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Clinical Study

Modern treatment of 84 newly diagnosed craniopharyngiomas

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ABSTRACT

There is debate regarding the appropriate treatment for craniopharyngiomas, which often present symptomatically given their proximity to critical brain structures, and pose significant surgical challenges. The goal of this study is to identify which patient and tumor characteristics are associated with specific preoperative symptoms, surgical complications, patient outcomes, and tumor recurrence in order to guide craniopharyngioma treatment. We retrospectively identified 84 patients with newly diagnosed craniopharyngiomas treated at our institution from 1986–2010. We used binary logistic regression and survival analysis to determine the effect of several variables (including sex, age, tumor size, location, surgical approach, and extent of resection) on preoperative symptoms and postoperative outcomes, including complication rates and tumor recurrence. Age and tumor location were associated with increased rates of preoperative symptoms, with children being more likely than adults to present with endocrine dysfunction, and intraventricular tumors being more likely than extraventricular tumors to present with headaches and hydrocephalus. A transcranial surgical approach was associated with 1.5 times higher rate of surgical complications than transsphenoidal surgery, while only intraventricular tumor location was associated with a poorer patient outcome. The main factor significantly associated with tumor recurrence was extent of resection. We conclude that intraventricular tumor location is most highly correlated with preoperative symptoms. If feasible, transsphenoidal approaches are preferred, as they result in fewer surgical complications, and gross total resections are optimal because they lead to lower rates of recurrence. When gross total resection is not possible, we favor multimodal treatment approaches.

1. Introduction

Craniopharyngiomas are rare epithelial tumors that are believed to arise from remnants of Rathke's pouch [1,2]. Although they represent only 1% of primary intracranial tumors in adults, they may represent up to 3% of intracranial tumors in children [1]. According to one epidemiological study, approximately 300 craniopharyngiomas are diagnosed in the USA each year; of these, nearly 100 are in children younger than 14 [3]. Histopathologically, craniopharyngiomas are classified into two types: adamantinomatous and papillary craniopharyngiomas (Fig. 1). Although craniopharyngiomas are histologically benign, their close proximity to several critical brain structures, including the optic chiasm, hypothalamus, pituitary gland, and third ventricle, make them frequently symptomatic and can render their treatment very morbid. Indeed, Harvey Cushing was noted in 1932 to have said that craniopharyngiomas "offer the most baffling problem which confronts the neurosurgeon".

There is considerable debate regarding the appropriate treatment for craniopharyngiomas. Many believe that gross total resection (GTR) is the only appropriate therapy, while others are beginning to advocate for multimodal therapy (subtotal surgical resection [STR] followed by radiation therapy) in order to minimize morbidity and improve patient outcomes. In 1986, Baskin and Wilson published a series of our institution's experience with craniopharyngiomas from 1969 to 1985, delineating patient demographics, preoperative symptoms, surgical approach, and outcomes in 74 patients [4]. In our current paper, we present the modern experience of 84 newly diagnosed craniopharyngioma patients treated at our institution between 1986 and 2010. Given the incomplete understanding of the variables that confer excess risk in surgery for craniopharyngiomas, we analyze the association of

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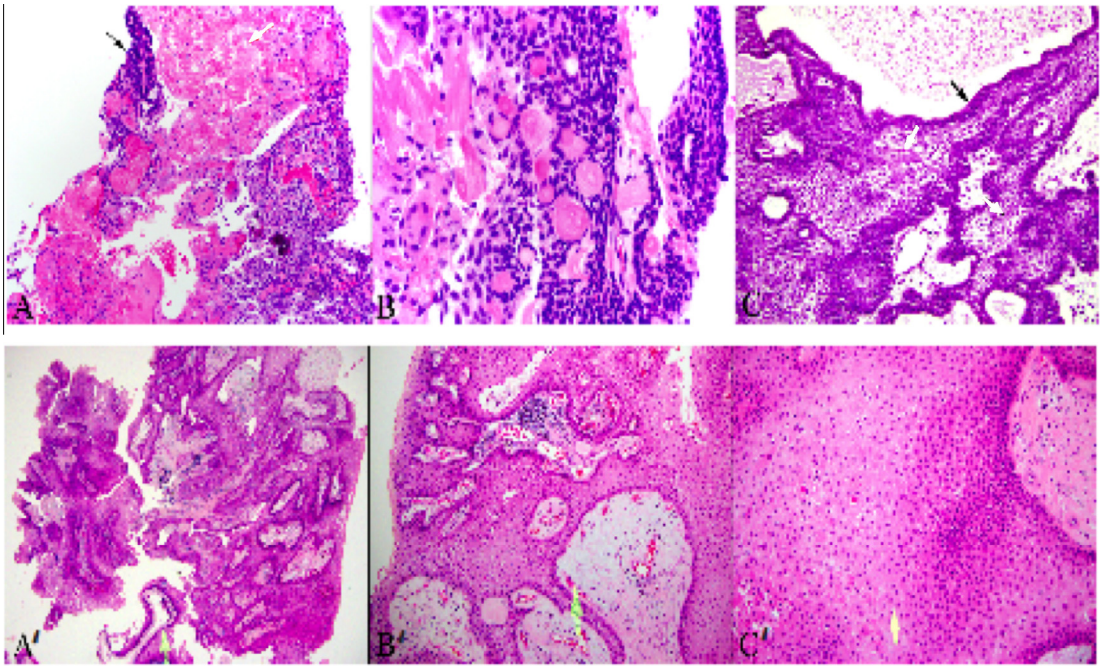

Fig. 1. Histopathologic features of adamantinomatous (A–C) and papillary (A′–C′) craniopharyngiomas in hematoxylin and eosin stained sections. (A) Epithelium with peripheral compact basal palisades (black arrow) as well as more central loose epithelium (stellate reticulum), and abundant wet keratin present with ghost like cell outlines (white arrow) (original magnification × 100). (B) Higher magnification shows wet keratin intermixed with anastomosing trabeculae of epithelium (original magnification × 400). (C) This example demonstrates multiple cysts lined by well-developed basal palisades (black arrow), loose stellate reticulum (white arrows) and intraluminal debris instead of wet keratin (original magnification × 200). (A′) Papillary lesion with central fibrovascular cores, which are lined by non-keratinizing squamous epithelium (original magnification × 40). Higher magnifications at (B′) × 100 and (C′) × 400 show well-differentiated squamous epithelium and mild chronic inflammation within the fibrovascular cores; these craniopharyngiomas lack the basal palisades, stellate reticulum and wet keratin of the adamantinomatous type. (This figure is available in colour at www.sciencedirect.com.)

several patient and tumor characteristics with pre- and post-operative symptoms, surgical complications, tumor recurrence, and patient outcome.

2. Methods

A retrospective review was performed of all patients undergoing craniotomy for resection of a craniopharyngioma at the University of California, San Francisco Medical center (UCSF) between January 1, 1986 and December 31, 2010. A database of all patients undergoing resection for brain tumors was generated from operating room logs, and was cross-referenced with a pathology dataset containing all patients with a histologically confirmed craniopharyngioma. Identifying patient characteristics, including name, diagnosis, and tumor location, were prospectively collected in these databases for all consenting patients undergoing neurosurgical evaluation at UCSF; this occurred in accordance with the Committee for Human Research (CHR# H7828-29842-01).

The medical records, radiographic imaging, pathology reports, and operative notes for each of these patients were reviewed. Data collected included patient demographics, preoperative symptoms, surgical approach, tumor size, location, histopathologic subtype, extent of resection, surgical complications, adjuvant therapy, tumor recurrence, and years of follow-up.

Preoperative symptoms were determined from the clinical records, and included descriptions of visual symptoms (more specifically, bitemporal hemianopsia, decreased or blurry vision), endocrinologic symptoms, headaches, seizures, and signs of hydrocephalus. Postoperative complications included endocrinologic complications related to tumor location (such as panhypopituitarism, diabetes insipidus), as well as surgical complications such as arterial/venous infarct and epidural/subdural hematoma.

2.1. Statistical analysis

All analyses were performed using the Statistical Package for the Social Sciences version 20 (SPSS, Chicago, IL, USA). We first analyzed differences between categorical variables using the Pearson's chi-squared (χ^2) test. Analysis of variance was used to evaluate for statistical differences between continuous variables.

Progression free survival was then assessed using Kaplan–Meier analyses. Between-group differences were first determined by the log-rank test, followed by Cox proportional hazards analyses to adjust for confounding variables including age, sex, tumor pathology, and adjuvant treatment. We also tested interaction terms between variables using backward conditional stepwise regression. After finding that none of the interaction terms would significantly alter the log likelihood of the regression model if removed (unadjusted $p > 0.20$ for all terms), we calculated the adjusted hazard ratios (HR) without adjusting for interactions. The goodness of fit of the regression model was confirmed by demonstrating a non-significant p value on the Hosmer–Lemeshow test.

3. Results

3.1. Patient and tumor characteristics

We identified 84 patients with newly diagnosed craniopharyngiomas treated by neurosurgeons at out institution over a 25 year period between 1986 and 2010; their demographic and clinical characteristics are delineated in Table 1. Of these, 40 patients (48%) were female and 44 patients (52%) were male. The average age at procedure was 36.7 ± standard deviation 22 years, with a bimodal age distribution peaking in the second and sixth decades of life. Almost all of our patients (97%) had craniopharyngiomas with extra or supra-sellar extension (Fig. 2); of these, 49% had