CASE REPORT

Functional pituitary gonadotroph adenoma in male patients: Case report

Nanik Ram,[1] Sajjad Ali Khan,[2] Bhagwan Das,[3] Najmul Islam[4]

Abstract

Pituitary gonadotroph adenomas are common but very rarely do they secrete biologically active luteinizing hormone (LH) and follicle-stimulating hormone (FSH). There have been case studies reporting high sex hormones (testosterone/estrogen) in the presence of high or normal LH and FSH. Here we report two cases (with their consent) who presented with visual disturbance and headache at a tertiary care hospital (Aga Khan university hospital) Karachi, Pakistan. Brain imaging revealed a pituitary macroadenoma. Further workup was consistent with pituitary gonadotroph adenoma with high FSH (case 1) and normal LH/FSH (case 2) and elevated serum testosterone in both cases. Transsphenoidal resection was performed and the tissue sample histopathology confirmed pituitary adenoma. Postoperatively, improvement in hormonal profile was observed along with a resolution of visual disturbances and headaches.

Thus, functional gonadotroph adenoma should be considered in the presence of elevated testosterone/estrogen and normal or elevated follicle-stimulating hormone (FSH)/ luteinizing hormone (LH). Early diagnosis leads to a better outcome.

Keywords: Pituitary Neoplasms, Gonadotrophs Adenoma, FSHoma.

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Introduction

Pituitary adenomas can present in different ways.[1] They are categorized as functional or non-functional.[2] While most of the pituitary adenomas are reported to be gonadotrophs, only one-third of them are functional, secreting LH, FSH or both. Though these tumours secrete luteinizing (LH) and follicle-stimulating hormone (FSH), they are often biologically inactive as the sex hormone levels are within normal ranges.[3] The actual incidence and prevalence of the functional gonadotroph adenoma are not known, there have been case reports and case series reporting them.[4-6]

[1,2,4]Department of Medicine, Aga Khan University Hospital, Karachi, [3]Cancer Foundation Hospital, Karachi, Pakistan.

Correspondence: Sajjad Ali Khan. Email: sajjadali_kmcite@yahoo.com

These tumours can be present because of the pressure-related symptoms like visual deterioration and headache or sexual dysfunction which may differ in males and females.[7] It is very important to consider functional gonadotroph adenoma in patients with space-occupying Central Nervous System lesions as it can prevent patients from permanent neurological and sexual dysfunction by offering treatment options in the early course of the disease.

Case Report

Case 1: A 61-year-old male patient with the history of diabetes mellitus, controlled with oral hypoglycaemic agents came to our hospital in February 2018 with history of visual disturbance for the last 8 months. It was gradual in onset, painless affecting the peripheral vision of both eyes. There was no history of change in the colour vision or night blindness. The accompanying symptom was gradually increasing headache, of mild intensity and no radiation, showing improvement with simple analgesics. Furthermore, there was no history of recent trauma to the head and neck region. The patient also denied any other systemic symptoms including weight loss, fever, excessive sweating, nipple discharge and change in the size of hands and feet. He was married with three children and denied any history of sexual dysfunction or family history of any significant disease.

Examination revealed normal vitals with a blood pressure of 120 /80 mm Hg and heart rate of 80 beats/ minute. On confrontation method he was found to have a bitemporal hemianopia. Genital examination was normal with both testes measuring about 25ml with pubic hair Tanner stage 5, and rest of the clinical examination was unremarkable.

Investigations for case 1 revealed elevated follicle stimulating hormone (FSH) 36.66 mIU/ml (N=1.4-15.4), testosterone of 952.7 mIU/ml (N=193-740) and high normal leutinizing hormone (LH) of 7.09 mIU/ml (N=1.2-7.8), and remaining tests were normal.

Gonadotropin measurement was done using the chemiluminescence method. (refer to Table-1 for complete workup details).

Initial imaging revealed a sellar mass of 27.5×25.4×3 millimeter (mm) extending in to cavernous portion of both internal carotid artery (ICA) and suprasellar cistern

Table-1: Case 1 lab reports.

Laboratory Investigations	Pre-operative	Post-operative	Normal Reference ranges
FSH	36.66 mIU/ml	4.97 mIU/ml	1.4-15.4 mIU/ml
LH	7.09 mIU/ml	0.99mIU/ml	1.2-7.8 mIU/ml
Testosterone	952.7 ng/dl	176.8 ng/dl	193-740 ng/dl
Cortisol	2.60 ug/dl	7.40 ug/dl	4.3 - 22.4 ug/dl
FT4	0.69 ng/dl	1.65 ng/dl	0.89-1.76 ng/dl
Prolactin	12.40 ng/ml		3-14.7 ng/ml
Growth hormone	Less than 0.50	0.06 ng/ml	2.0-5.0 ng/ml

FSH, Follicle stimulating hormone; FT4, Free Thyroxine; LH,Leutinizing hormone; mIU, milli-international units per milliliter; ng/dl,nanogram per deciliter; ug/dl, microgram per decilitre.

resulting in external compression over the optic chiasm and partial encasement of cavernous sinus (Figure-1 case one).

Preoperative hormonal assays revealed hypothyroidism and adrenal insufficiency, so hormone replacement of Hydrocortisone and Thyroxine were given. The patient underwent transsphenoidal surgical resection of the pituitary tumour. There were no immediate or late complications noted. Histopathology results were also consistent with pituitary adenoma.

Steroids and Thyroxine were stopped after surgery, once his hypothalamic-pituitary axis (HPA) and thyroid axis recovered.

On subsequent visits, the patient's lab parameters improved; FSH became normal (4.97 mIU/ml), LH & testosterone declined significantly 0.99 mIU/ml and 176.8 mIU/ml respectively. Moreover, patient's symptoms (vision and headache) improved significantly.

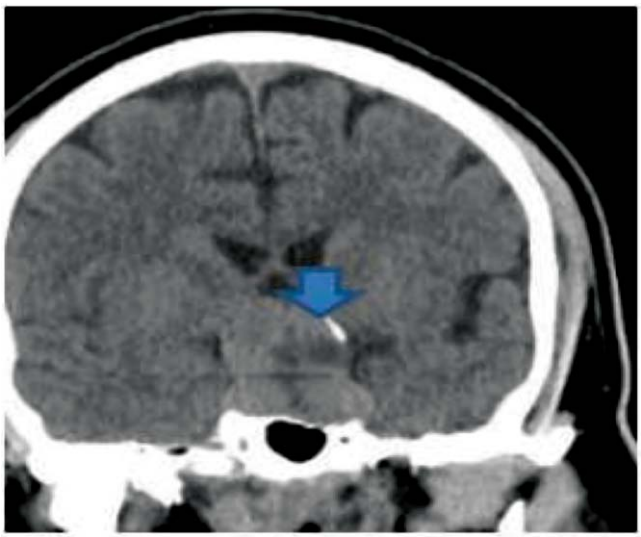

Figure-1: Case-1) CT Head showing a mass lesion extending in to the surrounding structures as pointed by the arrow.

Furthermore, there is a subjective feeling of psychological well being and occupational independence which was hampered by the disease before the surgery. Currently, the patient is on close follow up and is being assessed on regular basis for any new symptom or sign.

Case 2: A 52-year-old male married with two children and no prior comorbid condition presented to our hospital in March 2020 with a history of worsening of vision initially on the right side and then the left side during the preceding 6 months. It was gradual in onset with no history of recent trauma affecting the peripheral vision predominantly.

The patient also had mild headache on occasional basis which was not associated with any particular timings and it would improve with simple analgesics.

The patient denied any other symptoms to suggest any neurological or endocrinological disease. There was no other significant personal or family history of any other condition.

Examination revealed normal vitals with blood pressure of 110/75mmHg and heart rate of 85 beats per minute. Confrontation method revealed bitemporal hemianopia and the genital examination was also unremarkable with testis volume of 20 ml each.

Based on the above history and examination, a diagnosis of space occupying lesion of brain was suspected and further workup including laboratory investigations and brain imaging was considered.

Investigations revealed high normal follicle stimulating hormone (FSH) of 13.61 mIU/mL (N= 1.4-15.4) and high testosterone level of greater than 1500 ng/dL (N= 193-740) but normal luteinizing hormone (LH) 4.45 mIU/mL (N=1.2-7.8), cortisol of 12.60 ug/dL (N=4.3 - 22.4) and FT4 1.23 ng/dL (N=0.89-1.76). (refer to Table-2 for complete workup details).

Table-2: Case 2 lab reports.

Laboratory Investigations	Pre-operative	Post-operative	Reference ranges
FSH	13.61 mIU/ml		1.4-15.4 mIU/ml
LH	4.45 mIU/ml		1.2-7.8 mIU/ml
Testosterone	>1500 ng/dl	20.14 ng/dl	193-740 ng/dl
Cortisol	12.60 ug/dl	11.10 ug/dl	4.3 - 22.4 ug/dl
FT4	0.84 ng/dl	0.88 ng/dl	0.89-1.76 ng/dl
Prolactin	36.80 ng/ml		3-14.7 ng/ml
IGF-1	110 ng/ml		88.3-209.9 ng/mL
Growth hormone	0.13 ng/ml		2.0 -- 5.0

FSH, Follicle stimulating hormone; FT4, Free Thyroxine; LH, luteinizing hormone; mIU, milli-international units per milliliter; ng/dl, nanogram per deciliter; ug/dl, microgram per deciliter.

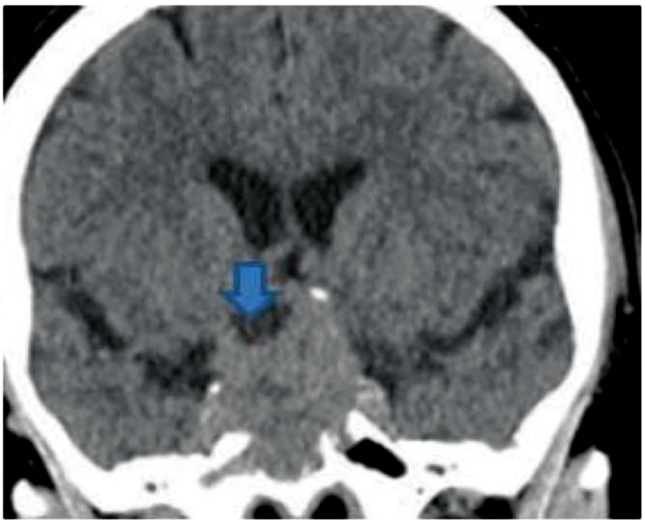

Figure-1: Case-2) CT Head showing a well-defined solid appearing mass lesion with some internal cystic component arising from the pituitary gland.

Imaging of the head revealed a well-defined solid mass arising from the pituitary gland and measuring approximately 45 x 39 mm on coronal sections extending into suprasellar region superiorly, sphenoid sinus inferiorly and abutting the cavernous sinuses bilaterally. (refer to Figure-1 case 2).

The patient underwent transsphenoidal surgical resection of the pituitary tumour. There were no immediate and late complications noted. Histopathology results were also consistent with pituitary adenoma.

Postoperatively, serum testosterone levels improved from over 1500 ng/dl pre-operatively to 20.14 ng/dl. Other laboratory parameters also improved.

The patient had a significant improvement in his vision and no other post-operative complications were observed. He had been on regular follow up and during his previous visit he reported to have low energy and decreased libido. He was started on thyroxine replacement and was monitored. During the subsequent visits the patient reported persistence of sexual dysfunction and testosterone in the replacement dose was started which showed a marked improvement in sexual and psychological well being.

Discussion

Most of the gonadotroph pituitary adenomas are non-functional and very rarely secrete biologically active steroid hormones in high levels (testosterone/estrogens). (4) Our case report is consistent with prior case reports and case series as both of our patients had a high level of serum testosterone before surgery and they improved significantly after surgery.

Studies show that the functional gonadotroph adenomas (FGA) often manifest secondary to pressure symptoms in the form of headache and visual disturbance and are associated with morbidity and mortality.[8]

Both of our patients had pressure symptoms in the form of visual deterioration and prolonged headaches. Furthermore, It has also been reported that these tumours may present with sexual dysfunction including hypogonadism and infertility.[5] In males, they can cause testicular enlargement or erectile dysfunction and in women, they can present with ovarian hyperstimulation syndrome.[9] In contrast, our patients denied any history of sexual dysfunction. Surgical intervention improved both the symptoms and biochemical changes.[3] There was a significant improvement in symptoms of headache and visual disturbance after surgery. Diagnosis was based on the biochemical and immunohistochemical staining of the tissue sample to differentiate these tumours from other lesions.[10] Biochemically, LH, FSH, or both could be high.[11] Both of our patients' serum testosterone levels were checked before and after the surgery which was significantly abnormal before the surgery and improved postoperatively.

One of the limitations of our cases was the lack of immunohistochemical diagnosis, because of the non-availability of the facility at our centre/country. In these two cases, the hormonal profile was highly suggestive of the functioning gonadotroph adenoma which was supported by the imaging studies.

Conclusion

Both our cases reveal important learning aspects. Case one presented with slowly progressing visual disturbance and headaches. Investigation showed high FSH in the presence of raised testosterone. He underwent surgery and post operatively his symptoms improved markedly. The second case also presented with visual defects and headache. His laboratory investigations showed elevated FSH and testosterone. He also underwent transsphenoidal surgery and his vision improved markedly. Hence, FGA should be considered in the differential diagnosis of pituitary tumours with visual problems.Biochemically, they can present with high FSH/LH and testosterone.Transsphenoidal resection is the initial treatment of choice and can reduce endocrine dysfunction, resolve headaches, improve visual impairment.

Disclaimer: None.

Conflict of Interest: None.

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