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What Remains of Transcranial Surgery in The Treatment of Pituitaryadenomas.

K.Bouaita[1], Shabay.Z[2], N.Ioualalen[3]
Department Of Neurosurgery, Hospital Ali Ait Idir, University Of Algeries, Algeria

Abstract: *The objective of this work is to elaborate the role and the indications of the trans cranial surgery in the treatment of pituitary adenomas.This is a retrospective series of 29 cases of pituitary macroadenomas operated at Ali Ait Idir hospital from 2010 to 2015. Mean age of the patients was 35 years. The sex ratio was 17females / 12males. The time to consultation was between 11 months and 2 years after onset of symptoms. Clinical signs were predominantlyopto-chiasmatic syndrome with blurred vision in 95% of cases. 10patients hormonal imbalance syndrome, a cavernous sinus syndromewith involvement ofunilateral third cranial nerve III in 04 patients (drooping of the upper eyelid). A syndrome of intracranial hypertension in patients with an incomplete frontal lobe syndrome 04pateints and generalized tonic-clonic seizures in two patients.All patients had preoperative MRI. Twenty-nine patients underwent transcranial surgery, the most common approachin all patients (100% of cases) is the frontotemporal approachwith opening of the Sylvian valley. Ten patients had already been operated at first by endoscopic endonasalapproach including five patients who were already operated twice transsphenoidal endoscopic approach.Improvementin visual function in 54.7% of cases, remained unchanged in 34.5% of cases and worsened in 13.8% of patients.*

Keywords: *endocrine disorders, pituitary adenoma, , visual function, total resection transcranial surgery.*

I. Introduction

Since the first description of acromegaly by PIERRE MARIE in 1886 andthe individualisation of its origin as an anterior hypophysis tumor (1), many things have changed in the field of pituitary adenomas especially in the diagnostic and therapeutic management. First by the re-introduction of trans-sphenoidal approach by Gérard GUIOT in (1958) under the image intensifier and there was additional finesse provided by the use of the microscope introduced by Jules HARDY to achieve a microscopic transsphenoidal surgery (2-3). With the development of technology and the introduction of minimally invasive surgery, a pure endoscopic transsphenoidal technique was introduced in 1997, JHO reported a series of 50 cases of which 46 were treated with this approach (4-5-6) . Paolo Cappabianca and Enrico DeDevitiis are among the first to report their experience in this field,by introducing the term « functional endoscopic pituitary surgery » (4-5-6).

Transcranial surgery was the first surgical approach used historically for the surgical treatment of pituitary tumors. Horsley described it in 1906, several cases operated successfully intracranially by sub-frontal approach(10). Cushing standardised the technique with a median direct sub-frontal approach.

Gazi Yaşargil demonstrated the benefits of transcranial surgery for sellar and suprasellar tumors using pterional approach minimizing brain retraction after opening the Sylvian fissure and arachnoid of the basal cisterns (2).

The progress of endocrinology, also changed the therapeutic attitude to the pituitary adenomas. The initial distinction between secreting adenoma and non-secreting adenoma, through endocrinological classification is more precise. Finally, a fundamental contribution is the development of modern imaging: CT and especially MRI, made accessible to therapists as a reliable and harmless imaging modality, enabling to address therapeutic indications which only take into accountthe disease itself and nothing else.The purpose of the pituitary surgery is the complete removal of the adenoma, and decompression of the optical canals. Currently the endoscopic endonasaltranssphenoidal approach is the most widely used in the surgical treatment of pituitary adenomas. Rare cases nevertheless may require a transcranial approach. In this series, we will specify the role and the indication of the trans cranial surgery in the treatment of pituitary adenomas.

II. patients and methodes

This is a retrospective study of 29 patients with pituitary macroadenomasoperated at Ali aitIdir hospital from 2010-2015.Mean age of the patients was 35 years. The sex ratio was 17females / 12males. The time to consultation was between 11 months and 2 years after onset of symptoms.All the patients were investigated in Neurosurgical and Endocrinological Departments. Visual acuity and visual field defects andcartographic fields were done by the department of ophthalmology in pre and post-operatively in eachvisit.Hormonal investigations include T4, TSH, blood Cortisol, follicle-stimulatinghormone (FSH), luteinisinghormone (LH), prolactine and Growth hormone (GH) for all patients pre and post-operatively.

Clinical signs were dominated by opto-chiasmaticsyndrome with visualdeficits in95% of patients**.** Diminution of visualacuitywas the major symptom.It was unilateral in 40% and bilateral in 60% of patients. We noted a high frequency of blindness (40%). Visual field deficits were observed in lesionscompressing the optic chiasma with retro chiasmaticextension (classicbitemporal in 13 patients). Endocrinal syndrome in10patients with amenorrhea –galactorrhea in females, cushing syndromeand diabetes insipidus.Cavernous sinus syndrome with unilateral IIIrd cranialnerve palsy in 04 patients (drooping of upper eyelid).

Intracranial hypertensionsyndrome(headaches and vomitting and on fundoscopy: bilateral papillary œdema) in patients withincompletefrontal lobe syndrome 04pateints.tonico-clonicgeneralised seizures in two patients.

All patients had an MRI preoperativelyin precise sagittal, coronal and frontal cuts; the form of the adenoma (hour-glass adenoma), size of tumor, the extent of the tumor and its close relationship with both supra-clinoid internal carotid arteries, the lateral extent of the lesion to the two cavernous sinuses and sub-frontal region.

The magnetic resonance imaging in coronal cuts can show the retro chiasmal extension of the tumor and towards the foramen of Monro which is responsible for a bi ventricular hydrocephalus. In addition, it shows the extension of the lesion in the sphenoid sinus to the clivus.

The CT scan is essential especially in coronal, axial cuts.It retains a significant interest in the study of the sphenoid sinus, morphology, the existence of any intra-sinus walls or pathology of the mucosa (importantly endoscopic endonasal approach).In the immediate postoperative period we performed a CT scan axial cuts to eliminate a surgical cavity hematoma or cerebral edema, postoperative MRI 3-6 months would be repeated annually there after. Eighteen of the 29 cases had giant adenomas with maximum tumor diameter exceeding 4 cm. Hydrocephalus was observed in 4 patients, two of which had a ventricular peritoneal shunt.

Twenty-nine patients were operated by transcranial route, the most common approach in all patients (100% of cases) is the frontotemporal approach with opening of the Sylvian valley.

The left frontotemporal approach was used in 05 patients (in 17.24% of cases), in whichthere was a tumor extension laterally to the left and a significant decline in visual acuity of the left side.Ten patients had already been operated atthe first stage by endoscopic endonasa lincluding five patients who were already operated twice bytranssphenoidal endoscopic approach.

These last patients had intra and suprasellar macroadenoma with a lower extension in the sphenoid sinus, the consistency of the tumor during transsphenoidal surgery was one of the factors that has limited the quality of resection, and the hourglass or figure eight shape of the adenoma.Nineteen patients were operated intracranially directly because of the importance and extent of the lesion especially lateral to the cavernous sinus and its extension in front and towards the clivus, macroadenoma with a small sella turcica, hourglass adenoma below and above the diaphragm.

III. Results

 Surgical Results: The extent of tumor excision was evaluated immediate postoperatively by a brain ct-scan and a brain MRI after 3 months post operatively.Surgical excision was complete in 10patients (34,5% of patients),subtotal in 13 patients (44,8% of patients) and partial in 6patients (20,7 % of patients),

Resection was considered subtotal if a tumor nodule had been left in place, either in the optic canal or adjacent the internal carotid artery, the pituitary stalk or adjacent the optic chiasm because of adhesions.

▲ **Visual Results**: The visual function analysis was first performed in the immediate postoperative period looking for a visual improvement or worsening by the neurosurgeon himself, followedby the ophthalmologistin the short and long term.

A visual function improvement was noted in 54.7% of patients, remained unchanged in 34.5% and worsened in 13.8% of patients. The visual field defect was improved after surgery in ten patients.

▲ **Endocrine Results**:The endocrine evaluation analysis in the immediate postoperative periodfound diabetes insipidus in eight patients, pan-hypopituitarism in six patients who needed replacement therapy postoperatoively.04 patients are still under treatment with Minirin for permanent diabetes insipidus.

All patients are monitored regularly by the Department of Endocrinology clinically, radiologically and by regular hormonal analysis.

The different types of adenomas found in our series; Chromophobic or non secretingadenomain nineteen patients (65.5%), prolactinomas in 6 patients (20.5% of cases), corticotrophic adenoma in 04 patients (14% of cases).

▲ **Postoperative Follow up**: All patients were regularly followed up clinically and radiologically by the neurosurgeon, endocrinologist and ophthalmologist.

The follow-up period ranged from a 1 to 5 years. All patients with residual tumor underwent radiological examinations especially brain MRI to assess the evolutionary potential of the lesion and to act accordingly.

4 cases of tumor recurrence within an average of 2 years were seen. They posed therapeutic choice difficulties. One patient was operated by endoscopic endonasaltranssphenoidal approach as the residual tumor was intra-sellar.The other three patients underwent radiotherapy. For patients in whomresectionqualitywassatisfactory, an MRI wasperformedevery six months the first year, everyyear for 5 years, and everytwoyearsthereafter.

 Mortality And Morbidity: Postoperative morbidity was dominated by;
a patient had aIIIrd cranial nerve palsy which improved partially after a long follow-up 16 months.
- Delayed cerebrospinal rhinorrhea that appeared in a patient operated for a macro-prolactinoma one year after the intervention by transcranial approach and bromocriptine as medical treatment, which was repaired by endoscopic endonasaltranssphenoidal approach.
- Transient diabetes insipidus in 06 patients which disappeared after an average of 4-5days,
-Eight patients developed hypopituitarism in immediate postoperative period needing replacement therapy.
Postoperative mortality was zero.

IV. Discussion

According to the different series in the literature, less than 10% of pituitary tumors require trans-cranial surgery. The main reason for this decline are the advancedtechniques and low mortality -morbidity after this surgery.

The results of transcranial pituitary surgery in literature namely the recovery of visual function, correction of hormonal hypersecretion or the quality of tumor removal and improved preoperative pituitary deficit are not homogeneous in comparison to the results of transsphenoidal surgery in the recent decades.

In large series of patients, it appears that one can have the best functional results after transcranial resection (7-8-9-10), as in the case of a series of 300 patients reported by Patterson et al (11). The normalization of vision has been reported retrospectively in 17% of patients after transsphenoidal procedures (n = 70) and 45% of patients after transcranial surgery (n = 94). After all, there are several authors who report similar or better results with the transsphenoidal approach in terms of the rate of recovery of visual functions; these results are similar and identical with our results regarding transcranial surgery for pituitary adenomas(11-12-13-14).

Fahlbusch et al,comparing the trans-sphenoidal surgery with transcranial surgery,reported a normalization and improvement of visual function in 80% and 48%respectively,for pituitary adenomas (3).Visual acuity and visual fields deteriorated in 2% of cases in the group operated transsphenoidally compared to 22% of cases in the group of transcranial surgery.At all times there is no doubt that the risk of postoperative pituitary hormonal dysfunction and anterior pituitaryfailureis more significant in the Transcranial than transsphenoidal approaches (15, 16).

On a retrospective series of 155 patients with non-secreting pituitary adenomas reported by Wichers-Rother et al, The corticotrophic axis and the thyroid axis were significantly altered after transcranial surgery than after transsphenoidal surgery atlong term follow up (17). As regards to the quality and extent of tumor resection, the series of Mortini et al. (9), concluded that 40% of cases operated by transsphenoidal approach (85 patients) underwent complete resection versus 42% for intracranial surgery (26 patients).

Mortiniet al have reported that there was a visual improvement in 55% of cases operated by transsphenoidal approach versus 74.5% of cases by transcranial pathway (9).The mortality rate for a transsphenoidal procedure in experienced hands should be less than 1%. In addition the literature suggests an overall morbidity lower 10%. These data have encouraged more and more surgeons to consider the pituitary transsphenoidal approach as a standard for almost all pituitary adenomas (8-18-19-20).However, there are still a number of different indications for transcranial approach for pituitary adenomas (3-10-21-22-23-24-25-26), one of the indications is the giant adenoma or with wide intra-sellaire component in combination with a smallsellaturcica.

Some surgeons advocate a trans-cranial first for hourglass shapedand sub diaphragmatic adenomas, these tumors perforate the diaphragm and do not present a clear capsule. We compared our indications and our experience with transcranial surgery for pituitary adenomas with those in the literature, We preferred trans-cranial approach for 3 patients with chromophobicmacroadenoma with a significant suprasellar extension on a small sellaturcica.

We operated 10 adenomas with a lateral extension to the supra-clinoidalinternal carotid artery where3 patients had already been operated by endoscopic endonasaltranssphenoidal approach leaving in place a part of the tumor that progressed after a follow-up 12 months. The giant adenomas with an asymmetrical lateral extension, makes them difficult to excise under endoscope despite the availability of endoscope 30 ° and 45 ° angle because of the risk of trauma to vessels and the inability to control bleeding as a consequence.

Some authors have discussed the use of intraoperative MRI after excision of the adenoma by transsphenoidal approach to determine the size and extent of residual tumor during surgery and then use a transcranial approach at the same sitting if the residue is significant (27). The extension of the adenoma in the

frontal region is an indication for the transcranial approach but sometimes this lesion can be resected by extended endoscopictranssphenoidaltransplanum approach.

Sometimes this tumor extension is asymmetrical to one sidelaterally,ensheathed with the A1 segment of the anterior cerebral artery, safe tumor resection becomes difficult using thetranssphenoidal route despite the availability of endoscopes with angles and therefore we propose the patient be operated by a transcranial route at a second sitting.On the contrary, some authors propose operating at the same sitting with a second approach which is the transcranial route. We had 05 patients operated with an adenoma in eight or hourglass shape with a double component supra and sub-diaphragmatic, by endoscopic endonasaltranssphenoidal technique and at a second time by transcranial technique where the quality of resection was limited to the sub diaphragmatictumor portion.It is well known that the consistency of the tumor plays an important role in achievingthe maximum possible tumor resection by transsphenoidalapproach (20-28).For example a giant adenoma may be amenable to total resection when the tumor is soft and easily removed by aspiration. On the other hand fibroids (representing 5-7.5% of large pituitary adenomas), are difficult to reduce despite using dissectors, curettes, ultrasonic aspiration. Inadequateexcision might deserve a transcranial approach, but it is not an absolute indication (10-20-28)

Snow et al have found that T2 weighted MRI can be a good preoperative predictor for solid tumors to determine the surgical approach (3).The three standard transcranial approaches for pituitary adenomas are pterional approach (frontotemporal) and variants of sub-frontal approach, as inter hemispheric fronto-basal approach and Sub temporal approach. In addition to these standard approaches and frequently used in the suprasellar region, there are other specific transcranial approaches used only in rare cases, for example, the orbitofrontal zygomatic or trans-callousal inter hemispheric approach.In our series we used thefronto-temporal approach for all adenomas. The fronto-pterional approach is the most frequently used approach. It enables the control the midline, andwork in the inter optic space.Dissection of the optic tract, carotid arteries and its collaterals, is done carefully.

***Complications**

Most potential complications in Transcranial pituitary surgerydo not differ much from common complications encountered in general transcranial neurosurgery; local infection at the craniotomy site, a collection of CSF in subcutaneous space or the occurrence of meningitis, a consecutive atrophy of the temporalis muscle, deterioration of functions of the cranial nerves, cerebral ischemia.Although the technical progress that has emerged over the past three decades, reduces morbidity and mortality associated with transcranial and also pituitary surgery. Symon and Jakubowski have reported a mortality rate of 0.99% for small adenomas and about 18% mortality for giant adenomas (3).

Van Lindert et al had a mortality rate of 5.7% with Transcranial pituitary surgery in a series that included all sizes of pituitary adenomas (3). Some authors have reported that the mortality rate for giant adenomas after transcranial surgery ranging from 4.6 to 18.7% of cases, while the morbidity rate is 10.4 to 23.2% of cases. (3-7-12-21-29)Recent studies indicate that the minor surgical morbidity can be high after transcranial surgery in 75% of cases for giant adenomas. Other complications of pituitary transcranial surgery; endocrine disorders postoperatively in connection with a disturbance or hormonal deficiency is more common in this surgery compared to the transsphenoidal surgery. In the series of Nomikos et al of 721 patients with non-functioning pituitary adenomas, 15% of patients showed a new hypopituitarism after transcranial surgery versus 1.4% of patients after transsphenoidal surgery. (30)

Taking into account that preoperatively, there were already some degree of hypopituitarism in 85% of patients in the group of transsphenoidal surgery, and 86.3% in the group of transcranial surgery (30).In 19.6% of the group of transsphenoidal surgery, patients resumed normal postoperative pituitary function, compared with none after transcranial surgery.The improvement of pituitary function was found in 30.1% of patients in the group of transsphenoidal surgery compared to only 11, 3% in the group of transcranial surgery.Pituitary deficit remained unchanged at 48.9% in the group of transsphenoidal surgery compared to 73.7% in the group of transcranial surgery (30). Diabetes insipidus, as a result of a manipulation of the pituitary stalk or hypothalamus is also more common in transcranial thantranssphenoidal surgery.

Nevertheless, transient diabetes insipidus is a common event in the immediate postoperative period after transcranial pituitary surgery (31). In a series of 721 patients with pituitary non secretingadenoma, transient polyuria with low urinary density occurred up to 34% of cases (30). However, permanent diabetes insipidus finally occurred in 3.2% of patients in the transcranialsurgery group3compared with 0.3% of patients in the group of transsphenoidal surgery (30).Other metabolic complication were hyponatremia (<132 mmol) as a result of water retention associated with inappropriate ADH secretion is also commonly seen in the postoperative period, mostly lasts a few days after the procedure.Visual impairment is a complication that is not uncommon in the pituitary transcranial surgery, the main cause of postoperative visual deterioration is the loss of blood supply of optic canals (deforming the small feeder vessels of the optic nerves and optic chiasm) after suprasellar

dissection of tumors (32) Loss of micro vasculature of the perforating arteries can also cause postoperative hypothalamic trauma, which is one of the most specific complications of transcranialsurgery for pituitary tumors.

Third (III)rd cranial nerve palsy is a common complication after transcranial supra-sellar tumors surgery- especially invasive para-sellar tumors involving the cavernous sinus (25)

Figures and Tables:

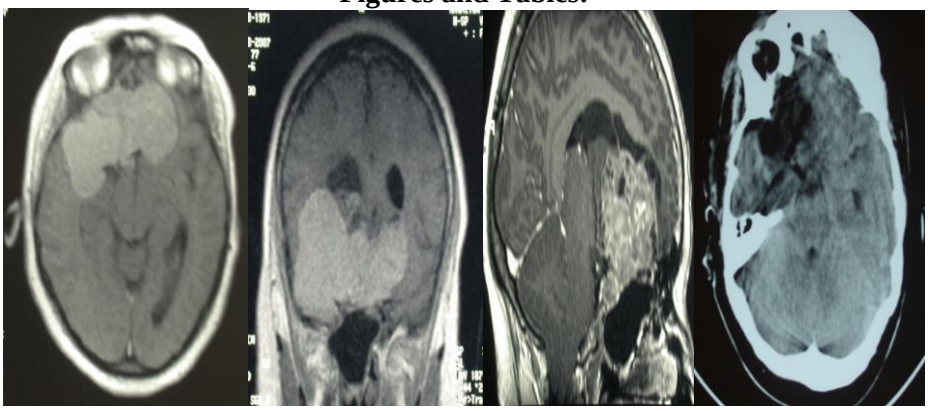
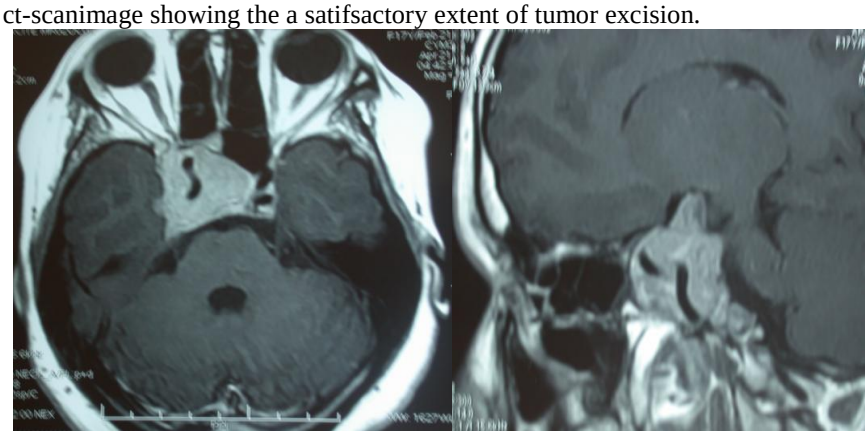


Fig1 :-MRIimages in saittal,coronal and axial cuts showing a giant adenomawith significant lateral extension to the right and towards the third ventricle.

- postoperative ct-scanimage showing the a satifsactory extent of tumor excision.



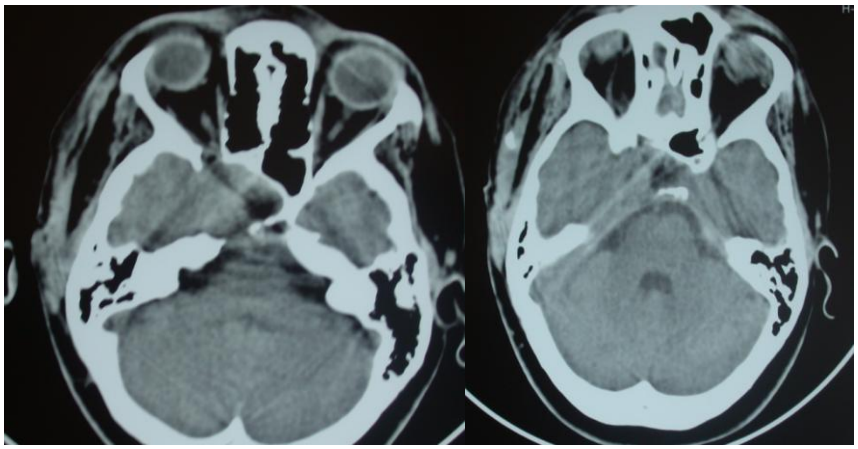


Fig2 :-imagesMRIin saittal and axial cuts showing a giant adenomawith lateral extension (the internal carotid artery appears to be encased by the tumor) right and below is in the sphenoidal sinus.

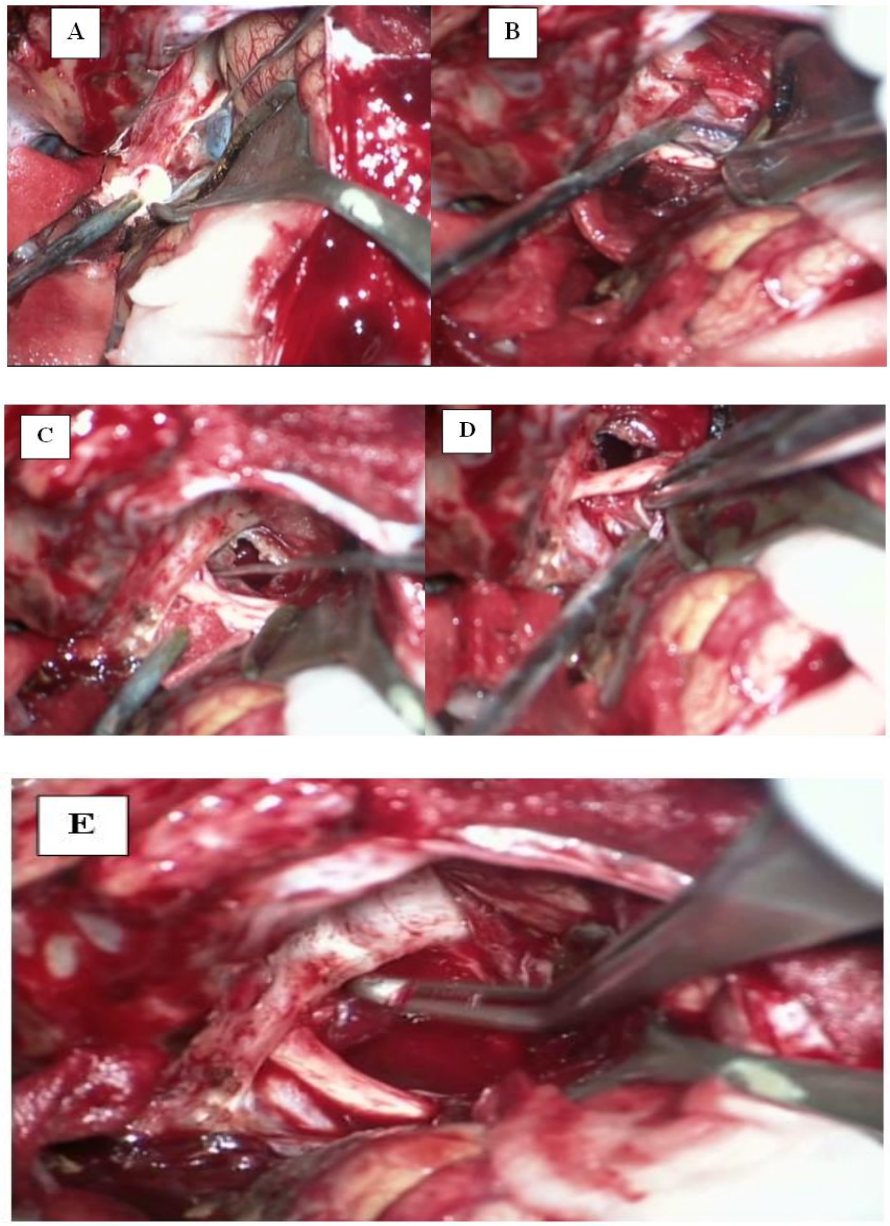


Fig3: peroperative images :

A : libération du nerf optique gauche**. B-** libération du nerf optique droit. **C** : adenoma resection in the inter optic space. **D** :'adenoma excision in the right inter optico-carotidspace. **E :** adenoma excision.

IV. Conclusion

In the surgical treatment of pituitary adenomas, the transsphenoidal surgery remains the most used approach by neurosurgeons, but transcranial surgery may be required in about 5% of cases according to the literature.In general, a transcranial approach should be considered when the size of the adenoma is large (giant adenoma) with lateral extension towards the cavernous sinus, anteriorly in the sub-frontal region or backwards towards the clivus.The most frequently used approach in this surgery is pterional or frontotemporal, unilateral sub-frontal and other approaches.The current literature focuses on outcomes and complications after transsphenoidal surgery with and without use of endoscopy and unfortunately only few recent data are actually available on results of transcranial procedures for pituitary adenomas. Generally in front of a giantadenomathe strategy to reduce the volume of the tumorfollowed by adjuvant radiotherapyshouldoffer the best resultswith regard to tumor control and patient safety.

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