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Université Sidi Mohamed Ben Abdellah

كلية الطب والصيدلة

FACULTÉ DE MÉDECINE ET DE PHARMACIE

PRISE EN CHARGE CHIRURGICALE DE CRANIOPHARYNGIOME

Mémoire présenté par

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OUTLINE

DEDICATION

First i would like to thank Professor Mohammed El Faiz Chaoui for accepting me into neurosurgical training and fatherly guidance he has shown through out the training in the department of neurosurgery. I would also particulary mention Professor Chakour khalid for going an extra mile in giving us dissection sessions, Professor Benzagmout Mohamed for his constant guidance on the subject of this memoire and Professor Lakhdar for his constant guidance in the department and not forgetting Professor Aggouri mohammed.

I would like to thank my wife Ellah and my two sons Malcom and Gregory as they have been the source of inspiration throughout my study period 2014 uptill now 2019. To my bigger family i hold the words of my two brothers , Macdonald has humbled himself despite holding a Phd himself to say i have gone further academically in the family and he feels proud, and Joseph who just said this neurosurgical training is for all of us and we need it the soonest. And i always laugh when my strong mother treats me as a baby upto now. To everyone i say thank you and the list is endless. But suffice to mention Professor majid Samii for the Africa 100 project initiative of which i partain to the first crop of the products and Professor abdussalam Khamlich our local coordinator for running a successful programme and being a father figure. Am really humbled to come this far and i promise to continue learning, and inspiring others to take up the carieer in neurosurgery especially in my country Malawi.

I would Lastly dedicate this work to my Late father Joseph Male Ndekha 'may his soul rest in eternal piece' who had constantly been an inspiration to my academic life, he was committed from my early age to see that i realise my full potential and his demise was a big blow but he will always remain my un sang hero.

LIST OF ABBREVIATIONS

ACTH : Adreno-Corticotropic Hormone

CT : Computed Tomography scan

CRH : Corticotropin Realising Hormone

DDVAP : D-amino-D-arginine Vasopressin

IGF1 : Insulin Like Growth Factor 1

ITS : Information Technology Systems

FSH : Follicle Stimulating Hormone

ETV : Endoscopic Third Ventriculostomy

ICB : Intracystic Bleomycin

ICP : Increased intracranial pressure

GH : Growth Hormone

GTR : Gross Total Resection

LH : Luteinizing Hormone

MRI : Magnetic Resonance Imaging

PL : Prolactine

STR : SubTotal Resection

TSH : Thyroid Stimulating Hormone

T3 : Tri-iodothyronine

T4 :Tetra-iodothyronine

VPS : Ventriculo-peritoneal Shunting

INTRODUCTION

Le craniopharyngiome est une tumeur rare, représentant environ 1% de l'ensemble des tumeurs intracrâniennes chez l'adulte et 5% chez les enfants. Il s'agit d'une tumeur bénigne en général classée grade 1 dans la classification de l'OMS 2016. Sa malignité relève de sa localisation au voisinage des structures neuro-vasculaires vitales, rendant ainsi difficile son exérèse chirurgicale avec un fort taux de morbi-mortalité. Il n'y a pas de présentation clinique spécifique, et les signes retrouvés sont communs à d'autres lésions de la région sellaire.

Patients et Méthodes :

Notre étude est rétrospective portant sur 30 cas de craniopharyngiome opérés au service de Neurochirurgie du CHU Hassan II de Fès entre Janvier 2009 et Décembre 2018.

Résultats :

Notre série comporte 18 enfants et 12 adultes. La moyenne d'âge chez les enfants était de 6,6 ans [Extrêmes : 5 et 11 ans] et 40,6 ans chez les adultes [Extrêmes : 17 et 63 ans] avec un âge moyen de la population de 23,1 ans. Le sex-ratio était de 2 ♂ pour 1♀ pour la population pédiatrique et de 1♂ pour 2♀ chez les adultes. 67% des enfants présentaient des signes d'hypertension intracrânienne et la symptomatologie dominante chez les adultes étaient des troubles visuels. Des troubles endocriniens étaient aussi retrouvés dans les deux groupes. Tous les patients avaient bénéficié d'une exploration neuroradiologique (scanner et/ou IRM) et d'un bilan ophtalmologique en préopératoire. Vingt-neuf patients (96%) avaient subi la chirurgie exérèse. L'abord chirurgical fronto-ptérional était le plus utilisé chez 27 patients. L'exérèse chirurgicale avait été totale chez 19 patients. 16,7% de récidive avaient été enregistrés.

Discussion :

Le craniopharyngiome dérive des restes embryonnaires des cellules épithéliales de la poche de Rathke et du conduit craniopharyngien. Il n'y a pas de prédominance de sexe même si certains auteurs rapportent une prédominance masculine chez les enfants et féminine chez les adultes. Il y a 2 pics d'incidence entre 5 – 15 ans et 40 – 55 ans. Deux types histologiques ont été décrits, adamantin et papillaire squameux. La présentation clinique est dominée par des signes d'hypertension intracrânienne, les troubles visuels, les signes d'atteinte des structures de voisinage, notamment l'hypothalamus et l'hypophyse. Le traitement de choix est chirurgical.

Conclusion :

La chirurgie reste le traitement de choix des craniopharyngiomes avec une évolution favorable. Certains auteurs ont évoqué le rôle des traitements adjuvants notamment la radiothérapie pour les cas d'exérèse subtotale et l'injection intrakystique de bléomycine pour les formes kystiques.

ABSTRACT

INTRODUCTION

Craniopharyngioma is a rare sellar region tumor. It is common in young age group but it can occur in all ages. It comprises almost 1% of all intracranial tumors in adults and about 5% in Children. It is a benign tumor in general, WHO 2016 classification grade I but can be adherent to vital neurovascular structures. This makes its surgical extirpation cumbersome and curries significant morbidirty and mortality according to most series in the literature. Its clinical presentation is usually non specific and can mimic other intra-cranial space-occupying lesions.

METHODOLOGY

This is a retrospective series involving 30 craniopharyngioma patients treated in the department of neurosurgery at Hassan II University Hospital from January 2009 to December 2018.

RESULTS

There were a total of 30 files that were analysed comprising 18 children and 12 adults. The mean age in children was 6.6 years and 40.6 years in adults and total population mean of 23.1years. The age range was 5 to 11years in pediatric population and 17 to 63 in adults. And the sex ratio was 2 :1 in children, and 1:2 in adults. Majority of children (67 %) presented with signs of increased ICP while almost all adults 100% presented with visual symptoms. Other symptoms presented were endocrine disturbance and hypothalamic dysfunction. All patients underwent Brain CT scan and MRI for diagnosis and pre-operative planning. Twenty nine patients (96.4%) underwent surgery. In 27 Patients, the approach was either right or left fronto-pterional. Gross Total Resection was achieved in 19 (65.5%) of operated cases. The recurrence rate was 16.7%. The postoperative complications included

diabetes insipidus, and panhypopituitarism among others.

DISCUSSION

Craniopharyngioma arises from ectodermally derived epithelial cell remnants of Rathke's pouch and craniopharyngial duct.There is no significant sex predominance even though some studies have shown a male predominance in childhood and female predominance in the adulthood. It usually has bimodal age distribution, thus there is peak incidence at ages 5-15 and at 40-55 years. Has two major histological subtypes; Adamantinomatous and papillary types.It is often revealed by signs of Increased intracranial pressure, visual disturbances and mass effect on surrounding structures; pituitary gland and stalk, hypothalamus. Most patients were managed by surgery that achieved GTR in more than half of our cases. No patients in our study benefitted from postoperative radiotherapy nor intra-cystic Bleomycin despite the extent of resection and the recurrence rate did not seem to defer.

CONCLUSION

Surgery constitutes the main treatment for craniopharyngioma with good outcome. However In view of recent published data there is need to integrate other treatment modalities like; Subtotal Resection with adjuvant radiotherapy or in case of recurrence and Intracystic Bleomycin for mainly cystic tumors.

Key words: Craniopharyngioma, increased intracranial pressure, MRI, surgery, prognosis

INTRODUCTION

"Craniopharyngioma" was the name introduced by Cushing for tumors derived "from epithelial rests ascribable to an imperfect closure of the hypophysial or craniopharyngeal duct". Craniopharyngiomas are relatively uncommon tumors (approximately 1% of all intracranial space-occupying lesions), with the annual incidence rate being between 0.5 and 2.5 new cases per million population per year. Craniopharyngioma has a higher annual incidence of 5.25 cases per million in the pediatric population in whom it accounts for 6% to 13% of intracranial tumors. In 60% of patients, craniopharyngioma is diagnosed after the age of 16 (47).

In 2007, the World Health Organization (WHO) grading system for craniopharyngioma defined two major subtypes of the tumor, adamantinomatous and papillary, with both corresponding to WHO grade I. These two histopathologic subtypes have significant implications regarding age at diagnosis. Adamantinomatous craniopharyngioma is observed to have a bimodal distribution, with one peak in children between 5 and 15 years old and a second peak in adults 45 to 60 years old. The papillary subtype occurs almost exclusively in adults at a mean age of 40 to 55 (47). Most large series do not show any consistent sex predilection for craniopharyngiomas. Some studies have shown a greater preponderance in males in childhood and females in adulthood.

Craniopharyngiomas may arise anywhere along the craniopharyngeal duct, but they most commonly arise in the sellar/ parasellar region. Four percent are purely intrasellar, 21% are sellar and suprasellar, and 75% are suprasellar alone, often with extension up into the third ventricle.

Geographic variation may also exist, with various reports citing craniopharyngiomas as accounting for 1.5% to 6.5% of all primary brain tumors. The low incidence of 1.5% in Australia contrasts with the 6.5% rate in China and a

possibly higher incidence in Africa (47)

Given the predominant location of these tumors in the sellar/ parasellar region, craniopharyngioma is characteristically manifested as three clinical syndromes: visual dysfunction, disturbance of the hypothalamic-pituitary axis, and raised intracranial pressure as a result of obstruction of flow of cerebrospinal fluid (CSF) hence hydrocephalus.

Craniopharyngiomas are dysontogenic tumors with benign histology but aggressive behavior. The surgical challenges posed by the tumor are well recognized hence the role of subtotal resection with adjuvant radiotherapy and the role of other treatment modalities as cited in a number of series in the literature with comparable efficacity.

The treatment and general therapeutic approach to craniopharyngioma have undergone several transformations, even within the modern neurosurgical era, with proponents of both radicalism and conservatism. Significant advances in preoperative imaging, surgical techniques, and adjuvant therapies have enabled neurosurgeons and neuro-oncologists to improve the quality of care that these patients receive.

I. MAIN OBJECTIVE

The aim of our study is to review the surgical management of craniopharyngioma in the department of neurosurgery university Hospital Hassan II, in the city of fez Morocco for a period of 11years, in order to compare our experience with surgical series in the literature and indeed evaluate other treatment options available.

II. SPECIFIC OBJECTIVES

i. Describe the demographic characteristics of our series.

ii. Show the clinical presentation of both children and adults, the radiological investigation done preoperatively and postoperatively.

iii. Descibe the surgical technique and approaches utilised.

iv. Descibe preoperative planning, intraoperative adjuncts.

v. Discuss intraoperative and post operative complication, their management and indeed overall outcome.

vi. And indeed review other surgical series to compare their treatment strategy and outcome.

REMINDERS

I. EMBROYOLOGY

Craniopharyngioma is thought to arise from ectodermally derived epithelial cell remnants of Rathke's pouch and the craniopharyngeal duct. Neoplastic transformation of cells derived from tooth primordia gives rise to adamantinomatous craniopharyngioma, whereas such transformation in cells derived from buccal mucosa primordia gives rise to the papillary type. By the fourth week of gestation, invagination of the stomodeum, lined by epithelial cells, takes place. This upward migration is met by a downward movement of neuroepithelium from the hypothalamus. This upward invagination, termed Rathke's pouch, is responsible for development of the adenohypophysis, whereas the downward growth of neuroepithelium is the precursor of the future neurohypophysis.

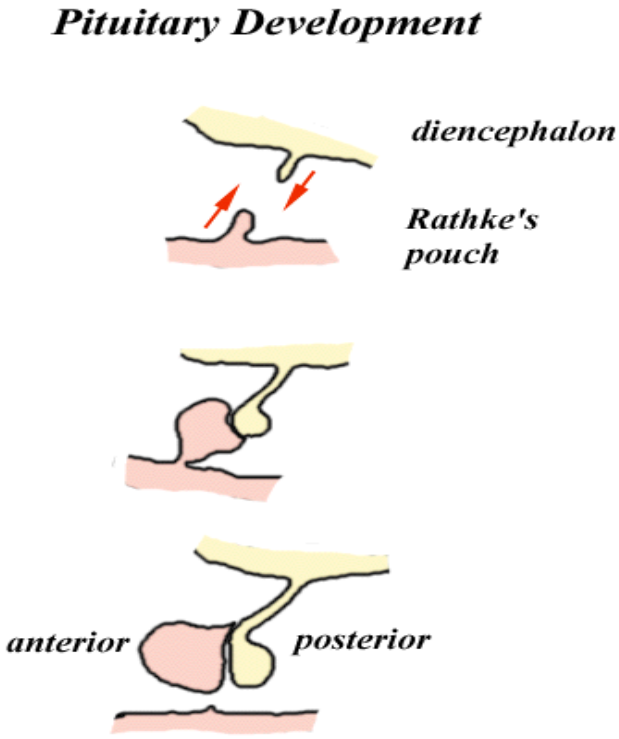


Figure 1: Rathke's pouch and diencephalon growing towrads each other.

As Rathke's pouch meets the infundibulum, it separates from the stomodeum and rotates around the anterolateral surface of the infundibulum. This rotation, which occurs during formation of the adenohypophysis, is responsible for delivering

embryonic rests to suprasellar or parasellar locations. This migration pathway from the primitive oral cavity is termed the craniopharyngeal duct. In 1904, Erdheim reported that the origin of craniopharyngiomas was based on incomplete involution of this pathway (47).

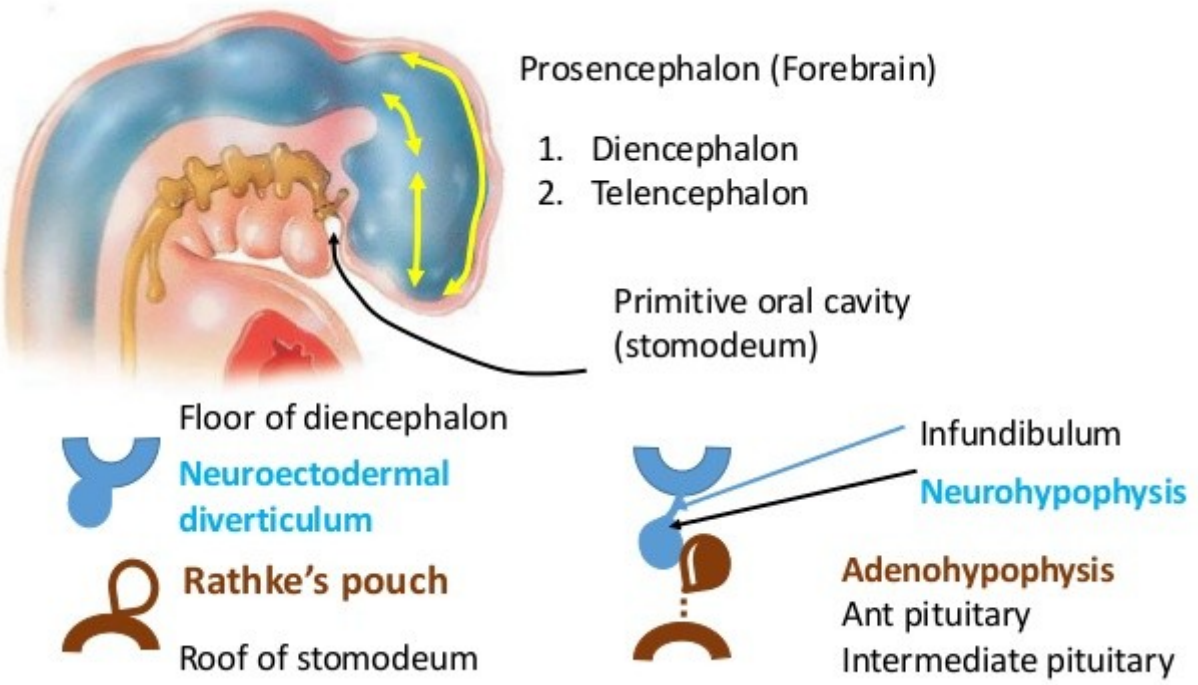


Figure 2: Developement of anterior and posterior pituitary gland

Recent evidence supports the hypothesis that embryonic rests of cells from the craniopharyngeal duct produce the pituitary gland, Rathke's pouch, and craniopharyngiomas. Both human chorionic gonadotropin and P-glycoprotein have been demonstrated to be produced by all these structures.

II. ANATOMY OF THE SELLAR REGION

The pituitary gland is a pea-sized endocrine gland that sits at the base of the brain. Often referred to as the "master gland", the pituitary gland synthesizes and releases various hormones that affect several organs throughout the body

Table 1: Table showing various hormones secreted by the anterior pituitary gland that becomes relevant in management of craniopharyngioma patients.

Hormone	Secretory Cell Type	Target	Effect
Growth hormone (GH)	Somatotrope	Liver and adipose tissue	Stimulation of growth and metabolism of carbohydrates and lipids
Prolactin (PRL)	Lactotrope	Mammary glands	Production of milk
Thyroid stimulating hormone (TSH)	Thyrotrope	Thyroid gland	Secretion of thyroid hormones
Follicle stimulating hormone (FSH)	Gonadotrope	Ovaries and testes	Regulates reproductive functioning
Luteinizing hormone (LH)	Gonadotrope	Ovaries and testes	Production of sex hormones
Adrenocorticotropic hormone (ACTH)	Corticotrope	Adrenal gland (cortex)	Secretion of glucocorticoids
ß-endorphin	Corticotrope	Opiod receptors	Inhibit pain perception

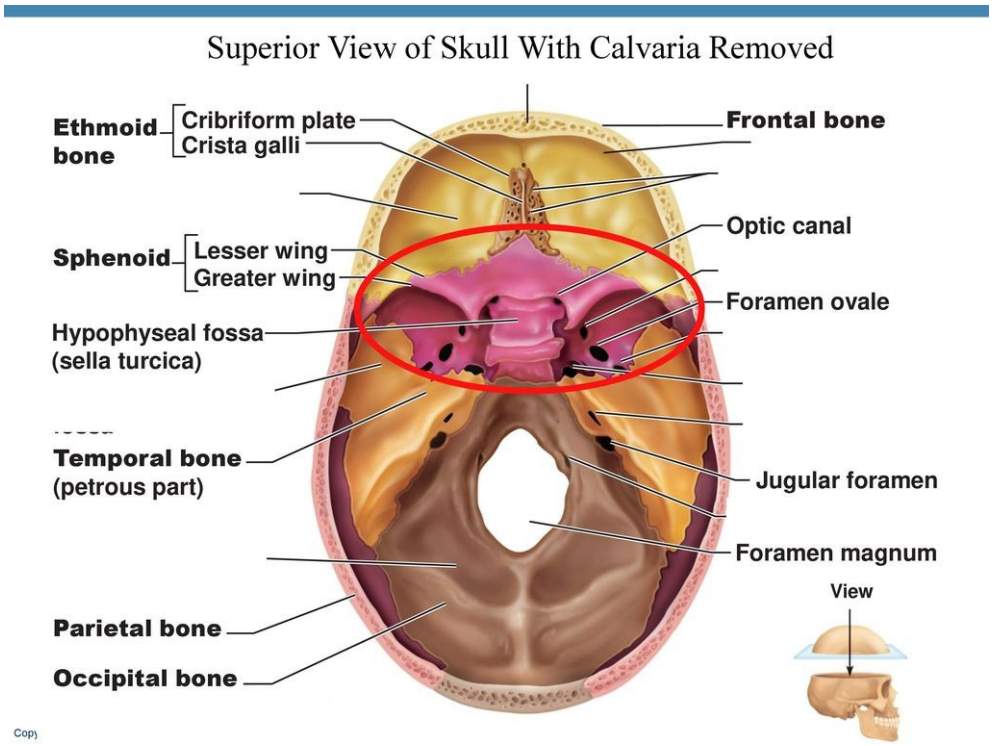


Figure 3: Skull base anatomy showing the anterior, middle and posterior cranial fossae indicating the sellar region as median part of middle cranial fossa.

The sella turcica is a central, saddle-shaped depression in the body of the sphenoid bone. The air-containing sphenoid sinus is directly below and anterior to the sella. The sellar floor is continuous with the tuberculum sellae anteriorly and the dorsum sellae posteriorly.

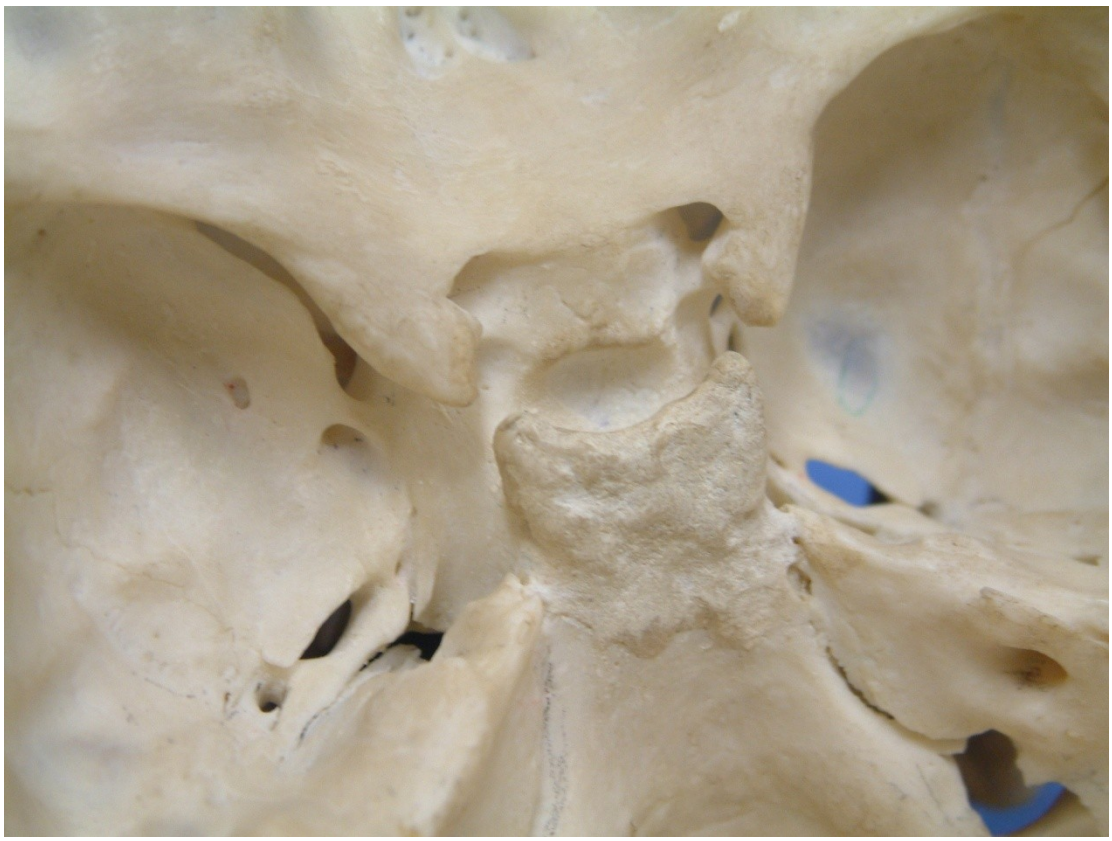


Figure 4: Showing the anatomy of the sellar turcica. Image from Anatomy dissection laboratory University of Sidi Mohammed Ben Abdellah.

The anatomy of the region of the sella and pituitary gland is known to vary considerably. The sellar floor can be asymmetrical (19%), flat (61 %), concave (36%), or convex (3%) – all types related to the pneumatization of the sphenoidal sinus (sinus presellar or sellar). There is no correlation between the degree of asymmetry of the sellar floor and the volume of the sella and the pituitary gland. Minor cortical changes of the sella turcica can be noticed (local thinning of the cortical layer, defect, bulge).

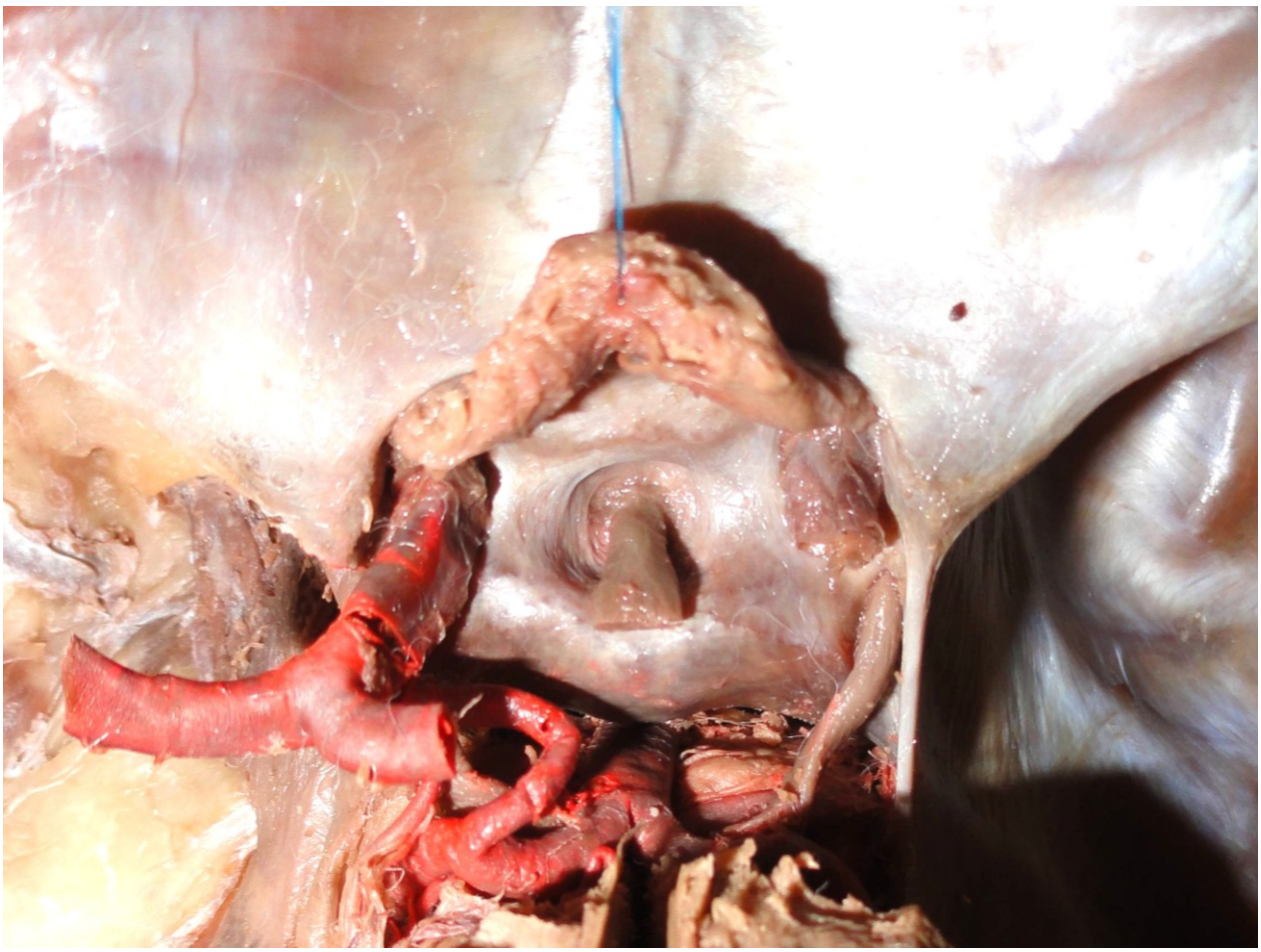


Figure 5: Anatomy Dissection Image of the sellar region in relation with other structures such as the carvenous sinus and visual apparatus. Note also the internal catotid artery and bifurcation

The normal sellar content consists of two distinct parts – the anterior lobe and the posterior lobe. The anterior lobe (adenohypophysis) is formed by proliferation of the anterior wall of the Rathke pouch, an ectodermal upward growth of the stomodeum or primitive oral cavity [29]. Rathke cleft cysts, a common finding at autopsy, can now be imaged as round midline structures often located in the anterosuperior portion of the sella [29]. The anterior lobe is composed of cells containing membrane-bound secretory granules specific to each type of cell. Fibrous tissue either in the form of local scars or diffusely spread can be seen in more than half of the cases occupying 1 % -15 % of the section area in the anterior

lobe [33]. The blood supply comes from the hypophyseal portal system except for small capsular branches arising from the internal carotid artery [9].

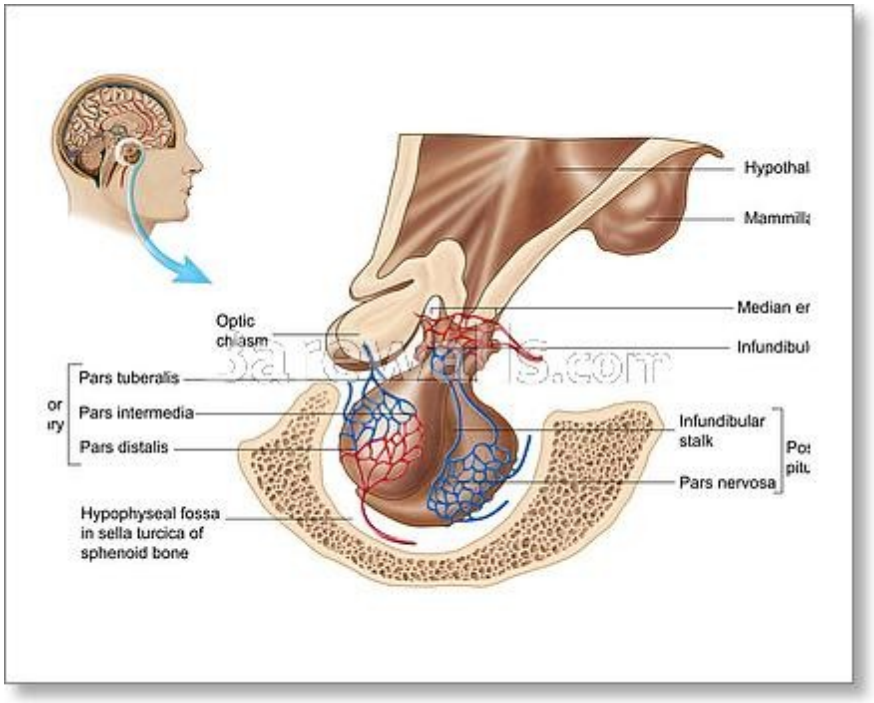


Figure 6: Blood supply and venous drainage of the pituitary gland and stalk

The anterior lobe is partly wrapped around the posterior lobe and separated from this lobe by the pars intermedia, which comes from the posterior wall of the Rathke pouch. It can contain small epithelial cysts believed to be derived from a remnant of the Rathke pouch [35]. The posterior lobe (neurohypophysis) comes from a downward extension of the diencephalon and consists of intrinsic pituicytes and a large bundle of unmyelinated nerve fibers, the bodies of which lie in the supraoptic and paraventricular nuclei of the hypothalamus. The axons and axon terminals include membrane-bound neurosecretory granules that contain specific hormones (vasopressin or ADH and oxytocin) synthetized by the hypothalamus and stored and released by the neurohypophysis [9,34,15]. The posterior lobe is often embedded in a convexly cupped dorsum sellae or posteroinferior sella floor. It is vascularized by branches of the internal carotid artery. The mean height of the pituitary gland is 5.5

mm (3- 9 mm) in the sagittal plan [45]. Mark [31] and Bonneville [9] observed no relationship between the size of the gland and the patient's sex or age; other authors found the length, width, and height of the gland to be significantly larger in women than in men. Decrease in height could correspond to regression of the glandular tissue from decreasing function, persistent CSF pressure over time, or ischemic changes in the anterior lobe [41]. The upper border of the gland is straight (60 %), concave (28 %), or convex (10.9 %). Convexity of the upper limit of the gland should not be considered abnormal (Fig. 1). The upper border of the gland is formed by the diaphragma sellae, a dural membrane that extends from the dorsum sellae to the tuberculum sellae and between the medial dural walls of the cavernous sinuses. The infundibulum or stalk extends from the hypothalamus to the posterior lobe of the pituitary gland through an opening of variable size of the diaphragma. Above the diaphragma, the CSF of the suprasellar cistern contains the superior portion of the infundibulum, the supraclinoidal carotid arteries and the circle of Willis, and the optic chiasm. The optic chiasm is formed anterior to the stalk by the optic nerves that emerge from the optic foramina and extend posteriorly, close to the inferior surface of the frontal lobe. The optic tracts run posterolaterally toward the lateral geniculate bodies. The optic chiasm has an average length of 6-1 0.6 mm. Its orientation in relation to the bony structures of the skull as well as to the brain is highly variable. The variability of the chiasmatic angulation combined with the variability of the distance from the hypophysis to the chiasm explain the variability of time elapsing between extension of a suprasellar tumor and mechanical compression of the chiasm initiating visual disturbances. The location of the chiasm compared to the sella is variable. In 9 % of cases it is prefixed (anterior border situated at the level of the tuberculum sellae), and in 6% -11 % of cases it is

postfixed (anterior border visible in front of the dorsum sellae) [35]. A posteriorly located chiasm could favor intra sellar expansion of the subarachnoid space and thus anterior cisternal herniation

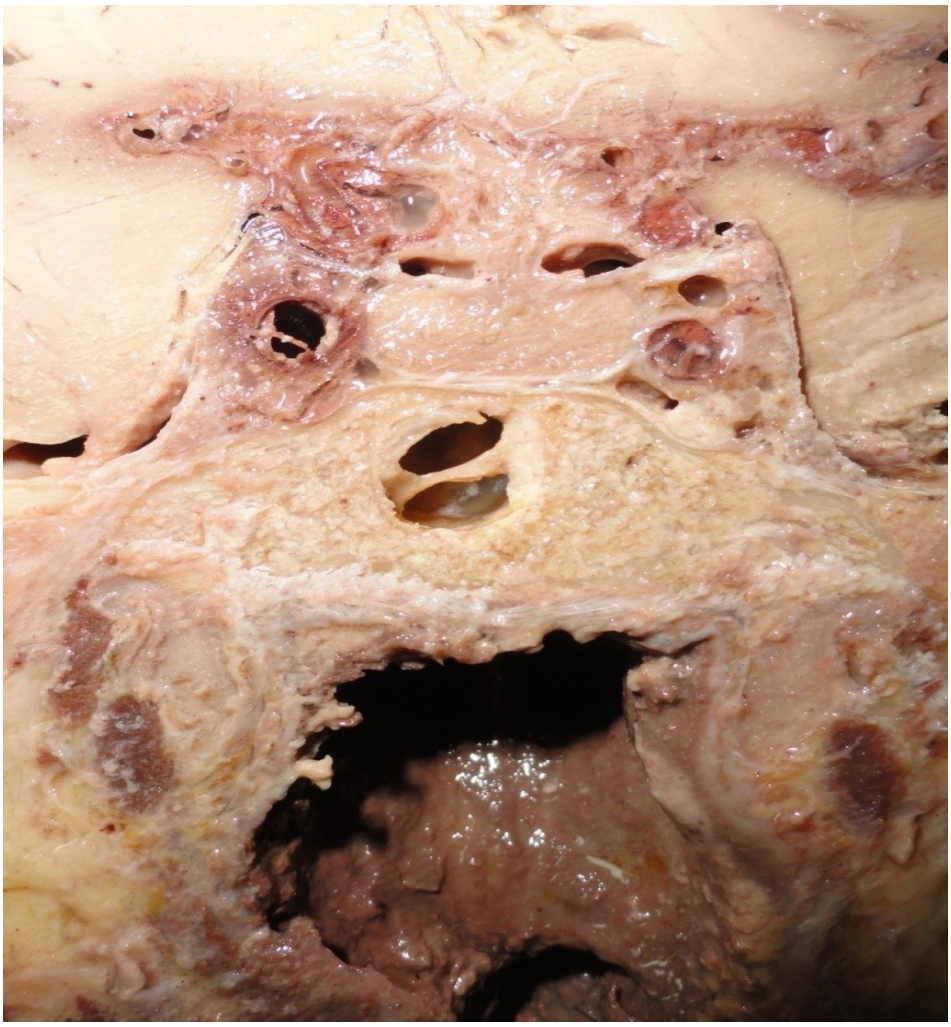


Figure 7: Coronal Section of Dissection Specimen showing Relation of the pitutary gland and Stalk to the carvenous and other neurovascular structures.

The sella is bordered laterally by the cavernous sinuses which contain the carotid arteries and cranial nerves III, IV, Vl, V2, and VI. The venous channels connecting the right and left cavernous sinuses (intracavernous sinuses) may be found at any site along the gland. Anterior intracavernous sinuses are reported to be twice as frequent as posterior ones (76% versus 32%). The empty sella is defined as partly empty when subarachnoid space extend to the tuberculum sellae and

occupies less than 80 % of the total height of the sellae. It is considered empty when the subarachnoid space occupies more than SO % of the sella, and the pituitary gland is reduced in size and shifted posteriorly and inferiorly. It can be associated with herniation of visual pathways and third ventricle, with or without visual impairment.

PATIENTS AND METHODS

This is a retrospective analysis of 30 cases managed for Craniopharyngioma in the department of neurosurgery at Hassan II Teaching hospital of Fez, Morocco from January 2009 to December 2018.

I. Data Sources

Case files were solicited from the records and some cases were followed up during hospitalisations in the department of Neurosurgery. Departimental and hospital archieves were the source of the old files which always have file numbers. I retrieved information concerning the demographic features, presenting symptoms, duration of stay, preoperative investigations, imaging data done outside the hospital before admission and histopathological data which were usually done both at the hospital and outside

Some clinical information, like post-operative theatre notes, Blood tests, histopathological results from hospital histo-pathology laboratory and most of post operative imaging was retrived from Hospital Information Technology System (ITS) Hosix.

Other valuable data were obtained from outpatients visits of the neurosurgeons and face to face interview with the responsible neurosurgeon.

II. Inclusion Criteria

All patients of all ages operated for craniopharyngioma in the department of surgery of Hassan II University Hospital between January 2009 and December 2018 were included.

III. Exclusion Criteria

Patients operated for sellar and supra-sellar tumors whose histopatholgy results did not confirm craniopharyngioma were excluded.

Patients followed up in our outpatients clinic but were not operated in our department were also excluded.

IV. Analysis

Collected data was analysed using Microsoft excel and SPSS and student t test, and chi-squared tests were used to test statistical significance.

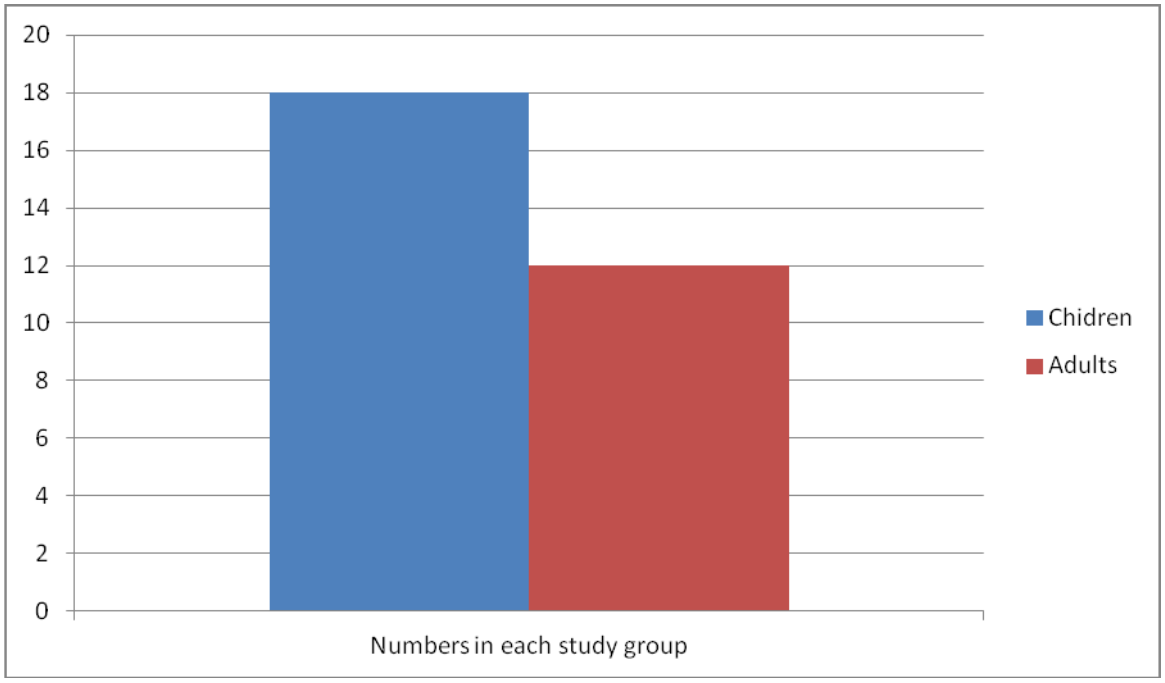
RESULTS

There were a total of 30 files that were analysed comprising 18 children and 12 adults. The mean age in children was 6.6 years and 40.6 years in adults and for the total population the mean age was 23.1 years. The age range was 5 to 11 years in pediatric group and 17 to 64 years in the adult group. The median age was 7 years in the childrens' group while that of the adult group was 38 years and 10 years was the median age of the whole study group. There were 16 male patients and 14 female patients in this study group representing a male female sex ratio of 1.14. Indeed, the sex ratio was 2:1 in the childrens group and 1:2 in adults group. Below is **Table 2** summarising the demographic characteristics of our study series.

Table 2: Demographic characteristics of craniopharyngioma patients in our study

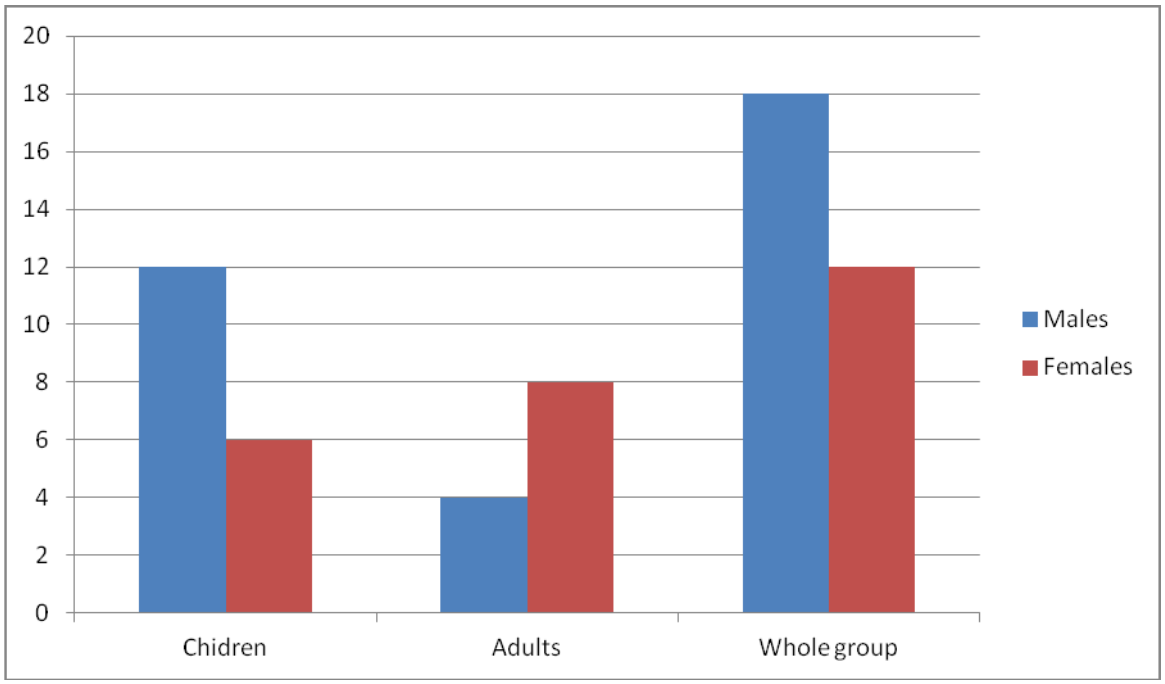
Statistical Parameters	Childrens group (number 18)	Adults group (number 12)	Whole series (Total number 30)
Mean age	6.6	40.6	23.1
Median Age	7	38	10
Age range (years)	5-11	17-63	5-63
Sex ratio male / female	2 :1	1-2	1.14 :1

Graph 1 below is a histogram showing the distribution of the study population between children and adults showing a bigger number of pediatric patients treated surgically for craniopharyngioma in our department during the study period spanning 11years.



Graph 1: Distribution of patients in each group study of craniopharyngioma

The second graph is another histograme showing distribution of sex among children, adults, and the whole group that clearly shows more numbers of males in chidren group as opposed to the adult group with reversal of ratios. Indeed, in the whole study group there was a male predominance.



Graph 2: Sex distribution in the peadiatric, adults and the whole study group of our series

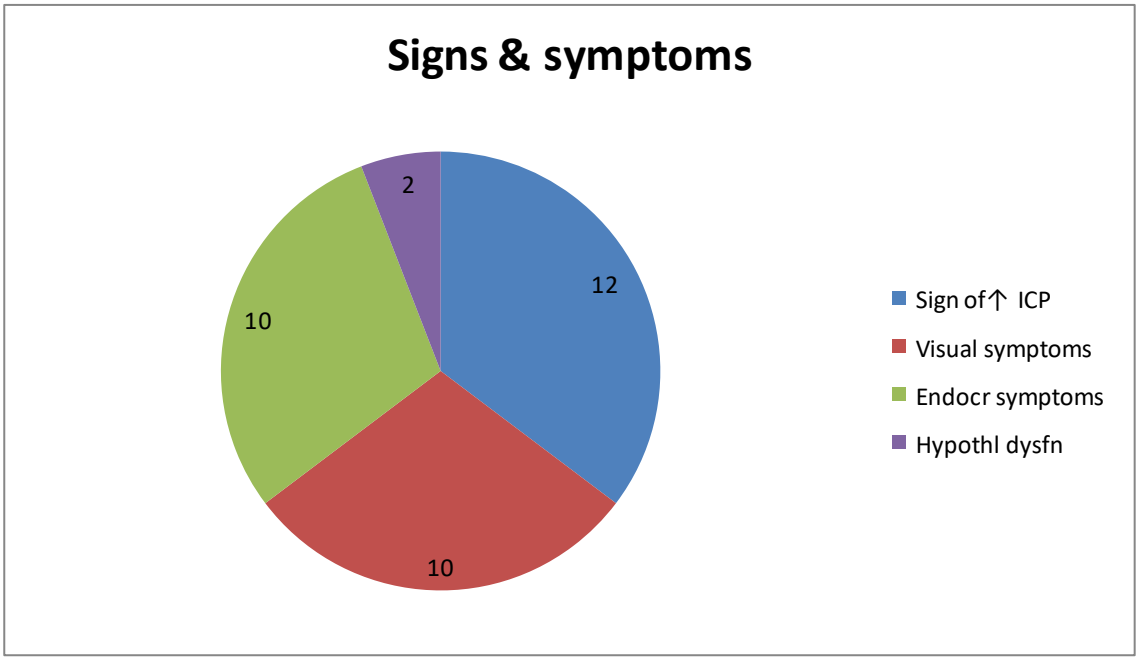
CLINICAL PRESENTATION

Classically, craniopharyngioma presents with symptoms that include the following; signs of increased intracranial pressure, disturbances of vision, endocrinopathies and symptoms of hypothalamic dysfunction. Table 3 summarizes our findings of presenting signs and symptoms in our surgical series.

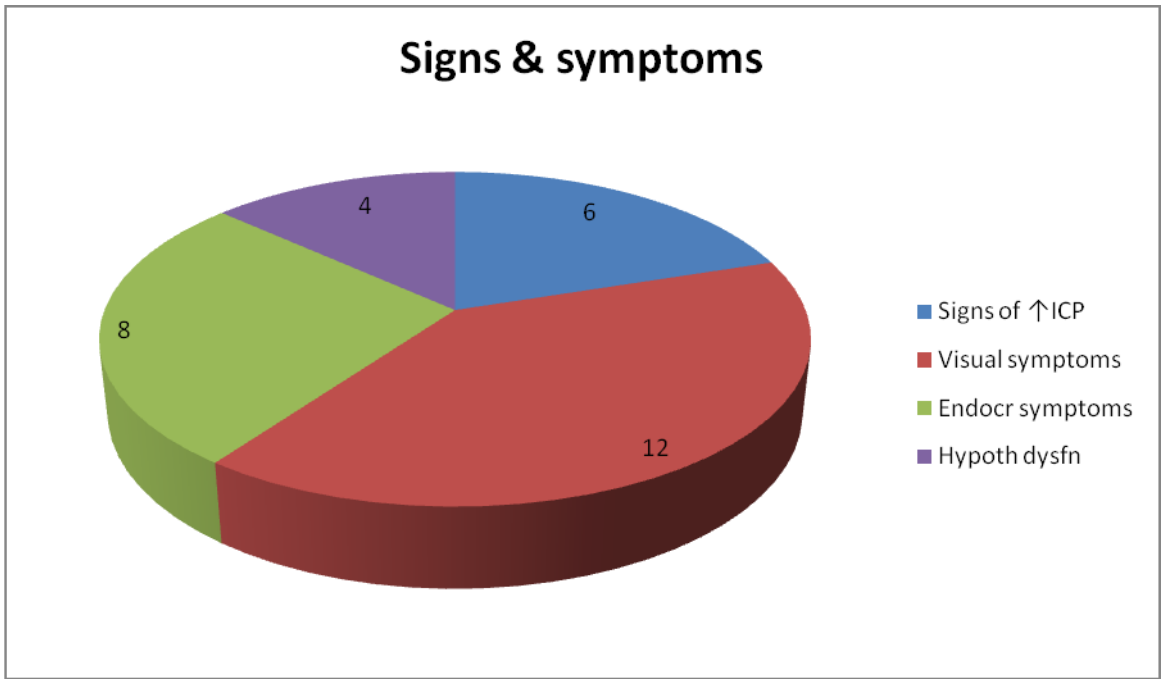
Table 3: Clinical symptoms and presenting signs with pediatric and adult subgroups

Symptoms/Signs	Children : Number (Proportion)	Adults : Number (Proportion)	Total : Number (Proportion)
Raised ICP	12(67%)	6(50%)	18(60%)
Visual Symptopms	10(56%)	12(100%)	22(73%)
Endocrine disturbance	10(56%)	8 (67%)	18(60%)
Hypothalamic dysfunction	2(11%)	4(33%)	6(20%)

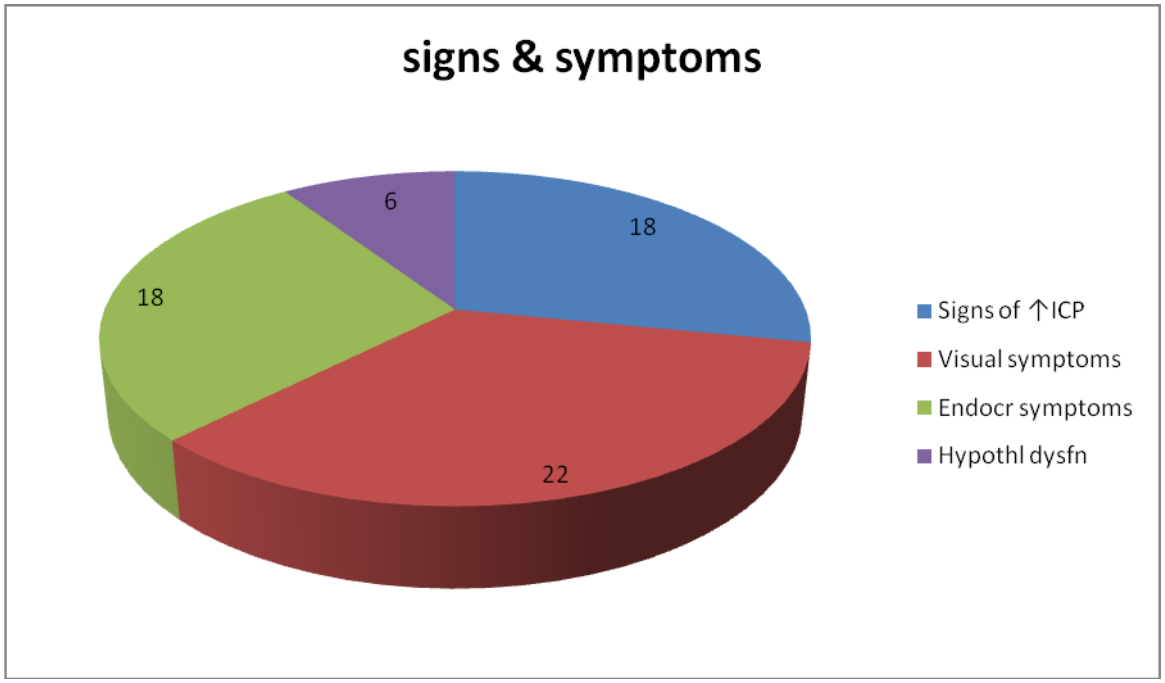
Graph 3, 4, and 5 are charts that show the distribution of the presenting symptoms among children, adults and the whole study group.



Graph 3: Distribution of signs and symptoms among childrens group



Graph 4: Distribution of signs and symptoms among adults group



Graph 5: Distribution of signs and symptoms among the whole group

I. DURATION OF HOSPITAL STAY

The mean duration of symptoms in our study was 17 months with a range that spanned 6 weeks to 6 years.

The mean hospital stay was 34 days, with a range of 4 to 86 days

II. PRE-OPERATIVE ASSEMENT

1. OPTHALMOLOGICAL EXAMINATION

All our 30 patients operated on for craniopharyngioma underwent objective opthalmological examination as basic part of preoperative assement of visual acuity, visual field defects, and papilloedema.

2. ENDOCRINOLOGICAL ASSEMENT

Endocrinological assessment was done systematic whether the patient has signs of insufficiency or not as a baseline to compare with post operative values. Hormones explored were all the anterior pituitary gland and hypothalamic hormones as follows : Growth hormone (GH) and Insulin like growth factors 1 (IGF1), prolactine (PL), Thyroid stimulating hormone (TSH) and serum T3 and T4, Cortico-tropin Releasing Hormone (CRH), Adrenocorticotropic hormone (ACTH) and free cortisal, follical stimulating hormone (FSH), and lutenizing hormone (LH).

3. NEURORADIOLOGICAL ASSESSEMENT

The whole patients underwent neuroradiological investigations using a brain computed tomography (CT scan) and brain nuclear Magnetic resonance imaging (nMRI). Below is a table showing imaging characteristics in our series in terms of lesion size, presence of calcifications, presence of cyst and hydrocephalus. We were able to analyse 26 cases of which we have had the images. Images of the remaining cases were not found in the files.

Table 4: Imaging characteristics in craniopharyngioma patients determined on brain CT scan and MRI

Imaging characteristic	Children	Adults
Max length ≤ 2cm	4	4
Max length ˃2≤6cm	8	6
Max length ˃6cm	2	2
Calcification on CT	8	2
Cystic lesion	4	1
Hydrocephalus	10	4

Below are samples of images showing various imaging characteristics on CT scan and MRI of our patients.

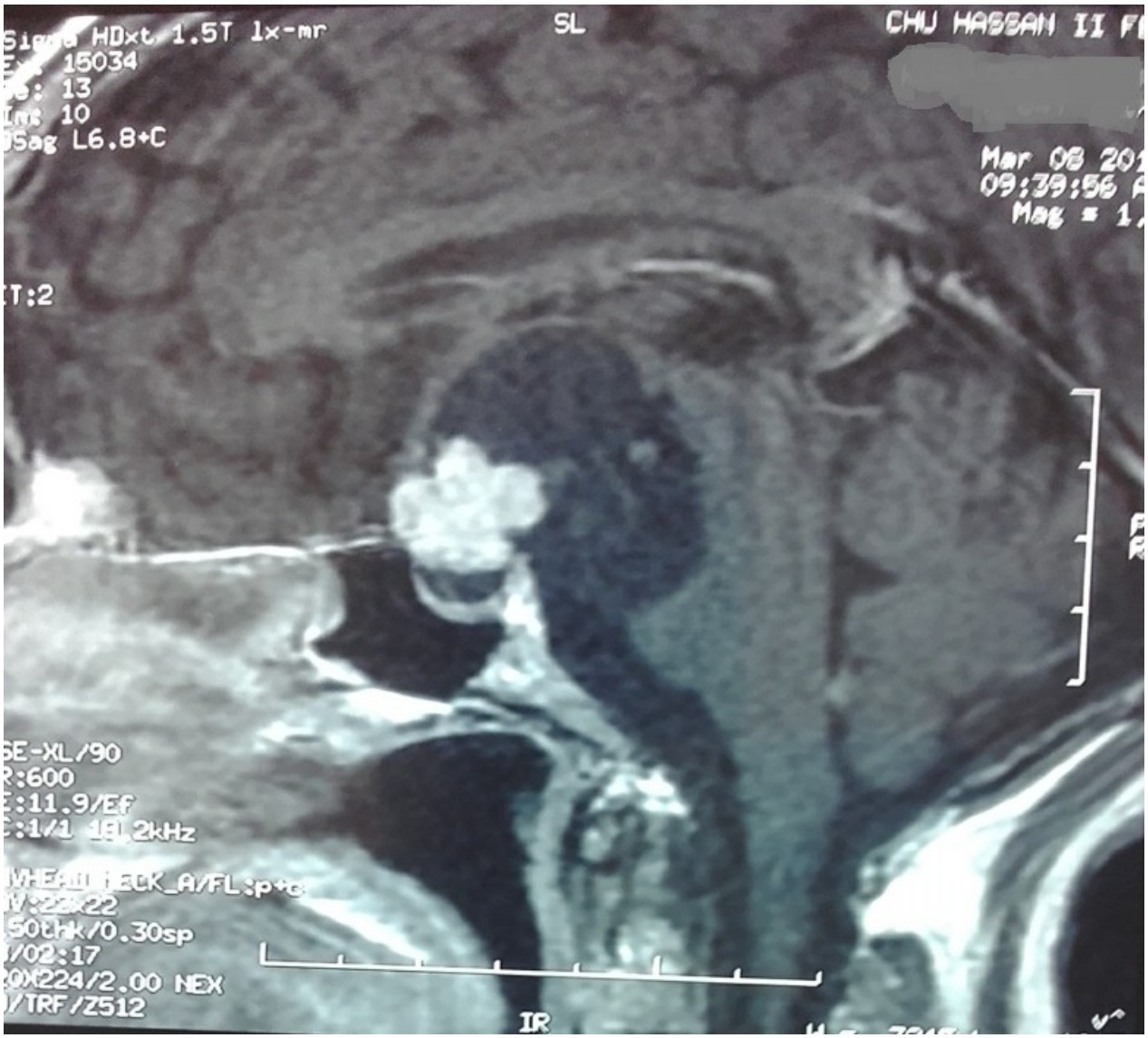


Figure 8: Sagittal gadolinium enhanced MRI showing a suprasellar mass that has a solid and a cystic portion measuring about 3.4 cm in maximun diameter.

This 64-year-old woman presented with signs of increased pressure, behavior change, decreased visual acuity of 2/10 in both eyes, right mydriasis, and hormonal deficiency of thyroid hormones T3, T4. She was operated in 2013 with total excision of the tumor. Histology results confirmed papillary craniopharyngima. Postoperatively, she presented with diabetes insipidus, and hypocortisolemia and treated successfully for respective complications with Minrin, and hormonal replacement with remarkable outcome.

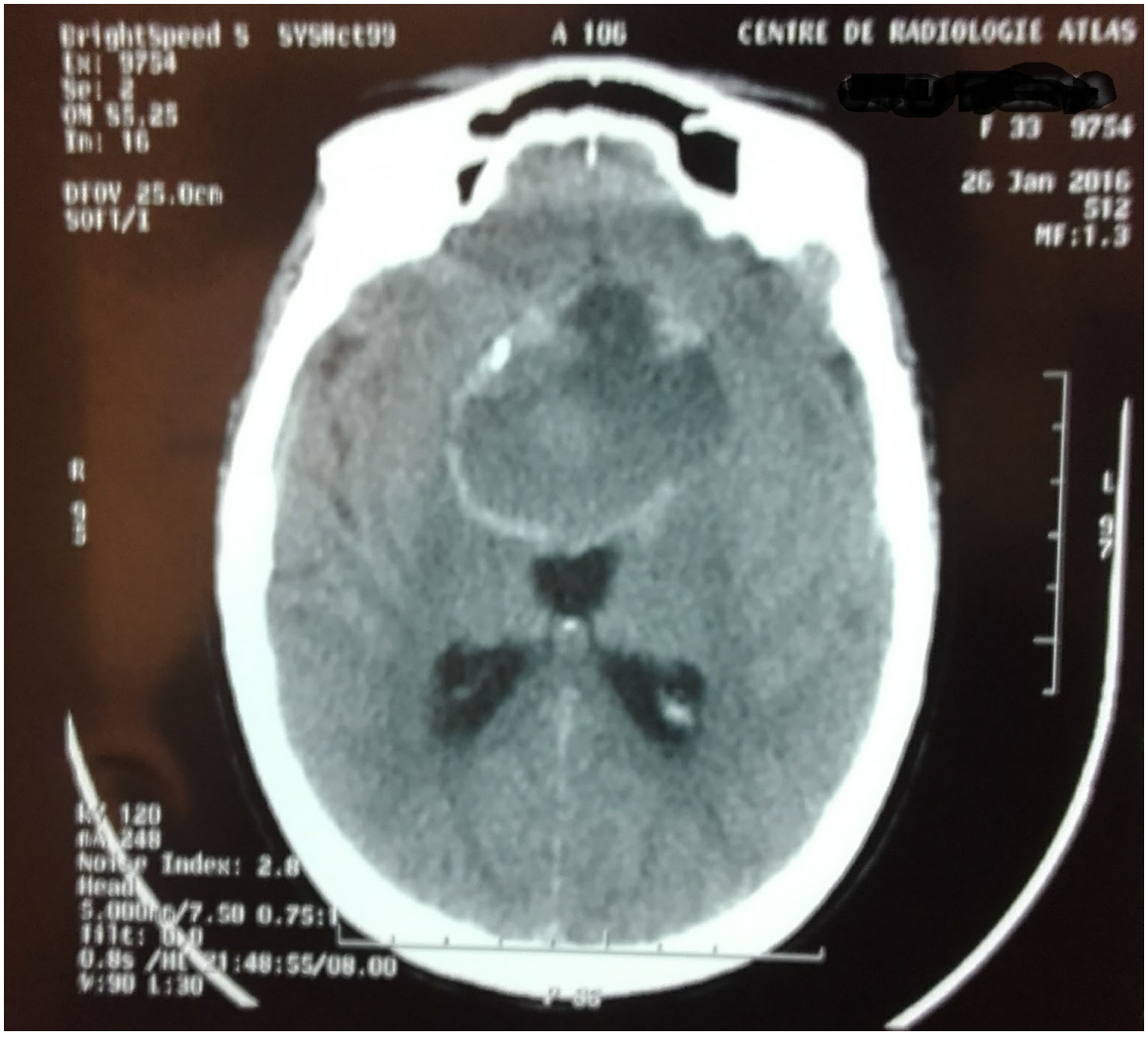


Figure 9: A brain contrast enhanced CT scan measuring 6 cm in a 33-year-old woman that presented with blindness.

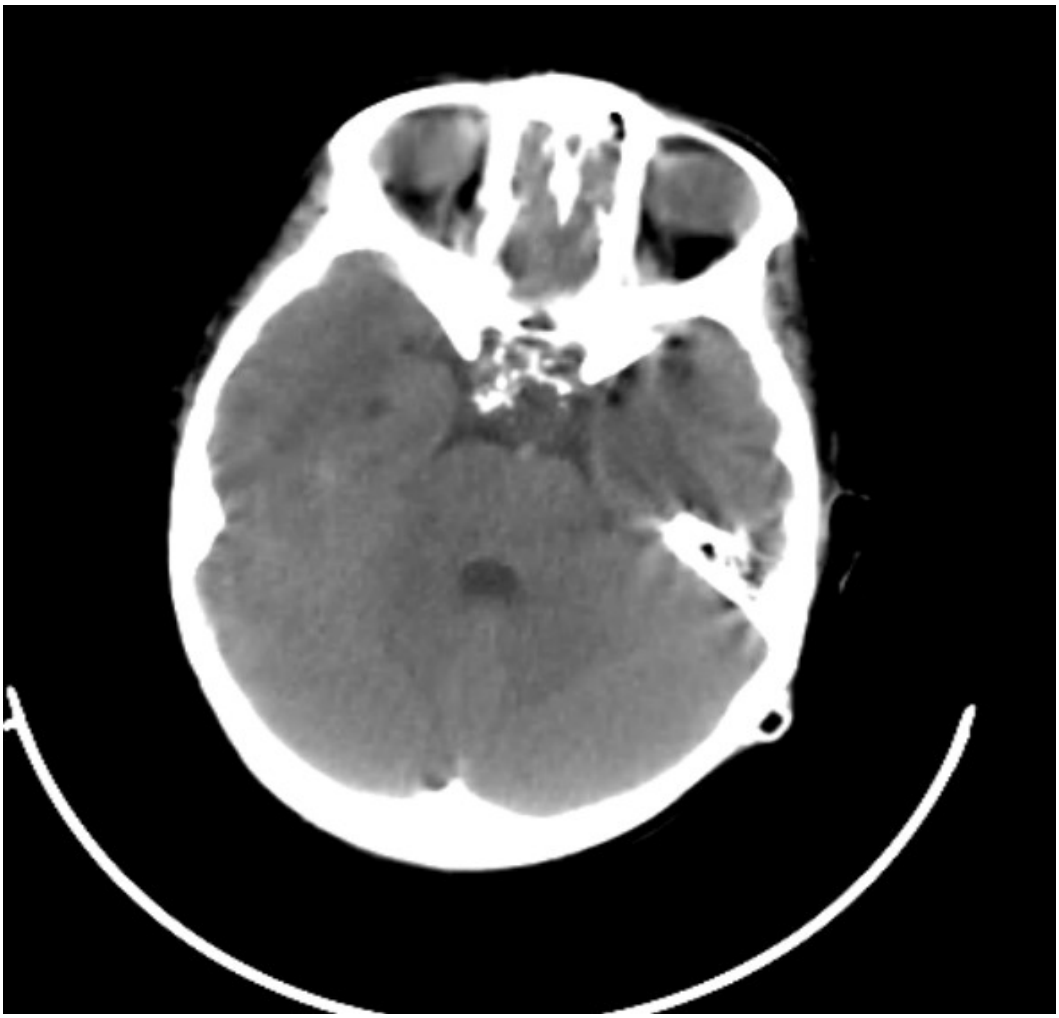


Figure 10: Axial brain non contrast CT scan of a 7 year old showing calcified tumor of the sellar region.

He presented with increased signs of increased intra-cranial pressure, decreased vision. He was operated and recovered partially his vision. In post operative period presented with diabetes insipidus, hypocortisolemia and thyroid hormones. He was put on minrin (ddvap), levothyrox, hydrocortisone and the drugs were withdrawn progressivelly with good tolerance. He is well and good and back to school.

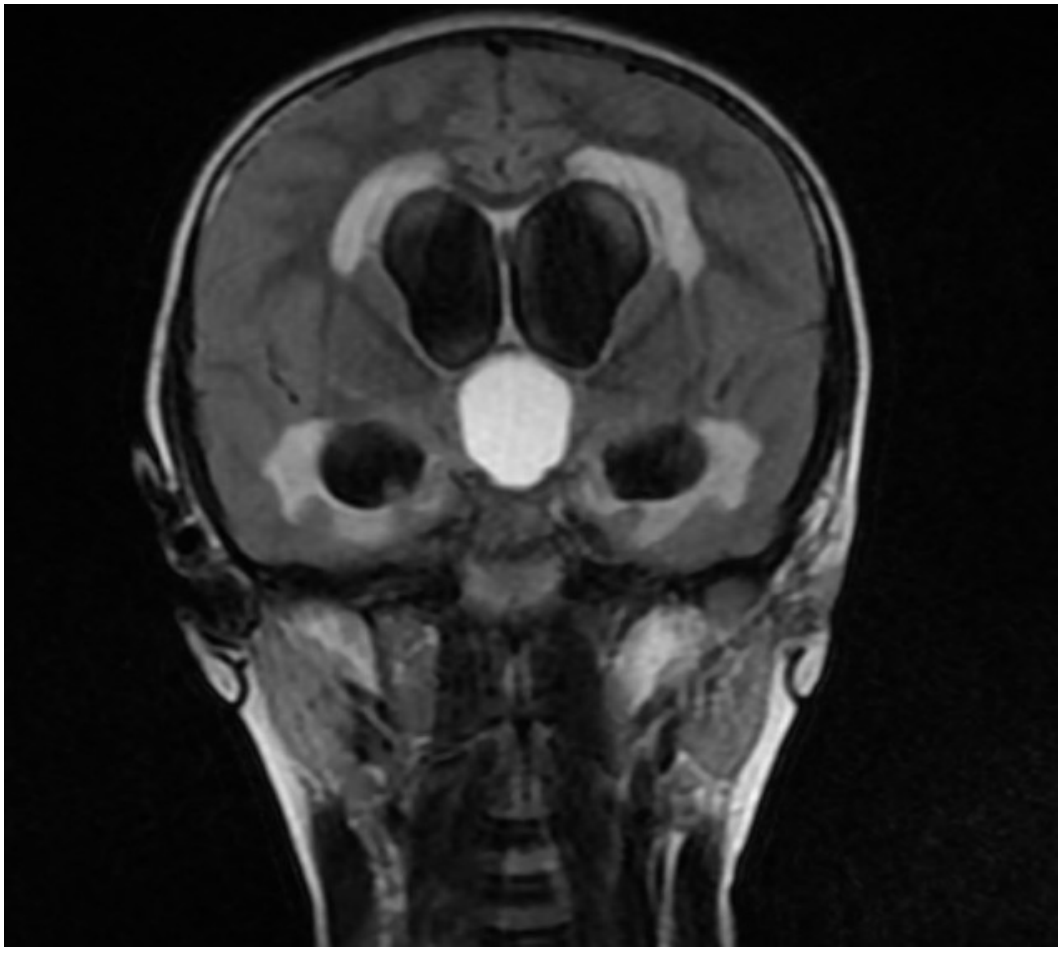
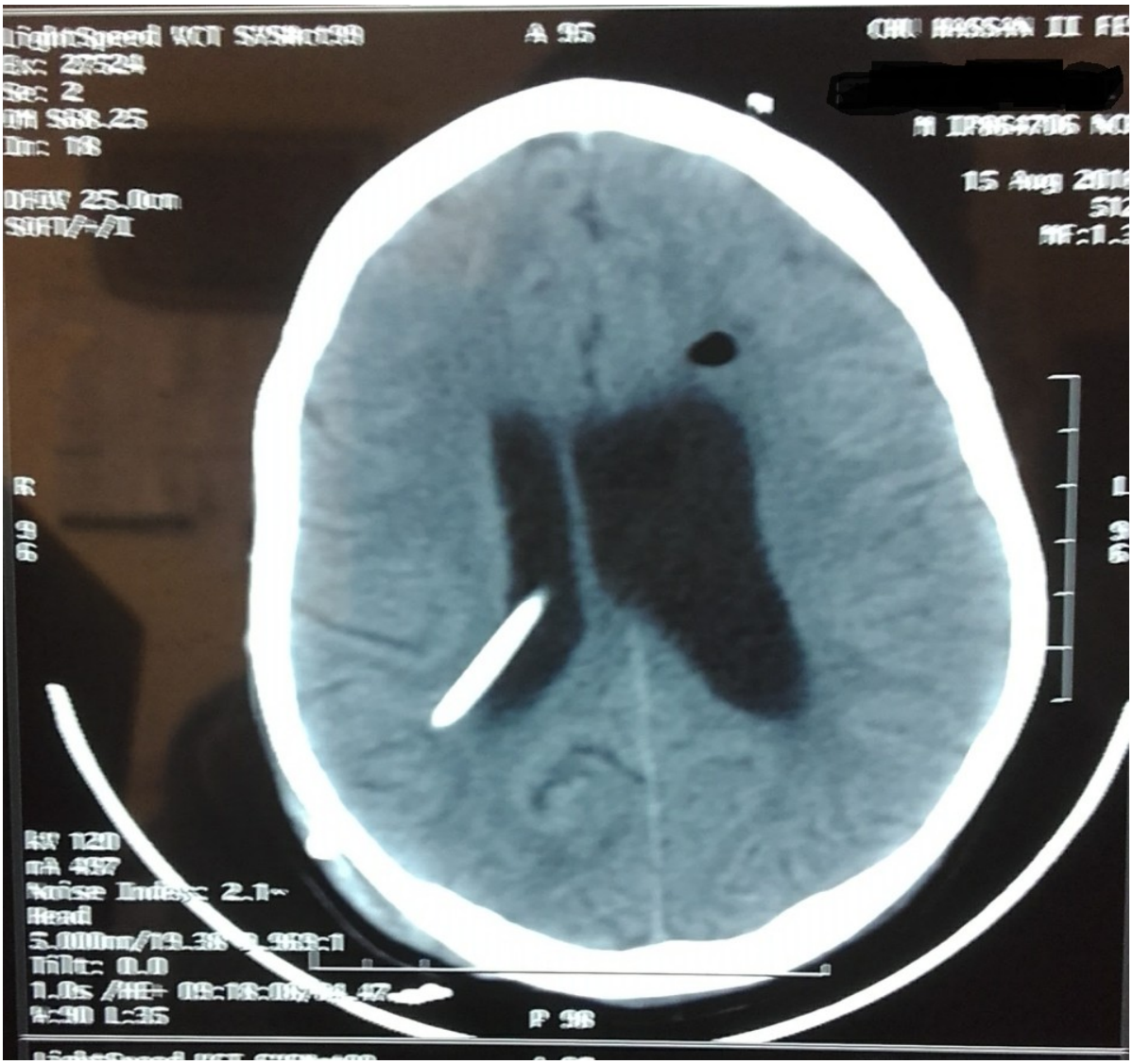


Figure 11: Pre-operative coronal T2 Flair MRI showing hydrocephalus in a patient subsequently treated for craniopharyngioma. Note the peri-epindymaire hyper-intense signal signifying active hydrocephalus.

III. PREOPERATIVE CEREBROSPINAL FLUID DIVERSION

A total of 10 patients (33.3%) in this group underwent cerebrospinal fluid diversion before definitive surgery to treat hydrocephalus and signs of increased intracranial preassure revealed on both CT scan and MRI. Opthalmological examination helped to reveal papilloedema which is a very sensitive sign of raised intracranial pressure.



Below is figure 12 that shows a brain CT scan after ventriculoperitoneal shunting with ventricular catheter put in the right lateral ventricle to treat hydrocephalus.

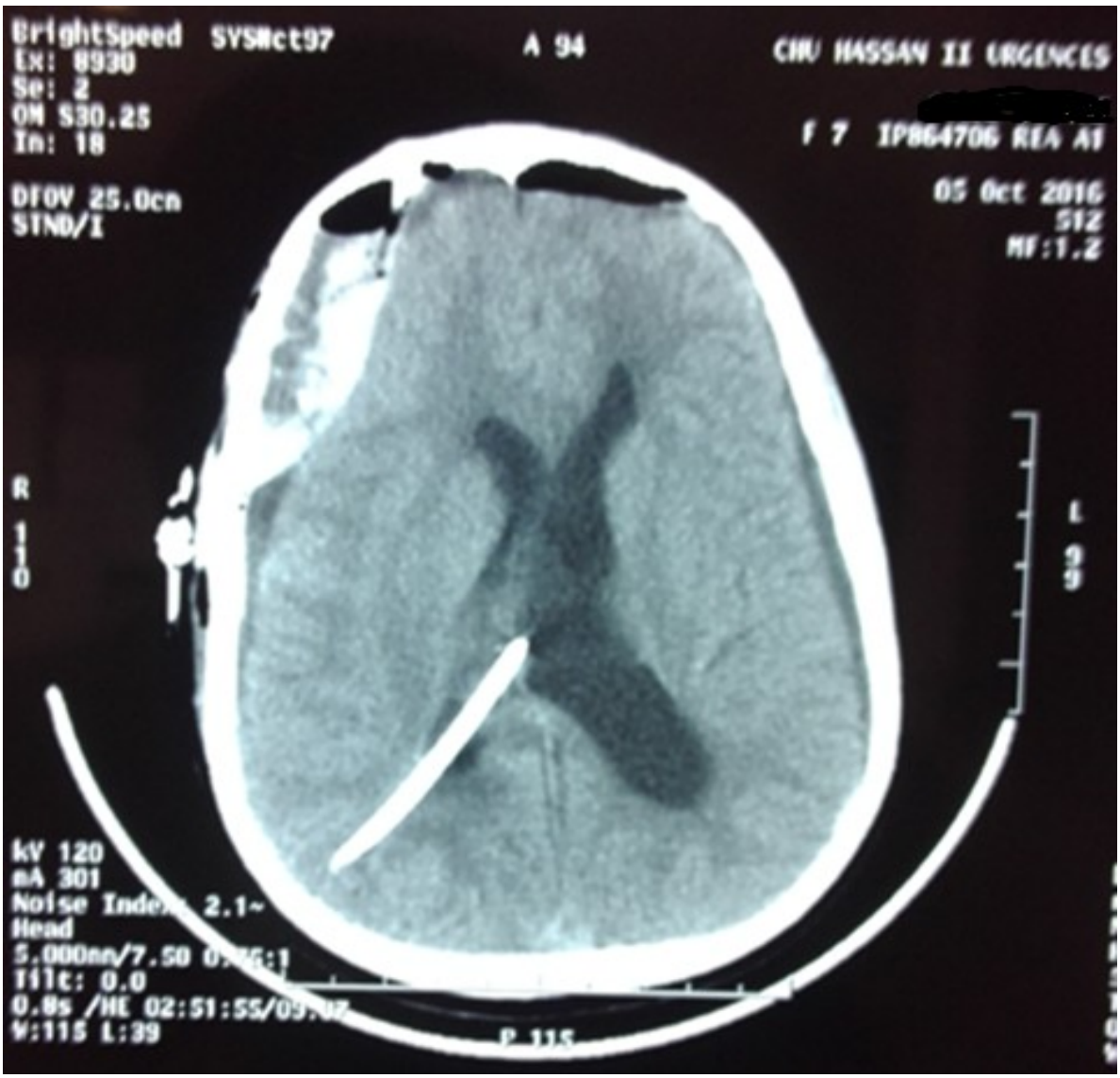


Figure 13: Postoperative CT scan in the above stated patient showing postoperative extradural hematoma and decreased vetricular dilatation as compared to pre-operative scan.

This scan belongs to a 10-years-old boy presented with two months history of headache, decreased vision associated to cranial nerve six pulsy and stunted growth. Neuroimaging showed craniopharyngioma with hydrocephalus. The patient underwent a CSF diversion on the right side but the tumor was blocking the foramen of monro so endoscopic septostomy was done to communicate the two lateral ventricloes after which his symptoms improved and was operated definatively for his craniopharyngima. In the above brain CT scan after the endoscopic procedure shows

pneumocephalus in the trajectory of the endoscope. **Figure 13** is post operative CT scan in the same boy that shows intraventricular catheter in place and post operative extradural hematoma that was treated conservatively and he did well with slight visual gain in long term.

IV. SURGICAL PROCEDURE

In our study group of 30 patients, the 29 patients (96%) underwent surgical procedure for removal of the lesion, while one patient was not operated due to her poor medical condition. Of the surgically operated patients, the surgical approach was either left or right frontal-temporal (pterional craniotomy) in 27 cases. One patient was operated with interhemispheric trans-callosal approach and the other one was operated using endoscopic transnasal trans-sphenoidal approach. I will describe the pterional approach first followed by the other two approaches.

1. FRONTO-TEMPORAL (PTERIONAL CRANIOTOMY)

SUITABILITY

It is the most favored approach for resection of craniopharyngiomas, and it would seem to best be suited for smaller tumors confined to the suprasellar space. It does allow access to both prechiasmatic and retrochiasmatic lesions, along with those above and below the diaphragma, and may be used in combination with interhemispheric-transcallosal or transcortical-transventricular approaches to remove larger lesions with significant suprasellar extension.

OPERATIVE DETAILS

The patient is positioned supine on the operating table with the head turned and elevated such that the malar eminence is uppermost. A frontotemporal incision is made (Figure 19), and the temporalis muscle can be raised with the skin as a myocutaneous flap or reflected anteriorly after interfascial dissection.

A frontotemporal bone flap is elevated, and the lateral aspect of the lesser wing of the sphenoid is drilled away. Frontal extension of the craniotomy is advocated by some authors to improve access. The dura is opened horizontally and reflected anteriorly. The sylvian fissure is split, and frontal and temporal retractors may be used judiciously to provide access to the tumor. Extension of craniopharyngioma into the third ventricle may be removed by opening the lamina terminalis.

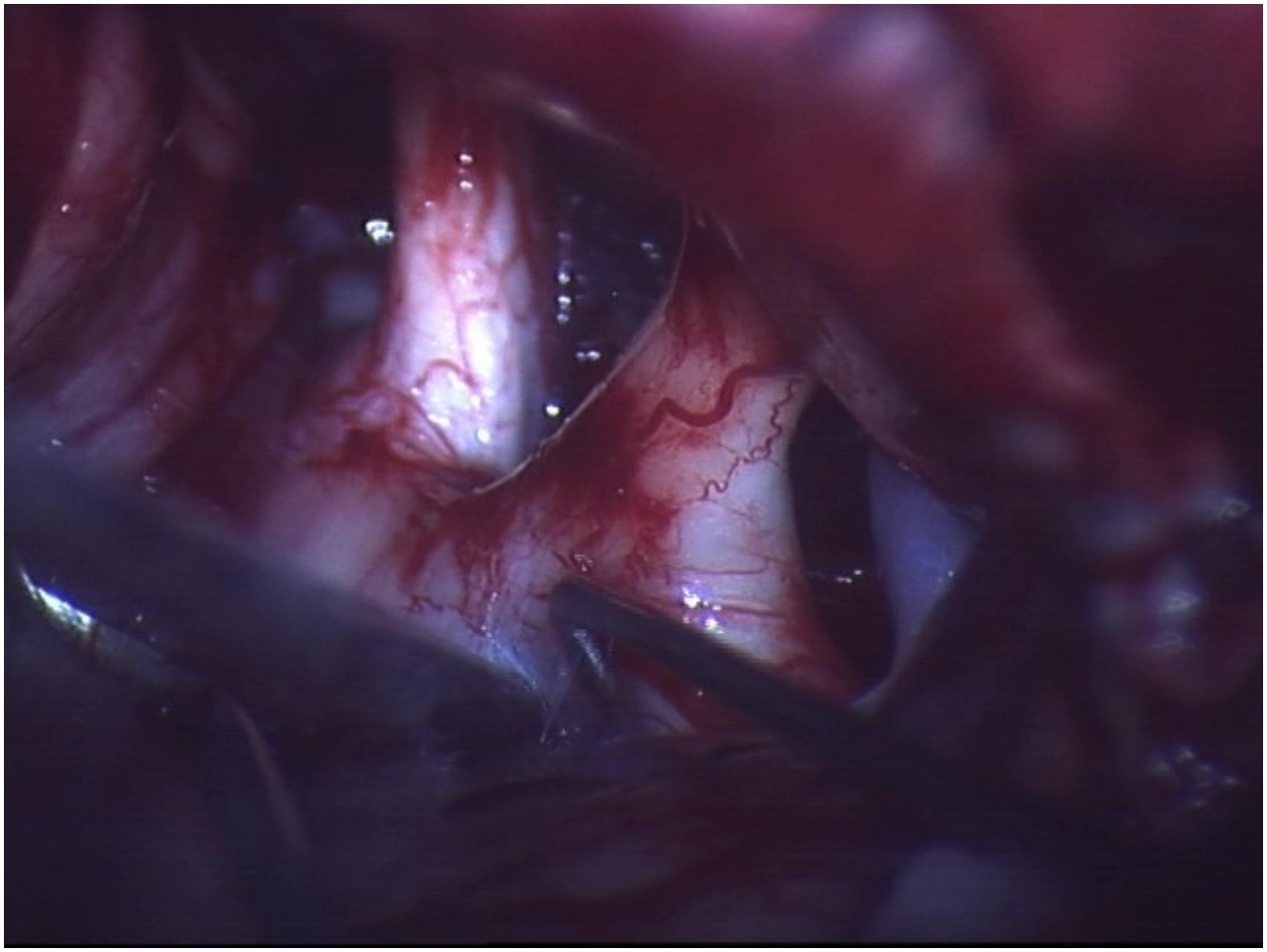


Figure 14: Biggining of surgical resection of retrochiasmatic craniopharyngioma. Image showing exposure of the bilateral optic nerves and chiasma. Note the sunction tip and dissection hook on the lamina terminalis.

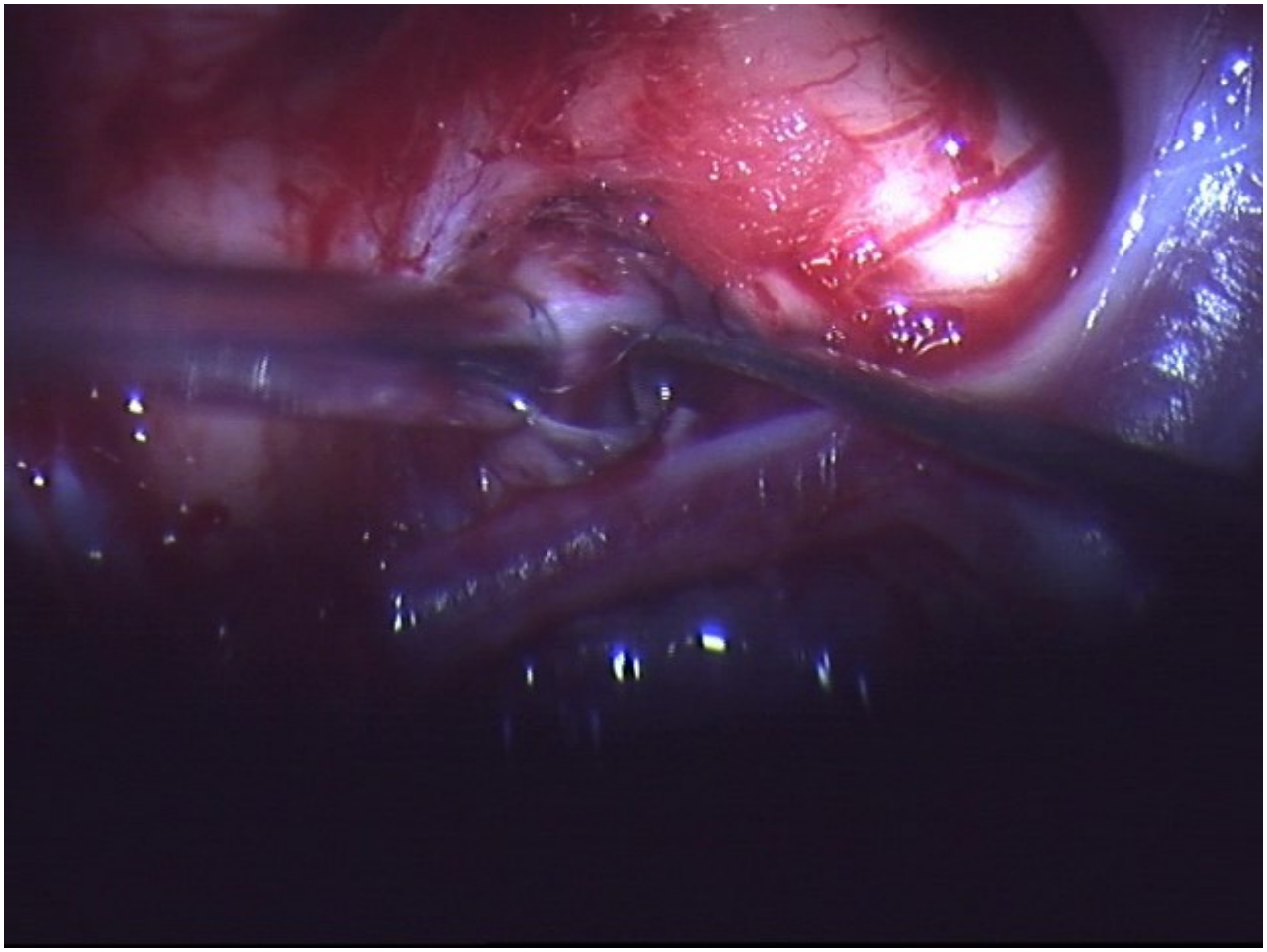


Figure 15: Opening of the lamina terminalis using hook and sunction in between the optic tracks. Note the anterior cerebral artery and internal carotid artery in the operative proximity of the tumor

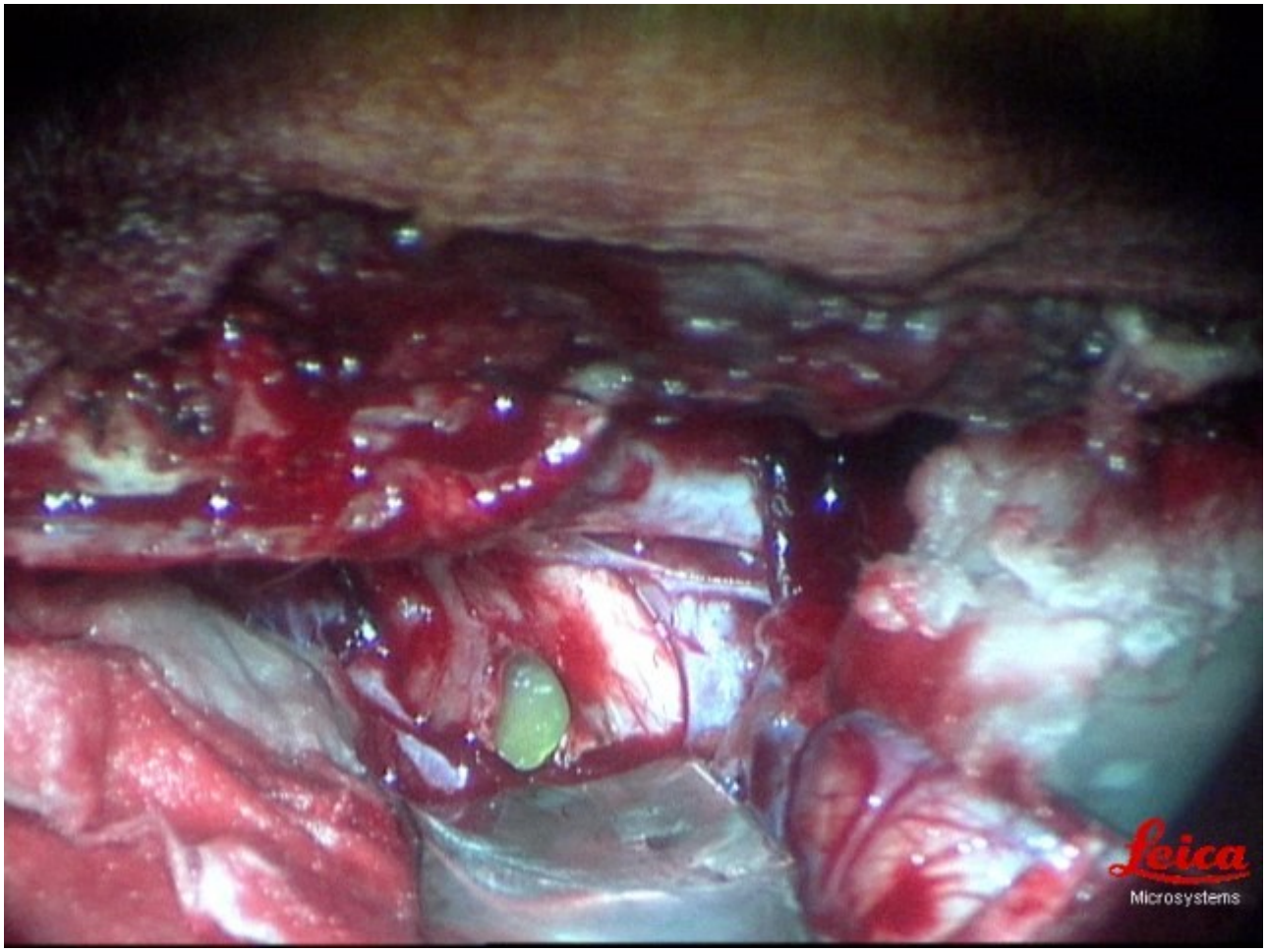


Figure 16: Microsurgical intraoperative image showing cystic craniopharyngioma with crunk case oil aspect of the cyst contents

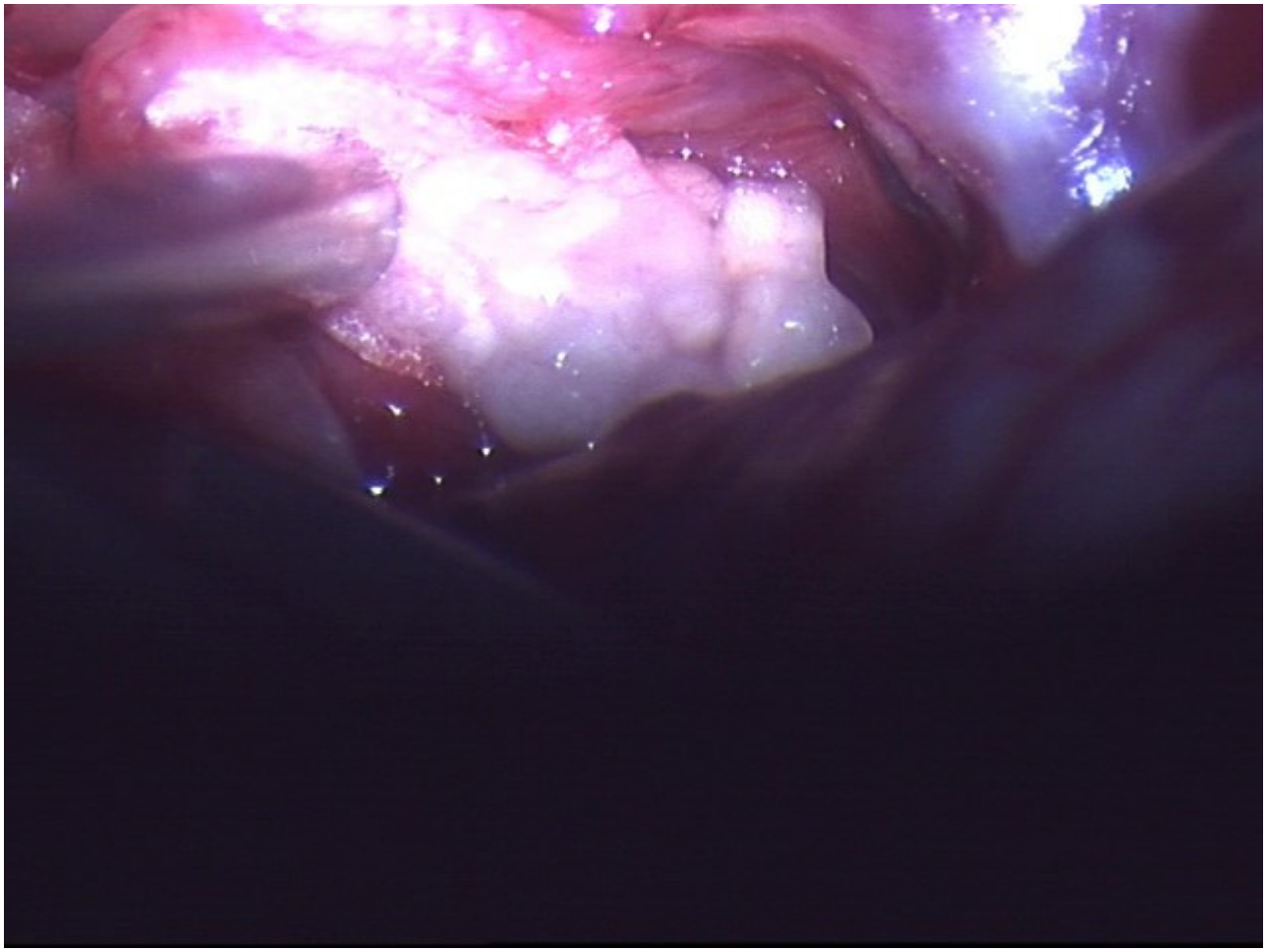


Figure 16: Microsurgical intraoperative image showing piecemeal resection of craniopharyngioma that is compressing the visual apparatus. See the removal of the intratumoral calcification.

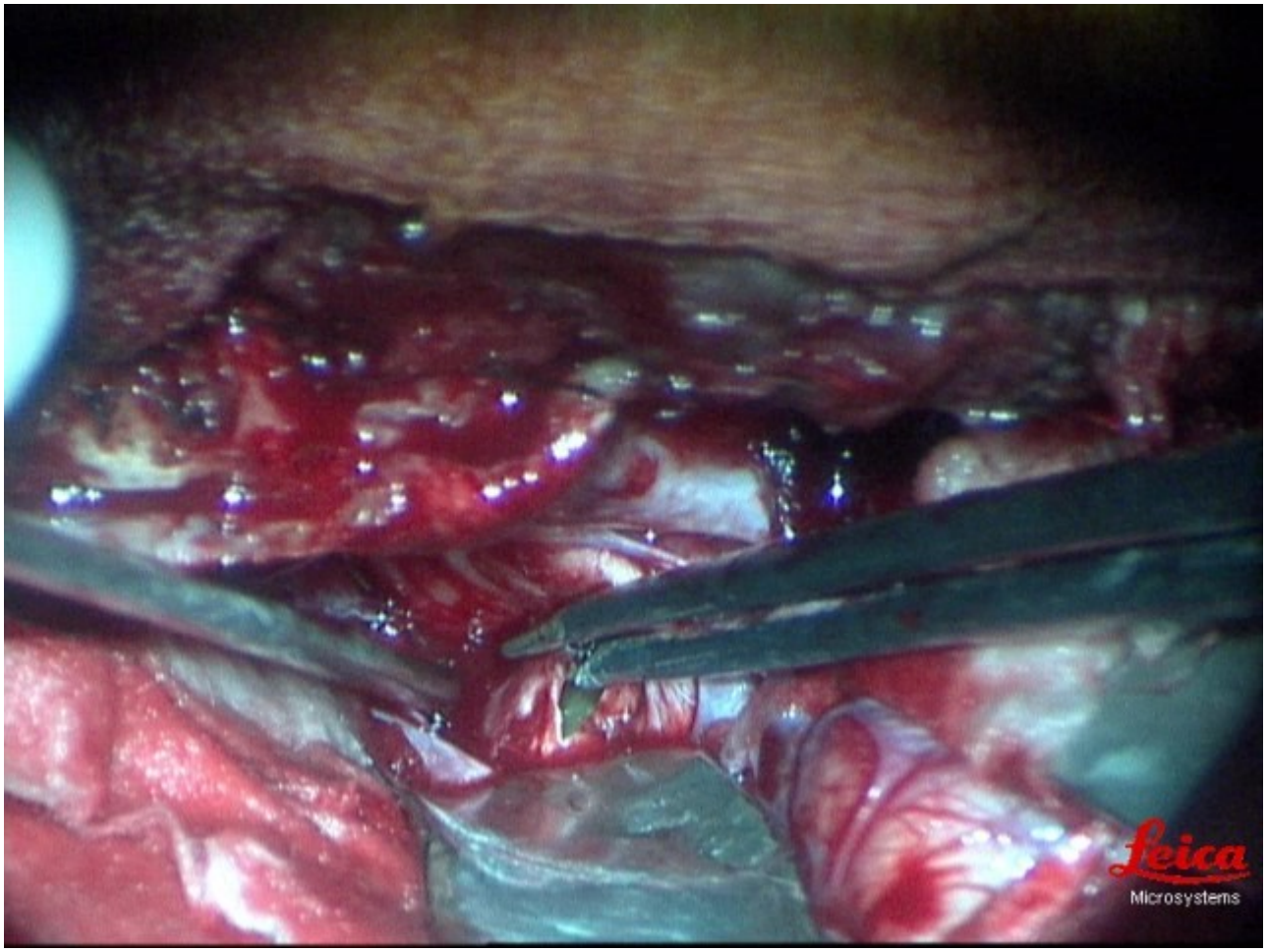


Figure 17: Microsurgical intraoperative image showing capsular dissection of a cystic craniopharyngioma

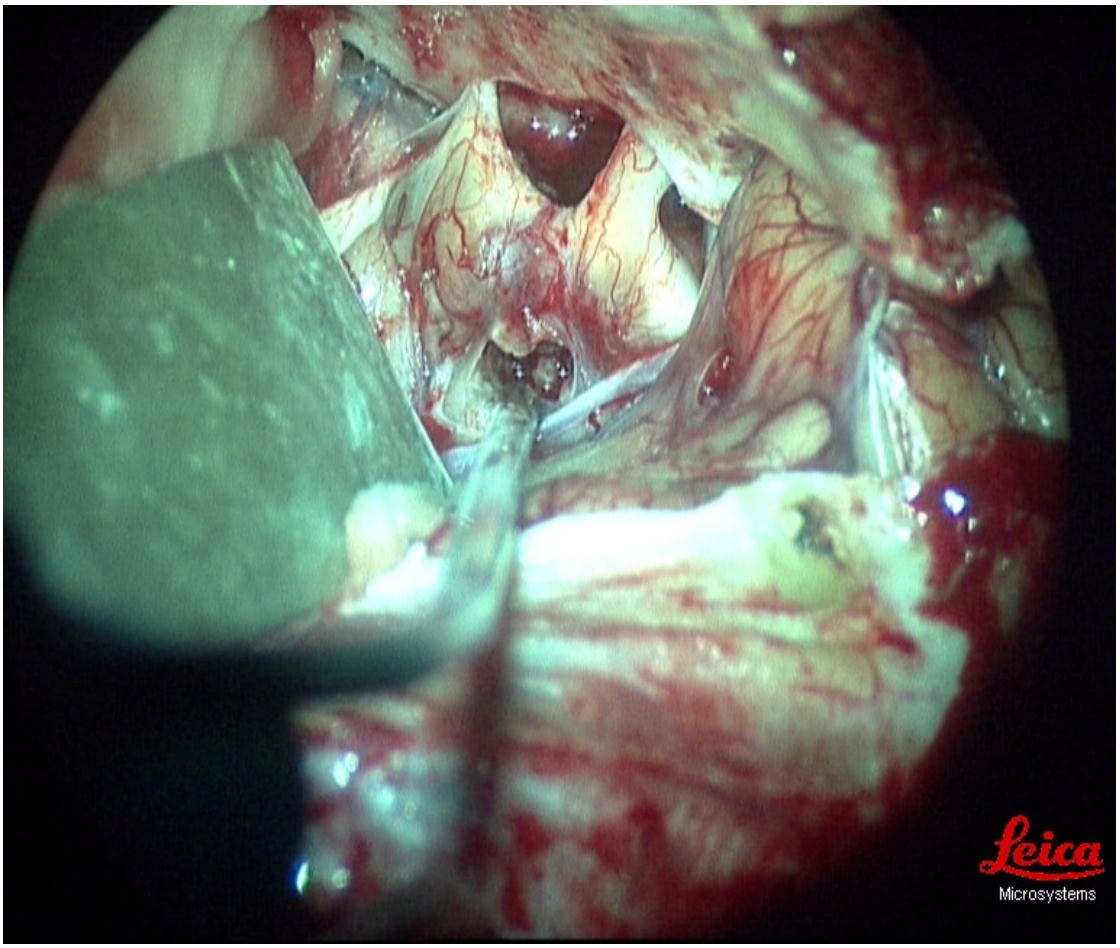


Figure 18: Microsurgical intra-operative image showing decompression of the optic apparatus in a patient operated for craniopharyngioma with GTR intra-operatively.

DIFFICULTIES

Difficulties primarily relate to visualization of the opposite carotid artery and access to the third ventricle. Brain retraction may be necessary. In the case of large retrochiasmatic or retrosellar lesions, the pterional approach offers a narrow window that may be obstructed by perforating vessels.

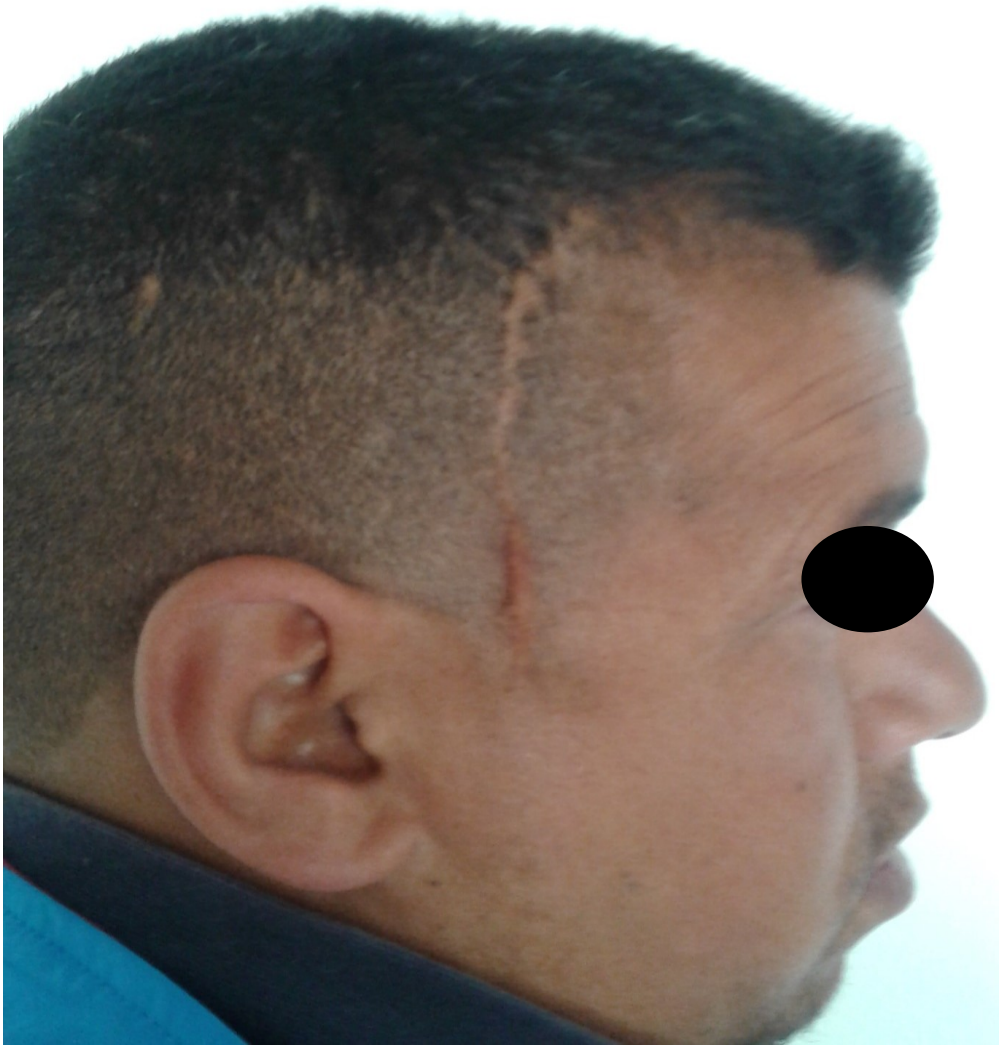


Figure 19: Old scar incision behind the hairline in a patient operated for craniopharyngioma

2. INTERHEMISPHERIC TRANSCALLOSAL APPROACH

SUITABILITY

Large midline tumors with suprasellar extension into the third and, potentially, the lateral ventricle can be removed if the interhemispheric-transcallosal approach is combined with a basal procedure. It may be satisfactorily used alone in the rare setting (3% to 10%) of a purely third ventricular craniopharygioma.

OPERATIVE DETAILS

The patient is placed supine in a Mayfield headrest with the head elevated 30 degrees and the neck flexed. A linear or U-shaped flap incision can be made anterior to the coronal suture. A craniotomy is performed that is predominantly over the nondominant hemisphere but with exposure of the sagittal sinus at approximately two thirds of its length anterior and one third of its length posterior to the coronal suture, although this location may be modified after use of a neuronavigation system. The dura is reflected toward the sinus while taking great care to preserve cortical venous drainage. The ipsilateral hemisphere is gently retracted to allow dissection in the interhemispheric space down to the callosum. Care is taken to identify and preserve the pericallosal arteries on the corpus callosum. A 1.5- to 2-cm incision is made in the corpus callosum, and the lateral ventricle is entered. Tumor may be resected through an enlarged foramen of Monro, or the choroidal fissure can be opened to allow greater access to the third ventricle. Alternatively, an interforniceal approach with direct access to the third ventricle can be used. Internal decompression with piecemeal extirpation of tumor is favored in this location.

DIFFICULTIES

The interhemispheric-transcallosal approach is generally used in combination with a subfrontal or pterional procedure. This approach puts at risk the medial hemisphere from retraction, in addition to the pericallosal arteries and fornix, as well as the veins and floor of the third ventricle.

V. TRANSSPHENOIDAL AND EXTENDED TRANSSPHENOIDAL APPROACHES

SUITABILITY

Smaller midline tumors within the sella or with an infradiaphragmatic suprasellar component may be removed by the transsphenoidal route. This route is most favorable for patients with enlargement of the sella. Significant suprasellar extension of craniopharyngiomas can be difficult to access from a transsphenoidal approach; however, the presence of cystic rather than solid disease makes its use more favorable. Advantages of this approach include the lack of need for brain retraction and potentially better visual outcomes than observed when using cranial approaches.

OPERATIVE DETAILS

The patient is placed supine on the operating table with the head elevated and slightly angled toward the surgeon. Use of a Mayfield headrest and neuronavigation devices can obviate the need for fluoroscopy, although either or both can be used. The procedure can be performed with an endonasal endoscope or by using the operating microscope with a nasal speculum. Sublabial, transseptal, and direct approaches to the sphenoid face have all been described. The mucosa is reflected, and the sphenoid sinus is opened with a drill or Kerrison punch. The mucosa of the

sinus is excised, and the anterior wall of the sella is removed to expose the sella dura. Anterior compression of the anterior pituitary is a common finding, and the gland may need to be divided to provide access to the tumor. For the extended transsphenoidal procedure, the tuberculum sellae can be removed, and additionally, excision of the planum sphenoidale will provide improved access to the suprasellar region. The dura may then be opened over the gland and the circular sinus and anterior to the sella to provide access to the suprasellar cistern. The dural defect is closed with a graft and supported by bone or synthetic plates, with fat placed in the sphenoid and a vascularized nasal flap added for coverage of the site of surgical access from the nasopharynx. Some authors advocate the use of postoperative lumbar drainage to reduce the risk for delayed CSF rhinorrhea.

DIFFICULTIES

Lateral extension of the tumor can be difficult to access from this approach, as can large tumors. Tumor involvement in the region of the anterior cerebral complex may expose the perforating vessels to risk for injury during surgery. Direct control of intracranial neural and vascular structures is inferior when using the transsphenoidal or extended transsphenoidal approach. Suprasellar calcifications are thought to be a contraindication to the use of this approach. This approach can be difficult or impossible to use in children with a poorly pneumatized sinus and in patients with nasal and sinus pathology. Reconstruction after tumor removal can be complicated, and high rates of CSF leakage have been reported in the literature, a problem that has not been completely resolved after extended transsphenoidal surgery. Use of a vascularized nasal mucosal flap is showing promise in this regard.

EXTENT OF RESECTION

Of the 29 patients operated surgically in this series, gross total resection (GTR) was achieved in 19 patients, representing 65.5% and among this group, during follow-up that ranged from 2 to 11 years we noted a recurrence among 03 patients, representing a 16.7% recurrence rate.

Figure showing pre-op and post operative MRI showing GTR of the tumor

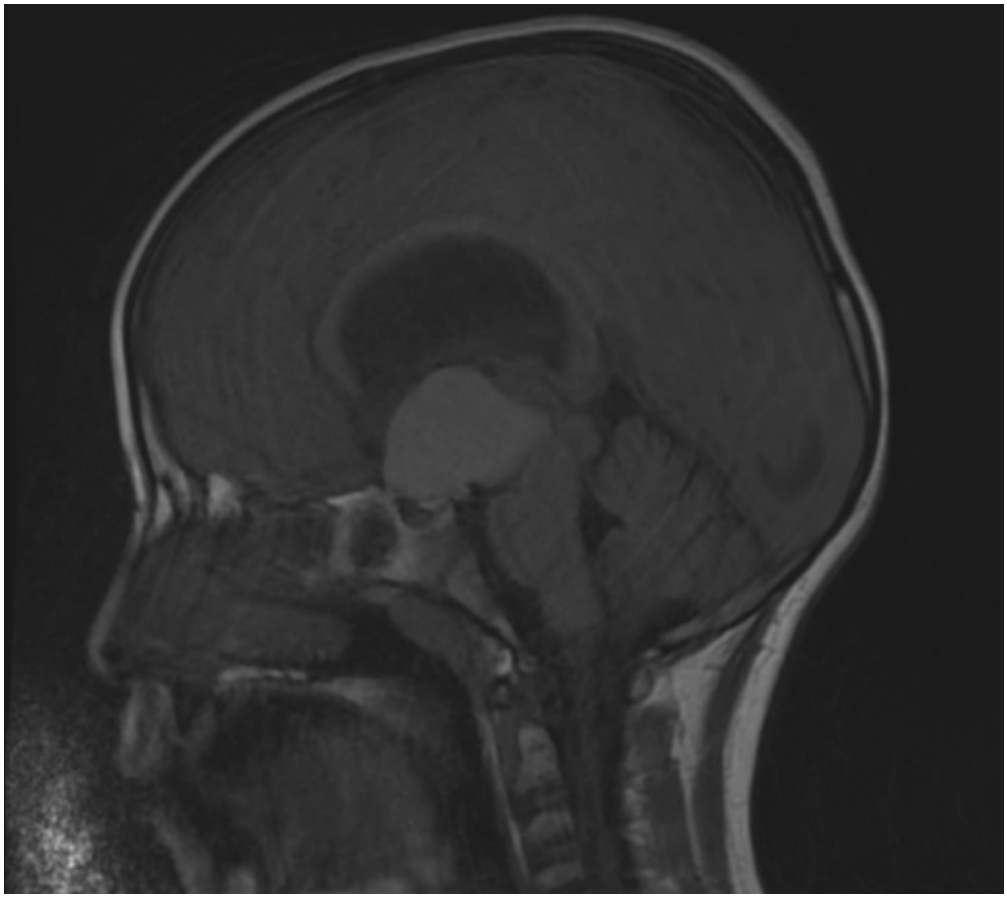


Figure 20: Pre-operative sagittal T1 Flair Showing a large cystic craniopharyngioma in 10 year old boy who presented with signs of increased intracranial pressure.

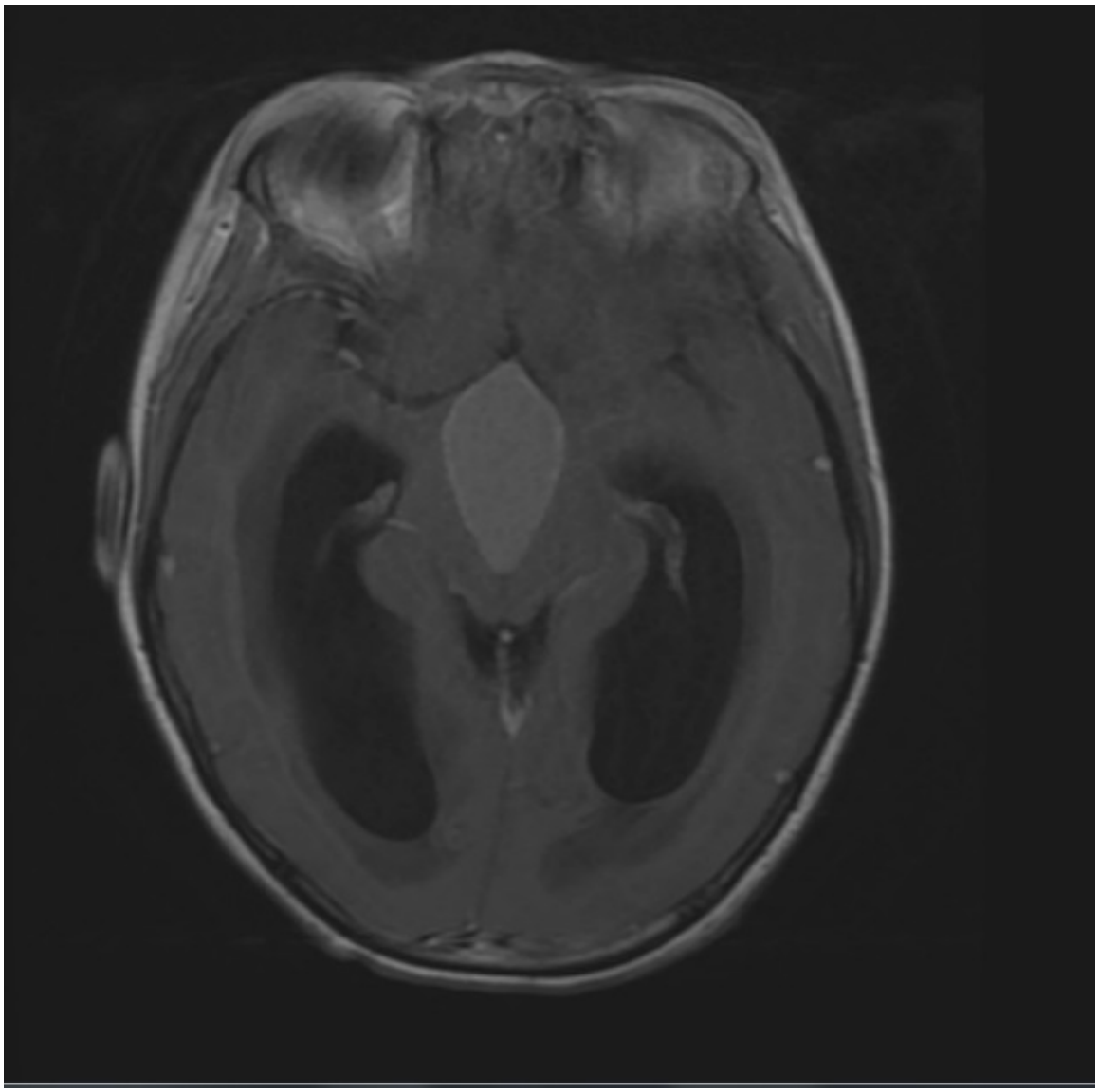


Figure 21: Pre-operative axial T1 Flair showing a large cystic craniopharyngioma in the same patient

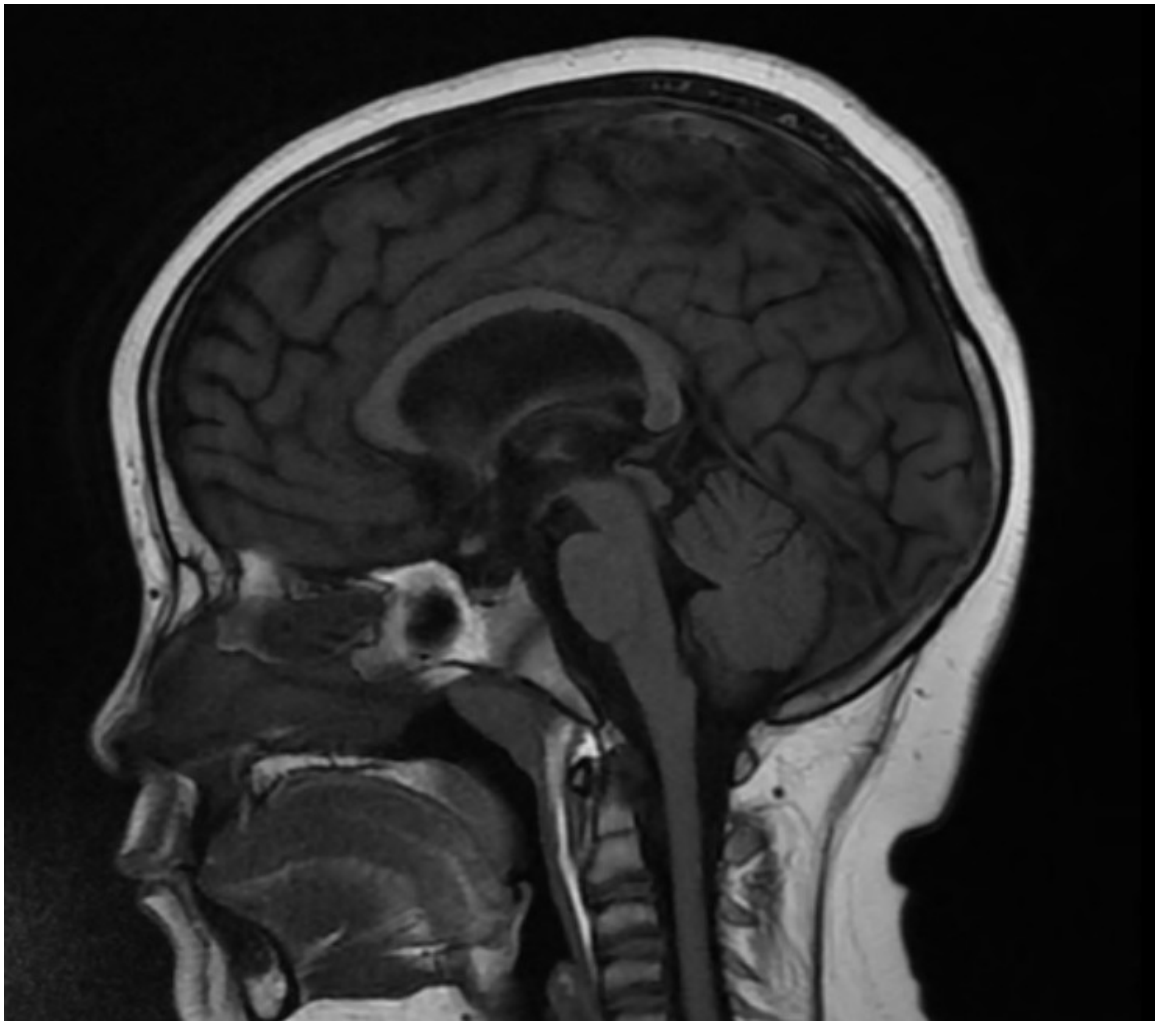


Figure 22: Post-operative mid-sagittal T1 MRI without contrast showing GTR of craniopharyngioma 2 years after surgery without recurrence.

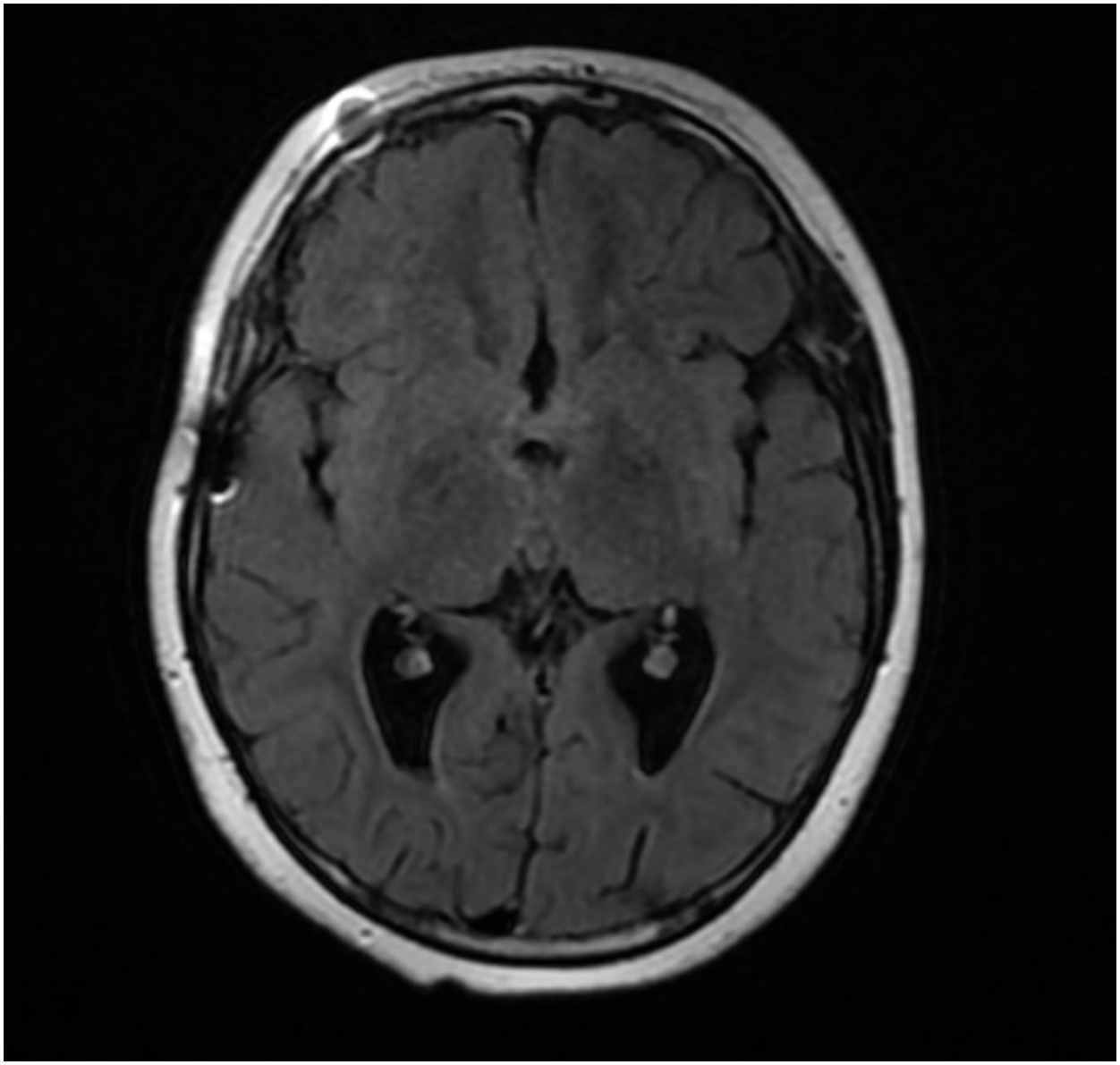


Figure 23: Post-operative Axial T1 Flair MRI without contrast showing GTR of craniopharyngioma 2 years after surgery without recurrence (same patient as figure 22).

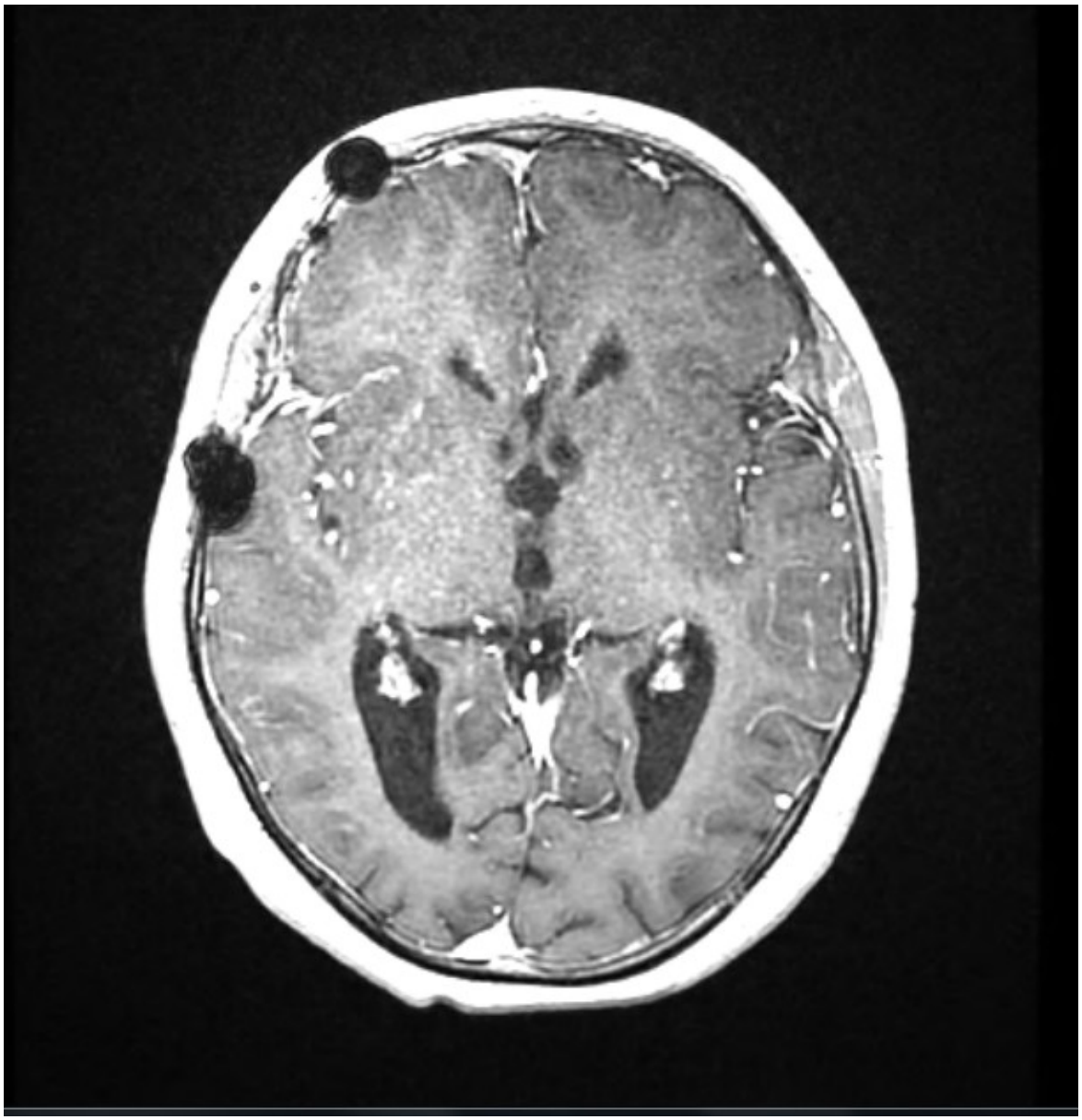


Figure 24: Post-operative Axial T1 MRI with Gadolinium contrast showing GTR of craniopharyngioma 2 years after surgery without recurrence (same patient as figure 22).

For the rest of the 10 patients who had subtotal resection the tumor, residue showed stability in size among the majority of cases except in 3 cases where there was steady growth of the residue with corresponding symptoms.

Figures below show pre-op and post operative MRI with tumor residue in what we call subtotal resection with progression.

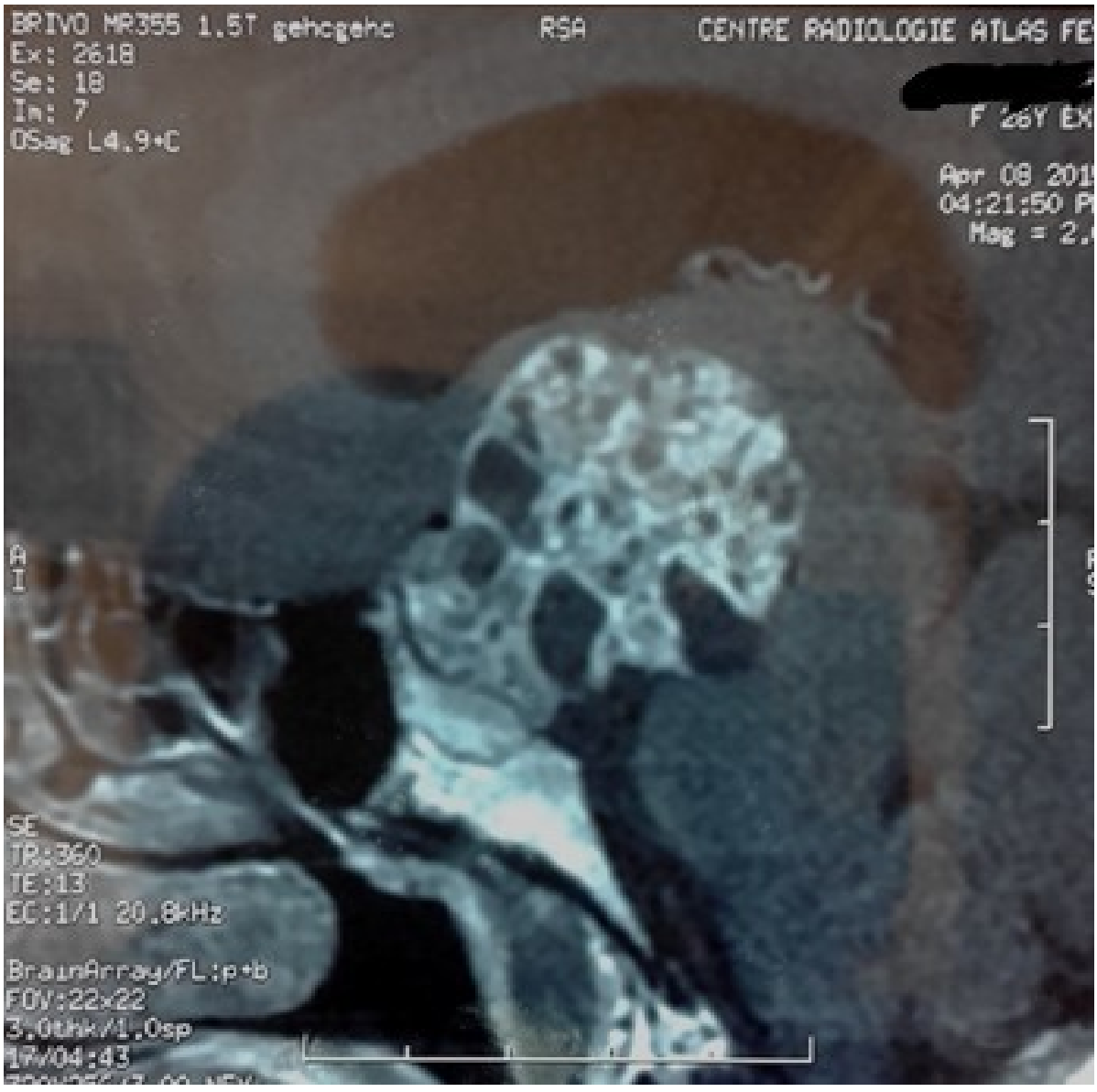


Figure 25: Pre-operative Sagittal T1 MRI with Gadolinium showing a large craniopharyngioma in a 32 year old woman.

This woman presented with a 4 years history of decreased vision, right side paresis and signs of increased intracranial pressure. She was operated by a left fronto-pterional approach and post operatively presented with worsening of the paresis and panhypopituitarism. She was put on high dose steroids and hormone replacement. She improved both her motor function and vision.

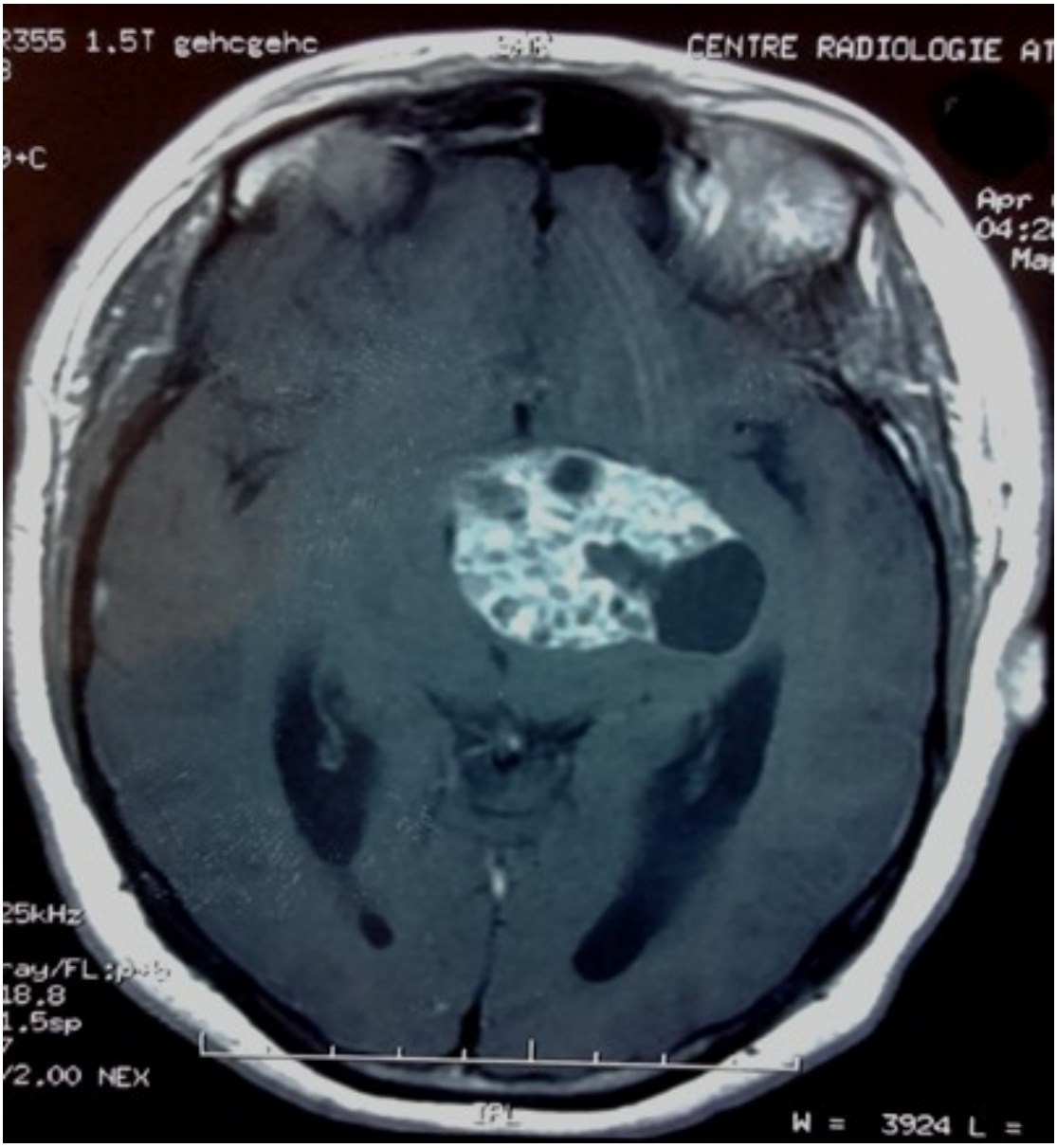


Figure 26: Pre-operative axial T1 MRI with Gadolinium showing a large craniopharyngioma in the same above patient..

The surgeon reported verbatim that he left some suspicious adherent tissue that was adherent to vital neuro-vascular structures. The brain CT scan done immediately and subsequent brain MRI showed no evident residue see figures below.

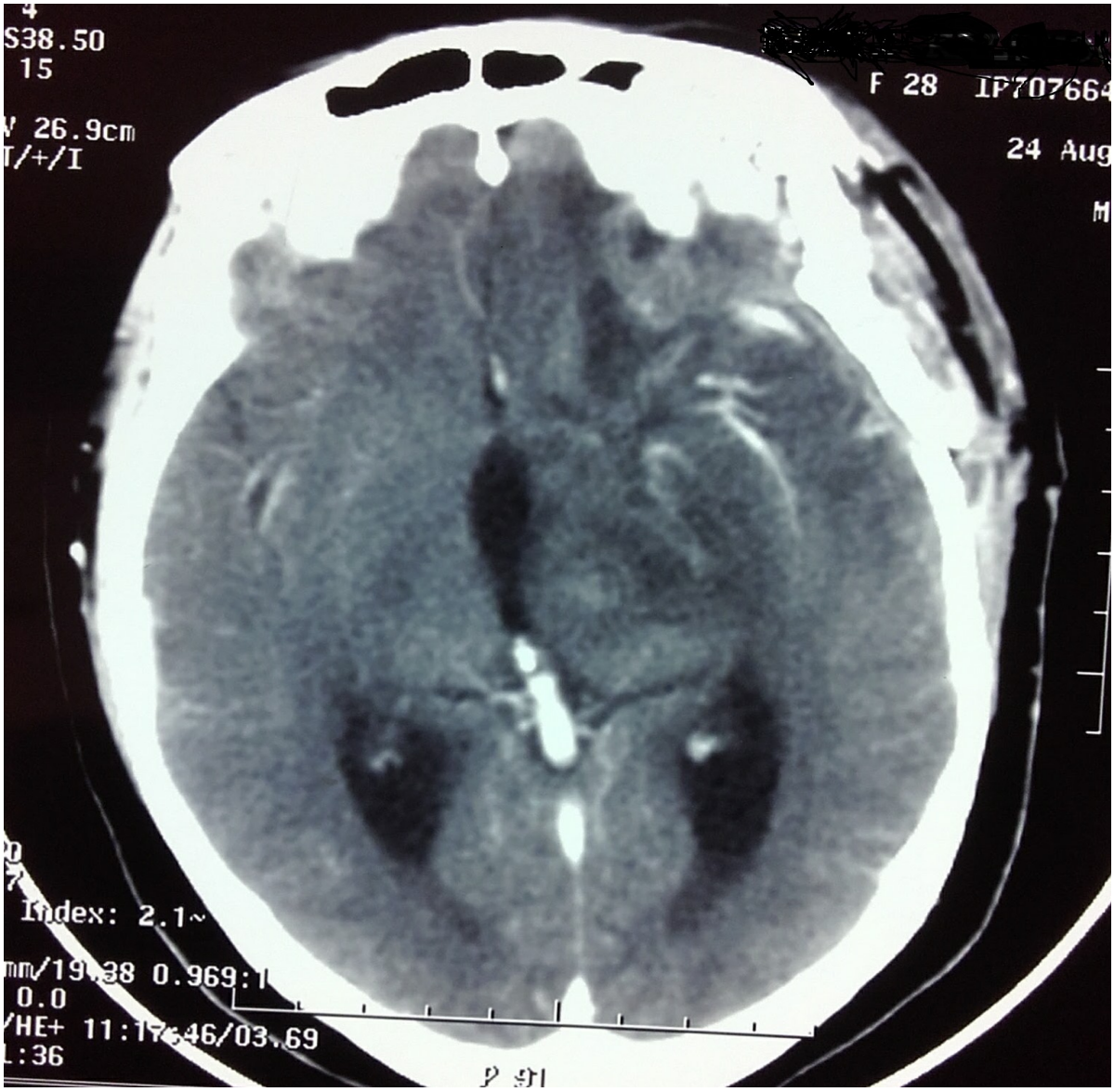


Figure 27: Immediate post-operative brain CT scan with contrast showing gross total resection without any post operative collection.

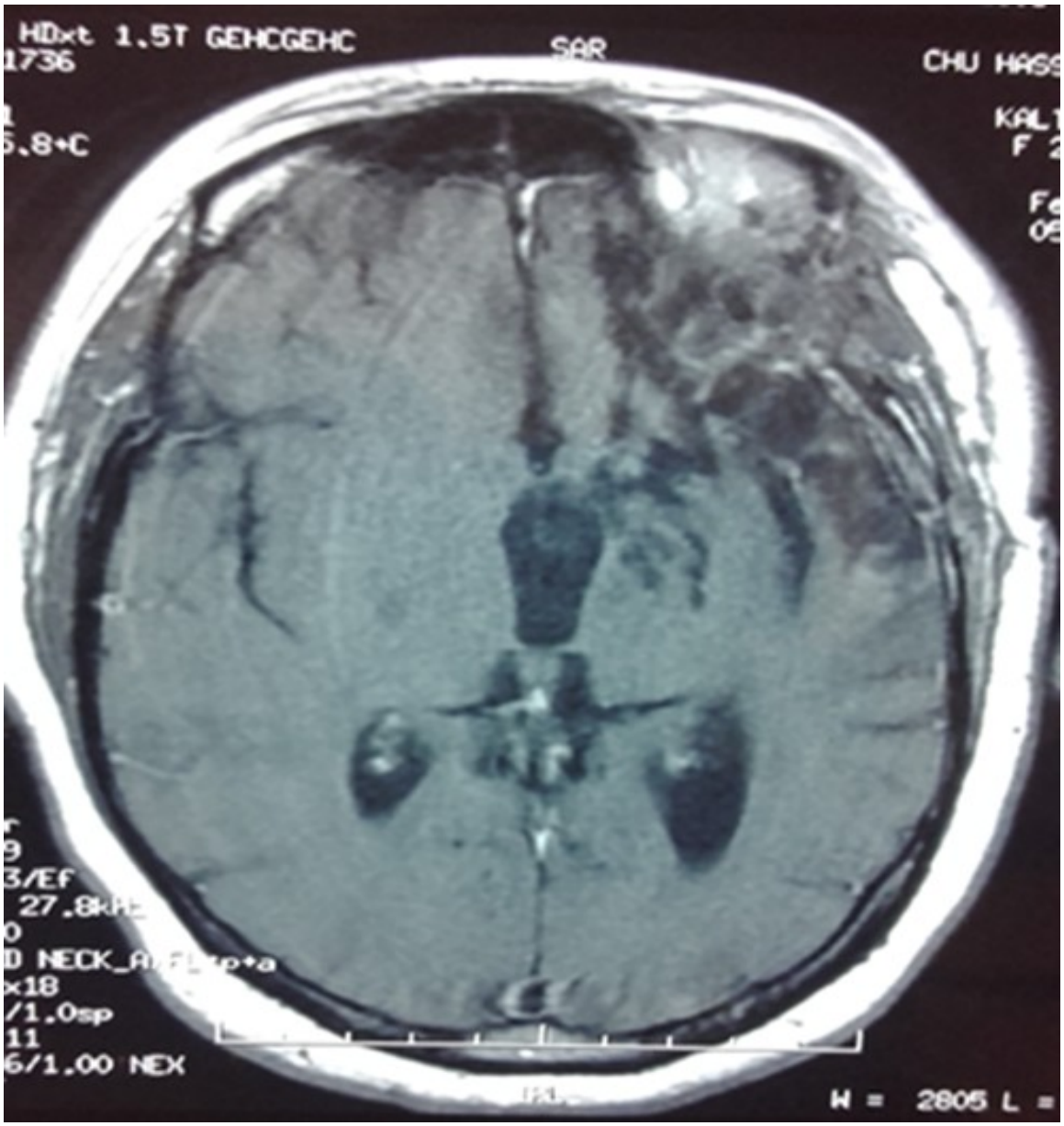


Figure 28: Post operative T1 Flair MRI with Gadolinium done within 6 months of surgery showing no tumor residue.

This patient reported some visual deterioration 3 years after surgery; hence another MRI was done see figures below.

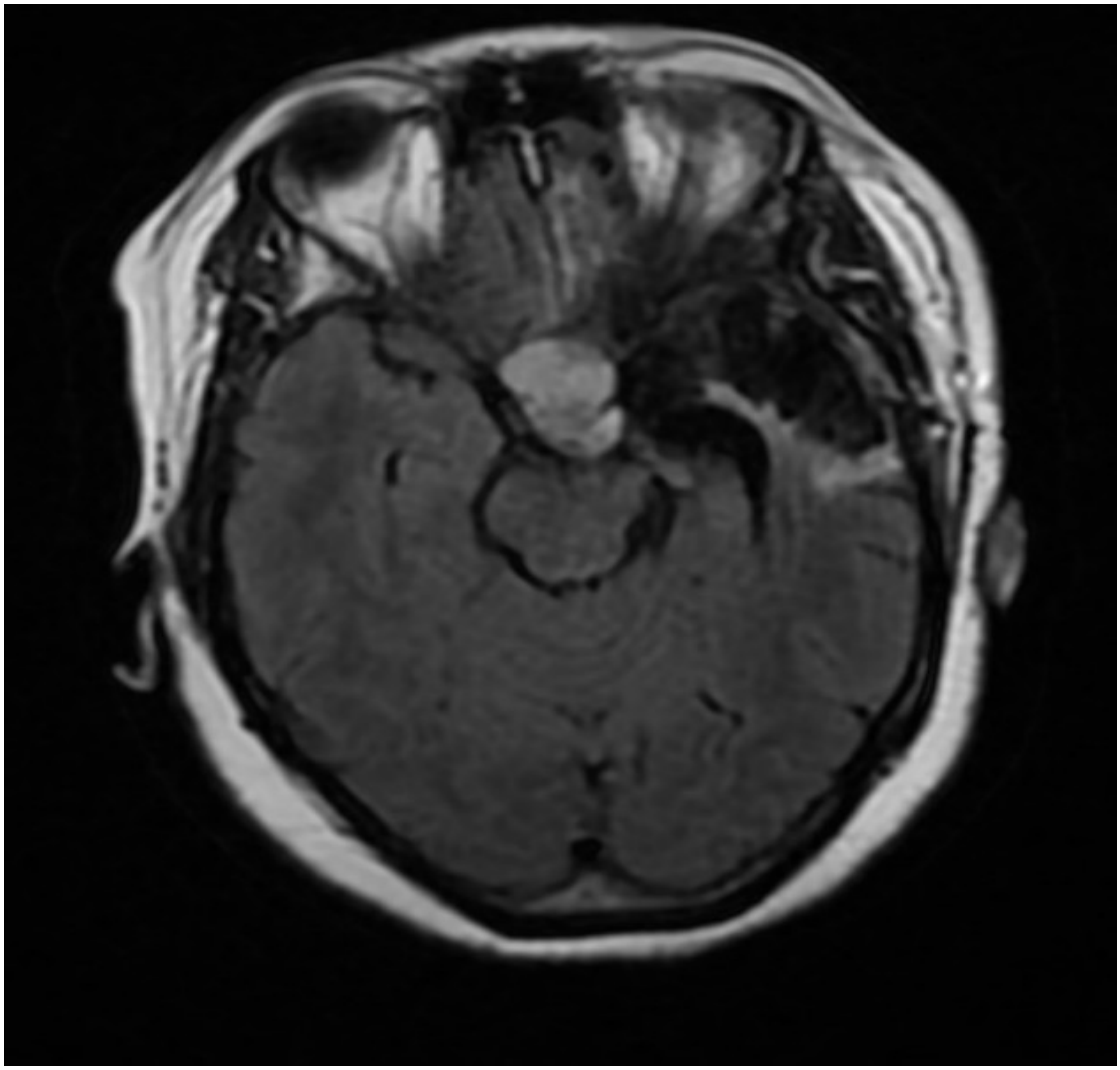


Figure 29: Post operative axial T2 Flair MRI after three years showing residual progression and reported visual deterioration (NB : Residue suspected intraoperatively and not seen on initial imaging)

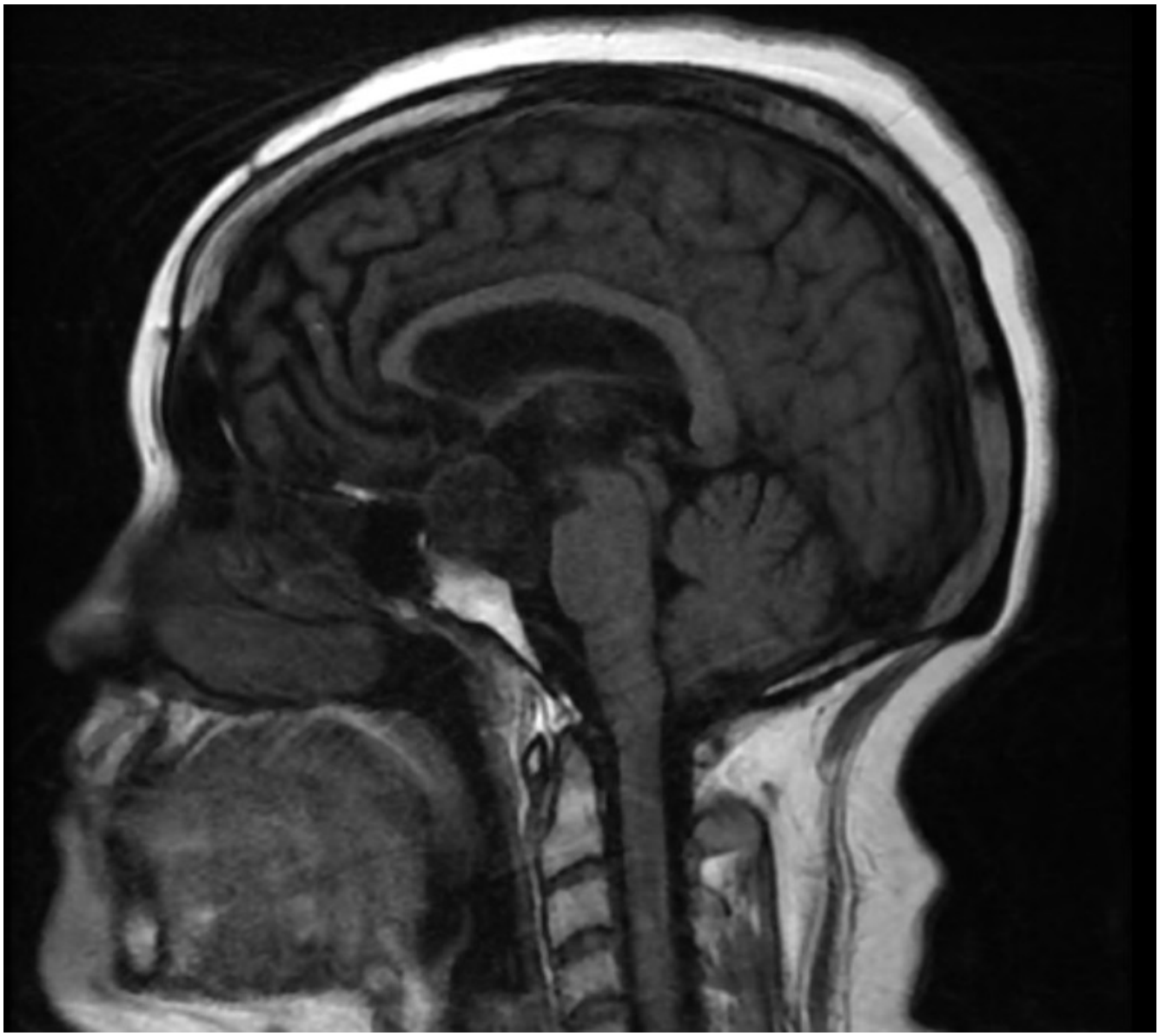


Figure 30: Post operative mid-sagittal T1 Flair MRI after three years showing extent of residual progression in the same patient above.

This patient is scheduled for re-operation

None of the patients has been reoperated for either recurrence or progression of the residue. Two patients are scheduled to be operated and are being followed up in the outpatient clinic with regular opthalmologic examination with neuro-imaging.

VI. OUTCOME AND COMPLICATIONS

In this surgical series, several complications were encountered in the post-operative period. The table below shows the number and proportion of complications that were encounted and how they were managed.

Table 5: Post-operative complications and their management

Complications	Number &Proportion	Management
Diabetes Insipidus (Isolated)	4 (16.7%)	Observation & DDVAP
Panhypopituitarism	6 (25%)	DDVAP, Levothyrox & Hydrocortisone
Post operative meningitis	2(6.9%)	Antibiotics
Seizures	2 (8.3%)	Anti-Epileptic drugs
Post-operative Hematoma Extra/subdural & op site	6 (25%)	Obsevation
Neurological deficits (cranial nerves+Others)	4 (16.7%)	Observation & High dose steroids

As we can see from the table above, the complications ranged from isolated diabetes insipidus in 4 patients treated with both observation and Minrin (DDVAP) with good evolution. The same applied to those who presented with multiple hormone deficiencies (panhypopituitarism) who were treated with hormonal replacement. Most of these hormones were reduced and stopped in the follow-up period leaving only a small percentage that remained dependent on supplimentation.

Post operative meningitis was diagnosed in 2 patients representing 6.79% and was ably treated by adequate intravenous antibiotics. Seizures also appeared in the post operative period in 2 patients and were controlled by anti-epileptic drugs. All patients underwent post operative brain CT scan in the immediate 48 hours and 6 had postoperative hematoma either in the operative site, subdural or extradural spaces and they were all treated conservatively. However, in one patient that was operated by endoscopic trans-nasal trans-sphenoidal approach the hematoma was large and the patient died in the immediate hours after surgery before being evacuated. This case represents one of the mortalities in this series.

Postoperative neurologic deficits in form of cranial nerve palsies and long tract signs also occured in 4 patients representing 16.7% and were treated with high dose steroids that were reduced progressively and stopped with improvement in all patients. One patient a 32 year old man who was operated with total tumor resection with the sacrifice of the pituitary stalk presented with polyphagia and significant weight gain post operatively. The patient is stable on hormone replacement with hydrocortisone, levothyrox and minrin and MRI done annually has not shown any sign of recurrence.

The number of deaths reported in our series was 3 representing a mortality rate of 10. 3%. One death occured in the immediate post operative period while the other two occured in subsequent weeks.

DISCUSSION

I. DEMOGRAPHIC FEATURES

There is no significant sex predominance even though some studies have shown a male predominance in childhood and female predominance in the adulthood. In our study we have seen a male female ratio greater in childhood of 2:1 and a reverse was observed in the adult group with a male female ratio of 1:2.

It is also important to mention that the majority of our patients were children comprising 60% of the total population in this study and this agrees with the assertion that craniopharyngioma is more prevalent in the pediatric population. The mean age in the pediatric cohort was 6.6years with an age range of 5-11 years and a median age of 7. The adult cohort had the mean age of 40.6years of age and age range of 17 to 63years old and a median of 38years. From these data we may deduce that craniopharyngioma has bimodal distribution with the majority of cases in the 1st and 4th decades of life. We also see a wider range in the adult cohort that starts in the 2nd decade to the 7th decade of life making this group heterogenous but due to the few number of cases, we treated them as one group. This heterogeneity brings into question the patient characteristics as related to age which may impact on several aspects of their management hence we were cautious about interpretation of the results in this group. This is a sharp contrast to the pediatric cohort which had a narrow range with almost all patients in the group below the age of 10years and this uniformity offered a unique opportunity to interpret the various aspects of clinical presentation and management in this group. Various studies in the literature involving either childhood or adult craniopharyngioma had their demographics similar to that of our study.

II. CLINICAL PRESENTATION

The median duration of symptoms in a series of 34 adult patients was 10 months. The pediatric cohort of patients in this mixed series had a median symptom duration of just 3 months. Adults are more likely than children to have symptoms of visual or endocrine abnormalities, whereas children more often have symptoms of increased intracranial pressure. In adults, headache, vomiting, and visual disturbance (hemianopia, uniocular visual loss, and diplopia) are the most common initial complaints. More than 80% of adult patients complain of some visual loss at initial evaluation and have evidence of a visual deficit on formal testing. In children, the most common initial symptom is headache, which occurs in 50% to 80%, followed by vomiting (21% to 68%) and visual deterioration (47% to 80%). The most common neurological signs relate to visual disturbance: visual field defects (35% to 79%), papilledema (10% to 50%), optic atrophy, and eye movement disorders. In adult patients, 29% have evidence of papilledema at initial encounter, compared with more than 50% in the pediatric population (47). In very young children, increased head circumference or a bulging fontanelle may be seen. Ataxia is described in about 20% of instances.

Approximately 30% of adults will initially have symptoms of endocrine disturbance. Gonadal insufficiency is the most common endocrine abnormality at diagnosis and consists of loss of libido and reduced masculine hair growth pattern in men. Women may complain of irregular menstrual periods or even amenorrhea. Other endocrinologic problems at initial evaluation include diabetes insipidus, hyperprolactinemia, adrenal insufficiency, and thyroid insufficiency.

Less than 15% of children with craniopharyngioma have complaints attributable to an endocrinologic deficit even though almost 90% have some

endocrine abnormality. Delayed puberty (4% to 24% of patients), obesity (8% to 15%), anorexia, short stature, and precocious puberty are all potential manifestations of craniopharyngioma (47) Growth hormone deficiency is the most frequently observed deficit, with more than 75% of patients being affected. Specific hormonal deficiencies are identified, with luteinizing hormone/follicle-stimulating hormone (40% of patients) more commonly affected than adrenocorticotropic hormone (25%) and thyroid-stimulating hormone (25%) (47) Diabetes insipidus is reported in up to 17% of children and 30% of adults.

Hydrocephalus is an important concomitant factor, particularly in pediatric craniopharyngioma. Hydrocephalus is identified at diagnosis in approximately a third of craniopharyngioma patients overall and in almost one third of children with craniopharyngioma and may require definitive treatment if primary tumor surgery fails to resolve the issue. And this was the case in our study where 10 patients were treated for hydrocephalus pre-operatively.

In one series, 43% of children went on to require long-term treatment of hydrocephalus. In another series, only 29% of adult patients had any evidence of hydrocephalus at initial evaluation, although there was a greater than 50% incidence of hydrocephalus in the pediatric population. Adequate treatment of hydrocephalus is imperative to minimize long-term cognitive deficits in these children, especially in those undergoing radiation therapy. There would seem to be a correlation between shunt requirement and worse outcome; however, it remains to be clarified whether this is directly related to shunting or is due to the presence of generally larger tumors with hypothalamic involvement in this group (47).

Neurobehavioral abnormalities appear to be more common in adults than in children. It has been estimated that more than 30% of adult patients with

craniopharyngioma older than 45 years have dementia or suffer from intermittent confusion, hypersomnia, apathy, or depression. Children may also suffer from neurocognitive decline and exhibit common clinical features such as abulia, psychomotor retardation, and flattening of affect. Adults are less often afflicted with the hypothalamic regulatory symptoms encountered in children with obesity, disturbances of thirst, and alterations in sleep cycles are disorders that seem to predominantly involve the pediatric population.

Very rarely, craniopharyngioma may develop acutely after intratumoral hemorrhage and rarely may rupture and result in aseptic meningitis or spontaneous drainage through the nasopharynx

There is considerable difficulty in diagnosing craniopharyngioma in young children because some may have relatively nonspecific symptoms such as vomiting and irritability, and visual field loss is often overlooked. A high degree of clinical suspicion is needed in such cases. It has been recognized that the diagnosis of brain tumors in children is frequently delayed in comparison to other childhood tumors (47).

In our study, we have also observed that a relatively bigger proportion of patients in the pediatric group presented with signs of increased intracranial pressure as compared to the adults at 67% and 50% respectively. However, when we consider the visual problems all patients in the adult group presented with it 100% while it was evident in only half of the pediatric cohort at 56%. There were comparable rates of endocrine deficiencies in the two groups pegged at 56% and 67% for pediatric and adult cohorts respectively. The hypothalamic dysfunction was seen three times more frequent in the adult cohort as in the pediatric at 33% and 11% respectively.

In a single center study in Taiwan at the department of Surgery, Kaohsiung Medical University Hospital, Chu et al (7) compared the clinic presentation and the surgical outcome of craniopharyngioma between children and adults we see several similaries with that of our study. The number of subjects in this Tawanese study was 40 with 17 children and 23 adults and it was done for surgical subjects from 1990 to 2012 a duration spanning 22 years. The difference with our study was that children were defined by age 20 or below and adults age greater than 20 and were subdivided into several age brackets a thing that we did not make in our study. In the table below, we see a comparable number of males and females in the childrens group while there was a significant proportion of females in the adult group with a male female ratio of 1:2 which was similar with what we found in the adult group in our study. As alluded to the sex ratio differed with what we saw in the childrens group in our study which had more males by a factor of 2.

In terms of the clinical presentation, we see that in this Taiwanese study there were comparable proportions in the visual problems in both groups and so was true with headache. Of note in this study is the significant number of patients in the childrens group who presented with the stunted growth. This study went on to compare the two groups in terms of the imaging characteristics like the tumor composition, size and presence of calcification and finally the histopathology results.

Table 6: Tabulation of the results in the above mentioned Taiwanese study

Characteristics	Total (n=40)	Children (n=17)	Adults (n=23)	p-value
Sex				0.283
Males	15 (37.5%)	8 (47.1%)	7 (30.4%)	
Females	25 (62.5%)	9 (52.9%)	16 (69.6%)	
Age				NA
0-10 yrs	6 (15.0%)	6 (35.3%)	0 (0%)	
11-20 yrs	11 (27.5%)	11 (64.7%)	0 (0%)	
21-30 yrs	9 (22.5%)	0 (0%)	9 (39.2%)	
31-40 yrs	3 (7.5%)	0 (0%)	3 (13.0%)	
41-50 yrs	3 (7.5%)	0 (0%)	3 (13.0%)	
51-60 yrs	5 (12.5%)	0 (0%)	5 (21.8%)	
61-70 yrs	2 (5.0%)	0 (0%)	2 (8.7%)	
>70yrs	1 (2.5%)	0 (0%)	1 (4.3%)	
Clinical presentation				
Visual problem	32 (80%)	13 (76.5%)	19 (82.6%)	0.702
Headache	26 (65.0%)	12 (70.6%)	14 (60.9%)	0.739
Stunted growth	10 (25.0%)	9 (52.9%)	1 (4.3%)	0.001*
Polyuria	9 (22.5%)	5 (29.4%)	4 (17.4%)	0.456
Changes in mentation	6 (15.0%)	2 (11.8%)	4 (17.4%)	1.000
Calcification				
Skull	26 (65.0%)	8 (47.1%)	18 (78.3%)	0.041*
CT	14 (35.0%)	9 (52.9%)	5 (21.7%)	0.749
Composition				0.074
Solid	5 (12.8%)	1 (5.9%)	4 (18.2%)	0.363
Cystic	13 (32.5%)	3 (17.6%)	10 (43.5%)	0.103
Solid & cystic	22 (55.0%)	13 (76.5%)	9 (39.1%)	0.027*
Size of tumor				<.001*
Small (<2cm)	5 (12.5%)	1 (5.9%)	4 (17.4%)	
Moderate (2-4cm)	16 (40.0%)	3 (17.6%)	13 (56.5%)	
Large (4-6cm)	14 (35.0%)	8 (47.1%)	6 (26.1%)	
Giant (>6cm)	5 (12.5%)	5 (29.4%)	0 (0%)	
Tumor histopathology				0.010*
Adamantinomatous	27 (67.5%)	15 (88.2%)	12 (52.2%)	
Squamous papillary	9 (34.8%)	0 (0%)	9 (34.8%)	
Mixed	4 (10%)	2 (11.8%)	2 (8.7%)	

yrs: Years; NA:Not Assessed.
Data are presented as n(%) by group and were compared using Pearson chi-square or Fisher's exact test.
* Indicates significant difference between children and adults. ($P<0.05$)

III. PREOPERATIVE INVESTIGATIONS

Other than undergoing routine blood investigations that includes full blood count, urea and electrolytes, hemostasis, and blood typing it was mandatory for all patients to have baseline serum hormone levels for hypothalamic and anterior pituitary hormones whether the patient has an abnormality or not. This served as a baseline to compare with postoperative values and its well known that many hormone deficiencies in such patients are clinicallay silent hence helps the surgeon to be aware of such to prevent catastrophic events for example in case of hypocortisolemie which may need treatment before surgery and so is diabetes insipidus. This also helps the surgeon with intraoperative decisions as regards to pituitary stalk which may sometimes need to be sacrificed to achieve gross total resection.

The other important pre-operative examination that was done routinely was an ophthalmological examination done by an ophthalmologist to see the state of visual acuity and visual field defects. Being a sellar and suprasellar tumor with various combinations of extention the craniopharyngioma can compress the visual apparatus be it the uni or bilateral optic nerve and chiasma or the optic tract. Also due to its space occupying effect with increasing growth the raised intracranial pressure can also result in papilloedema and optic atrophy. It is also important to note that the raised intracranial pressure could be due to obstructive hydrocepahalus hence the ophthalmological examination may help in the decision to treat the hydrocephalus so as to stabilise the clinical condition before definitively treating the lesion surgically. This inital exam also serves to follow improvement in vision in the post operative period or worsening. In terms of tumor reccurence it can also guide in the decision to re-operate.

1. RADIOLOGICAL ASSESSMENT

This is an integral part of craniopharyngioma diagnosis and management since the presentation is generally non specific and mimicks any space occupying lesion and neuro-radiological assessement by computed tomography scan and nuclear magnetic resonance imaging helps in diagnosis, preoperative planning, diagnosis of hydrocephalus and postoperative assessment of extent of resection and tumor reccurence. And we can loosely say that without neuroradilogical investigation there can be no surgical treatment of craniopharyngioma. In our study 26 files were analysed and as illustrated in **table 4**, we see equal comparable proportions of tumor size in both groups, thus pediatric and adult groups. The tumors were radiologically measured on either CT or MRI for their maximum diameter. The tumors were classified as small, medium, and large/giant. The diamensions were abitrarily subdivided as 2cm or less, between 2 and 6cm and greater than 6cm respectively. Another aspect was the presence of calcification, cystic portion, and hydrocephalus. All these aspects help the surgeon to plan surgery in terms of approach and envision whether gross total resection may be achieved without significant morbity. The MRI with its multiplanar sections can be used to classify the topography of craniopharyngioma. A number of classification schemes have been proposed to assist in decision making regarding surgery, particularly concerning the approach and its concomitant risks.

Hoffman and colleagues (20) proposed intrasellar, prechiasmatic, and retrochiasmatic as three basic subtypes, whereas Samii and Bini devised a five-tier grading system based on vertical height of the tumor. Yasargil and associates (47) recommended grading with respect to the diaphragma and the third ventricle. The most recently proposed grading system, from Puget and co-workers (37) relates to

the degree of involvement of the hypothalamus to further define resectability. No one system has come into widespread use, but all have useful elements for approaching these tumors surgically, considering their position in relation to the chiasm, or taking into account their vertical height and hypothalamic involvement. Giant craniopharyngiomas have been defined as tumors that have a maximal diameter greater than 5 cm. They are frequently cystic in nature and may extend into the anterior, middle, and posterior fossa.

The table 7 below shows the various topographic classification as reported in the literature in chronological order from early 1990s to as recent as 2014.

Summary of topographical classification of craniopharyngiomas from published literature

Authors	Year	Basis of classification	Classification system
Yasargil et al[57]	1990	Relation with diaphragm	Purely intrasellar–infradiaphragmatic Intra- and suprasellar, infra- and supradiaphragmatic Supradiaphragmatic parachiasmatic, extraventricular Intra- and extraventricular Paraventricular in respect to the third ventricle Purely intraventricular
Hoffman[1]	1994	Relation with ventricle	Preventricular Subventricular Retrochiasmatic Intraventricular
Samii and Tatagiba[58]	1997	Tumor extension	I: intrasellar or infradiaphragm II: occupying the cistern with/without an intrasellar component III: lower half of the third ventricle IV: upper half of the third ventricle V: reaching the septum pellucidum or lateral ventricles
Kassam et al[59]	2008	Relation with stalk	Preinfundibular Transinfundibular Retroinfundibular Isolated intraventricular

Pascual et al[39]	2004	Relation with third ventricle	Suprasellar tumor pushing the intact third ventricle floor upward Suprasellar mass breaking through the third ventricle floor and invading the third ventricle cavity Intraventricular mass within the third ventricle cavity and floor, the latter being replaced by the tumor Intraventricular mass completely located within the third ventricle cavity and with the intact floor lying below its inferior surface
Qi et al[60]	2011	Growth pattern of arachnoid envelope around the stalk	Infradiaphragmatic Extra-arachnoidal Intra-arachnoidal Subarachnoidal
Fatemi et al[61]	2009	Anatomic extension of tumor	Retrochiasmal Sellar and suprasellar Cavernous sinus invasion Far lateral extension
Jeswani et al[42]	2016	Endoscopic view of Infundibular	Infundibular I Infundibular II Infundibular III
Matsuo et al[62]	2014	Anatomic association between CP and sellar diaphragm, hypophyseal stalk, and optic nerve	Relation with diaphragm Subdiaphragmatic (complete, incomplete) Supradiaphragmatic Relation with hypophyseal stalk Preinfundibular lateroinfundibular retroinfundibular transinfundibular Relation with optic nerve Prechiasmatic type Retrochiasmatic type Other (pure intrasellar) Tumor extension Third ventricle Interpeduncular cistern Prepontine cistern Frontal base Cavernous sinus Sphenous sinus Sellar type Presellar type Concha type

In our series when we compare the two groups in terms of proportion of calcification as seen on pre-operative brain CT scan we found 44.4% in pediatric group while the proportion was 16.7% in adults which was significant (statistical significance calculation). The presence of calcification in a way also alerts the surgeon as to the degree of tumor adherence to surrounding neurovascular structure which may affect the safety of having gross total resection without unacceptable morbidity and or mortality.

Another aspect is the presence of the cystic lesion which we found in 4 children and in 2 adults. The presence of this cystic component has several implications that include the surgical approach as described in the literature. In our cases however the surgeon was confortable with the frontal pterional approach whatever the aspect of the lesion, i.e solid or cystic.

The neuro-radiological investigation also reveals the presence of hydrocephalus associated with the craniopharyngioma. Hydrocephalus was seen more frequent in childrens'group at 55.6% and merely 16.7% in the other group. The pathophysiology and etiology of hydrocephalus in craniopharyngioma patients is multifactorial and originates from various tumor extensions that cause obstruction. The decision to treat hydrocephalus associated with craniopharyngioma is not simple one. But in general patients diagnosed with craniopharyngioma and hydrocephalus with signs of increased intracranial pressure and decreased level of conscienceness generally benefit from CSF shunting to stabilise their condition before definive surgery. Neurosurgeons are reluctant to put ventricular peritoneal shunts (VPS) in patients to avoid the inherent complications of this procedure that remain significant in terms of mechanical failure and infections complications.

As already alluded to a total of ten patients had VPS done to treat hydrocephalus in our series. In one patient the tumor was obstructing the foramen of monro and unilateral ventricular catheter did not resolve his hydrocephalus hence he underwent endoscopic septostomy to perforate the anterior part of the septum pellucidum to communicate the two ventricles.

IV. SURGICAL PROCEDURE

As already alluded to in our results of the 30 patients in our series 29 patients underwent surgical extirpation of the craniopharyngioma and the one remaining patient was not operated due to very poor medical condition that included advanced age, and medical co-morbities that deemed surgery too risky. It is important to note that the majority of the patients in our series were operated by one surgeon except one case that was operated by another surgeon. The most used approach was either left or right fronto-pterional approach and the choice of this approach did not differ in the two groups. Early in the series one patient was operated by anterior interhemispheric transcallosal approach and no more patients were operated by this approach. The one patient operated by the other surgeon was operated by endoscopic trans-nasal transphenoidal approach. This patient died in intensive care unit in the immediate post-operative period due to hemorrhage in the operative site as shown on post operative brain CT scan. And being a single case we can not generalise the outcome since there are several reports that have highlighted the good outcome especially in sellar or suprasellar craniopharyngioma with largely cystic component.

In a study performed in Germany by Rudolf Fahlbusch et al (42) termed surgical treatment of craniopharyngioma: experience with 168 patients they reported that the pterional approach was most frequently used (39.2%), followed by the transsphenoidal approach (23.6%). For large retrochiasmatic craniopharyngiomas, the bifrontal interhemispheric approach was used increasingly over the pterional approach and led to improved surgical results. Total tumor removal was accomplished in 45.7% of transcranial and 85.7% of transsphenoidal procedures.

Another study in Paris- France published in 2002 by Rémy van Effenterre and Anne-Laure Boch (40) termed craniopharyngioma in adults and children: study of 122 surgical cases. In this study, all patients were operated and followed up by one neurosurgeon (RVE). The operation was performed via a frontopterional approach in 112 cases and a transsphenoidal approach in 10 cases. The tumor removal was considered total in 59%, subtotal in 29%, and partial in 12%. The surgical mortality rate was 2.5%. Even when tumor removal was not complete, radiotherapy was not systematically administered; it was reserved for cases of recurrence. The authors have studied clinical signs, operative characteristics, and ophthalmological, endocrinological, and functional outcomes, as well as recurrence risk and long-term patient survival. The mean follow-up period was 7 years. The functional results in these patients were excellent in 85%, good in 9%, fair in 5% (usually because of ophthalmological sequelae), and poor in 1%. Tumors recurred in 29 patients, but the salvage treatment, by operation or radiotherapy, was successful in 83%. The actuarial patient survival rate was 92% after 5 years and 85% after 10 years. These results compared favorably with the data reported in the literature and that of our series, suggesting that radical surgery of craniopharyngiomas allows good outcome in terms of survival, full recovery, and quality of life for both adults and children.

Jin-Li Jiang et al. (24) have performed a study in Beijing- China concerning microsurgical treatment of craniopharyngioma: Experiences on 183 consecutive patients. In this study, there were no cases of death during operations. The extents of tumor resection were determined by intraoperative judgments and postoperative iconography. There were 133 cases (72.68%) experiencing total tumor removal, 37 cases (20.22%) undergoing subtotal resection, and 13 cases (7.1%) suffering partial removal. There was no statistically significance on total removal rate between the 2

major surgical approaches (frontopterional approach vs anterior interhemispheric approach). During the microsurgery, intact pituitary stalks presented in 111 case, partially preserved stalks showed in 26 patients. Besides, 23 stalks were resected with tumors and 24 cases had no stalks. 9 cases of giant craniopharyngioma (maximum diameter > 6 cm) were removed with the assistance of intra-operative magnetic resonance imaging, including total resection in 6 cases and subtotal resection in 3 cases.

When we compare what we found in the literature, our results are comparable to that of other single center studies and or even better. As illustrated in our results approximately two thirds of our operated patients benefited from gross total resection with acceptable level of morbidity.This could be attributed to surgeons experience with a single mastered approach that he perfected with a steady learning curve. And in majority of patients that had sub-total resection the residue remained stable and did not benefit from radiotherapy. However a number of cases progressed either as residue or as recurrence. Examining this outcome we put into question the benefit of gross total resection with its inherent risk of morbidity when recurrence still occurs hence various schools have advocated the role of subtotal resection with or without radiotherapy.

V. OUTCOME AND COMPLICATIONS

As in any surgical series several complications were reported in our study and included the following, diabetes insipidus, panhypopituitarism, cranial nerve palsy, meningitis, seizures, and postoperative hematomas. In general these complications would be classified as mild to moderate and were treated accordingly with satisfactory outcome. Suffice to say that a number of patients in both pediatric and adult groups required life long hormone replacement especially, hydrocortisone, levothyrox, and minirin (DDVAP). Even though most tolerate the treatment but being on life long treatment is in it self cumbersome. Because of the few number of complications in both groups we treated them together and we tried to see the results of other series reported in the literature.

In a study by Gucev Z.S et al (16) in Macedonia in 13 childrens, 9 males and 4 females , 12 out of 13 children underwent subtotal removal and one had intracystic beomycin the follow up was 6-229 months. All children had multiple pituitary deficiencies after surgery but no deaths were reported in the entire follow-up period.

In another study by Michael E. et al. on endocrinological, neurologic and visual morbidity after craniopharyngioma published in the journal of neurosurgery in 2011. 540 patients underwent surgical resection of their tumor. 138 received biopsy alone followed by some form of radiotherapy. The mean follow up was 54 + /-1.8months. The overall rate of new endocrinopathy was 37% (95% CI=33-41). Patients receiving GTR had over 2.05times the rate of endocrinopathy compared to patients receiving STR (52 vs 19 X2 P<0.00001.

In a Finish study by R.Sorva and O. Heiskanen (43), 123 patients with craniopharyngioma were managed between 1951 and 1982. 45 patients under 16

years while 78 over 16 years with peak incidence in 11-20 years and 47-50 years. 115 patients were operated on and 67 cases (58%) had radical resection and the surgical mortality was 13%. Recurrence occured in 26 patients (21%): 11 after radical and 15 after non radical resection. They concluded that radical operation was the best treatment. For patients with a non radical operation or with a recurrence modern radiotherapy gives long lasting relief.

Ajay Aggarwa et al.(1) in an article , radiotherapy for craniopharyngioma, states that radiotherapy remains the mainstay of multi-disciplinary management of patients with incompletely resected and recurrent craniopharyngioma. Advances in imaging and radiotherapy treatment technologies offer alternatives with the principal aim of improving the accuracy of treatment and reducing the volume of normal brain receiving significant radiation doses.

Saira Alli et al.(43) published an article in November 2016 in the journal of neuro-oncology titled ; microsurgical removal of craniopharyngioma, endoscopic and transcranial techniques for complication avoidance. They said that craniopharyngioma remains a challenging entity for neurosurgeons because of its midline, deep seated location and intimate relationship withcritical neurovascular structures. They also sais that although GTR is ideal, the need to reduce surgical morbidity and preserve quality of life has led to a number of neurosurgical approaches which have attained this goal.

Yuan J. Rao et al (39) in 2017 published an article in the journal of neuro-oncology titled patterns of care and treatment outcomes of patients with craniopharyngioma in the national cancer database (NCDB). This study included 697patients, (166 children and 531 adults) treated for craniopharyngioma between 2004 and 2014 in the NCDB. Adjuvant radiotherapy was defined if given within

6months of surgery. Limited surgery was defined as biopsy or subtotal resection. Mean follow up was 46months. 21% received ajuvant radiotherapy. The 5 year survival among limited resection, limited resection + radiotherapy and GTR were 75%, 85% and 82% p=0.2. On multi-variate analysis of the 195 patients with known surgical extent limited resection + radiotherapy was associated with improved overall survival compared to limited resection.

Simon J.B and team reported in Pituitary in 2016 in a paper titled pronounced response of papillary craniopharyngioma to treatment with vemurafenib a BRAF inhibitor. This was a case of somatic BRAF V 600^{E} mutation, the tumor responded promptly and progressively to monotherapy with vemurafenib. The molecular targeted use of BRAF inhibitor Vemurafenib and excellent tumor response by support a pathological role for the BRAF V 600^{E} mutation in papillary craniopharyngioma. Craniopharyngioma have not been previously considered as treatable with cytotoxic or targeted agents. BRAF inhibitors may be an effective treatment option as part of the multimodal therapeutic armamenterium for this condition. The successful use of vemurafenib in this patient is a proof of concept that justifies further clinical studies and represents a potential paradigm shift in the medical management of patients harbouring craniopharyngioma.

VI. SYNOPSIS OF THE DISCUSSION

From the discussion of our surgical series which we have done systematically from our results several issues stand out clear and these include

i. Our patient's characteristics resembled that of other studies in the literrature of same design.

ii. The clinical presentation varied to some extent in the two groups and is in agreement with that reported in other studies.

iii. Our patients were thouroughly explored pre-operatively in terms of endocrinological, ophthalmological and neuro-radilogical investigation however there is paucity of follow up data and neuropsychological testing which plays a significant measure of outcome.

iv. As single center single surgeon experience it has compared well with a study done in a developed, resource rich setting hence our findings could be generalised to some extent.

v. Our study has been limited since no case of recurrence was reoperated mainly due to accessibility problems.

vi. It is clear in this study that the approach did not differ between the two groups and the single approach mastered had generated satsisfactory results as compared to all the approaches described relevant to defferent topography of the lesion.

vii. The most frequent complications were the endocrinological and were also reported in the various papers reported and of importance is that most of them were treated symptomatically and only few led to permanent sequalae.

viii. Our level of mortality and morbity did not differ significantly and

conclusion could be drawn as regards to surgical management of craniopharyngioma

ix. In general management of craniopharyngioma comprise surgery by different approaches that could be supplimented by various forms of radiotherapy as judged necessary. In cystic tumors, intracystic chemotharapy with Bleomycin and other molecules has been reported. The use of cytotoxic drugs has been tested e.g Vemurafenib though still in the stage of clinical trial.

CONCLUSION

From our study and those studies found in the littérature we come to conclude that craniopharyngioma management still rests of surgical extirpation. While GTR is the desired outcome, it remains challenging and it is not feaseable in considerable number of proportion of patients. But as we have seen STR still offers reasonable quality of life with or without adjuvant radiotherapy. Considerable level of complications are associated with the surgical management of craniopharyngioma but most are amenable to treatment and good quality of life after surgery could be assured. While we advocate surgery for craniopharyngioma as the main treatment paradigm each case must be treated on individual basis and the availability of other treatment options like adjuvant radiotherapy, steriotactic radiosurgery, intracystic Bleomycin, and other systemic chemotherapy which are still in trial phase must be explored.

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