Craniopharyngioma: same dangers, different age...

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Craniopharyngiomas are rare epithelial tumors arising from Rathke’s pouch remnants, originally described by Zunker in the late 19th century. They constitute approximately 3% of all intracranial neoplasms and 10% in pediatric population. They are the most common pediatric brain tumor of nonglial origin, representing 54% of all sellar and suprasellar tumors.

Its developmental path extends from the pharynx to the floor of the sella turcica, and tumors may be completely intrasellar (5-6%), extrasellar (20-41%), or a combination of both. Although typical locations are sellar and suprasellar, craniopharyngiomas have frequently been identified in several other locations.

In spite of benign histological characteristics and slow growth, these tumors frequently exhibit malignant behavior, with locally infiltrative and recurring potential, even after apparently curative therapy. Anecdotal cases of malignant transformation and of ectopic and metastatic recurrence have been described after surgical treatment.

Data from the US reveal an overall incidence of 0.11 per 100,000 person/years, with no significant gender variance. The tumor may be diagnosed at any age, but a bimodal distribution occurs, with peak incidences in children between 5 and 14 years, and adults between 55 and 74 years. Almost half the cases occur in the adult population, and it has been suggested that these tumors bear significant clinical, biological and pathological differences among age groups.

Histologically, craniopharyngiomas are predominantly cystic or mixed lesions, the solid ones accounting for less than 20% of cases. About 80-87% of craniopharyngiomas are calcified, and calcifications are more common in children (90%) than in adults (50%).

Two distinct types have been identified, with important age-distribution differences. The adamantinomatous type is the most common, and predominantly affects children and adolescents. These are commonly cystic tumors, usually with a solid component, and a wide size variation at the time of diagnosis. Extensive fibrosis and inflammation are observed, resulting in dense adhesion to adjacent structures and contributing to the difficulties in complete resection of these tumors.

The papillary variant is almost exclusive of adults and usually involves only a solid component, typically with no calcifications. In contrast to the adamantinomatous type, these tumors are generally well circumscribed, with less infiltration of adjacent brain tissue, and therefore more amenable to surgical resection.

The clinical features associated with craniopharyngioma, consist of a broad spectrum of signs and symptoms, reflecting the pressure effects of the tumor on the surrounding brain structures (hypothalamo-hypophyseal axis, visual pathways, brain parenchyma, blood vessels and ventricular system). Symptoms frequently develop insidiously, and become apparent only after the tumor has reached significant dimensions. Thus, clinical presentation ranges from asymptomatic to endocrine, visual, intracranial hypertension-related or psychological abnormalities, some of which evolve largely unnoticed by patients, especially those of pediatric age.

The severity of the clinical manifestations relates to the location, dimensions and growth of the tumor, and 3 major syndromes have been described accordingly:

Prechiasmal localization – visual symptoms predominate.
Retrochiasmal location – signs of raised intracranial pressure (ICP).
Intrasellar craniopharyngioma – headache and endocrinopathy.

Age-related clinical differences have also been postulated, with raised ICP predominating in children, sexual development abnormalities in adolescents, visual defects and hypopituitarism in adults and cognitive impairment in the elderly.

In the pediatric population, the most frequent presenting manifestations include signs of increased ICP: growth failure and visual disturbances. Headache is present in 60-80% of patients, vomiting (frequently without nausea) in 35-70% and papilledema in 25-
in cardiovascular and cerebrovascular mortality
endocrinological effects), but also to treatment compli-
suggested in some studies (with better prognosis for
ment modalities, on survival
ding the effects of age, histological type, or even treat-
patients surviving at 10 years
rates for craniopharyngioma, with more than 90% of
contributed to an improvement in overall survival
also common, as are psychological problems
of thyroid dysfunction. Poor school performance is
ence can occur. These signs most likely are the result
palsies in children, revealed no other clinical differ-
nausea and vomiting, papilledema and cranial nerve
ICP are much less common than in children.
chiatric symptoms. Symptoms related to increased
tive defects (memory loss, apathy, confusion) and psy-
amenorrhea. Large tumors in adults can cause cogni-
tumors produce endocrine and visual abnormalities, as
well as neurological defects such as ataxia and con-
vulsions. Eighty-eight percent of men experience de-
creased sexual drive and 82% of women complain of
amenorrhea. Large tumors in adults can cause cogni-
tive defects (memory loss, apathy, confusion) and psy-
psychiatric symptoms. Symptoms related to increased
ICP are much less common than in children.
A recent literature analysis involving almost 1,000
patients, apart from a higher frequency of headache,
nausea and vomiting, papilledema and cranial nerve
palsies in children, revealed no other clinical differ-
ences between age groups.
Recent advances in endocrinology, neuroradiology,
radiation oncology and neurosurgical techniques have
contributed to an improvement in overall survival
rates for craniopharyngioma, with more than 90% of
patients surviving at 10 years.
Mortality is not only related to the tumor (local and
endocrinological effects), but also to treatment compli-
cations and, particularly in adults, to a marked increase in
cardiovascular and cerebrovascular mortality.
Data from different series are not consistent regard-
ing the effects of age, histological type, or even treat-
ment modalities.
Differences between pediatric and adult patients are
suggested in some studies (with better prognosis for
either age groups, but not in others. However, in
some subgroups, such as neonates and children under
5 years at the time of diagnosis, a worse outcome has
consistently been demonstrated.

Histological type or the location of the tumor have
not been associated with significant differences in sur-
vival, in spite of some studies suggesting a better
prognosis for the squamous papillary variant, while
others did not support this opinion. Tumor type or lo-
ocation apparently has no effect on recurrence, albeit age less than 5 years has
been found a significant predictive factor for the reap-
pearance of the disease. Most, if not all the imaging
features associated in some reports, with increased
recurrence risk (tumor dimensions, location, calciﬁca-
tion), appear related to resectability, and may influ-
ence recurrence only indirectly, by inﬂuencing sur-
gecal results. Finally, no data have convincingly estab-
lished differences in prognosis between the 2 major
historical types, although the squamous papillary
type has been associated to a better outcome in most
series.

Long-term morbidity is frequent, and is caused by
the disease (either primary or recurrent) or by its treat-
ment. Manifestations broadly involve endocrine, vis-
ual and neuropsychiatric deﬁcits, and, once again, no
differences between pediatric and adult populations
have consistently been established in the literature.
Endocrine dysfunction is common, with at least 3
pituitary hormone deﬁciencies reported in 50-100%
of patients. Particular hormonal deﬁcits vary be-
tween 88 -100% for GH, 80-95% for FSH/LH, 55-
88% for ACTH, 39-95% for TSH and 25-85% for
ADH. Diabetes insipidus is found in 25%-86% of
survivors. Eighty percent of patients in one se-
ries were receiving hormonal replacement at fol-

Major visual deﬁcits are found in 10-50% of pa-
patients, and again, are not signiﬁcantly associated
with age at diagnosis.

Hypothalamic involvement produces a disruption in
hunger, satiety and energy balance control, with obesi-
ty as one of the prominent features. This manifestation
is reported in 25-75% of surgically treated patients,
and is related to hypothalamic invasion by the tumor
and/or surgical or radiation sequela. The degree
of obesity can be profound, leading to metabolic syn-
drome, and at present, there is no effective treatment
available.
Patients treated for craniopharyngioma can also present memory, cognitive and emotional and behavioral deficits, that contribute to the poor academic and work performance and may compromise familial and social functioning[3,4]. In conclusion, craniopharyngiomas remain a puzzling and challenging disease, in spite of all the advancements in diagnosis and treatment modalities.

This clinical entity merges a spectrum of different epidemiological, clinical and pathological processes that share a common histological benignity, the same mechanisms of injury and the potential of recurrence. Significant clinical and prognostic differences between children and adults, the two peak-incidence populations, have not consistently been found. However, the disease rarity and the wide variability and heterogeneity of the results found in most series, do not contribute to the consistency of these conclusions. Even in the absence of such differences, and with the good survival results, it has a different and more profound impact in a developing organism than in an adult one.

Efforts must address not only the development of better and less harmful therapies to achieve tumor and recurrence control, but also the preservation of life quality and normal development. Meticulous attention to issues such as hormone deficiencies, visual loss, cognitive and emotional disorders, is essential to a good outcome, especially in children. This lifelong management process must be assured by a multidisciplinary and committed team of healthcare providers in order to achieve satisfactory long term results.

REFERENCES


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