IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 2 Ser. 8 (February. 2019), PP 51-55
www.iosrjournals.org

Pituitary Adenomas, Challenges and Prospects of Management: A Case Report

Ignatius Ezeani,[1](FMCP) Chidozie Maduka,[1](MWACP) Francis Ugoeze,[2](FMCP)

Department of Medicine, Federal Medical Center, Umuahia, Abia state, Nigeria
Department of Medicine, Federal Medical Center, Asaba, Delta state, Nigeria
Corresponding Author: Dr. Ignatius U Ezeani,
Department of Medicine,Federal Medical Center,P.M.B 7001, Umuahia
Abia State, Nigeria

Abstract:
Introduction*: Advances in Endocrinology and Neuro-radiology research in recent years have allowed earlier recognition and more successful therapy of pituitary adenomas. Prolactinomas are the most common type. Early clinical recognition of the endocrine effects of excessive pituitary secretion has led to early diagnosis of pituitary tumors before the appearance of late manifestations such as sellar enlargement, panhypopituitarism, and suprasellar extension with visual impairment. We report 2 cases of pituitary adenoma seen at our Endocrine clinic and to highlight the importance of early recognition and management.*
Clinical presentation*: Case 1 is a 62 year old female, businesswoman, Igbo who presented with complaints of visual blurring and recurrent headache of one month duration. Eye symptoms were painless and progressively worsened to develop into partial loss of vision on her right eye and later on her left eye. Case 2 is a 50 year old male, Igbo lawyer who presented with a history of: recurrent visual blurring, poor vision and headache all of 3years duration. There was associated tearing, poor range of vision and persistent eye discomfort.*
Conclusion: *Pituitary adenomas are treated with surgery, irradiation, or drugs to suppress hypersecretion by the adenoma or its growth. The aims of therapy are to correct hypersecretion of anterior pituitary hormones, to preserve normal secretion of other anterior pituitary hormones, and to remove or suppress the adenoma itself. Prognosis depends on tumor type, size and degree of invasion into surrounding structures. Most patients can be approximately treated and will lead full productive lives. Some require long term medications, repeat surgery or radio-surgery to keep their tumor under control. Some may require temporary or lifelong hormone replacement medications.*
Running title*: Pituitary Adenomas*
Keywords*: Pituitary adenoma, macroadenoma, prolactinoma, trans-sphenoidal surgery*

Date of Submission: 30-01-2019 Date of acceptance:16-02-2019

I. Introduction

The pituitary gland functions as a master controller of the activities of other endocrine gland in maintaining normal homeostasis and reproductive cycle.[1] The secretory function of the anterior pituitary is influenced by releasing factors from the hypothalamus. These releasing factors stimulate different cell-types of the anterior pituitary to produce their hormones which control the activities of different target organs. Other chemicals secreted by the hypothalamus known as inhibiting factors inhibit the production of anterior pituitary hormones, thereby preventing their activities on the target organs. The posterior pituitary is not influenced by releasing or inhibiting hormones.

Pituitary adenomas are relatively common forms of primary brain tumors. They usually arise from a single transformed cell and thus are monoclonal in origin. [2]Majority of them are benign and are adenohypophyseal in origin.

They can be classified into functional and non-functional tumors. Most functional tumors are prolactinomas,[3] followed by growth hormone secreting tumors, then ACTH-secreting tumors, gonadotrph (FSH and LH) secreting tumors and least commonly, thyrotroph adenomas (accounting for less than 1% of pituitary tumors). They can also be classified by size as microadenoma and macroadenoma. Microadenomas are less than 1cm while macroadenomas are greater than 1cm in diameter.[4] Microadenomas are more predominant and are largely asymptomatic while macroadenomas may cause mass effect leading to compression of nearby structures like the optic chiasma superiorly, the carvenous sinus and its content laterally or even compression of the

pituitary gland itself leading to hypopituitarism. Most of the non-functional adenomas are gonadotroph cell tumors and one third of pituitary adenomas are not associated with symptoms and signs of hormone excess. [5,6] Pituitary adenomas do not usually progress to malignant carcinomatous state unlike other solid tumors.[7,8,9,10] The uniqueness of this case lies in the fact that these patients were initially misdiagnosed when they presented earlier at various hospitals before they were referred to an endocrinologist. Moreover, even when they presented to our endocrinology clinic, we encountered challenges of where to send them for specific laboratory investigations. These patients opted to be referred out of the country on personal grounds, but we are worried that there many other cases that are been misdiagnosed and even for those that have been accurately diagnosed, challenges of financial constraints may be a stumbling block. There is need for physicians practicing in poor resource settings like ours to have a high index of suspicion and to refer immediately to the specialist. We believe that this article will be of immense benefit to physicians.

II. Case Presentation

Case 1:

Is a 62 year old female, Igbo businesswoman, who presented with complaints of visual blurring and headache of one month duration. Symptoms were insidious in onset, painless and progressively worsened to develop into partial loss of vision on her right eye and later on her left eye. Headache was throbbing, initially localized in the frontal region but later became generalized; relieved transiently by ingestion of analgesics however, there was no known aggravating factor. She presented at a peripheral health center where a diagnosis of enteric fever was made and she was commenced on antibiotics and analgesics which she took for 10days. However, symptoms still persisted which prompted her referral to our clinic. Examination revealed that visual acuity: was hand movement in right eye and 6/18 in the left eye, visual field (VF): temporal hemianopia in the left eye in automated perimetry. Brain computerized tomography scan was suggestive of a pituitary tumor. Magnetic resonance imaging (MRI) revealed a pituitary macroadenoma (2.7 cm high, 2.1 cm wide and 2.0 cm deep). It extended up and out of the sella turcica, stretching the optic chiasm and optic nerves. Hormonal profile showed decreased LH, FSH and cortisol. Based on her request, she was referred to India for further evaluation and possible surgery. She underwent Endoscopic Trans-sphenoidal approach and excision of pituitary tumor in India.

Case 2:

Is a 50 year old male, Igbo, lawyer who presented with a history of: recurrent visual blurring, poor vision and headache all of 3years duration. There was associated tearing, poor range of vision and persistent eye discomfort. He was referred to an ophthalmology clinic where he was given chloramphenicol eye drops which he used for several weeks with minimal relief. At this point, the ophthalmologist then advised him to see an endocrinologist. Clinical examination was essentially normal. Brain computerized tomography scan was suggestive of a pituitary sellar mass measuring 2.6 x 1.7 x 2.3 cm with suprasellar extension compressing the optic chiasma and a conclusion of giant macroadenoma was made. Sagittal T1-weighted MRI shows a non enhancing pituitary macroadenoma. Hormonal profile showed decreased testosterone and increased TSH, others parameters were normal. Histopathological report showed medium-sized adenoma containing moderate to abundant amounts of finely granular cytoplasm and round to oval nuclei showing finely-stippled chromatin and indistinct to small nucleoli. The cytoplasm was basophilic with absent mitoses. Few pleomorphic tumor cell nuclei were seen. Tumors were arranged in pseudo-acinar formations with a central lumen-like space and there were no reticulin network within it. An assessment of pituitary macroadenoma was made and he requested to be referred to India where he had an MRI which also revealed a giant macroadenoma. He subsequently underwent a trans-sphenoidal surgery.

III. Follow Up And Outcomes

Patient 1 presented for follow up visit a month after the surgery, symptoms of headache and visual blurring have improved significantly although she complained of blood tinged mucous dripping from the nostrils early in the morning. She was sent for repeat hormonal test (TSH, LH, FSH, ACTH, prolactin, cortisol) which were all within normal limits. We reassured her and referred her to the ENT surgeons who commenced her on otrivin nasal drops which she used for 2weeks and discontinued when the nasal dripping resolved. The second patient presented to our clinic 2weeks after the surgery but had no complaints. Symptoms of visual blurring, poor vision pre-surgery have resolved however, he did not present for follow up visit again.

IV. Discussion

The overall incidence of pituitary adenoma varies from 10- 22%.[11,12] In a population-based study in the USA, incidence rates of pituitary adenomas are higher in females in early life and higher in males in later life.[13] Rates generally increase with age with blacks having higher rates compared to other races.[13] Males are

diagnosed with larger tumors than females.[13] In a retrospective study of the incidence of brain tumors in Jos, Plateau state, Nigeria, anterior pituitary tumors made up about 21%.[14]

Clinical features of pituitary adenoma include features of adenohypophyseal hypersecretion (according to cell origin), and features of mass effect. Symptomatic microadenomas present more with features of hormone excess while symptomatic macroadenomas present with features of mass effect. The two index cases presented with visual blurring and recurrent headache which was transiently relieved by analgesics. It is important to note that the eye symptoms: visual blurring, progressive loss of peripheral vision and frequent tearing appeared to have progressively worsened from onset till just before they both presented to the Endocrinologist. If the optic chiasm and/or one or both optic nerves are compressed by upward growth of a pituitary tumour, the patient may notice blurred vision in one or both eyes as seen in our two index cases. This can be quite subtle early on, and the blurring may be all over the vision, or in just part of the side vision. Some patients also notice that colours do not seem to be as bright as they used to be, for example bright red coloured objects are seen as a washed-out pink colour instead. This is because compression of the optic nerve or chiasm often causes loss of colour vision before it causes loss of visual acuity. Peter H. in a case report from Australia revealed progressive visual loss in a 53 year old Caucasian who was discovered to have giant macroadenoma.[15] A report from Taiwan which studied the Influence of Pituitary Adenoma Size on Vision and Visual Outcomes after Trans-Sphenoidal Adenectomy in 78 patients that pituitary adenomas larger than 2 cm cause defects in vision while adenomas 2 cm or smaller do not cause significant visual impairment: this is similar to the findings in our patients.[16] Recent reports[17,18,19] have even revealed a relationship between the size of pituitary adenoma and VF defects. These studies clearly illustrated that patients with larger tumors tended to have VF abnormality, and that the severity of VF defects is closely related to tumor. The two patients presented early with visual blurring which progressively became worse, there is need for physicians especially those working in poor resource settings to have a high index of suspicion whenever a patient presents with symptoms of visual blurring, headache and progressive loss of vision.

Management of pituitary adenomas, especially macroadenomas is largely multidisciplinary including the Endocrinologist, Neurosurgeon, Neuro-ophthlmologist, and metabolic laboratory scientists. Treatment target is to achieve total cure when possible, or tumor size reduction, hormone function restoration and normal vision restoration, where complete cure is not achievable. This involves medical management, surgical intervention, radiotherapy or combination of these.

Medical management is usually specific for tumor type. Prolactinomas respond well to dopamine agonists. Surgery and radiotherapy are not often used.[20] For growth hormone-secreting tumors, somatostatin analogues like octreotide are used after surgical debulking of the tumor. Centrally-acting medications like bromocriptine, cyproheptadine and peripherally-acting agents that reduce or block cortisol actions like ketoconazole, mitotane, are used in the medical treatment of corticotropin secreting tumors, though surgery and radiotherapy are more effective. Thyrotropin secreting tumors and non secreting macroadenomas are treated by surgery and radiation (for thyrotropin-secreting tumors).[20]

Surgical therapy, mostly using trans-sphenoidal approach (which was introduced in the 80s) is the treatment of choice for macroadenomas and may result in tumor cure.[15] The introduction of endoscopic trans-nasal trans-sphenoidal techniques in the subsequent decade allowed a simpler and more direct approach to the sella, resulting in increased patient comfort, decreased use of nasal packing, decreased hospital stay and a wider panoramic view of the surgical field using angled endoscopes.[21-24] Surgical complications include transient diabetes insipidus in five to 15 per cent of patients and less commonly, infection and leakage of cerebrospinal fluid. The endoscopic Trans-sphenoidal approach was the technique used for our index cases although the first patient had extended nasal packing due to the prolonged blood tinged early morning nasal dripping from her nostrils post surgery. The visual acuity in both patients significantly improved post surgery. This is similar to findings from earlier studies.[25-27] A gradual improvement in visual acuity continues over the next few months with the visual field improving in a triphasic response, taking months to years to regain its function.[28] Another study from China reported that visual improvement occurred in 88.7% of patients.[16] Previous series have reported that visual improvement depends on the surgical approach, ranging from 74.7–93.4%.[29,30] In our report, the two patients had large macroadenomas and this may explain why they experienced greater visual improvement after surgical resection although patients with smaller pituitary adenomas may still have better visual outcome.

Traditional Radiotherapy using external beam radiation and radiosurgery using gamma knife are useful in inoperable tumors or when patient declines surgery.[31] It is also useful as a complementary treatment with medical and/ or surgical treatment.

Follow-up will include tumor size monitoring, hormone level monitoring and identification of features of hypopituitarism, hormone replacement and complementary therapy for iatrogenic hypopituitarism (especially post-surgical and radiotherapy), identification and treatment of complication.

Teaching points

The two cases highlight the challenges encountered by physicians practicing in poor resource settings: unavailability of needed laboratory equipments and facilities for diagnosis. These calls for concerted efforts by government and all stakeholders to ensure that hospitals are upgraded and specialist clinics are well equipped.

The two patients presented early with visual blurring which progressively became worse, there is need for physicians especially those working in poor resource settings to have a high index of suspicion whenever a patient presents with symptoms of visual blurring, headache and progressive loss of vision. In other word, the uniqueness of these two cases is that both patients presented with eye symptoms which was initially misdiagnosed and initially mismanaged until they presented at the endocrine clinic. We believe there are more cases that may have been misdiagnosed in our locale. Unfortunately these patients may not get to see a specialist in time, hence the need to submit these two cases to increase awareness among physicians.

The need for multi-disciplinary team approach to management of these patients is vital: there should be inter-specialty discussions (between the Endocrinologist, Ophthalmologist, Neurosurgeon, Histopathologist and Chemical pathologist) periodic clinical grand rounds and updates to enhance patients care and improve outcome. The general practitioners should be encouraged to choose the option of early referral once a patient presents with worsening visual disturbance and recurrent headache.

V. Conclusion:

Pituitary adenoma is a relatively common brain tumor which may be incidentally found without symptoms, or may be an active microadenoma with features of hyperpituitarism, or a macroadenoma with features of mass effect. Treatment modality is multidisciplinary and tailored towards the type and/or size of tumor and its complication. A high index of suspicion is necessary in achieving correct diagnosis.

VI. Consent Statement

Written informed consent was obtained from the patients for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

VII. Declarations

Ethical approval: The Ethics and Research committee of the Federal Medical Center, Umuahia gave the ethical approval. The two patients discussed in this case report did it voluntarily, and they wrote an informed consent

Competing interest: The authors declare that they have no competing interests.

Source of funding: none

Availability of data and material: Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Authors Contribution

IE conceived of the study, carried out the sequence alignment and drafted the manuscript. FU participated in the sequence alignment. CM participated in the design of the study and helped to draft the manuscript. All authors read and approved the final manuscript.

The manuscript has been read and approved by all the authors, the requirements for authorship have been met, and each author believes that the manuscript represents honest work.

Acknowledgement

We thank staff of the Department of Medicine, Federal Medical Center, Umuahia, Abia state, Nigeria who contributed towards the article by making substantial contributions to conception and revision of manuscript for important intellectual content.

References

[1]. Amar AP, Weiss MH. Pituitary anatomy and physiology. Neurosurg Clin N Am. 2003. 14; 1: 11-23.
[2]. Alexander JM, Biller BM, Bikkal H, Zervas NT, Arnold A, Kilbanski A. Clinically nonfunctioning pituitary tumors are monoclonal in origin. J Clin invest. 1990; 86:336-340.
[3]. Famine P, Maya MM, Melmed S. pituitary magnetic resonance imaging for sellar and parasellar masses: ten –year experience in 2598 patients. J Clin Endocrinol Metab.2011. 96; 6: 1633-1641.
[4]. Arafah BM, Nasrallah MP. Pituitary tumors: pathophysiology, clinical manifestations and management. Endocr Relat Cancer. 2001; 8: 287-305.
[5]. Krysiak R, Okopien B, Korzekwa M. Atypical pituitary tumors. Pol Merkur Lekarski.2012; 32:323-328.
[6]. Chanson P, Brochier S. Non-functional pituitary adenomas. J Endocrinol Invest 2005; 28:93-99.
[7]. Asa SL, Ezzat S. The cytogenesis and pathogenesis of pituitary adenomas. Endocr Rev. 6666 1998. 19:798-827.
[8]. Colao A, Ochoa AS, Auriemma RS, Faggiano A, Pivonello R, Lombardi G. Pituitary carcinomas. Front Horm Res.2010. 38: 94-108.
[9]. Farrell WE, Clayton RN. Molecular genetics of pituitary tumors. Trends Endocrinol Metab 1998. 9:20-26.

[10]. Melmed S. Update in pituitary disease. J Clin Endocrinol Metab. 2008. 93: 331-338.
[11]. Buurman H, Saeger W. Subclinical adenomas in postmortem pituitaries: Classification and correlations to clinical data. Eur J Endocrinol. 2006; 154:753-758.
[12]. Costello RT. Subclinical adenoma of the pituitary gland. Am J Pathol. 1936; 12:205-216.
[13]. McDowell BD, Wallace RB, Carnahan RM, Chrischilles EA, Lynch CF, Schlechte JA. Demographic differences in incidence of pituitary adenoma. Pituitary. 2011; 14(1):23-30.
[14]. Igun GO. Diagnosis of brain tumors at Jos University Teaching Hospital Nigeria. East Afr Med J. 2001; 78:3:148-151.
[15]. Peter Herse. Pituitary macroadenoma: a case report and review. Clin Exp Optom 2014; 97: 125–132.
[16]. Ren-Wen Ho, Hsiu-Mei Huang, Jih-Tsun Ho. The Influence of Pituitary Adenoma Size on Vision and Visual Outcomes after Trans-Sphenoidal Adenectomy: A Report of 78 Cases. J Korean Neurosurg. 2015. 57:1; 23-32.
[17]. Levy A. Pituitary disease; presentation, diagnosis, and management. J Neurol Neurosurg Psychiatry. 2005.75:3; 47-52.
[18]. Monteiro ML, Zambon BK, Cunha LP: Predictive factors for the development of visual loss in patients with pituitary macroadenomas and for visual recovery after optic pathway decompression. Can J Ophthalmol. 2010; 45: 404-408.
[19]. Rivoal O, Brézin AP, Feldman-Billard S, Luton JP. Goldmann perimetry in acromegaly: a survey of 307 cases from 1951 through 1996. Ophthalmology. 2000; 107:991-997.
[20]. Shlomo M, Jameson JL. Disorders of the anterior pituitary and hypothalamus In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL,editors. Harrison's Principles of Internal Medicine, 18th ed. New York: McGraw Hill; 2012; 323: 2876–2902.
[21]. Mampalam TJ, Tyrrell B, Wilson CB. Trans-sphenoidal microsurgery for Cushing disease: a report of 216 cases. Ann Intern Med 1988; 109: 487–493.
[22]. Swearingen B, Biller BMK, Barker FG II, Katznelson L, Grinspoon S, Klibanski A, Zervas NT. Long-term mortality after trans-sphenoidal surgery for Cushing disease. Ann Intern Med 1999; 130: 821–824.
[23]. Jho HD, Carrau RL. Endoscopy assisted trans-sphenoidal surgery for pituitary adenoma. Acta Neurochir (Wien) 1996; 138: 1416–1425.
[24]. Cappabianca P, Alfieri A, de Divitiis E. Endoscopic endonasal trans-sphenoidal approach to the sella: towards functional endoscopic pituitary surgery. Minim Invasive Neurosurg 1998; 41: 66–73.
[25]. Nasseri SS, Kasperbauer JL, Strome SE, McCaffrey TV, Atkinson JL, Meyer FB. Endoscopic transnasal pituitary surgery: report on 180 cases. Am J Rhinol 2001; 15: 281–287
[26]. White DR, Sonnenburg RE, Ewend MG, Senior BA. Safety of minimally invasive pituitary surgery compared with a traditional approach. Laryngoscope 2004; 114: 1945–1948.
[27]. Spencer WR, Das K, Nwagu C, Wenk E, Schaefer SD, Moscatello A. Approaches to the sellar and parasellar region: anatomic comparison of the microscope versus endoscope. Laryngoscope 1999; 109: 791–794.
[28]. Kanski JJ. Clinical Ophthalmology 648,49th ed. London, UK: Butterworth Heinemann, 2007. p 811
[29]. Mortini P, Barzaghi R, Losa M, Boari N, Giovanelli M: Surgical treatment of giant pituitary adenomas: strategies and results in a series of 95 consecutive patients. Neurosurgery 60: 2007: 993-1002; discussion 1003-1004.
[30]. Müslüman AM, Cansever T, Yilmaz A, Kanat A, Oba E, ÇavuSoglu H, et al.: Surgical results of large and giant pituitary adenomas with special consideration of ophthalmologic outcomes. World Neurosurg 76: 2011: 141-148; discussion 63-66.
[31]. Paek SH, Downes MB, Bednarz G, Keane WM, Werner-Wasik M, Curran WJ Jr, et al. Integration of surgery with fractionated stereotactic radiotherapy for treatment of nonfunctioning pituitary macroadenomas. Int J Radiat Oncol Biol Phys. 2005; 61; 3: 795-808.

Ignatius Ezeani. "Pituitary Adenomas, Challenges and Prospects of Management: A Case Report." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 2, 2019, pp 51-55.