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A Review of Visual and Endocrine Outcome Following Surgery for Pituitary Adenoma in a Tertiary Hospital

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Abstract

Background: Pituitary adenomas present with hormone and visual dysfunction requiring surgical treatment. Evaluating benefits of treatment becomes expedient in our emerging tertiary practice.

Aims and Objectives: Evaluating benefits of treatment pituitary adenomas in a tertiary hospital, North Central Nigeria.

Methods: Retrospective review of cases of surgery for pituitary adenomas (Jan 2013 to Dec 2017). Study parameters were visual and endocrine functions evaluated up to 12 months post-op. Simple descriptive statistics was used for data analysis.

Results: Total 28 out of 57 cases (49%) had surgery. M:F 3:1. Mean age of 44 years (range 21 to 72 years). 23/28 (82%) were referred from eye clinics. Commonest presentation was visual impairment (100%). Bitemporal field loss in 12/28 (42.8%) and complete blindness in 10/28 (35.7%). Low cortisol and low thyroid hormone were observed in one case each (3.5%). Of the four functional cases, three were prolactin secreting and one growth hormone secreting. Mean time to presentation was 29 months (Range- 1 to 108 months). Commonest neuroimaging modalities were contrast enhanced CT and MRI. Commonest pre-op diagnosis was non-functional adenoma 24/29 (85.7%). Commonest surgical approach was transsphenoidal surgery 20/28 (70.1%). CVF at 12 months follow up recorded visual improvement in only 11/28 (39.2%). Hormone profile at 12 months showed improved status from 21/28 (75%) to 25/28 (89%) but residual prolactinemia in 2/28 (7.1%) and persisting GH secreting in 1/28 (3.5%). Check MRI at 12 months revealed no significant residual/recurrent tumor and no chiasmal pressure in 16/27 (59.2%). Commonest histology report was pituitary adenoma with diffuse FSH/LH expression in 15/28 cases (53.5%). Further treatments were re-do operation and radiotherapy referral in 3/27 (11.1%) each.

Conclusion: Following surgery, a marginal improvement in vision was observed but hypocortisolism and low thyroid hormones were restored to normalcy at 12 months. However, despite surgical/medical interventions GH remained high at 12 months in lone case of acromegaly and prolactinemia persisted in two out of the three cases.

Keywords: Pituitary adenomas; Visual impairment; Pituitary hormones; Transphenoidal surgery

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Abbreviations

CVF: Central Visual Field; TSH: Transphenoidal Hypophysectomy; MRI: Magnetic Resonance Imaging; FSH/LH: Follicle Stimulating Hormone/Luteinizing Hormone

Introduction

Pituitary adenomas constitute the third most common intracranial neoplasm in adults after gliomas and meningiomas [1] and make up approximately 10%. Some studies done in our environment show similar prevalence of 16.8% to 21% [1,2]. They are normally benign tumors but can cause significant morbidity either due to pressure effects on surrounding structures or due to associated hormonal imbalance from dysfunction of the pituitary gland [3]. It has been observed in this environment that most present in advanced stages of the disease with marked

pressure symptoms and or hormone imbalance. Due to the close anatomical relationship between the adenoma and the visual apparatus, visual field loss is a prominent symptom of mass effect. But equally important is the intrinsic pressure of the adenoma on the gland itself which sequentially takes down the secretory cells starting first from the less important ones (growth hormone, follicle stimulating hormone/luteinizing hormone) to the most important ones (thyroid hormones and Adrenocorticotrophic hormones) [4]. The resultant effect is hypopituitarism which is of a major therapeutic and anesthetic consideration especially for surgical candidates. It is expected that surgical decompression of the adenoma removes the pressure on these cells to optimize their chances of restoration of the secretory functions. It is also a fact that some pituitary tumors are secretory ab initio. Aside prolactinomas, the rest (Cushing's disease and Growth hormone secreting Acromegaly) are surgical candidates ab initio. For the prolactinomas, surgery is only indicated when it becomes a persistent pressure producing macroadenoma not responding to medical treatments (bromocriptine and cabergoline). But what is not clear right from the outset is how much benefit is derivable from surgical intervention when the adenoma has caused neurological deficits already before presentation e.g. visual field loss. Although reports from elsewhere in Nigeria [5] suggest benefit from surgical intervention even at late stages it is our intent to provide our local evidence through a retrospective review of local experience.

Aims and Objectives

Aims and objectives of this retrospective study is to evaluate the changes in visual functions and endocrine status in patients surgically treated for symptomatic pituitary adenomas.

Methodology

Ethical approval was sought for and obtained from National Hospital Abuja Institutional Review Board to conduct a retrospective review of cases of surgery for pituitary adenomas from Jan 2013 to Dec 2017. Major study parameters of interest were visual and endocrine functions evaluated up to 12 months follow up. Only patients who had surgery for pituitary tumors were selected for this study. Other skull base tumors were excluded. The parameters studied were clinical presentation especially visual and endocrine status, radiological diagnosis (CT and MRI), surgical approaches, histological pattern and outcome of surgery over a follow up period of at least one year with particular reference to visual and endocrine status. Data were assembled on a spreadsheet and analyzed with simple descriptive statistics and presented in tables.

Results

About half (49%) of all confirmed cases of pituitary adenoma who presented to our service during the study period consented and paid for all logistics of surgery (Table 1). Quite a significant number 15/57 (26%) though willing and consented to have surgery were unable to proceed due to lack of funds to meet up logistics demands. Some 6/57 (10.5%) out rightly rejected surgical treatment while the rest 8/57 (14%) accepted surgical treatment but sought referral to other centers. The main focus was therefore on those who underwent surgical treatment in our center. Sex ratio of M:F 3:1 favored males. Mean age was 44 years (range 21 to 72 years). Mean time to presentation was 29 months (Range 1 to 108 months). 23/28 (82%) were referred from eye clinics. All patients presented with visual impairment (Table 2) Bitemporal field loss pattern was found in 12/28 (42.8%), followed closely by complete blindness in 10/28 (35.7%). Unilateral loss with completely normal contralateral visual fields was observed in 2/28 (7.1%) while unilateral loss with partial loss on the contralateral side was observed in 4/28 (14.2%). Pituitary hormone profiling confirmed non secretory status on 24/28 (85.7%) pre-operatively (Table 3) with associated chronic hypocortisolism (Addison's disease) in one case (3.5%) and hypothyroidism in two cases (7.1%) of the four functional cases, three were prolactin secreting (10.7%) and one (3.5%) growth hormone secreting (acromegaly). Therefore, seven cases with dysfunctional pituitary hormones were observed in this study. Commonest neuroimaging modalities were contrast enhanced CT and MRI confirming sellar/suprasellar mass with compression of visual apparatus which are features consistent with pituitary adenoma. Commonest pre-op diagnosis was non-functional adenoma 24/29 (85.7%) out of which two required pre-op thyroid replacement therapy while one required cortisol replacement in addition. Of the four functional ones, the three macroprolactinomas already failed hormone treatment with both bromocriptine and carbegoline and presented with worsening vision and pressure effects while the acromegalic one only showed modest response to somatostatin. Commonest surgical approach was transsphenoidal surgery 20/28 (70.1%), mostly the microscopic (16/20) but also endoscopic (4/20). Transcranial approach was the

Table 1: Disposition of patients presenting with Pituitary Adenoma during the study period.

Patient Grouping	Freq	Percentage
Consented for operation and able to bear cost of treatments	28	49.1
Consented for operation but unable to bear cost of treatment. Then lost to follow up	15	26.3
Sought and obtained referral for treatment elsewhere including abroad	8	14
Out rightly rejected surgical treatment in preference to traditional/faith healing centers	6	10.5
Total	57	100%

Table 2: Visual field changes following surgical intervention.

Pattern of visual field loss	Pre-op	12 months post op follow up	Vision unchanged	Vision improved	Worsened vision
Bitemporal	12	4	4	8	-
Bilateral blindness	10	8	8	2	-
Unilateral blindness with normal contralateral vision	2	2	2	-	-
Unilateral blindness with Contralateral temporal loss	4	3	3	1	-
	28		17	11	-

Table 3: Pituitary hormone changes following surgical intervention.

Pituitary hormone secretory status		Pre-op	6 months post op	12 months post op	Normalized hormone status	Non normalized hormone status
1-Non secreting adenomas	1a-Normal pituitary hormones	21	24	24	24	-
	1b-Low thyroxine	2	-	-	2	-
	1c-Low cortisol	1	-	-	1	-
2-PRL secreting adenomas		3	2	2	1	2
3-GH secreting adenomas		1	1	1	-	1
Total		28			25	3

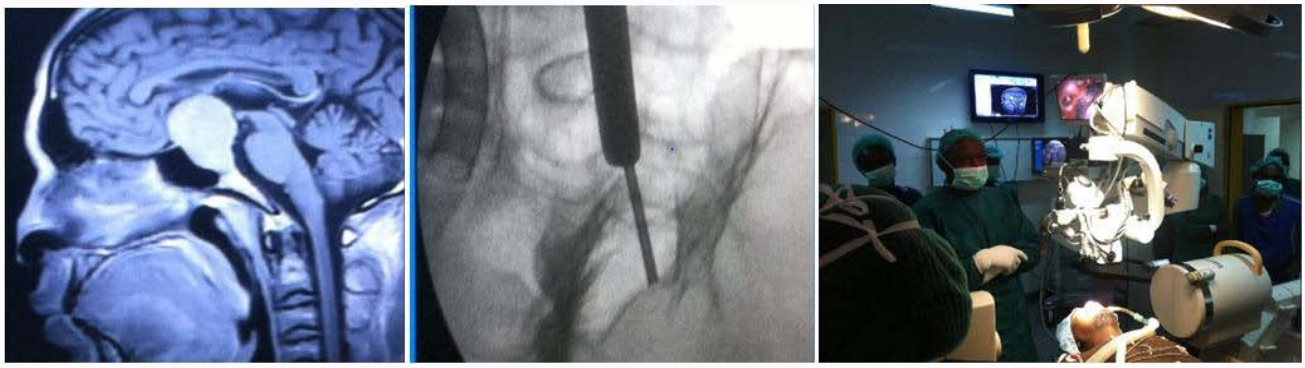

Figure 1: 1a) Gad+ MRI Brain, 1b) Intra-op navigation with C-arm and 1c) operating microscope.

preference in 8/28 (28.5%) due to tumor extension to suprasellar compartment. Commonest post-op complication was nasal bleeding in 6/28 (21%) but most important was DI in 3/28 (10.7%) and CSF leak in one case (3.5%). CVF assessment at 12 months follow up recorded restoration of normal vision in 8/12 cases of previously bitemporal field loss but vision remained unchanged in the rest 4. Only 2/10 of the previously bilateral blindness recorded some improvement with surgery and the rest remained blind. Out of the four cases of unilateral blindness with contralateral temporal loss, only one recorded a near complete restoration of the contralateral temporal field loss. There was no change in the two cases with unilateral blindness and normal contralateral side. No worsening of vision was recorded. Hormone profile at 12 months showed normalization of hormone status from 21/28 (75%) preoperatively to 25/28 (89%) postoperatively but residual prolactinemia in 2/28 (7.1%) and persisting GH secreting in 1/28 (3.5%). Check MRI at 12 months revealed no significant residual/recurrent tumor and no chiasmal pressure in 16/28 (57.1%). There was significant residual/recurrence but no chiasmal pressure in 10/28 (35%). In two cases (7.1%) there was significant pressure on the visual apparatus necessitating further treatments re-do operation and radiotherapy referral. Commonest histology report was pituitary adenoma with diffuse FSH/LH expression cells in 15/28 (53.5%) followed by Null cells in 9/28, Prolactin expression cells in 3/28 and GH expressing cells in 1/28.

Discussion

Late presentation with a mean time to presentation of 29 months (range 1 to 108 months) was phenomenal and was responsible for some irreversible deficits recorded at presentation such as blindness. It is rather disturbing that just about half of the total eligible patients had access to surgical treatment for reasons ranging from financial constraints, preference for unconventional treatment options and seeking help elsewhere. Perhaps more disturbing are those 15/57 (26%) who displayed willingness to have surgery and so consented but were unable to proceed due to lack of funds to meet up logistics demands and the group (10.5%) who out rightly rejected surgical treatment for less conventional treatment options. These constitute a significant challenge for the advancement of pituitary surgery and assessment of derivable benefits in this environment. It is particularly sad to note that a sizeable number were denied treatment due to lack of any insurance in place to cater for them. Family and community insurance which most rely on for these high-end operations was not available for them. This may have contributed to seeking less conventional, alternative treatment options and eventual loss to follow up. It is most likely that the disease progressed until further complications and demise. It is also important to note that some of the patients who sought referral elsewhere including abroad may have done so because they were not convinced of the local expertise based on the available statistics. It is also pertinent to note that the mean time to presentation of 29 months (Range 1 to 108 months) is rather unacceptable and is directly related to economic constraints and abysmal health insurance policy or alternative funding strategies. The twin issues of late presentation and poor compliance with surgical treatment have become intertwined and recurring decimal in our environment and really deserve a special attention. Delay in effecting appropriate surgery for pituitary adenomas is known to upset desired results and was already reported by Magulike et al. [6] in Nigeria. This report also advocated that fear of surgery should be timely dispelled so that victims could understand their situations better and efforts made to encourage them to take the right decisions. Mezue et al. [5] also corroborated the fact that tumors of the pituitary gland present late in developing countries with an obvious increase in morbidity but that surgical intervention even at this late stage should not be withheld because it often results in visual improvement.

Majority of the patients (82%) were referred from eye clinics. This finding is in keeping with other studies [5,7] and is rather not

surprising because the initial port of complaint for visual impairment is usually the optometry and ophthalmology clinics. They often have used eye drops for years and changed glasses severally before brain imaging is conducted and appropriate referral to the neurology and neurosurgery clinic. The rest also experienced headaches and had a lot more insight into their problems and presented straight to the neurology/neurosurgery clinics. It is therefore not surprising that all patients presented with visual impairment (Table 2). Bitemporal field loss pattern was found to be the commonest (42.8%) field defect in this study. Sullivan et al reported that bitemporal field defects were present in 89% of their series at St Vincent [8]. Although bitemporal hemianopsia is a classic presenting visual field deficit in pituitary adenomas due to pressure effect on the undersurface of the chiasma by an enlarging adenoma, additional visual disturbances can result from these tumors due to pressure extending to either or both optic nerves with a resultant optic atrophy causing unilateral or bilateral blindness [9]. In this study, complete blindness was observed in 10/28 (35.7%) of cases. Unilateral loss with completely normal contralateral visual fields was observed in 2/28 (7.1%) due to unilateral extension of adenoma causing optic nerve atrophy.

As observed, 24/28 (85%) of cases were non-functional macroadenomas which have grown so large to exert tremendous mass effects resulting in associated visual deficits as detailed above and also hyposecretion of TSH and ACTH in one case each. Functional macroadenomas were quite rare in this study constituting only about 15%, three prolactinomas and one growth hormone secreting (acromegaly). The rarity of growth hormone secreting pituitary macroadenomas in this environment has been reported by Idowu et al. [10]. Who described a case series of only three cases in a tertiary institution in Lagos, Nigeria over a period of two year. In our practice environment therefore, it is a correct assertion that nonfunctional macroadenomas are by far the commonest presenting for neurosurgical intervention. Our findings were clearly at variance with previously known facts that functional pituitary adenomas were far commoner constituting 65% (48% prolactin, 10% GH, 6% ACTH and 1% TSH) [11]. The recorded late presentation of average 29 months is also not surprising because the functional ones which would normally present early due to the physiologically upsetting hormone excess 12 were in the profound minority in this study. Quite a few of the non-functional have associated hormone hyposecretion especially thyroid and adrenocortical hormones which were of pre-operative anesthetic interests. Both MRI (Figure 1a) and CT were invaluable imaging modalities in understanding the detailed anatomic relationships of the adenoma to the surrounding vital neurovascular structures for appropriate surgical planning.

Commonest surgical approach was image guided (C-arm) transsphenoidal surgery 20/28 (70.1%), mostly the microscopic (16/20 = 80%) but also endoscopic (4/20 = 20%). Transcranial approach was the preference in 8/28 (28.5%) due to tumor extension to suprasellar compartment. This is in line with the current trend in surgery for pituitary adenoma. The use of modern neurosurgical equipment such as intraoperative image intensifier introduced by Guiot et al. [13] in 1958 and also the neurosurgical operating microscope introduced by Hardy [14]. Since 1969 have revolutionized and widened the safety margin for minimally invasive transsphenoidal access to the sellar region especially for pituitary adenomas. It has been a tremendous landmark improvement on the previous works on pituitary surgery by Victor Horsley [15] as reported in 1906, and later improvements on his techniques by Harvey Cushings [16]. It is important to note that the perfection achieved by this solid foundation set the pace for current advances in endoscopy, neuro-navigation and intraoperative imaging (CT/MRI) which allows for real time assessment of instrument placement, anatomical localization and determination of extent of tumor resection. Indeed, it has been an eventful past century in the evolution of modern, safe and minimally invasive surgery for pituitary adenomas but the sad truth is that a sizeable number of pituitary adenomas still require a transcranial approach mainly due to sheer size and extension to the suprasellar compartment as evidenced by the 28% in this study. Other indications for transcranial approach [17] include minimal enlargement of the sellar, with large suprasellar component, significant extrasellar extension to the cavernous sinus and middle fossa, incidental finding of aneurysm, unusually fibrous adenoma which caused incomplete excision in a previous transsphenoidal attempt, recurrent tumor etc.

It is important to note that whereas surgical decision was straight and easy for most of the non-functional ones 22/24 (91.6%), it wasn't so for the lone case of hypothyroid and also the lone case of hypocortisolism who were first treated by the endocrinologists with hormone replacement therapy until hormone balance was restored. Then surgery proceeded uneventfully. Similarly, surgical decision for the functional tumors was equally challenging. The three cases of prolactinomas underwent initial attempt to control the tumor medically with dopamine agonists. But it has been documented that failure to achieve medical control do occur sometimes and surgery is particularly advocated in this situation especially when pressure symptoms threaten irreversible visual failure. Reinstitution of adjuvant medical therapy has been reported to normalize prolactin levels [18]. For the lone case of acromegaly, the only application of medical treatment (octreotide and bromocriptine) was to pre-operatively improve the success of the planned surgical treatment. The high cost of prolonged medical treatment with no commensurate benefit especially in a resource poor setting has been captured in the report by Idowu OE et al [1]. Which clearly showed preference to early surgery for acromegaly. Moreover, according to different neuroendocrinology societies and pituitary centers surgical treatment provides rapid control of GH/IGF-I levels and is the first line of treatment for GH-secreting adenomas [19].

Assessment vision at 12 months follow up recorded restoration of normal vision in eight out of 12 cases of bitemporal field loss but vision remained unchanged in the rest four (Figure 2a, 2b). Only two out of ten previously bilateral blindness recorded improvement while the rest remained blind. And, out of the four cases of unilateral blindness with contralateral temporal loss, only one recorded a near complete restoration of the contralateral temporal field loss. Although no worsening of vision was recorded, improvement in vision was only recorded in 11/28 (39.2%). This is quite low in comparison to results from elsewhere. Whereas Sullivan LJ 8 reported 68% improvement (p less than 0.001), Powell M [20] reported 88% improvement in vision following surgery. However, our results compare with 31.8% visual improvement reported by Mezue from South East Nigeria. Perhaps the twin challenge of late presentation and poor access to early surgical treatment provides a possible explanation for these poor results in this environment. That underscores the need for continued advocacy for early presentation and improved access to treatment.

Re-evaluation of pituitary hormone profile at 12 months showed normalization of hormone status from 21/28 (75%) preoperatively to 25/28 (89%) postoperatively. Out of the three cases of macro-

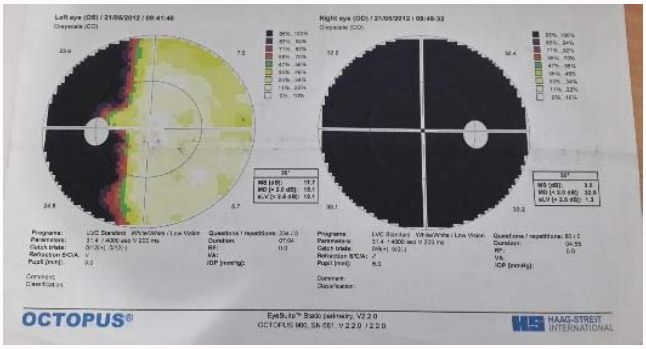

Figure 2a: Pre-op CVF- Left temporal loss. Right blindness.

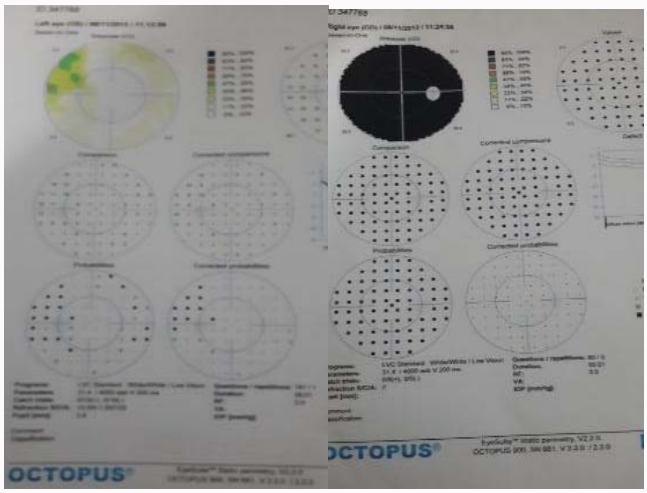

Figure 2b: 12 months post op- Resolved left temporal field, right same.

prolactinoma, only one responded to surgery and adjuvant dopamine agonists (bromocriptine). The rest two, though still on drugs, still had persisting prolactinemia and in line with current recommendations, will continue on medications for up to four years [21]. But, one required further surgery due to MRI evidence of significant chiasmal pressure from a residual adenoma. Similarly, persisting GH secretion and residual adenoma with chiasmal pressure on check Gad + MRI in the lone case of acromegaly dictated referral for redo-operation via a transcranial approach to be followed with adjuvant radiotherapy.

From the commonly observed histology findings, including adenoma with diffuse FSH/LH expression cells, Null cells, prolactin expression cells, and GH expressing cells there was no evidence to suggest high mitotic index or malignant potentials. Therefore, complete surgical excision where possible remains to aim to guarantee cure.

Conclusion

Recovery of lost vision for advanced stages of pituitary macroadenomas as observed in this review cannot be guaranteed despite surgical intervention. However, surgical intervention when safe should not be withheld especially when minimally invasive approach is available. It is important to note that following surgical intervention for macroadenomas, the chances of normalization of endocrine functions from a hyposecretory status is probably higher than from a hypersecretory status.

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