Craniopharyngioma

Analysis of factors that affect the outcome

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ABSTRACT

Objective: The aim of this work is to find out factors that affect the outcome of treatment of patients with craniopharyngioma treated at King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia.

Methods: This study was carried out retrospectively by reviewing the medical records of all patients with craniopharyngiomas treated at King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia in the last 10 years (January 1990 through to December 1999), and collecting clinical, radiological, surgical, and follow-up data and performing statistical analysis to find out factors that affect the outcome of such cases.

Results: There were 11 females (61%), and 7 males (39%), the median age was 24 years. The main presenting symptoms were reduced vision in 66.7%, symptoms of raised intracranial pressure in 50%, endocrinal problems in 33.3%, seizures in 16.7%, and hemiparesis in 5.6%. Radiologic studies showed 72% of tumors had mixed solid and cystic components, calcification in 83%, and ventricular dilatation in 50% of cases. The tumor extended to the posterior fossa in 11%, and to both middle and posterior fossae in 11% of cases. Eighty-nine percent of patients had tumor excision through pterional craniotomy and 11% through subfrontal approach. Gross total removal was achieved in 17% and subtotal resection in 83%. Tumor recurred in 9 patients (50%), 4 of them (44%) had postoperative radiotherapy. The outcome was good in 10 patients (56%), poor in 6 patients (33%), and 2 patients died (11%). The patient age, radiological appearance of tumors and their location were significantly correlated with the outcome (p 0.02, 0.02, 0.04).

Conclusion: Craniopharyngiomas are a common tumor in children. Ophthalmologists and Pediatricians should be aware of the clinical presentation and refer patients to specialized centers for treatment. Total resection of the tumor should be the goal of the Neurosurgeon as it offers the best chance of cure.

Keywords: Brain tumors, craniopharyngioma, pediatric tumors, outcome.

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Craniopharyngiomas (CRF) are benign epithelial tumors of the skull base. It is the most common intracranial neoplasm of non-glial origin in children, representing 9% of pediatric brain tumors.[1] It was first described by Erdheime in 1903, and 7 years later, Lewis reported the first attempt to remove it.[2,3] It arises from epithelial rests (remnants of Rathke's pouch) located on an axis extending from the sella turcica along the pituitary stalk to the hypothalamus and the floor of the 3rd ventricle.[2] The initial presentation of CRF in children is characterized by visual loss, endocrine disturbances or manifestations, or both, of raised intracranial pressure (ICP). Microscopically, CRF are composed of nests or trabeculae of epithelial cells or epithelial-lined cysts, or both, embedded in a loose connective tissue or

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glial stroma. The epithelial cells are arranged in 2 distinct patterns, adamantinomatous (common type) that occurs more often in children, usually shows calcification, frequently invade the brain and can recur. The other pattern form the squamous papillary type that occur almost exclusively in adults, rarely calcify, do not invade the brain and do not recur.[4,5] Mixed CRF showing features of both types is well described. The management of CRF is challenging, as complete surgical removal is sometimes difficult to achieve and is usually associated with substantial morbidity and mortality. On the other hand, other therapeutic modalities such as radiotherapy and chemotherapy are of limited efficacy by their own, and they are used as adjuvant to surgical treatment.[6]

Information regarding the clinical characteristics and management results of patients with CRF in the Kingdom of Saudi Arabia is scarce. In this study the authors retrospectively reviewed all the cases of CRF that were treated at King Khalid University Hospital (KKUH) during the last 10 years to define the clinical features and find out factors that could potentially affect the outcome of treatment of CRF patients in the KSA.

Methods. The material of this study included 18 consecutive patients with CRF treated at KKUH during the period January 1990 through to December 1999. The patient files were reviewed and all biographic, clinical, radiological and treatment data were uniformly collected according to a previously designed data sheet. The collected data included: patient's age (patients <18 years were considered as children), sex, nationality, duration of illness, and the presenting symptoms such as visual, endocrinal, symptoms due to raised intracranial pressure (ICP), seizures or hemiparesis, or both. The physical signs documented in the notes were recorded including visual acuity and field, presence of optic atrophy on fundus examination, endocrinal findings as short stature and the development of secondary sexual characters. Serum hormones (thyroxin, cortisol, growth hormone, follicle stimulating hormone and leuteinizing hormone) when available were also recorded. The radiological findings from plain x-rays, computerized tomography (CT-scan) and magnetic resonance imaging scans, **(Figures 1, 2, 3),** such as, large sella turcica, presence of calcification, appearance of tumor (cystic or solid), location of the tumor (prechiasmatic or retrochiasmatic), extension of the tumor to frontal and temporal lobes and to the posterior fossa, as well as hydrocephalus were also recorded. Operative data was documented including the surgical approach (pterional, subfrontal or trans-sphenoid), the extent of tumor excision whether subtotal resection (STR) or gross total removal (GTR). Postoperative treatment with radiotherapy was also recorded. Tumor recurrence was defined as

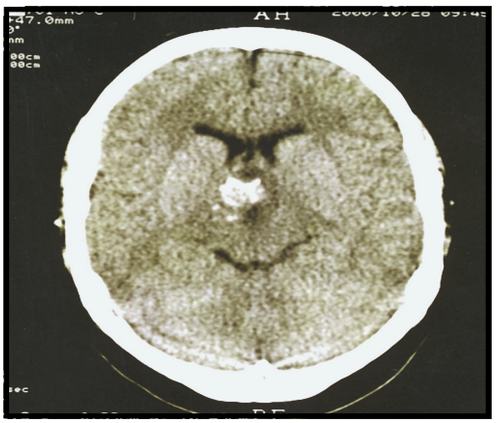

Figure 1 - Precontrast computerized tomography scan showing the cystic and calcified components of the tumor.

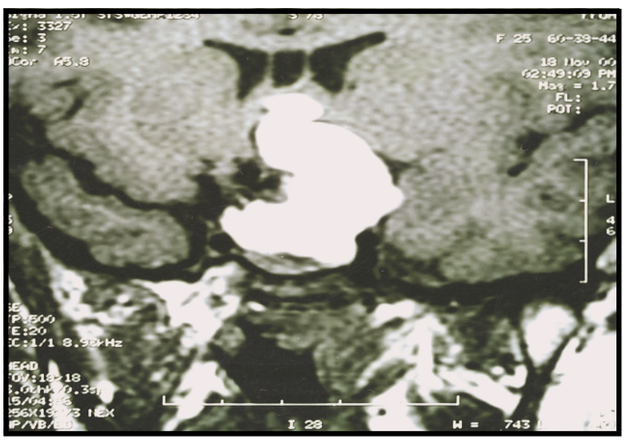

Figure 2 - Precontrast T1 magnetic resonance imaging coronal scan delineating the lesion and showing the upward extension of the tumor. There is an incidental cavum septum pellucidum.

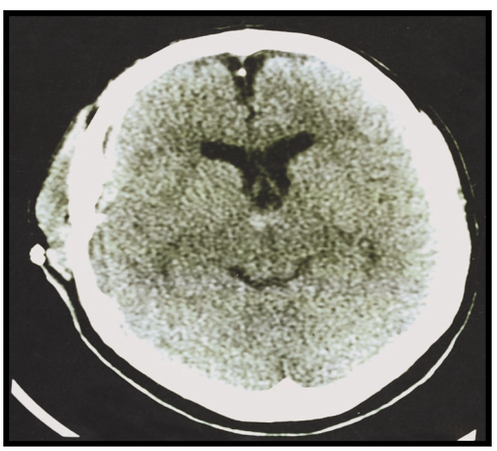

Figure 3 - Postoperative computerized tomography scan showing complete removal of tumor.

regrowth of tumor as appeared in the follow up CT and MRI scans or both even if the initial excision was subtotal. Follow up notes were reviewed and the patient's clinical, endocrinological and radiological findings were documented. The outcome of treatment was considered good (if the patient is alive, having stable useful vision, good school performance or can cope with his job, poor (if not fullfilling the above criteria), and dead.[7-9]

Data were entered into data sheets using SPSS version 9, and analysis of variants and bivariate analysis was carried out looking for factors that correlated with the outcome. Results were considered significant if the P = 0.05 or less.

Results. The study included 18 patients, 7 patients were males and 11 were females, their age ranged from 1-55 years with a median age of 24 years (mean 23.3). Eleven patients (61%) were Saudi, and 7 (39%) were non-Saudi. The duration of symtoms ranged from 2 weeks to 7 years with a median of 13 weeks. **Table 1** summarizes the clinical and radiological findings of the patients. The pterional craniotomy was the approach used in 16 patients (89%) and the subfrontal approach was used in 2 cases (11%). One patient had initially trans-sphenoid drainage of the cyst, 6 months later he had tumor recurrence that was treated through a pterional approach. Gross total resection of the tumor was achieved in 3 cases (17%) and STR was carried out in 15 (83%) cases. Histologically, in all of our cases the CRF were described as adamantinomatous and squamous papillary type was identified. Early postoperative complications included chemical meningitis in 2 patients, hemiparesis in 2 patients (was transient in one patient), persistent hydrocephalus (needed shunt) in 3 patients, and wound infection in one patient. Eleven patients (61%) needed permanent hormone replacement Desmopressin, 1-desamine-8-D-arginine-vasopressin (DDAVP) in 9 patients, hydrocortisone and thyroxin in 7 patients). Regrowth of tumor was detected in 9 cases (50%), 75% of tumor recurrence were in children. Postoperative radiotherapy was given to 7 (39%) cases. The follow up period ranged from 1-7 years (median was 36 months). The outcome was good in 10 patients (56%), poor in 6 patients (33%), and 2 patients died (11%), the first patient died 2 days after surgery from severe hypothalamic dysfunction following GTR of the tumor, and the 2nd patient died one and half years after surgery from persistent hypothalamic dysfunction.

Discussion. Although benign neoplasm, CRF has an aggressive course and still represents a formidable challenge to neurosurgeons and cure is difficult to achieve. Despite the advances in diagnosis and treatment, no single mode of treatment has proved to be uniformly satisfactory. The incidence of CRF is high in children, less than 50%

Table 1 - Clinical and radiological features at presentation.

Features	N (%)
Clinical Features	
Reduced vision	12 (67)
Unilateral	2 (11)
Bilateral	10 (56)
Total blindness (both eyes)	5 (28)
Optic atrophy	9 (50)
Papilledema	3 (17)
Raised ICP	9 (50)
Endocrinal disturbances*	6 (33)
Seizures	3 (17)
Hemiparesis	1 (5.6)
Radiologic Features	
Pre-chiasmatic	8 (44)
Retro-chiasmatic	7 (39)
Pre & retro-chiasmatic	3 (17)
Calcification	15 (83)
Cystic only	4 (22)
Solid only	1 (5.6)
Mixed solid & cystic	13 (72)
Extension to posterior fossa	2 (11)
Extension to middle & posterior fossa	2 (11)
Dilated ventricles**	9 (50)

* Two patients had short stature one of them had undeveloped secondary sexual characters, one patient had infertility and diminished libido and 4 had reduced T4 and cortisol. **Three patients required ventriculo-peritoneal (V-P) shunts after tumor excision, one of them had bilateral shunts, ICP=intracranial pressure, N-number

Table 2 - Factors affecting the outcome.

Clinical Parameter	Outcome Good	Poor	Dead	Significance
Age				
Child	2	5	0	0.02
Adult	8	1	2	
Sex				
Male	4	2	1	0.9
Female	6	4	1	
Nationality				
Saudi	6	4	1	0 .9
Non-Saudi	4	2	1	
Appearance				
Cystic	1	2	1	0.02
Solid	0	0	1	
Mixed	9	4	0	
Location				
Pre-chiasmatic	6	2	0	0.04
Retro-chiasmatic	4	1	2	
Both	0	3	0	
Hydrocephalus				
Present	4	4	1	0.6
Not present	6	2	1	
Extent of excision				
GTR	3	0	0	0.2
STR	7	6	2	
Radiotherapy				
Given	3	3	1	0.7
Not given	7	3	1	
Recurrence				
Documented	3	6	0	0.008
Not documented	7	0	2	

GTR=gross total resection of the tumor, STR=subtotal resection

of CRF's occur in children, however it can occur in old age up to 70 years, and it has equal sex distribution.[1,3] In the present study, 44% of tumors occurred in children and there was a strong correlation between the age and outcome of patients in our series (P0.02), as 28% of the child group had good outcome while 72% of the adults had good outcome. The reported outcome is better in adults than children, as the tumor recurrence is more common in children (75% versus 25% in our series), radiotherapy is better tolerated by adults than children and adults often had long-lasting benefit from combined surgery and radiotherapy.[10-12] In addition it is well documented that once recurrence occurs, the course of the disease changes dramatically and progressively.[7,13]

In the present study, loss of vision was the most frequent presentation, and it was unusually higher, (67%), than what is reported in the literature. The reasons for the increased incidence of loss of vision in our series could be attributed to 2 factors; first the delay in presentation and the 2nd is that 11 patients (72%) had tumors in the prechiasmatic region. Yasargil[14] has attributed the visual deterioration to 2 factors, the first is due to stretch of the optic nerves by the growing tumor underneath pushing them against the tough dura of the optic canal, and the 2nd is due to the pincer action on the chiasm (being pushed from below by the tumor against the anterior cerebral arteries crossing over the optic chiasm).

Comprehensive preoperative neuroimaging is essential before surgical removal of CRF. It provides the neurosurgeon with a road map that enables complete removal of the tumor.[15] Computerized tomography scan was carried out in all cases included in our study, it clearly showed the nature of the lesion (solid or cystic) as well as calcification (83% of cases). The contrast enhanced scans showed clearly the solid portion of the tumor as well as the cyst wall. The preoperative diagnosis of our cases was based primarily on the CT findings. Recently (last 3 years), MRI scan was carried out in all cases. The T2 axial, and T1 contrast enhanced coronal and sagittal views showed the exact extension of the tumor and its relation to the surrounding arteries as well as the tumor-brain interface. Most neurosurgeons[2,10,11,16-19] agree that total removal of CRF is the best modality of treatment and offers the best chances of cure, however the extent of invasion of the tumor as well as the surgeon's expertise will determine whether GTR is feasible or not, taking in consideration the associated significant morbidity. The surgery in most cases was carried out using the pterional approach. The pterional approach was found adequate in all cases. By splitting the Sylvian fissure widely the tumor was fully exposed except into cases where the tumor has grown up into the posterior part of the 3rd ventricle. Only 3 patients had GTR as confirmed by postoperative imaging. In the rest of the patients, it was felt by the operating surgeon that total removal is hazardous; as it was difficult to dissect the tumor of the surrounding arteries and optic pathways, and its capsule was firmly adherent to the hypothalamus. Although 15 patients had STR only 7 of them had postoperative radiotherapy, the reasons for not giving radiotherapy to the remaining 8 were, one patient was one year old, one patient had poor general condition to have radiotherapy, 2 patients were thought to have GTR, and the rest were non-Saudi patients where there were difficulty in referring them for radiotherapy.

The outcome of treatment of CRF is well described in the literature, however there are wide variations. Most large series report mortality rates of 5%-10%.[1] Reports of good results[2,3,10,11] range from 60%-70%. In Yasargil series, considered as the largest personal series in the literature, the long-term (20 years) survival was 90% after primary surgery and 60% after re-operation, and the recurrence rate in his series was 7% after complete removal (lowest reported recurrence rate).[20] Choux et al,[21] in the multi-center study of 474 children, reported 4% surgical mortality for primary surgery and 13% after secondary radical surgery. Although CRF's are radiosensitive tumors, many neurosurgeons,[2,13,20] recommended not giving radiotherapy after total tumor removal confirmed by imaging. A small fleck of calcification without enhancing tumor was considered as total resection.[13]

The mortality rate in our study was 11% (2 patients). Fifty six percent of our patients had good outcome while 33% had poor outcome. The poor outcome in our series could be attributed to the delay in presentation, low rate of total excision, difficulty in referring non-Saudi patients for radiotherapy, and to the recurrence of tumor. The recurrence rate in craniophyngioma ranges from 10%-90%.[7,13,22] It depends mainly on the amount of resection, which is determined by the surgeon's judgement during surgery and on whether post-operative radiotherapy was given or not. For surgery alone without post-operative radiotherapy, the reported recurrence rate is 7%-25% after GTR confirmed by post-operative imaging.[13,20] Hoffman 1992[8] reported 34% recurrence rate in patients he felt had complete resection. Recurrence is unavoidable after STR alone without radiotherapy, usually it occurs after a short period of tumor quiescence.[7,10,11,13,20,22] Wara et al[22] reported a 95% 5-year survival after STR and radiotherapy, and 78% at 15 years. However, they did not comment on the quality of survival in their series. Choux reported a recurrence rate of 19% after GTR, 30% after STR followed by radiotherapy and 57% after STR alone (30% overall recurrence rate).[21]

Fifty percent (9 patients) of our patients developed recurrence, all had STR but only 44% had post-operative radiotherapy due to the above-mentioned reasons. The hazards of radiotherapy especially in

children should not be forgotten. It includes, cognitive impairment, secondary tumors, Moya Moya vasculitis, panhypopituitrism, and cranial nerve neuropathy and radiation necrosis of the brain.

Analysis of the clinical and radiological factors that might affect the outcome of our cases showed that the age is significantly correlated with the outcome, adult had better outcome than children, (P 0.02). The tumor appearance and location as seen in the scans were also correlated with the outcome, invasive tumors extending to both pre- and retro-chiasmatic regions had poor outcome (100%) than tumors located only in the pre-chiasmatic region (25% poor outcome), due to attachment to the hypothalamus (P 0.04). **Table 2** shows factors affecting the outcome.

From our series which included patients from different regions in the KSA, we could see that there was significant delay in referring patients for treatment (67% had significant deterioration of their vision, and 28% had complete blindness). Regular follow-up of CRF patients is essential for early detection and treatment of tumor recurrence. Complete pre- and post-operative hormonal assessment is necessary in the treatment of patients with CRF.

In conlcusion, craniopharyngioma are benign tumors, however they can cause significant visual and endocrinal problems. Ophthalmologists and Pediatricians should be aware of the clinical presentation so that they can early diagnose the tumor and refer patients to specialized centers for treatment. Total resection of the tumor should be the goal of the Neurosurgeon as it offers the best chances of cure.

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