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Çocukluk Çağı Kraniyofaringiyoma Olgularının Klinik ve Laboratuvar Bulguları

Clinical and Laboratory Follow up of Pediatric Craniopharyngioma Cases

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ÖZ

GİRİŞ ve AMAÇ: Bu çalışmada çocukluk çağı kraniyofaringioma olgularının klinik ve laboratuar bulguları ve izlem süresince karşılaşılan endokrin sorunların değerlendirilmesi amaçlanmıştır.

YÖNTEM ve GEREÇLER: Çalışmaya Ocak 2010-Aralık 2017 arasında kraniyofaringiyoma tanısı alan olgular dahil edildi. Demografik ve klinik veriler Uludağ Üniversitesi Tıp Fakültesi Çocuk Endokrinoloji poliklinik dosyalarından retrospektif olarak değerlendirildi. İstatistiksel analizler için SPSS software version 21 kullanıldı.

BULGULAR: Sekiz yıllık süreçte tanı alan 28 olgu çalışmaya dahil edildi. Olguların yaşları 60-207 ay arasında değişmekte olup median yaş 138,5 aydı. Cinsiyet dağılımlarına bakıldığında %53 erkek(n=15) ve %47 kızdı (n=13). En sık başvuru bulguları sırayla başağrısı, görme bozuklukları ve boy kısalığıydı. Tanı anında olguların %71'inde (n: 20) tümör boyutu 3 cm'den büyüktü. Preoperatif dönemde büyüme hormonu eksikliği %17(n=5) ve hipotiroidizm %14(n=4), hipokortizolemi %10 (n=3), diyabet insipit %7,1(n=2) sıklıkta saptandı. Postoperatif dönemde olguların %89,3'ünde çoklu hipofizer hormon eksikliği saptandı.

TARTIŞMA ve SONUÇ: Kraniyofaringiyomalar yavaş büyüyen tümörler olup genellikle geç tanı alır. Geç tanı ve tümör boyutunun büyük olması sıklıkla endokrin kayıpların daha ciddi olmasına yol açar. Büyümede duraksama ve ilerleyici kilo artışı hipofizer kitlelerin erken tanısı açısından uyarıcı bulgulardır.

Anahtar Kelimeler: kraniyofaingiyoma, santral hipotiroidi, hipopituitarizm

ABSTRACT

INTRODUCTION: The aim of this study was to evaluate the clinical and laboratory findings and follow up of endocrine status of pediatric craniopharyngioma cases.

MATERIALS and METHODS: The patients diagnosed with craniopharyngioma between January 2010-December 2017 were included in this study. Demographic and clinical findings were retrospectively examined from medical records of Uludag University Medical Faculty Pediatric Endocinology Department. Statistical analyses were performed using the SPSS software version 21.

RESULTS: We identified a total of 28 patients with craniopharyngioma during this period. The age of the patients ranged from 60 to 207 months, with a median age of138.5months.Fifty-three percent (n=15) of cases were male and forty-seven percent (n=13) of the cases were female.The most common presenting complaints were headache, visual impairment, and short stature in decreasing order. Tumor size was greater than 3 cm in 71% (n: 20) of patients at the time of diagnosis. When the endocrine status of the patients were examined in the preoperative period, it was determined that 17% (n: 5) of the cases had growth hormone deficiency, 14% (n: 4) had hypothyroidism, 10%(n: 3) had cortisol deficiency, and 7.1% (n: 2) had diabetes insipidus. In the postoperative period, panhypopituitarism developed in 89.3% (n: 25) of the cases.

CONCLUSIONS: Craniopharyngiomas are slow-growing tumors, the tumor is usually diagnosed lateand reaches large sizes. Late diagnosis and large tumor size often lead to more serious endocrine losses. Failure to thrive and progressive weight gain are stimulating findings for early diagnosis of pituitary masses.

Key words: craniopharyngioma, central hypothyroidism, hypopituitarism

INTRODUCTION

Craniopharyngiomas are benign tumors that affect the endocrine system due to the critical site of origin. They may cause multiple hormone deficiency and visual impairment both before and after surgery because of their close localization to the optic chiasm, hypothalamus and pituitary gland. They are rare epithelial tumors and originate from Rathke's pouch remnants (1).

Craniopharyngiomas are 5-15% of childhood intracranial tumors, usually occur between 5-14 years of age and are rare before 2 years of age(2). In pediatric population, the tumor has a cystic component in 90% of the cases. The clinical symptoms of craniopharyngioma are; headache, nausea, and vomiting due to increased intracranial pressure; visual impairment, and visual field defects, short stature or slow growth, increase in thirst or urination, weight gain, changes in personality or behavior. It is estimated that 70-80% of the cases have endocrine disorders at presentation and the most common hormone deficiencies at presentation are growth hormone (75-100%), adrenocorticotropic hormone (20-70%) and thyrotrophic hormone (3-30%). Hyperprolactinemia and diabetes insipidus can occur due to pituitary stalk compression of the mass. Delayed or arrested puberty in adolescents or precocious puberty in prepubertal children can be detected at presentation(3). Although lateral skull X-ray demonstrates enlargement or distortion of sellaturcica and suprasellarcalcification, and computed tomography is sensitive for small amounts of calcification or cystic abnormalities, MRI is the most sensitive imaging method for the diagnosis.(4) Craniopharyngiomas are benign and do not make metastasis to other parts of the brain or to other parts of the body. However, they may grow and press on critical areas of the brain. Although they are benign, they need to be treated for compression effects. The aim of the study was to evaluate the clinical features and outcomes of pediatric craniopharyngioma cases in our pediatric endocrinology department.

MATERIALS and METHODS:

Patients admitted to Uludag University Medical Faculty Pediatric Endocrinology department and diagnosed as craniopharyngioma between January 2010 and December 2017 were included in this study. Ethics committee approval was obtained for the study. The inclusion criteria comprised minimal interval of six months after surgery for evaluation of postsurgical hormone deficiencies. Growth hormone deficiency was diagnosed in the patients with short stature (height Z score< -2 SD), low growth velocity for age, negative response to growth hormone stimulation tests with a peak less than ≤ 5 µg/l (clonidine or glucagon), and low insulin-like growth factor-1 (IGF-1) level for age. Obesity was defined as body mass index (BMI)> 2 SD as determined by the World Health Organization (WHO).

Statistical analyses were performed using the SPSS software version 21. The variables were investigated using visual (histogram, probability plots) and analytic methods (Kolmogrov-Smirnov/Shapiro-Wilk's

test) to determine whether or not they are normally distributed. Descriptive analyses were presented using proportions, medians, minimum, and maximum values as appropriate.

RESULTS:

During 8-year period, a total of 28 patients, 46.4% (n=13) female and 53.6% (n=15) male, were diagnosed as craniopharyngioma.The age range was from 60 month to 207 months with a median 138.5 months.The follow-up period ranged from 6 to 14 months, with a median of 6 months.Headache was the most common presenting complaint (71.4%, n=20). The other complaints and their frequency are summarized in Table 1.

Table 1. Frequency of complaints and symptoms at initial examination.

Complaints	**N (%)**
Headache	20(71.4)
Visual impairmentandnistagmus	15(53.6)
Shortstature	11(39.3)
Nauseaandvomiting	8 (17.9)
Obesity	5 (17.9)
Seizure	5 (17.9)
Papilledema	5(17.9)
Hydrocephalus	5(17.9)
Hemiparesis	1(3.6)

Of all the patients, 39.3% (n=11) had short stature, 5 of these patients (17.9% of all patients) had laboratory consistent with growth hormone deficiency. Growth hormone deficiency was the most common endocrine disorder in the preoperative period. Other endocrine disorders in the preoperative period were summarized in Table 2. Five patients had hydrocephalus in the preoperative period. All patients in this study were treated with surgery by transcranial approach. Total excision was achieved in 82% of the cases. The histological subtype of the tumor was adamantimatous in 53% (n=15) of the cases and pathology data could not be reached in 13 patients. Ten (35.7%) of the patients needed re-surgery due to recurrence.

Multiple pituitary hormone deficiency developed in 89.3% of the patients after surgery. In the postoperative period, hypothyroidism and adrenal insufficiency were the most common endocrine disorders and affected 85.7% (n=24) of the patients. Clinical findings due to hormone deficiency at admission and after treatment are summarized in Table 2.

Table 2. Clinical findings due to hormone deficiency at admission and after treatment.

	Preoperative N(%)	**Postoperative N(%)**
Growth hormone deficiency	5(17.9)	21(75)
Hypothyroidism	4(14.3)	24(85)
Hypocortisolism	3(10.7)	24(85)
Diabetes insipidus	2 (7.1)	23(82)
Precocious puberty	1(3.6)	-
Hyperprolactinemia	1(3.6)	-
Hypogonadism	-	23(82)

Five patients had radiotherapy due to residual tumor after surgery. All patients who required radiotherapy had an initial tumor size over 3 cm.

DISCUSSION

Craniopharyngiomas are rare epithelial tumors and originate from Rathke pouch remnants(1).The incidence of craniopharyngioma is 0.5-2 cases per million per year and 30-50% of these cases are children and adolescents(5,6). There is a bimodal age distribution, with one peak in children between 5 and 14 years, and a second peak in adults between 50 and 75 years of age(2).Age distribution in our study group was similar to the literature,ranged from 60 month to 207 months with a median 138.5 months.

Craniopharyngiomas are slow-growing tumors and the clinical picture at the time of diagnosis is often dominated by non-specific manifestations of intracranial hypertension, such as headache and nausea(4). In our study group headache was the most common complaint at the time of diagnosis, 71.4% presenting with this complaint. Visual impairment (62–84%) and endocrine deficits (52–87%) may lead to diagnosis(4). Similar to the literature, visual impairment was the second most common presenting complaint (53.6%). Frequency of complaints and symptoms at initial examination are summarized in Table 1.

Pituitary hormone deficiencies are common in craniopharingiomas. At the time of diagnosis, 40%–87% of children present with at least one hormonal deficit, frequency of growth hormone deficiency is 75%, gonadotropins 40%, adrenocorticotropic hormone 25%, and thyroid stimulating hormone25% and central diabetes insipidus is present preoperatively in 17% of patients (7–10).In our study group; 39.3% (n=11) had short stature, 5 of these patients (17.9% of all patients) had laboratory consistent with growth hormone

deficiency. Growth hormone deficiency was the most common endocrine disorder in the preoperative period. Other endocrine disorders in the preoperative period were 14.3% (n=4) hypothyroidism, 10.7% (n=3) hypocortisolism, 7.1% (n=2) diabetes insipidus, 3.6% (n=1) precocious puberty and 3.6% (n=1) hyperprolactinemia. Central diabetes insipidus was detected in 7.1% (n=2) of the patients. These results suggest that failure to thrive could be the first sign of craniopharyngioma.

Surgery is the most preferred method of treatment. The aim of surgery is to achieve complete resection by preserving visual and hypothalamic functions. For the tumors too close to or too entangled with the optic nerve or hypothalamic structures; surgery targets to eliminate the compression effect of the mass and remove the tumor as much mass as possible(11).Complete resection can be defined as no residual tumor in the operative field and no contrast-enhancing lesion detected in postoperative contrast-enhanced MRI. According to the literature, total resection ratio ranges between 26.3% and 82.5% and in our study total excision was achieved in 82% of the patients (12–16). Various surgical approaches are used for craniopharyngioma. All of patients in our study were treated by cranial approach. Five (17.4%) patients had radiotherapy after surgery due to residual tumor. Although rates of recurrence after surgery varies between 0.02-33% in the literature, the rate of recurrence in our study was 35.7% (n=10). Tumor size at diagnosis was >3 cm in 85.7% (n=24) of the patients, and the higher recurrence rate in our study may be due to late diagnosis and increased tumor size. Although there is a correlation between tumor size and recurrence rate, there is no clear information about the cutoff point of diameter that can predict recurrence(12,14,16–18).

Two or more hormone deficiencies were detected in 89.3% (n:25) of the patients in the postoperative period. While growth hormone deficiency was the most common endocrine disorder before surgery, adrenal insufficiency and secondary hypothyroidism were the most common endocrine disorders with a rate of 85.7% (n:24) in the postoperative period. The rate of post-surgical pituitary hormone deficiencies increaseswith regard to the tumor's localization (hypothalamus and pituitary involvement) and size. The rate of permanent post-surgical diabetes insipidus ranges between 40% and 93%. Similar to the literature, permanent diabetes insipidus was detected in 82% (n=23) of the patients. (8,9,19–22). Treatment modalities change over the years and while total excision has been recommended previously, in recent years, hypothalamus-sparing surgical strategies are recommended in order to prevent hypothalamic damage and associated severe neuroendocrine sequele and irradiation of residual tumor is efficient in preventing tumor progression(23).

Early recognition of craniopharyngioma cases may reduce endocrine losses that may develop in the postoperative period. Although headache, nausea-vomiting, and visual field defects mostly occur in late period, failure to thrive and progressive weight gain may be warning signs for pediatricians. A multidisciplinary approach is essential in both diagnosis and treatment.

Conflict of Interest: We declare that there is no conflict of interest.

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