ORIGINAL ARTICLE

Craniopharyngioma Total or Near Total Surgical Resection: An outcome based learning experience

Saeed Mazher[1], Junaid Ashraf[2]

ABSTRACT

Background: Craniopharyngiomas are benign slow growing tumours that are located within the sellar and para sellar region of the central nervous system. It is a rare but significant health problem in Pakistan. The point prevalence of this tumour is approximately 2/100,000.

Objective: To determine the outcome of complete resection in patients with craniopharyngioma and to determine the relationship of different factors with outcome at 3 months of follow up.

Methods: A case series study conducted in thirty five patients, who were diagnosed as cases of craniopharyngioma on the basis of history, clinical examination, CT and MRI appearances and histopathological examination. All patients underwent complete resection of craniopharyngioma. The study was conducted at the Department of Neurosurgery, Dow University of Health Sciences/ Civil Hospital, Karachi from 27thth December, 2006 and 27th December, 2007.

Results: Good outcome was seen in thirty four (97%) patients, one (3%) had poor outcome in term of mortality. Age, Preoperative presence of neurological deficit, localization of the lesion and preoperative hydrocephalus just before placement of VP shunt and radical excision were the most important predictor of good outcome. The rest of factors studied such as Glassgow coma, duration of illness, and signs of meningeal irritation postoperative hydrocephalus had no effect on outcome.

Conclusion: A complete excision of the tumour is recommended, if there is no hypothalamic invasion and in the presence of hypothalamic invasion, near total resection with post-operative radiotherapy. Endocrine disturbances need careful follow up and replacement.

KEY WORDS: *Craniopharyngioma, Radiotherapy, Sellar And Para Sellar Region, Complete Resection, Outcome.*

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INTRODUCTION

Craniopharygiomas, which account for 3% of intracranial neoplasms. Craniopharygiomas are benign tumors developing from remnants of the embryonic craniopharyngeal duct .Though present from early fetal life, they present with symptoms related to pressure on local structures or raised intracranial pressure and demonstrate a bimodal distribution of age at presentation, the first peak being between 5 and 14 years and the second at 50-74 years. They are rare (incidence 0.13 per 100,000 people per year).[1]

Initial management is surgery to remove the tumour, followed, if indicated, by radiotherapy. A small proportion of patients are managed with more conservative measures such as cyst aspiration, followed by radiotherapy with or without shunt insertion. There is still controversy with respect to what is the optimum treatment.[2, 3]

A high proportion of patients have endocrine defects before and after surgery due to damage to the anterior pituitary and distribution of communication between the hypothalamus and pituitary.[4] Complete excision can be technically very difficult and recurrence may occur, the cumulative incidence of recurrence after 10 years being 33% with about one in 10 patients eventually dying of the tumour.[5] Because Craniopharygiomas are usually sited in the region of sella turcica, tumour growth may cause neurological and/or endocrine symptoms. Early complications consisted of diabetesinsipidus {24cases(75%)}, hyponatremia {six cases(19%)}and hypernatremia {five cases(15.5%)}.Late post operative complications included 15 cases of tmour recurrence (46.8%),nine cases of panhypopituitarism (28%),hydrocephalus in nine patients (28%), hypophagia in four patients (12.5%).[6] The most frequent complaints were headache and vomiting (74%).The main endocrinological complaints were polyuria, polydipsia (15%) and lassitude (10.6%).Although short stature was a symptom in 9.1% of patients, it was a finding in 39.7% of patients. Plain skull X-rays raised the suspicion of intracranial tumour in more than 90% cases.[7]

The actual term craniopharygioma was coined by Charles Frazier in 1931 and was popularized by Harvey Cushing 1932.[8]The middle cranial fossa has a median portion and two lateral compartments. The median part is formed by the body of the sphenoid which is followed out to form the pituitary fossa (the sella tursica).Anteriorly a tranverse ridge, the tuberculum sellae, separates the fossa from the shallow optic groove which leads to the optic canal on each side. Posteriorly a plate of bone, the dorsum sellae, projects upwards and forwards; its two corners are the posterior clinoid processes. On each side of the fosse a shallow carotid groove leads posteriorly to the foramen lacerum. The body of the sphenoid contains the sphenoidal air sinuses lies under the pituitary gland and cavernous venous sinuses and above the nasopharynx[9]. Almost all of these tumors have both solid and cystic portions, and even portions that appear densely calcified on diagnostic studies usually contain small cysts. The fluid in these cysts may be yellow, light tan greenish, dark black (machine oil) or even milky white. The range of viscosity is wide from watery to sludge like. Cystic Craniopharyngioma fliud contains suspended cholesterol crystals, which can be recognized by their characteristic birefringency[10].Craniopharyngiomas produce symptoms like headaches, nausea, and projectile vomiting. Headaches were usually bifrontal or frontotemporal, throbbing, progressive, and associated with retroorbital pain in patients with visual deficiencies. Headaches without a coexisting endocrine disturbance were uncommon in association with Craniopharyngioma (7%). [12]

Clinical features essentially include visual disturbances, endocrine deficiencies, and neurological signs. The vast majority of craniopharyngiomas are located in the suprasellar region and most commonly present with symptoms of visual problems, headaches, and pituitary dysfunction. The perichiasmal location of craniopharyngiomas results in visual dysfunction (such as blurred vision, hemianopsia, or polymorphism) at the time of presentation in 40% to 70% of patients. Chen and colleagues found that in children[13] the visual symptoms usually presented after a history of systemic symptoms, whereas in adults the visual symptoms were usually the initial manifestation of the disease. Recognition of visual dysfunction in children is often delayed until serious damage to the visual pathways has already occurred Tumor growth can also result in compression of the third ventricle, presenting with signs of increased intracranial pressure as well as hypothalamic dysfunction. Fifty percent of

patients with craniopharyngiomas complain of severe headaches. Other signs include vomiting and papilledema, and, in rare cases, children have presented with acute alterations in consciousness.Endocrine dysfunction is present in 80% to 90% of children with craniopharyngiomas, but rarely do patients present with such symptoms Adults with growth hormone deficiency both isolated and with hypopituitarism, have features of metabolic syndrome including excess abdominal adiposity, insulin resistance and dyslipidemia this has been implicated in increased cardiovascular mortality.[14]

There are two main management pathways with regards to the treatment of the tumour. The first involves attempted gross total resection of the tumour [18, 19, 20], the second approach is for more limited surgery, aimed at debulking the tumour to reduce the mass effect on the optic pathways and to re-establish the cerebrospinal fluid pathways, followed by radiotherapy.[21]

The second pathway was developed because of the high morbidity experienced with the gross total resection of tumours that invade the hypothalamus.[22] The morbidity can be considered in terms of hypothalamic dysfunction and an altered neuropsychological profile.[23] In an attempt to balance the advantages of an aggressive surgical resection against the risk of significant morbidity associated with this, a pre-operative grading system has recently been proposed that considers the extent of invasion of the hypothalamus by the tumour as opposed to the traditional anatomical localisation. In recent large adult series only about 50% of patients are having a gross total resection, which is similar to pediatric series, because of the recognized significant morbidity associated with surgical injury to the hypothalamus[24]. The management options for these tumours also include the stereotactic placement of a catheter to allow repeated aspiration. Furthermore, the use of intracystic radiotherapy (Yttrium-90 or Phosporus-32) or chemotherapy (Bleomycin) has had some success.[25]

The purpose of this study is to observe surgical outcome. Firstly to analyze all surgical cases of craniopharyngioma as well as the various methods used to attain best surgical prognosis in the department of Neurosurgery of Dow Medical College and Civil Hospital, Karachi over a period of one year.

METHODOLOGY

This study was conducted in the Department of Neurosurgery, Dow University of Health Sciences/ Civil Hospital, Karachi**.** One year and two weeks between 27th[th] December, 2006 and 27[th] December, 2007. All the patients coming with Craniopharyngioma are included in the study duration with minimum of 35 cases. The applied technique was Non probable purposive sampling. Patients of all ages of either sex proven to be of Craniopharyngioma based on history, clinical features, CT / MRI appearances were included in the study. While patients with Non Craniopharygeal masses like other sellar and supra sellar masses and who are not operated due to any reason were excluded. The study design was Case Series. Surgical outcome means effect of response of complete resection in terms of early and late complications and mortality. Early complications (within 24hrs to 7 days) like death secondary to bleeding, diabetes insipidus and hyponatremia. Late complications from (7 days till 3 months) such as electrolyte imbalance, infection, convulsions, thermodysregulation, panhypopituitarism and death.

After detailed history and clinical examination, patients were admitted and subjected to routine laboratory investigation to assess their fitness for surgery that include CBC, BSR, Urea, Urine DR, CXR in all patients and creatinine, electrolytes and ECG when indicated. Afterwards patients were asked to get their full visual assessment in eye department meanwhile patient's hormonal assays (growth hormaone, morning cortisol levels and thyroid profile) were send for assessment of the hormonal status. Then patients were given preoperative medications according to the requirement such as steroids/mannitol if marked symptoms of raised ICP and peri tumoral edema is evident. Anti epileptics if there is positive history of fits. One dose of prophylactic antibiotic was given, in the morning of the day of surgery. All operations were performed in the supine position under general anesthesia. There were two approaches used one was transcranial and the other one was transsphenoidal. In cases of large craniopharnygioma extending out of the sella transcranial approach was used. On the other hand small lesions were excised through transcranial route. In transcranial route head fixed in a May field then (frontal) Operative area washed with pyodine solution and covered

around with drapes. Head positioned is adjusted in such a manner so that least retraction required, subfrontal flap incision given, skin and bone flaps elevated. To slag down the brain the CSF is aspirated. With the retraction of frontal lobes we approached to the sellar area near by neurovascular region. Excision of the lesion done under operating microscope while avoiding any insult to stalk, hypothalamus and other vital structures like neurovascular apparatus. Good hemostasis achieved. Closure done. Postoperative care included fluid and electrolyte monitoring and replacement. If the urinary output exceeded by 200ml per hour, patients were given desmopressin through intramuscular or nasal route. In the first post operative day serum electrolyes and urine DR (sp gravity) were observed every six hourly then next it was shifted to twelve to twenty four hourly according to the severely of diabetes insipidus. In the first twenty four hours patients underwent postoperative CT SCAN Brain to exclude hemorrhage, hydrocephalus, brain edema and residual lesion if remaining. Patients were discharged when they no longer required parenteral desmopressin usually within one to two weeks.

Follow up has been taken at one month, second month and third month after complete resection in the tumour outpatient clinic. Patients were assessed for early and late complications. The main outcome measures were post operative complications neurological status and mortality.

Patients with Craniopharyngioma admitted through outpatient department or emergency at Neurosurgery Department, Civil Hospital Karachi will be included in this study after taking informed consent. The diagnosis of Craniopharyngioma based on history of patients, clinical features, CT and MRI appearances. History of patient will be taken to determine the age, the volume and the localization of the mass and quality of life considerations. All patients were examined clinically just before complete resection to assess the preoperative neurology. All patients fulfilling the inclusion criteria will be underwent a complete under general anesthesia. Patients were followed up at 1^{st} month, 2^{nd} month, 3^{rd} month interval in the outpatient department to determine the complications.

The whole data will be collected on a proforma specially designed for this study in consultation with the experts. After collection of proforma, the data was entered in SPSS (Statistical programme for Social Sciences) version 11. Frequencies and percentages of early and late complications in operated patients were analyzed. Age, preoperative neurological status and localization of the lesion were compared with complications for evaluation of their impact on the final outcome.

RESULTS

A total of 35 craniopharyngioma patients were treated by gross total resection from 27^{th} of December 2006 to 27^{th} of December 2007.Out of these 25 patients were males and 10 were females, their age ranged from 4-51 years with a median age of 19 years (mean 21.63) and standard deviation of 13.42 Figure 2. Most common presentations were with neurological sign and symptoms such as visual symptoms (65.7%), raised ICP (37.1%), hormonal disturbances (22.9%) and fits (2.9%).

The duration of symtoms ranged from 1 month to 15 months with a median of 1.37 about 71% had the duration of 1 to 5 months, 20% were having symptoms for 6 to 10 months and 9% were with symptoms for 11 to 15 months. The subfrontal approach was the approach used in 30 cases (85.7%) and the transsphenoidal approach was used in 5 cases (14.3%). Complete resection of the tumor was achieved in all cases. Histo1ogically, in all of our cases the craniopharyngioma were described as adamantinomatous and squamous papillary type was identified.

The most frequent findings were related to the visual pathways. Papilledema, bitemporal hemianopsia and optic atrophy were frequently observed. There were about 37% patients who had neurological deficit present at the time of presentation. (Table 1)

Tumour localization data were gathered in 35 patients. Tumours were located in the sellar, suprasellar and parasellar regions of 9, 13 and 13 number of patients respectively. Hydrocephalus was present in 37.1% of patents. Moreover the data about the extent of removal was maintained in all patients. The tumour had been removed totally in 28 and near totally in 7 patients due to inoperable extension of the

lesion. In patients with gross hydrocephalus ventriculoperitoneal shunt placement was done in about 13 cases before removal of the tumour. There were seven patients received external conventional radiotherapy after a median of 2.5 months from the operation. No patient had received radiotherapy before the operation.

Most of the patients stayed in hospital department for few weeks and out of 35 patients of the series one died within one week after operation. The remaining 34 were followed up until 3 months. During follow-up documented observed early complications were diabetes insipidus in 24 patients, hyponatremia in 5 patients (was transient in one patient), and wound infection in one patient. Twenty four patients (68%) needed transient hormone replacement Desmopressin, hydrocortisone in all patients. Three of the patients had growth and thyroid hormonal disturbances in each. Therefore they were followed in our tumour clinic and referred to the endocrinologist for dose adjustments and monitoring. Postoperative radiotherapy was given to 7 (20%) cases. The follow up period ranged from 1-3months (median was 2 months). The outcome was good in terms of mortality as only one patient died (2.8%). It was poor in term of early complications as present in about twenty nine patients (82%) (Figure 3) but they were treated successfully. About 90% patients showed development and improvement. The cause of the death on the same day of surgery was severe hypothalamic dysfunction following the resection of tumor recurrence. Whereas late Postoperative complications included hydrocephalus in four Patients (Figure 4), panhypopituitarism in eight patients and no late death.

In patients age ranges were seen according to the complications and it was noted that in the age group of 11-20yrs complications were mostly seen, while in the age group of 21-30 complications were second most commonly observed. Complications were least likely found in extreme age groups.

Similarly in the study, patients with neurological deficits were observed in relation to the complications and it was noted that positive preoperative neurological deficit had some correlation with the presence of postoperative complications.

Lastly complications are increasing with the extension of sellar lesion out of sella which was found in seeing the complications according to the tumour localization by MRI (Table 2). This can be due to compression symptoms of the lesion or delay in presenting to the neurosurgical experts.

Figure 1: Male Female Ratio/ gender distribution (N-35)

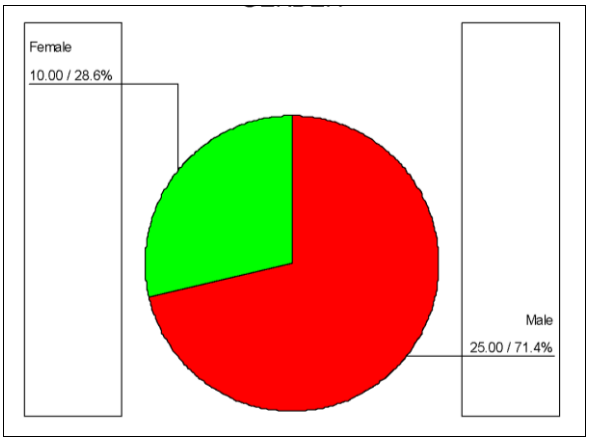


Figure 2. Age Distribution

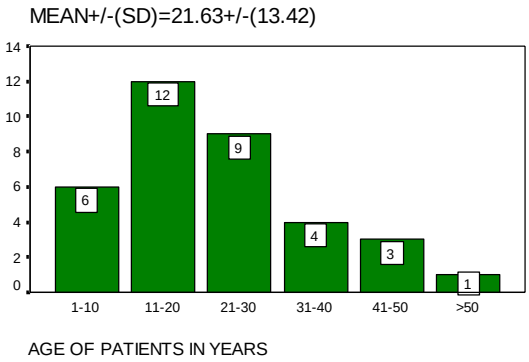


Table 1. Neurological Deficits

Neurological Deficit	Frequency	Percent
Present	13	37.1
Absent	22	62.9
Total	35	100.0

Table 2. MRI Findings with Respect to Complications

MRI Brain	Complications Absent	Complications Present
Sellar mass	3(50%)	6(21%)

Suprasellar mass	2(33%)	11(38%)
Parasellar mass	1(17%)	12(41%)

Figure 3. Complications

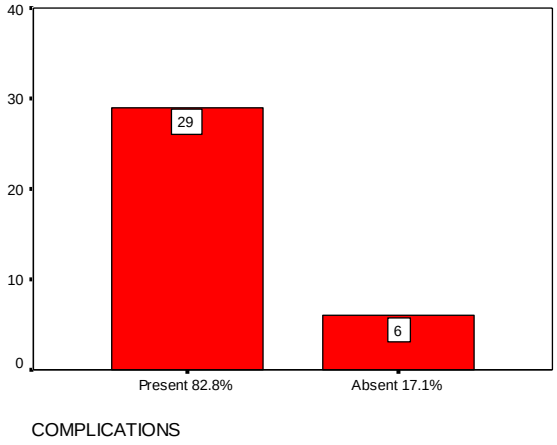
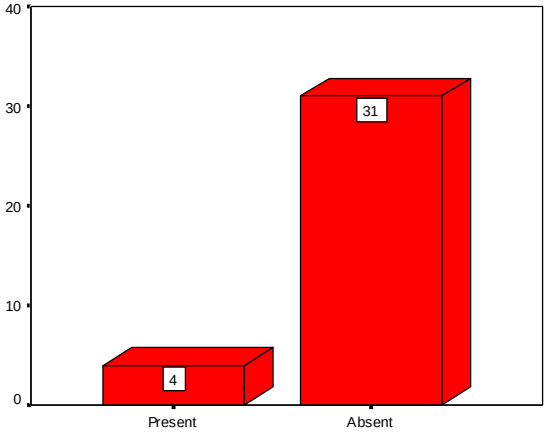


Figure 4. Post-operative Hydrocephalus



DISCUSSION

This study describes results of near total surgical excision of caraniopharyngioma including early and late complications. Craniopharygioma is the third most common tumour in children. It is histologically benign tumour but can behave aggressively and the recurrent rate is high. Due to its localization, close to the visual pathways, hypothalamus and pituitary hormone numerous sequelae, including multiple pituitary hormone insufficiency, hypothalamus dysfunction and visual impairment[7]. Craniopharygioma accounts for between 1.7 and 4.6% of brain tumours, with peak incidence between the ages of 6 and 14 years. The youngest ever reported was a neonate presenting with obstructive hydrocephalus reported[9]. his tumour also appears in older age groups and almost 60% of the cases are found in adults[5]. The mean age of our patient population was 18.3.

In our study the mean age was 21.63. Six percent of cases occur in the first decade of life, twelve percent in the second decade, three percent in fifth decade and one percent in sixth decade. In our study the oldest patient was 51 years. Whereas in the international study published in European journal of cancer of care 2004.Twenty two percent of cases occur in the first decade of life 29% in the second decade, 8% in the sixth decade 3% in the seventh decade in one study, the oldest patient was 70 years old Among adults a predominance of cases has been reported in men 64.6% and 34% were women.[6] Similarly we had male predominance of 71.4% and 28.6% were females in our study.

In previous international study the predominant symptoms were endocrinological in 93% of children while in our study we had more prominence towards visual symptoms which was in 65% cases second common presentation was symptoms of raised intracranial pressure in 37% and hormonal disturbances were found in 22.9% cases as our study was not specific for children we had all patients with any age and of either sex.

According to surgical experience of 309 cases of craniopharygioma in China[26] they concluded that pre-surgery neuroimaging evaluations have improved our knowledge of intricate anatomical relationship between craniopharyngioma and the structures of the hypothalamus, pituitary stalk, and optic apparatus, which make total tumor resection feasible with the preservation of these vital structures to ensure a lower recurrence rate with acceptable mortality.

In our study neuroimaging helped in evaluation in terms of preserving vital structure and surgical planning. As far as tumour recurrence is concern our study has limitation because it requires a long term follow up and retrospective data has more significance in this regard which is beyond our spectrum. Although we had lower mortality of 2.8% (graph 10) in comparison to other international study, conducted at Hacettepe University Turkey, which was 23.6% but solely in

pediatric age group. Most large series reported mortality rates of 5%-10%.While in Yasargil series, considered as the largest personal series in the literature, the long-term (20 years) survival was 90% after primary surgery and the mortality was 4%.There were two more large studies conducted in china on 309 and 284 craniopharyngioma patients, recently published reported 2% and 3 % mortality respectively. One percent mortality had also been reported in one of the studies conducted at King Khalid hospital Kingdom of Saudia Arabia.

Craniopharyngioma tend to have suprasellar location 90%; however 18% of craniopharygioma extend in to the sella and 5% of these tumours are purely intrasellar these tumours can also extend to the anterior, middle and posterior cranial fossa rarely craniopharygioma arise primarily in unusual lacations such as the nasopharynx sphenoid bone third ventricle the cerebellopntine angle and within the optic chiasm it may be solid or cystic more commonly mixed. Calcification, cyst formation and intravenous contrast enhancement in a suprasellar and intrasellar mass are the hallmarks of craniopharyngioma in CT. Computed tomography is superior to MR in detecting calcifications, but MRI preferred in the evaluation of a tumour's extent for therapeutic planning[15] .

Similarly we had craniopharygioma purely intrasellar in 25.7% rest of all were having extra sellar extensions like suprasellar and parasellar, with the involvement of neighbouring structures among 74.2% in aggregate.

Although benign neoplasm, craniopharygioma 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. There was another study carried out on craniopharyngiomas patients, treated at King Khalid University Hospital, Riyadh, Kingdom of Saudia Arabia which included 18 patients. They comment that most neurosurgeons agree that total removal of craniopharyngioma 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 gross total resection is feasible or not, taking in consideration the associated significant morbidity. The surgery in most cases was carried out using the pterional approach[27].

However we preferred sub frontal approach and it was found adequate in our most cases however in few cases we required lamina terminalis approach to accomplish difficult complete excision. In cases where the extrasellar involvement was absent or minimal we had approached the tumour through transphenoidal route.

In a retrospective study performed, 73 of the 121 patients evaluated had a good outcome, with a mean follow-up period of 10 years. Good outcomes were associated with survival at the follow-up examination; the absence of major motor deficits related to treatment or tumor progression; functional vision; a Katz grade of A, which denotes independence and not requiring any supervision in feeding, continence, transferring, using the toilet, dressing, or bathing; school status at no more than 1 year behind the expected grade or employability for an adult of working age; the absence of incapacitating psychological or emotional problems; and a Karnofsky Performance Scale (KPS) score of at least 80. The KPS is an assessment tool for evaluating functional status or impairment that is widely used by clinicians. It consists of an 11-item rating scale, with scores that range from 100 (normal function) to 0 (nonfunctional or dead).

In a study performed on 143 patients underwent endocrinological testing before and after surgery[12]. Ninety-two patients had a transcranial approach, while 35 patients had a transsphenoidal approach. (The remaining 16 patients underwent limited procedures such as stereotactic-guided cyst puncture or CSF shunt placement.) Panhypopituitarism increased from 10.9% before surgery to 34.8% after surgery for those treated transcranially; the increase was 40%-42.9% for those treated via the transsphenoidal approach. Honegger et al. concluded that there was no significant difference in the DI occurrence between the two groups. Regardless of the surgical approach, DI is an expected consequence of craniopharyngioma resection

In general, the prognosis for patients with craniopharyngioma is good, with an 80-90% chance of permanent cure if the tumor can be completely removed with surgery or treated with

high doses of radiation. However, the prognosis for an individual patient depends on number of factors including the ability of the tumor to be completely removed, and the neurological treatment, and most of the treatment of total resection is the best chance for cure.

CONCLUSION

The study revealed that radiographically total excision of even large craniopharyngiomas can be safely achieved by one or a combination of several advanced microsurgical techniques, sometimes by radiotherapy if might not excised completely and staged strategy. Major morbidities can be avoided, although moderate deficits and hormonal imbalances caused by the tumor and the treatment. Most of the problems with hormones and vision do not improve with

morbidities occur and require management with close follow up. Moreover we can protect the hypothalamic structures and its perforating arteries by choosing surgical approaches according to the location of craniopharygioma relative to the third ventricular floor and it is critical to deal with dehydration and endocrine disorders for a sound outcome of craniopharyngioma surgery. In other words for achieving best outcome it should be a multidisciplinary effort by neurosurgeons endocrinologists ophthalmologists and oncologists.

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