Craniofaringiomas: a literature review
Craniofaringiomas: uma revisão de literatura

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ABSTRACT
This is a comparative review of diagnostic and therapeutic models of craniopharyngiomas. Craniopharyngiomas are rare tumors, almost invariably benign, extra axial and non-glial of the central nervous system. They are most commonly located in the sella turcica and the suprasellar region. These tumors have clinical presentation based on the mass effect on adjacent structures, such as loss of vision, pituitary development disorders and endocrinopathies. This study was based on informations collected from the Virtual Health Library (VHL), PubMed and LILACS databases, excluding duplicate references at the end of the search. Selected articles were published between 2001 and 2019. From the research undertaken, it is possible to conclude that, even though CPH’s (Craniopharyngiomas) are a rare form of tumors, they have been widely reported all around the medical community with extensive and corresponding clinical presentations. These findings have direct practical relevance and corroborates our intention of summarizing reliable information regarding this disease.

Keywords: Review; Diagnostic; Therapeutic; Suprasellar; Sella turcica; Tumors; Craniopharyngiomas

RESUMO
Esta é uma revisão comparativa dos modelos diagnósticos e terapêuticos dos craniofaringiomas. Os craniofaringiomas são tumores raros, quase invariavelmente benignos, extra-axiais e não gliais do sistema nervoso central. Eles estão mais comumente localizados na sela turcica e na região suprasellar. São tumores cuja apresentação clínica se baseia no efeito de massa em estruturas adjacentes, como perda de visão, distúrbios do desenvolvimento hipofisário e endocrinopatias. Este estudo foi elaborado a partir de informações coletadas nas bases de dados da Biblioteca Virtual em Saúde (VHL), PubMed e LILACS, excluindo referências duplicadas ao final da busca. Os artigos selecionados foram publicados entre 2001 e 2019. A partir da pesquisa realizada, é possível concluir que, embora os CFs (craniofaringiomas) sejam uma forma rara de tumores, eles têm sido amplamente divulgados em toda a comunidade médica com apresentações clínicas extensas e correspondentes. Esses achados são de relevância prática direta e corroboram nossa intenção de reunir informações confiáveis a respeito dessa doença.

Palavras-chave: Revisão; Diagnóstico; Terapêutico; Supraselar; Sela turcica; Tumores; Craniofaringiomas

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Craniopharyngiomas (CPH) are rare tumors, almost invariably benign, extra axial and non-glial, of the central nervous system. They are most commonly located in the sella turcica and suprasellar region. These tumors have clinical presentation based on the mass effect on adjacent structures, such as loss of vision, pituitary development disorders and endocrinopathies\textsuperscript{1,2}. The correct diagnosis remains a challenge for professionals due to the wide clinical characteristics, important hormonal disorders and visual impairments. Also, the appropriate therapeutic options for most cases remain uncertain in the literature. This disease remains a significant challenge for endocrinologists and neurosurgeons due to frequent post-surgical recurrences that impact in morbidity and mortality of adult and pediatric patients. The importance of understanding the clinical profile of CPHs, as well as the best therapeutic approach, will contribute to a better prognosis, with a significant impact on quality of life after correct treatment\textsuperscript{1}. The aim of this study is to carry out a literature review of CPH's in adults and children.

The search was performed using the databases of the virtual health library (VHL), PubMed, LILACS, excluding duplicate references at the end of the studies. Selected articles were published between 2001 and 2019. The keywords were: diagnostic, therapeutic, and craniopharyngiomas. Inclusion criteria were review or original articles, published in the period described with an experimental design (clinical trials or not) or observational studies performed on humans with more than 40 subjects for diagnosis, treatment and rehabilitation. Mortality, quality of life, adverse effects, and hormonal function after treatment were the used outcomes.

Even though it is a tumor with benign characteristics, it can produce symptoms related to the compression of neighboring structures, including optic chiasm, pituitary gland, hypothalamus, third ventricle and other structures, thus decreasing the quality of life of patients\textsuperscript{7}.

Among the clinical features, those related to the mass effect may cause nonspecific headaches, nausea and other subsequent symptoms related to optic campimetry, pituitary disorders, dysfunctions in the CSF circulation and hypothalamic
It is noteworthy that the campimetric alterations are dependent on the anatomical region being compressed by the tumor \(^7\). Campimetric changes usually result from compression of the optic nerve and chiasma. Medial to the optic chiasm in the decussation region, bitemporal heteronymous hemianopsia is expected. If the tumor has an asymmetrical growth frontolaterally, there may be unilateral amaurosis with temporal alteration of the contralateral eye. Quadrantopsias are not well reported in sellar tumors. Other reported optical symptoms are sensation of retroocular pressure and loss of visual focus \(^10\). In the suspicion of sellar or parasellar tumors, a careful visual examination should be included. One must look for visual field defects, disorders of ocular motricity and the presence of papilledema on ophthalmological examination.

The most common endocrinopathies are anterior pituitary dysfunctions, causing a disruption in the production of growth and gonadotrophic hormones \(^10\). Intracranial hypertension due to obstruction of the Monroe foramen is more common in children compared to adults. It causes severe headache and vomiting accompanied by nausea due to hydrocephalus. As a result, it is important to place the CPHs in differential diagnoses when there is a syndrome composed of moderate to severe headache, visual deficits, and decreased polydipsia/polyuria \(^11\). Galactorrhea is common when the tumor grows to the point starts from the beginning of a location close to the pituitary stem, generating a dopaminergic counter-block \(^7\).

Any suspicion of lesions close to the pituitary gland must be accompanied by a complete hormonal profile exam, such as in the Table below:

**Table 1. Prevalence of clinical alterations:**

<table>
<thead>
<tr>
<th>Campimetric visual alterations</th>
<th>62% to 84%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inappropriate GH secretion</td>
<td>75%</td>
</tr>
<tr>
<td>Inappropriate FSH and LH secretion</td>
<td>40%</td>
</tr>
<tr>
<td>Inappropriate TSH secretion</td>
<td>25%</td>
</tr>
<tr>
<td>Inappropriate ACTH secretion</td>
<td>25%</td>
</tr>
</tbody>
</table>

**Table 2. Hormonal profile in craniopharyngioma patients**

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seric prolactine</td>
<td>Usually elevated</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>Usually diminished</td>
</tr>
<tr>
<td>IGF-1</td>
<td>Usually diminished</td>
</tr>
<tr>
<td>Luteinising hormone (LH)</td>
<td>Usually diminished</td>
</tr>
<tr>
<td>Follicle-stimulant hormone (FSH)</td>
<td>Usually diminished</td>
</tr>
<tr>
<td>Seric testosterone</td>
<td>Usually diminished</td>
</tr>
<tr>
<td>Thyroid-stimulant hormone (TSH); T3 and T4</td>
<td>Usually diminished</td>
</tr>
<tr>
<td>Adenocorticotropin hormone (ACTH)</td>
<td>Variable</td>
</tr>
</tbody>
</table>

Computed tomography (CT) or magnetic resonance imaging (MRI) can highlight the presence of a tumor with solid-cystic components in any of the regions already described. Clearly, MRI is best used in the evaluation of anatomical components, both tumoral and circumscribed, whereas CT has a greater sensitivity in the presentation of calcified components, which are present in about 90% of cases in children, and around 70% of the cases in adults \(^12\). The suspicion of CPH should be made when there is a sellar or chiasmatic component with dystrophic calcification, a cystic and/or solid component.
with contrast uptake\(^\text{13}\) (Figure 1). CT is the best way to detect or exclude calcifications in CPH tissue (90% of sensibility). MRI T1-weighted images are best suited to search for cystic components with a high protein concentration, mixed with solid components. T2 and FLAIR-weighted images show heterogeneous signs in solid components, low signal due to calcification and hyperintensity in cysts.

CPHs are benign tumors that are presented with a variable cystic content. There may be two variations. The adamantinomatous variation is characterized by strands or nests of multi-stratified squamous epithelium, composed of polygonal or columnar cells, and presented in a pseudo-pallid arrangement on the periphery, while in the central regions there is a reticular texture. The most frequent findings in the adamantinomatous variant are calcifications. These findings are not observed in the papillary variant. The cysts’ are composed of simple pavement epithelium. Compact keratin granules that have a tendency to dystrophic calcifications, content rich in cholesterol, fibrosis and chronic reaction inflammation are important diagnostic elements\(^\text{14,15}\).

The fluids in papillary variant are neither keratin nor cholesterol rich, being composed of fibrovascular papillae that are covered by multi-stratified squamous epithelium.

The therapeutic difficulty associated with the treatment of CPH is based on the choice of the multiple different approaches considering the different types, behaviors, sizes and location of these lesions. Currently, the most accepted therapeutic models for CPH treatment involves surgical resection, followed by radiation treatment, including radiosurgery, and endocrine therapy with immunomodulatory therapy. The three therapeutic modalities may or may not be associated depending on the patient’s situation\(^\text{16}\).

As for the surgical resection, tumors located at the skull base, especially near structures such as the pituitary gland and optic chiasm, are never easily resected. The aim is to achieve complete or maximum resection of the tumor with total postoperative viability of the visual and endocrine capacities, especially in well-located, non-aggressive tumours. Eventually this is not an achievable goal, depending mostly on the adhesions of the tumor pseudocapsule to the neighboring structures. There are multiple surgical approaches used in the treatment of CPH’s. Transcranial approaches involve the use of a craniotomy to reach the tumor. It is best suited for CP with suprasellar extension. The difficulties encountered are based on the limitation of the surgeon’s vision due to the presence of the optical chiasm adjacent to the tumor and its possible extension to the pituitary gland, because of the viewing angle. Tumors with extension to the third ventricle or the Monroe’s foramen may be accessible with the opening of the lamina terminalis.

The pterional approach and its variants should be considered for the resection of small tumors located close to the optic chiasm and extending unilaterally. The subfrontal and interhemispheric approaches are considered for tumors located before the optic chiasm or after the lamina terminalis, and those extending upwards in the direction of the third ventricle, with limited spreading bilaterally\(^\text{9}\).

The transsphenoidal approach is mostly used in partially or totally intrasellar tumors. Tumors located in the sphenoid cleft may be approached through an extendable endoscopic skull base approach\(^\text{9}\).

For patients who have had an incomplete resection, there is the conventional external beam radiation therapy. There is...
the possibility to continue the treatment considering the re-operation and/or therapy\(^{18}\).

Radiotherapy is a therapeutic method that is based on the emission of high-energy ionizing radiation to destroy or inhibit the growth of abnormal cells that form a tumor. When X-rays pass through tissues, they release so much energy that electrically charged particles appear and atoms of oxygen, extremely reactive, will react with the DNA molecules, causing changes in the double helix leading to cell death, either by the mechanism of apoptosis or by the loss of the ability to divide itself. It is a method that is used in different situations, such as in the postoperative period to destroy remaining tumor cells, as the main treatment for a brain injury or even to relieve symptoms of the disease in terminally ill patients\(^{18}\).

In the context of CPH’s, there are basically two methods that are used: conventional radiotherapy (RT) and stereotactic radiotherapy/radiosurgery. Despite the benefit related to RT, especially after partial resection of these tumors, the risks of complications related to conventional RT are not low, especially in the pediatric age group\(^{19}\). It is important to highlight its complications in the administration of radiotherapy in the vicinity of important structures. Consequences are frequently seen, as visual deterioration (more significant at higher doses), worsening of endocrine deficits, higher incidence of cerebrovascular disease due to arterial involvement (carotid and Willis Polygon), and increased risk of developing secondary neoplasms (reported in a minimum number of cases)\(^{18}\).

Stereotactic radiosurgery is a method that has been used in recent years in an attempt to replace conventional radiotherapy, as it presents a more precise and focal radiation emission at the injury site. With this technique, greater precision is obtained in the application of the treatment accompanied by greater protection of healthy tissues. Some studies suggest that the efficacy of single session radiosurgery might be lower than multi-session radiosurgery\(^{19}\). Partial excision of the tumor followed by fractionated radiotherapy can lead to a decrease in tumor mass, with disease-free survival of 97% (3 years) and 92% (5 years), with low risk of toxicity\(^{20}\). It is important to emphasize that this technique can be considered in the case of patients with recurrent tumors of small dimensions (≤3cm), mostly solid, and that are at least ≥3mm distant from the critical structures (brainstem, chiasm and optic nerves)\(^{18}\).

### CONCLUSION

The revised data discussed in this literature review approach the diagnostic and therapeutic models related to craniopharyngiomas, based on the most recent articles and books available. From the research undertaken, it is possible to conclude that, even though CPHs are a rare form of tumors, it has been widely reported all around the medical community, with extensive and corresponding clinical presentations. These findings have direct practical relevance and corroborates our intention of summarizing reliable information regarding this disease.

### REFERENCES


