceleri, tedaviye tümör yanıtı, hipofonksiyonlarda iyileşme, görme alanı ve biyokimyasal kontrol arasındaki farklar kaydedildi ve iki grup arasında karşılaştırıldı.Çalışmaya dev prolaktinoma tanısı konulan toplam 41 hasta dahil edildi. Hastaların %82.93'ünde hipopituitarizm, %80.59'unda hipogonadizm, %51.22'sinde GH eksikliği, %36.59'unda ACTH eksikliği ve %41.46'sında TSH eksikliği saptandı. Görme alanı defekti %60.53 oranında saptanmıştır. Tanı anındaki tümör hacmi Grup M'de anlamlı olarak daha yüksekti ($p<0.001$). Tümör hacmindeki ortalama azalma sadece medikal tedavi ile %75.22 ve cerrahi+medikal tedavi ile %60.20 idi ($p=0.36$). Son vizitte PRL düzeyleri açısından gruplar arasında istatistiksel olarak anlamlı bir fark bulunmadı ($p>0.05$). Bu çalışmanın sonuçları, dev prolaktinomalı hastalarda tümör hacminin küçülmesi ve PRL değerlerinin normalleşmesi açısından tek başına medikal tedavi ile cerrahi+medikal tedavi arasında anlamlı bir fark olmadığını göstermektedir. Cerrahi, ciddi bası durumları için saklanmalı ve potansiyel olarak gereksiz cerrahi yaklaşımlardan kaçınılmalıdır.

Anahtar Kelimeler: Dev prolaktinoma. Tümör hacmi. Prolaktin. Dekompresyon. Medikal tedavi.

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Dr. Filiz MERCAN SARIDAŞ
Bursa Uludağ University Tıp Fakültesi,
Department of Endocrinology ve Metabolism,
Bursa, Türkiye.
Phone: 0224 295 11 40
E-mail: filizmercandr@gmail.com

Authors' ORCID Information:
Filiz MERCAN SARIDAŞ: 0000-0002-3135-9388
Erhan HOCAOĞLU: 0000-0002-6299-9513
Müge YAŞAR: 0000-0002-6545-8640
Kadircan KARATOPRAK: 0000-0001-5205-9539
Özen ÖZ GÜL: 0000-0002-1332-4165
Soner CANDER: 0000-0001-6303-7896

Prolactinomas represent the most frequently occurring hormone-secreting pituitary tumors, comprising around 40% of all pituitary adenomas, with a reported prevalence ranging from 3.5 to 5 per 10,000 individuals[1]. Although classified as World Health Organization Grade I tumors, prolactinomas manifest with significant sequelae due to mass effect and/or increased prolactin (PRL) levels[2,3]. Most prolactinomas are microadenomas with a diameter of less than 10 mm and are typically observed in women. In contrast, macroprolactinomas, defined as adenomas larger than 10 mm in diameter, are more commonly found in men, likely due to delayed diagnosis, and often necessitate more intensive treatment[4]. Prolactinomas larger than 40 mm are classified as giant prolactinomas, which are rare, representing only 0.5-4.4% of all prolactinomas. These giant tumors are more prevalent in men, with a male-to-female ratio of 9:1. The median age at diagnosis is approximately 40 years. These tumors are mostly benign and have similar histological and clinical characteristics to macroprolactinomas, although they rarely include atypical adenomas or develop into PRL-secreting carcinomas[5].

The diagnosis of giant prolactinomas can be complex, as their large size, aggressive behavior, and invasive characteristics may lead to delays in diagnosis, misdiagnosis, or inappropriate treatments[6]. Giant prolactinomas are characterized by prolactin levels exceeding 1,000 mcg/L and are commonly accompanied by clinical manifestations of hyperprolactinemia or symptoms resulting from mass effect. Most patients have hypogonadism due to low testosterone levels and, at least partly, hypopituitarism[7].

Prolactinomas can be treated successfully with medical therapy. Dopamine agonists decrease prolactinoma size by inducing a reduction in cell volume, promoting perivascular fibrosis, and leading to partial necrosis of tumor cells[8]. Dopamine agonists are successfully used in the first-line medical treatment of prolactinomas[9]. Among these, cabergoline, a long-acting D2-selective dopamine agonist, has demonstrated exceptional efficacy in normalizing PRL levels[10]. On the other hand, surgery becomes the appropriate second-line treatment when patients' PRL levels do not turn to normal range or when there is a lack of radiologic shrinkage of the tumor with medical treatment[11]. Some patients may not tolerate the side effects of medical treatment, including headache, cognitive problems, mood changes, insomnia, orthostatic hypotension, and nausea/vomiting are candidates for surgical intervention[3]. However, pharmacological responses are lower in giant prolactinomas compared to micro- and macroprolactinomas, and therefore, surgery is performed more frequently in these patients[12]. Surgical treatment alone is insufficient to achieve normalization of PRL levels in the majority of giant prolactinomas, making long-term medical treatment necessary even after surgery[13]. Studies in the literature regarding giant prolactinoma are mostly in the form of case reports, case series, or lack of comprehensive evaluation. In this single-center retrospective study, we aimed to evaluate the results of medical therapy in giant prolactinoma patients who previously underwent surgery or not.

Material and Methods

Study Design and Patients

Before the beginning, the local ethics committee approved the study protocol. Patient consent was waived because of the retrospective nature of the study. This study followed the ethical principles of the 1964 Declaration of Helsinki (DoH) and its later amendments.

The medical records of 41 patients diagnosed with prolactinoma and monitored in our clinic between 2015 and 2020 were reviewed. Patients with serum prolactin levels higher than 1000 mcg/L at the time of diagnosis and the largest tumor diameter of more than 40 mm were classified as giant prolactinoma and included in the study[1]. Patients who co-secreted adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), and or growth hormone (GH) as identified by pituitary hormone function tests or positive staining in the immunocytochemical evaluation post-surgery were excluded from the final analysis[4]. In addition, patients with missing MRI follow-up information were also excluded from the final analysis.

Patients were grouped as those who underwent surgery plus medical therapy as secondary treatment (Group S+M) and the patients who received medical therapy alone (Group M) as primary treatment. Patients' demographics, such as age and gender, and age at the time of the diagnosis were recorded. Differences between the pre-and post-treatment tumor size, PRL levels, Knosp grades, tumor volume response to treatment, improvement in hypofunctions, visual field, and biochemical control were recorded and compared between the two groups. In addition, side effects associated with the treatment and follow-up visits were also analyzed.

The longest tumor diameter at diagnosis was 51.44 ± 12.66 mm in Group M and 34.71 ± 14.45 mm in Group S+M. The tumor volume at diagnosis was 28.82 (9.10 - 232.96) mL in Group M and 9.36 (0.17 - 76.05) mL in Group S+M.

The assessment of prolactin levels was conducted for Group M before initiating medical therapy and six months following its commencement. For Group

S+M, prolactin levels were evaluated before surgery and six months after the administration of medical therapy post-surgery. Blood samples were collected in yellow-capped tubes before and after treatment, then centrifuged at 3500 rpm for 10 minutes in the biochemistry laboratory. Measurements were performed using the Abbott ARCHITECT I2000SR immunoassay analyzer, employing the chemiluminescent microparticle immunoassay (CMIA) two-step direct ratio-RLU method as the analytical technique.

Treatment Procedures

All patients received medical treatment, which was the initial therapy for 18 patients (43.90%) and a secondary intervention following surgery for 23 patients (56.10%). Cabergoline was the drug of choice, administered at an average weekly dose of 2 mg. In cases demonstrating resistance, the dose was increased to a maximum of 7 mg per week. For patients diagnosed with giant prolactinomas at our center, primary medical treatment is the favored approach unless there are severe or life-threatening compression symptoms. Surgical treatment option is considered in patients unresponsive to medication or those who have experienced serious side effects. Patients who undergo primary surgical intervention are generally those initially referred to the surgical department. In these cases, the primary criterion for opting for surgery is the presence of severe compression symptoms, particularly those that pose a threat to vision.

Data Evaluation

Tumor size was assessed using magnetic resonance imaging (MRI) by measuring three diameters and calculating the volume with the Di Chiro and Nelson formula (height × length × width × π/6), which is based on the geometry of an ellipsoid. This formula incorporates the height (H) and length (L) of the pituitary fossa measured from a lateral skull radiograph, as well as the width (W) of the floor obtained from a posteroanterior projection[14]. The percentage changes in the tumor's longest diameter and volume before and after treatment were subsequently evaluated. The change in tumor size was assessed following a similar protocol using pituitary MRI images obtained six months after the initiation of medical therapy. By previous studies, a reduction of 30% in tumor diameter or 50% in tumor volume was considered significant[15,16].

The extent of invasion of the lesion was evaluated on pre- and post-treatment MRI images, and the degree of invasion was determined based on the modified Knosp Classification suggested by Micko et al.[17]. Neuroradiological evaluation was performed according to this classification and graded according to whether the tumor crossed the medial and lateral tangents of the intra- and supra-cavernous internal carotid arteries (Grade 0 to 4). The changes in the extent of invasion were categorized as increased, unchanged, or improved (18).

The percent changes in PRL levels were determined in the sixth month of the treatment. A reduction >95% of the baseline PRL or returning to normal levels was considered biochemically remission, and a reduction ≥ 30% was considered partly remission and, otherwise, no improvement, and the groups were compared in this respect[13]. The differences between pre-and post-treatment visual fields were grouped as full recovery, partial recovery, no change, and worsening of vision, based on normal, up to a quarter, quarter-to-half, and more than-half vision fields.

Hypopituitarism was determined based on the levels of thyrotropin, gonadotropins, and target hormone levels, the results of dynamic tests for ACTH and GH, and the patients' hormonal therapy. The improvement in hypopituitarism was evaluated six months after the treatment, and the normalization of hormone levels after discontinuation of hormonal therapy. Group S+M and Group M were compared in terms of the changes in the studied parameters between the pre-and post-treatment measurements.

Statistical Analysis

The study data were statistically analyzed using SPSS Statistics for Windows version 23 software (SPSS, Statistical Package for Social Sciences, IBM Corp. Armonk, NY, USA). Normality in numerical variables was tested with the Shapiro-Wilk method. Normally distributed variables (age and longest tumor diameter at diagnosis) were expressed as mean±standard deviation, while non-normally distributed variables (age, PRL levels, tumor volume at diagnosis, Ki67 indices, and follow-up times) were expressed as median (min-max) values. Categorical variables are reported as frequencies (numbers and percentages). Quantitative variables were compared using Student's t-test or the Mann-Whitney U test, while categorical variables were analyzed using the Chi-square test or Fisher's exact test. A p-value of <0.05 was regarded as statistically significant.

Results

A total of 41 patients with giant prolactinoma, 36 (87.80%) males and 5 (12.20%) females with a median age of 43 (min-max: 21-85) years, were included in the study. The mean age at diagnosis was 39.00±12.57 years. The mean longest tumor diameter was 42.44±15.90 mm, and the mean tumor volume was 31.95±43.02 cc. The median follow-up time was 44 (min-max: 6-180) months. The mean pretreatment PRL level was 7054 ± 9684 mcg/L. However, it should be noted that initial PRL measurements were

performed in different health centers and, therefore, showed high variability.

According to the hormonal evaluation, hypopituitarism was found in 34 (82.93%), hypogonadism in 33 (80.59%), GH deficiency in 21 (51.22%), ACTH deficiency in 15 (36.59%), and TSH deficiency in 17 (41.46%). Visual field defects occurred in 23 (60.53) patients, but the evaluation was made in 38 patients. The most common symptom associated with giant prolactinoma was decreased libido in 31 (75.61%), followed by erectile dysfunction in 28 (77.77%, males), headache in 17 (41.46%), menstrual irregularity in 3 (60%, females) and galactorrhea in 3 (7.21%) patients. Demographic and clinical features of all patients included in the study are given in Table I.

Table I. Demographic and clinical characteristics of all patients

Characteristics	
Number of patients	41
Gender M/F	36:5 = 7.2
Age (years)	43 (21-85)
Age at diagnosis (years)	39.00±12.57
Follow-up (months)	44 (6-180)
Longest tumor diameter at diagnosis (mm)	42.44±15.90
Tumor volume at diagnosis (mL)	31.95±43.02
PRL level at diagnosis (mcg/L)	7054 ± 9684
	n (%)
Hypopituitarism	34 (82.93%)
Hypogonadism	33 (80.59%)
GH deficiency	21 (51.22%)
ACTH deficiency	15 (36.59%)
TSH deficiency	17 (41.46%)
Visual field defect	23 (60.53%)
No visual field defects	15 (39.47%)
Menstrual irregularity (females)	3 (60%)
Decreased libido	31 (75.61%)
Erectile dysfunction (males)	28 (77.77%)
Galactorrhea	3 (7.21%)
Headache	17 (41.46%)
Categorical variables are expressed as n (percentage), while continuous variables are reported as the mean (± standard deviation) for data with a normal distribution and as the median (range: minimum–maximum) for data with a non-normal distribution.	

ACTH: Adrenocorticotropic hormone, GH: Growth hormone, TSH: Thyroid-stimulating hormone, PRL: prolactin, F: Female, M: Male.

The baseline values of the variables compared between Group M and Group S+M are presented in Table II. Accordingly, the median age was 41.50 (min-max: 27-77) years in Group M and 46.00 (min-max: 21-85) years in Group S+M. The mean age at the time of diagnosis was 38.50±10.73 years in Group M and 39.39±14.07 years in Group S+M. The median follow-up duration was found to be 29 (min-max: 6-75) months in Group M and 75 (min-max: 15-180) months in Group S+M. There was no statistically significant difference between the two groups in terms of pituitary dysfunction and hormone deficiencies (Table II).

Table II. Baseline values of the examined parameters according to groups

Characteristics	Group M	Group S+M	P value
Number of patients	18	23	
Gender M/F (Male)	17 (94.4%)	19 (82.6%)	0.36
Age (years)	41.5 (27-77)	46.00 (21-85)	0.11
Age at diagnosis (years)	38.5 ± 10.73	39.39 ± (14.07)	0.82
Follow-up (months)	29 (6-75)	75 (15-180)	**0.001**
Longest tumor diameter at diagnosis (mm)	51.44 ± 12.66	34.71 ± 14.45	**<0.001**
Tumor volume at diagnosis (mL)	28.82 (9.10 - 232.96)	9.36 (0.17 - 76.05)	**<0.001**
Pituitary dysfunction	15 (83.33%)	19 (82.61%)	0.95
Hypogonadism	15 (83.33%)	18 (78.26%)	0.68
GH deficiency	8 (44.44%)	13 (56.52%)	0.53
ACTH deficiency	5 (27.78%)	10 (43.48%)	0.34
TSH deficiency	4 (22.22%)	13 (56.52%)	0.05
Visual field defects	11 (61.11%)	12 (52.17%)	0.57
Categorical variables were analyzed using Chi-square or Fisher's exact tests. The Student's t-test was employed to compare the longest tumor diameter and age at diagnosis, while the Mann–Whitney U-test was utilized for comparisons of tumor volume at diagnosis, age, and follow-up duration.			

ACTH: Adrenocorticotropic hormone, GH: Growth hormone, TSH: Thyroid-stimulating hormone, F: Female, M: Male.

Group M and Group S+M were also compared in terms of the changes in the studied parameters between the pre-and post-treatment 6th-month measurements using the change percentages. The mean reduction in tumor volume was 75.22% with medical therapy alone and 60.20% with surgery plus medical therapy, and the difference between the two groups was not statistically significant (p=0.36). The rate of decrease in PRL levels was found to be 93.45% in Group M and 94.38% in Group S+M, and the mean decrease was significantly higher in Group S+M (p=0.04). However, no statistically significant difference was found between the groups at the 6th month measurements that showed the last status of the patients (p=0.927) (Figures 1 and 2). Similarly, no significant differences were found in terms of the 6th-month tumor height, width, and length values (for all, p>0.05).

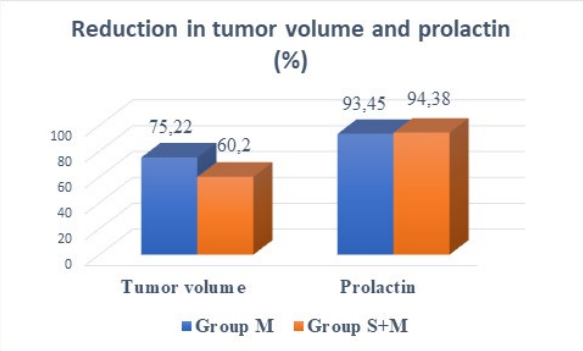

Figure 1:
Percentage change in tumor volume (p=0.36) and prolactin levels (p=0.04) of the groups before and after treatment

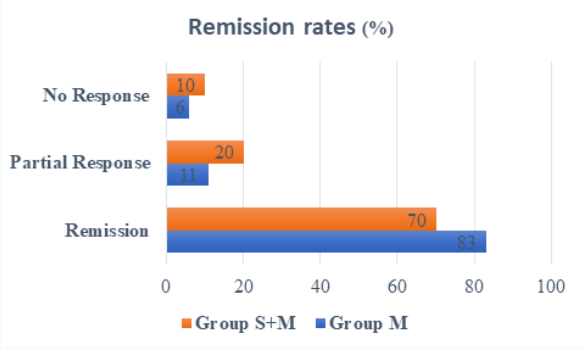

Figure 2:
Remission rates after treatment between the groups

In general, hormonal deficiencies improved at the 6th-month follow-up in both groups in various degrees, but no statistically significant difference was found between the groups in terms of the changes in hormonal deficiency parameters. The improvement in the visual field was higher in Group M compared to Group S+M, but the difference did not reach statistical significance (p=0.13). Changes in hormonal parameters at the 6th month after treatment compared to baseline values are given in Table III according to the groups.

Discussion and Conclusion

Giant prolactinomas are rare, large, and invasive lesions of mostly benign nature. Management of giant prolactinomas poses an important challenge due to their mass effects, high degree of invasiveness, and diffuse neurologic complications. On the other hand, dopamine agonists (DAs) are extremely effective in reducing tumor volume in giant prolactinomas as well as micro- and macroprolactinomas. DAs have been shown to normalize elevated PRL levels effectively, rapidly relieve neurological symptoms, and significantly reduce tumor volume[6]. Compression symptoms are prominent in giant prolactinomas. In the presence of acute severe compression, surgical treatment is performed in these patients[13]. In patients with resistance to DAs, surgical debulking is performed to induce rapid optic decompression and visual impairment[11,19]. However, most patients require medical therapy despite surgical treatment. Surgical results are unsatisfactory and rarely provide a cure due to the location, size, and invasiveness of the tumor[20]. In addition, surgery for giant prolactinomas is associated with high morbidity and mortality rates[6].

In the present study, the results of the patients receiving medical therapy alone due to giant prolactinomas were compared with those receiving surgery plus medical therapy as a secondary line treatment. This is one of the few studies in the literature reporting the effect of surgery on giant

Table III. Changes in the examined parameters at the 6th month after treatment compared to the baseline values for both groups

Response	Group M				Group S + M				p
	A	B	C	D	A	B	C	D	
Visual field defects		6.3%	31.3%	62.5%		22.7%	45.5%	31.8%	0.13
Hypogonadism	5.6%	61.1%	11.1%	22.2%	4.3%	69.6%	17.4%	8.7%	0.64
Pituitary dysfunction									
GH deficiency	5.6%	16.7%	50.0%	27.8%	4.3%	39.1%	39.1%	17.4%	0.47
ACTH deficiency	5.6%	22.2%	66.7%	5.6%	0.0%	39.1%	56.5%	4.3%	0.50
TSH deficiency	0.0%	22.2%	77.8%	0.0%	4.3%	52.2%	39.1%	4.3%	0.08
Hypopituitarism	5.6%	61.1%	11.1%	22.2%	0.0%	78.3%	17.4%	4.3%	0.20

Worsening (A): The occurrence of an increase in visual field defects or a deterioration in pituitary hormonal functions following treatment.
No Response (B): The absence of improvement in visual field defects or pituitary hormonal functions after treatment.
Not Worsening (C): The lack of visual field defects and no deterioration in pituitary hormonal functions observed both before and after treatment.
Improvement (D): The presence of improvement in visual field defects or pituitary hormonal functions after treatment.

ACTH: Adrenocorticotropic hormone, GH: growth hormone, TSH: Thyroid-stimulating hormone

prolactinomas since most publications are in the form of case reports or case series[7,20]. As the main findings of this study, tumor volume significantly decreased at the end of the 6-month treatment both with medical therapy alone and with surgery plus medical therapy, but there was no significant difference between the two treatment modalities.

Giant prolactinoma is a male sex predominant disease with a male-to-female ratio of 9:[14,21]. In the present study, gender distribution was determined as 87.80% male and 12.20% female patients, in line with the literature. The discrepancy between genders has been attributed to the later presentation of male patients due to a longer asymptomatic phase[22]. In addition, the growth potential of these tumors is also greater in males. In our study, higher tumor volume and PRL levels in males compared to females support this opinion. Patients with giant prolactinomas are usually diagnosed around 40 years of age. Iglesias et al. reported the mean age at diagnosis as 40 years, Liang et al. as 40.36 years, Acharya as 36.1 years, Almalki as 38.1 years, and Lisa also reported 38 years in a systematic review of 196 giant prolactinoma cases. In our study, the mean age at the time of diagnosis was found to be 39 years, and this was within the age range reported in the literature[6,22-25].

In giant prolactinoma, men may complain of visual field problems, hypogonadism, erectile dysfunction, weakness, and headaches, while women may present with visual deterioration, headache, menstrual irregularities, and, in the younger group, galactorrhea[7]. According to these findings, in our study, patients in both groups had the above-mentioned symptoms with decreased libido, additionally, at various rates. In the present study, the most common complaint at the time of presentation was decreased libido, followed by visual defect, erectile dysfunction in male patients, headache, menstrual irregularity, and galactorrhea in female patients.

Visual field deterioration due to compression of the optic chiasm or tracts is one of the most common and serious complications of giant prolactinomas. It causes a significant decrease in patients' quality of life (QoL). Decompression can provide the possibility for visual field improvement. Medical therapy with cabergoline has been proven to provide improvement in the visual field within days to weeks. Shimon et al., Corsello et al., and Lv et al. reported visual field recovery as 88.9%, 85.7%, and 83.3%, respectively. In the present study, we found visual improvement in 62.5% of the patients. The lower result in our study might have resulted from the definition of visual improvement among the studies.

Endocrine disorders, including hormonal deficiencies, frequently accompany giant prolactinomas. In the present study, hypogonadism was the most common hormonal deficiency, followed by GH, ACTH, and TSH deficiencies. At the last follow-up visits, hypopituitarism was improved by 12%, hypogonadism by 14.6%, GH deficiency by 41%, ACTH deficiency by 4.9%, and TSH deficiency by 2.4%. However, these rates are measured at 6 months after initiating medical therapy, and further improvements could be seen in the longer term. The above-mentioned studies reported various results on hormonal deficiencies, but an exact comparison does not seem reliable because of several factors, including the number of patients, preferred treatment regimens, and patient grouping.

The two commonly recognized criteria to evaluate the effectiveness of a treatment method for medical or surgical management of giant prolactinomas are tumor volume and PRL levels. Treatment aims at normalization of PRL levels (<1000 mcg/L) and reduction of tumor value. Response of tumor and PRL levels to medical therapy has been reported in a few studies. In a study by Lv et al., PRL concentration decreased by more than 95% and tumor size by 75%[26]. Similarly, in our study, PRL levels decreased by 93.97% and tumor volume by 67.32%. Our findings are consistent with the previously reported values. In this study, the PRL and tumor volume reductions were 93.45% and 75.22% in the medical treatment alone group and 94.38% and 60.2% in the surgery plus medical treatment group, respectively. Although a higher percentage in normalization of PRL levels was achieved with surgery plus medical therapy approach, no significant difference was found between the groups in PRL values measured at the last visit, which reflects remission.

Study Limitations

This study has some limitations. The major limitation of the study is its retrospective design and being conducted in a single center. Therefore, treatment approaches and outcomes of this study can not be generalized. In addition, the duration of follow-up could be longer. However, there are few studies in the literature to compare the outcomes of medical therapy alone and surgery plus medical therapy[26-28]. The remaining few studies have compared the therapeutic approach between giant- and macroprolactinomas[23,29], cabergoline, and bromocriptine therapy[6] and the long-term outcomes of cabergoline[22]. Other publications in the literature include case reports and case series. We believe that our results will guide further studies to elaborate more definitive indications for the surgical treatment of giant prolactinomas.

The results of this study indicate no significant difference between medical therapy alone and surgery plus medical therapy in terms of the reduction of tumor volume and normalization of PRL values in patients with giant prolactinomas. In our opinion, surgery should be reserved for severe compression conditions, and potentially unnecessary surgical

approaches should be avoided to prevent complications of surgery, to use limited health resources more reasonably, and to lower treatment costs.

Ethics Committee Approval Information:
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Idea and design: F.M.S., E.H., M.Y., K.K., Ö.Ö.G., S.C.; Data collection and processing: F.M.S., E.H., M.Y., K.K., Ö.Ö.G., S.C.; Analysis and interpretation of data: F.M.S., E.H., M.Y., K.K., Ö.Ö.G., S.C.; Writing of significant parts of the article: F.M.S., E.H., M.Y., K.K., Ö.Ö.G., S.C.;
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