Actualization of treatment options in Craniopharyngioma: a comparative analysis of different therapeutic modalities.

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Abstract

In this manuscript, the authors review current treatments of craniopharyngioma, focusing on new trends and making a comparison between them and the classical surgical approach. Modern treatment options include radical or conservative surgery, radiosurgery, external beam radiotherapy, interstitial radiotherapy, stereotactic cyst aspiration and interferon. Differences in tumor size, location and shape, as well as other circumstances like recurrence and previous treatments, should preclude the neurosurgeon to decide the best options in each patient.

Key words: Craniopharyngioma, Treatment options, Radiosurgery, Interferon, Stereotactic aspiration.

Introduction

Craniopharyngioma is a complex pathology that is histologically benign, centrally located, related to optic chiasm, pituitary stalk and hypothalamus, and formed by solid and liquid components. It affects children and the economically active population, though it is relatively uncommon if compared with other tumors. Undoubtedly, it is still a challenge for the neurosurgeon and requires a multidisciplinary approach for its most effective treatment.

Throughout the last century, many different techniques were developed for the treatment of these tumors. These techniques vary in their goals (healing or palliation), prognosis, difficulty, experience in number of cases, etc. Results from the different therapeutic forms, however, are usually successful in their goal, generating confusion on which technique should be used in each individual case.
The present article analyzes four recently published articles. To conclude, current possibilities for each therapeutic option and their advantages and limitations are discussed.

1) SURGICAL TREATMENT OF CRANIOPHARYNGIOMAS: EXPERIENCE WITH 168 PATIENTS

Fahlbusch R, Honegger J, Paulus W, Huk W, Buchfelder M
J Neurosurg (1999) 90:237-250

Information

This article analyzes a series of 168 patients who were operated between 1983 and 1997. The pterional approach was used in 39.2% of them, whereas 23.6% underwent surgery through the transsphenoidal route. However, the authors claim that in the past few years they have frequently chosen the subfrontal interhemispheric approach (11.5%) for larger tumors, because it lends a greater percentage of complete resections. A total excision of the lesion was performed in 49.3% of the 148 patients that underwent open surgery as initial treatment, and in 85.7% of those where the nasal approach was used. Subtotal excision was performed in 22.3%, partial excision in 14.2% and only in 2.7% of the 148 patients a biopsy was carried out. Reasons for incomplete resection were a firm adherence to hypothalamus in 26.8% of cases, obstructed vision in 21.4%, large calcifications in 14.3%, adherence to perforating vessels in 10.7% and adherence to greater vessels in 7.1%. Perioperative mortality was 1.1% in first-time surgical patients and 10.5% in cases of recurrence. Morbidity was 12.8% for transcranial surgery and 5.7% for transnasal approaches, including hypothalamic dysfunction, meningitis, seizures, diabetes insipidus and pituitary deficiency. The rate of patients free of recurrence after a longer period than 5 years was 86.5 % after 5 years and 81.3% after 10 years in total resections, against 48.8% for subtotal resection and 41.5% after partial excision, both after 5 years. All in all, 79% of the 148 patients initially operated are currently leading independent lives without limitations, being the survival final percentage 92.7% after 10 years.

Analysis

The present article is the larger series published in the recent years. It includes a detailed study of patients' clinical and imaging signs and symptoms, with a complete analysis of their endocrine functioning, developed in a subsequent article (14). The exposed results back up the use of surgery as first therapeutic option in patients with craniopharyngioma, although they emphasize the importance of the surgeon's experience to reach good results. Likewise, knowing when to stop tumor resection if evidence of hypothalamic invasion or dissemination to other noble structures is found is stressed to the utmost. Therefore, in subsequent evolutionary terms, the authors conclude that, when it is indicated, there is a greater benefit for the patient if an incomplete resection is performed than when a total resection is attempted and it results in a patient with serious sequelae or even dead.

2) GAMMA KNIFE RADIOSURGERY FOR CRANIOPHARYNGIOMAS

Wen-Yuh CH, Hung-Chi P, Cheng-Ying SH, Wan-Yuo G, Ling-Wei W
J Neurosurg (Suppl 3) (2000) 93:47-56

Information

The use of radiosurgery with other adjuvant treatments is analyzed in this article. A series of 31 patients is presented, 25 of which were treated with radiosurgery after other initial therapy, and 6 of which received radiosurgery as first therapy. If there was found an important cystic component making the localization of optic nerves and chiasm difficult, a stereotactic aspiration was performed prior to irradiation. Authors define as complete response the disappearance of more than 80% of residual tumor volume, whereas a progression was demonstrated when a tumor decrease below 20% of initial volume or an increase of tumor size was found. There was a complete response in 32.3% of cases (10 patients), a partial response in 32.3%, no changes in 22.6%, and a tumor volume increase in 12.8%, which was defined as failure of treatment because it induced the authors to apply a therapeutic method other than radiosurgery to control tumor growth. The evolution was excellent in 29% of cases, good in 38.7%, regular in 16.1%, and poor in 6.5%, according to the authors' classification. Three patients (9.7%) died during postoperative follow-up. The average follow-up for this series was 36 months. Morbidity was very low, including one patient with a post-radiosurgery quadrantanopia.

Analysis

This series is one of the largest series under radiosurgical therapy for craniopharyngiomas. The study demonstrates that the reported morbidity is inferior to the one described for open surgery approaches, although favorable response to therapy is also reduced. There was a positive response to volume reduction of the solid component in a high percentage of cases, although the short follow-up does not provide ground for definitive conclusions at present. It is worth mentioning that 23 of the 31 patients underwent open surgery as initial treatment. Therefore, the series is composed mostly of already operated patients with postoperative recurrence, making it difficult to reach a definitive conclusion regarding the role of radiosurgery as initial therapeutic alternative for craniopharyngiomas. Likewise, no appreciations are made regarding the surgical experience of the centers where the surgical resections were performed, which, as it is widely known, is central for the evolution of operated patients.

3) STEREOTACTIC INTRACAVITARY THERAPY OF RECURRENT CYSTIC CRANIOPHARYNGIOMA BY INSTILLATION OF 90YTTRIUM

Blackburn TP, Doughty D, Plowman PN
British Journal of Neurosurgery (1999) 13(4):359-365

Information

The use of intracavitary radiotherapy with 90Yttrium in six patients with recurrent craniopharyngiomas is described in this article. Six patients with eminently cystic recurrence were chosen, requiring periodically repeated aspirations due to the persistence of the tumors, for which other therapeutic approaches had completely been exhausted. Seven cysts were treated with this method, resulting in a permanent remission in five cases which required no further aspirations, although in two of them there was the need of 90Yttrium reinstillation. One case had no favorable response, showing a recurrence both solid and cystic, and the other case died a month afterwards due to solid complications. No patient developed worsening after the procedure, neither visual nor endocrine. The average follow-up was 3.5 years. An extensive review of all irradiated cysts presented in the literature was performed.

Analysis

The use of intracavitary radiotherapy has proven to be a valid alternative in selected cases of tumors with cystic components. The recurrence of those cysts is very low after treatment. Although morbidity and mortality are also very low, the present study does not show significant endocrine or visual improvements after the procedure. While this would be explainable by the fact that these patients present recurrence of previous therapies that may have generated irreversible ophthalmologic or endocrinological deficits, improvement in the cases treated from the beginning and reported in the world literature analyzed in this article is not proved. Therefore, this therapy would be reserved for cystic tumors against which other treatments had failed, without the primary goal of improving symptoms but of definitively decreasing the volume occupied by the cystic component in the lesion.

4) PHASE II EVALUATION OF INTERFERON ALPHA 2A FOR PROGRESSIVE OR RECURRENT CRANIOPHARYNGIOMAS

Jakacky RI, Cohen BH, Jamison CH , Mathews VP, Arenson E, Longee DC, Hilden J, Cornelius A, Needle M, Heilman D, Boaz JC, Luersen TJ
J Neurosurg (2000) 92:255-260

Information

Fifteen patients, younger than 21 years old, were analyzed in this article, all of which had a progression of tumor growth evidenced in seriated MRIs. Three patients were separated from the study before finalization, which rounded the final count of assessed patient to twelve. Out of those twelve, three had a favorable response to treatment, with one complete response, one partial response and one minimal response. One patient presented visual improvement. All three cases had a predominantly cystic component. On the other hand, it was proved that three patients presented progression of the disease during therapy. Toxicity from interferon was high, causing hepatic and neurological dysfunctions that lessened when the drug was discontinued or the dose decreased.

Analysis

The use of interferon against craniopharyngiomas is based on the principle that states that craniopharyngioma cells derive from the same linkage as squamous cells skin tumor, which has a favorable response to interferon. Infantile population is proved to have a favorable response to this treatment in a low percentage of cases (25%), and its high toxicity and cost do not yet warrant it for a routine utilization. However, the effects of interferon on adults, in different doses and schemes, are still to be defined.

Synthesis and Comments

Harvey Cushing, pioneer in craniopharyngioma surgery and to whom these tumors owe their name (31), was perhaps one of the first in being discouraged by only being able to perform partial resections in his 87 cases, where he performed 180 operations (35). This clearly proves the high rate of recurrence that developed in that foundational series.

Morbidity and mortality in the primary series was lowered to a nonetheless overwhelming 50% by the middle of the twentieth century (5,25,28), based on hormonal substitution therapy and the development of new surgical and anesthetic techniques. These figures caused the initial development of alternative techniques such as applied radiotherapy, by Kramer (17,18), and intracystic 32P injection, by Leksell (22), either accompanied or not by surgery being less invasive from the oncological perspective.

Largest surgical series dating the end of the 80’s support a total resection as the treatment goal (12, 13, 39, 40). However, morbidity and mortality of these series are still high, as well as recurrence.

Limited surgery plus radiotherapy remained a valid therapeutic alternative by the end of last century, with various series (23, 34) published in response to morbidity and mortality rates that were still present in surgical series. The authors admit excellent results from radiotherapy alone, surgery alone or radiotherapy after limited surgery, and they hold that the risk of endocrinological and ophthalmological alterations after treatment is greater with invasive surgery. In any case, the series are not large and the authors themselves accept that the groups under treatment may not necessarily be comparable because the selection of groups was not randomized.

The place of radiosurgery in the treatment of craniopharyngiomas is still to be defined (15, 30, 38). The series published up to the present are very small and a prudential follow-up period, which would allow for valid conclusions, has not yet lapsed. Lunsford suggests that the use should be restricted to tumors smaller than 20 mm placed farther than 5 mm from the optic nerves, which restricts the number of tumors that could be treated thus.

Another therapeutic alternative for craniopharyngiomas is stereotactic intracavitary brachytherapy. In all, 200 cysts have been published since the aforementioned works by Leksell, which started in 1951 and were continued by Backlund (3) with a long series. The foundation of this therapeutic approach is the local irradiation on cysts epithelium with beta particles, which have low penetration and short half-life. This causes the cysts to stop growing and require no repeated punctures to keep them evacuated anymore. It is not yet proved, as the analyzed article states, that endocrine and visual symptoms improve, at least when the cysts treated are recurrences of cysts previously treated with other therapies. In any case, cyst control reaches rates of 96% (26), and morbidity and mortality rates are really very low. Apart from the mentioned treatment possibility of monocystic recurrence, intracavitary irradiation is a viable alternative for the treatment of tumors with a significant cystic component as a first step prior to microsurgical excision or radiosurgery applied to the solid portion of the lesion.

Our initial therapeutic decision regarding craniopharyngiomas is surgery as first choice. Resection should be total in all the cases that lend to it. In any case, we prefer not to compromise the neurological and metabolic health of the patient trying to perform total resections where the tumor cannot be completely excised. Patients' evolution after subtotal or partial resection (which is technically persistence, not recurrence) is usually favorable, improving initial neurological symptomatology for years, and in some cases, definitively.

In the personal experience of the senior author(AB), in a series of 86 cases operated in the last twenty four years, a complete resection was obtained in 61.6% of the adult, and 69% of the pediatric population. In those cases where a total resection could be made, 76% remain free of tumor for five years, meanwhile only 40% of the subtotal resection remain free of tumor recurrence for the same period of time.

Alternative therapeutic approaches to surgery, such as radiotherapy, brachytherapy and radiosurgery, are excellent supplements to keep recurrence and persistence under control, and even healing in some cases. The ceiling quoted by Fahlbusch (10) of a maximum of 60-80% of good results with total

resections should be the goal to pursue with surgery as the first treatment option. On the other hand, we should emphasize that the previous experience of the surgeon is a deciding factor for the postoperative evolution of the patient (33), because someone experienced may probably suspend the operation at the appropriate moment, without innecessary risking the good evolution of the patient but, at the same time, performing a resection of the lesion as complete as possible. Persistent or recurrent tumors may be managed by surgery again or other treatment option, tailoring the treatment specifically for each patient.

Papers reviewed

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