Case Report

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Pituitary macroadenoma with panhypopituitarism masquerading as schizophrenia: a diagnostic dilemma managed conservatively

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Introduction and importance: Secretory pituitary macroadenoma also known as prolactinoma are benign neoplasm comprising very minimal cases of intracranial masses. Among the various presentation suggestive of panhypopituitarism, psychosis, and features of schizophrenia is very rarely seen. In the majority of cases, neurosurgical intervention for the excision of tumor is considered a standard treatment modality but conservative management with dopamine agonist and steroids have also been shown to provide an optimal level of care also improving the quality of level of patient.

Case presentation: A 42-year-old Asian male presented with a history of talking to self, delusion of persecution, over talkativeness, hallucination, increased suspiciousness, and history of lost and found in the streets where he was working as a migrant worker. The patient was initially managed in line of schizophrenia with the antipsychotics drug of choice. On further assessment there was no improvement of psychiatric symptoms but they further deteriorated with additional neuropsychiatric symptoms; hence, MRI brain was carried out. Following which, the diagnosis of pituitary macroadenoma was confirmed and further more hormonal analysis was done, which showed findings suggestive of panhypopituitarism. The patient was then managed conservatively with dopamine agonist and steroids, which showed rapid improvement of psychiatric symptoms with a massive reduction in the size of the pituitary macroadenoma.

Clinical discussion: With the incidence of 100 per million cases pituitary adenomas are considered locally invading with the characteristic compression of the surrounding structure, presenting as visual hallucinations, olfactory hallucinations, episodes of losing time, apathy, and features suggestive of adrenal insufficiency, hypogonadotrophic hypogonadism, and symptoms secondary to hormonal imbalance such as hypothyroidism. Psychiatric symptomatic presentations are considered a very rare presentation in cases of pituitary macroadenoma. Also, psychiatric features and symptoms of psychosis are associated with prolcatinomas through idiopathic mechanism and the basic casualty has not been established. Surgical intervention such as trans-sphenoidal resection of the mass can be undertaken in case where mass effects is present but long-term remission and prognosis is found not to be fruitful. Conservative treatment with dopamine agonist such as cabergoline and steroids also plays a meaningful role in abrupt management in such cases.

Conclusion: Pituitary macroadenoma presenting as a patient of schizophrenia is noted very rarely in medical literature; hence, investigations in view of neurosurgical diagnosis in cases presenting as psychosis should be considered for ideal holistic management. Conservative management can also be a breakthrough treatment modality in complete recovery of pituitary macroadenoma.

Keywords: case report, pituitary macroadenoma, prolactinoma, schizophrenia

Introduction

Pituitary adenomas are neoplasms of benign origin comprising 10–15% of all intracranial masses[1]. Among various types of pituitary adenomas prolactinomas comprises 57%, nonsecretory pituitary adenomas 28%, hormone secreting pituitary adenomas 11%, corticotroph adenoma 2%, and 2% of unknown functional status[1]. Based on size variation pituitary adenomas are categorized into macroadenoma (>10 mm) and microadenoma

HIGHLIGHTS

- Secretory pituitary macroadenoma also known as prolactinoma are benign neoplasm comprising very minimal cases of intracranial masses.
- With the incidence of 100 per million cases pituitary adenomas are considered locally invading with the characteristic compression of the surrounding structure.
- Psychiatric features and symptoms of psychosis are associated with prolcatinomas through idiopathic mechanism and the basic casualty has not been established.
- Investigations in view of neurosurgical diagnosis in cases presenting as psychosis should be considered for ideal holistic management.
- Conservative treatment with dopamine agonist such as cabergoline and steroids also plays a meaningful role in abrupt management in such cases.

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(<10 mm)[2]. It is been reported that microadenoma shows female preponderance and macroadenoms are equally prevalent among male and females. Additionally, the level of serum prolactin depends upon the size of adenoma and prolactin level greater than 250 ng/ml denotes mostly a macroadenoma[3]. Functionally, prolactinomas are prolactin secreting pituitary tumors originating from the lactotrophs of the anterior pituitary gland. Hyperprolactinoma is considered when serum prolactin above the normal range (20–25 ng/ml in premenopausal women, 15 ng/ml in men and postmenopausal women)[3]. Symptomatically, prolactinoma present as galactorrhea, amenorrhea, sexual dysfunction, and infertility, as well as symptoms due to tumor expansion, such as headache and visual changes[4]. The spiking levels of serum prolactin have been found to bring out psychiatric symptoms such as mood and behavior changes with associated symptoms of depression, anxiety, mania, and hostility[5,6]. Moreover, the underlying pathophysiology resulting in psychotic features in pituitary macradenoma is still unclear but a basic existing theory states that the release of prolactin from the pituitary is inhibited by dopamine, whereas a deficiency of this neurotransmitter increases prolactin secretion[7,8].

We here present a case of an adult male with the changes in behavior and personality that is consistent with a psychotic illness, but were nonspecific and did not fit neatly into any single psychiatric diagnostic category. There was no singular feature of this patient's presentation that pointed to the possibility of a mass lesion, highlighting the importance of considering the diagnosis of a brain tumor and a thorough medical investigation in patients with psychiatric symptoms. This case report has been written according to Surgical Case Report (SCARE) guideline[9].

Case summary

A 42-year-old Asian male was seen for an initial evaluation in our psychiatry outpatient department for over talkativeness, destructive behavior, talking to self, and delusion of persecution in 2021/08/20. There is a preceding history of the patient being lost and found in the streets of Malaysia, where he was working as a migrant worker. His past medical history does not consisted of any kind of comorbidities and chronic illness. Social history was positive for active or past tobacco use, alcohol but not illicit drug use. There was not as such as any home medications that the patient was using and no any over-the-counter medications.

According to the first-degree relative and working friends of the patient, they reported a history of a behavioral changes such as the patient talking to himself over the phone, alleging to his friends that they are conspiring to kill him, hallucination, increased suspiciousness, hyperactive, and agitated since the last 4–5 months; hence, initially a working diagnosis of mania with psychotic symptoms (F30.2) was designated and further drug therapy of Haloperidol, phenargan, Diazepam, Olimet was started. He denied vomiting, dizziness, orthostatic symptoms, galactorrhea, and reported no significant changes in his facial features, shoe size, or ring size. Furthermore, psychiatric mental state examination was carried out and on detailed questioning, general attitude and behavior (GAB): does not greet on interview, rapport could not be established, avoid eye contact, speech: pressured speech, increase in tone, rate, volume, irrelevant, and incoherent speech, mood: elated, thought: linear and goal directed, delusion could not be established, perception: no perceptual abnormalities reported. Hence, the patient was diagnosed as schizophrenia and medical management in that line was started. In the subsequent period of hospital admission there was not any improvement in the symptoms of the patient and further more Lithium drug therapy was also started from 32nd day of admission and Trihexyphenidyl Hydrochloride in view of anti N-Methyl-D-aspartate(NMDA) receptor encephalitis. On 40th day of admission, the patient started having involuntary bilateral lower limb movement, drowsiness, and hallucination in the background of his initial symptoms hence MRI with contrast was done, which showed a well-defined sellar mass with suprasellar extension measuring about $28 \times 30 \times 26$ mm suggestive of pituitary macroadenoma, with lesion iso to hyperintense in T1, heterogeneously hyperintense on T2\FLAIR with few areas of hypointensity within (Figs. 1A–D). Hence, for further continuing care patient was then handed over to the department of neurosurgery at 42nd day of admission and patient planned for a craniotomy and tumor excision. Furthermore, ophthalmology consultation was carried out further as the patient had blurring of vision since 2 years. Visual parameters such as visual acuity, power, near vision, extra ocular movement, convergence, slit lamp, color vision, amslers grid, and fundus examination all were within normal ranges but Humphrey 30-2 program showed decreased bilateral temporal vision. On the 38th day of admission hormonal profile was sent after consultation with an endocrinologist and Luteinizing hormone (LH), Follicular stimulating hormone (FSH), Free triiodothyronine (Ft3), Free thyroxine (Ft4), Thyroid stimulating hormone (TSH), Adrenocorticotropic hormone (ACTH), Basal cortisol, Growth Hormone (GH) (30 min after 75 gm glucose), serum procalcitonin were sent. Thyroid function tests at this time showed low free T4 of 0.35 ng/dl (0.6–1.24 ng/ml), low Free T3 of 1.66 pg/ml (2.3–4.2 pg/ml) with low normal thyroid stimulating hormone (TSH) of 5.38 uIU/ml (0.300–4.000 ulU/ml) with decreased levels of LH, FSH, Corrtisol, GH with severely raised serum procalcitonin the findings were consistent with secondary adrenal insufficiency, secondary hypothyroidisim, and hypogonadotrophic hypogonadism) suggestive of panhypopituitarsim (Table 1).

In view of the lab reports, Tab Thyroxine 100 microgram was started along with hydrocortisone, which was later changed to prednisolone and surgery was halted due to the risk of myxedema coma. In subsequent days patient got symptomatically better and Thyroid function tests were normal on levothyroxine replacement and levothyroxine was continued (Table 1). After 60th day of admission was planned for discharge with medical therapy consisting of cabergoline 0.25 mg, prednisolone 20 mg, calcium and vitamin D supplements. At 1 month follow-up patient showed complete recovery of symptoms with normalized hormonal profile and further MRI done at 2 months and subsequently at 1 year follow-up showed reduction of adenoma size by almost 50% with good quality of life of the patient.

Discussion

Prolactinomas or prolactin secreting pituitary tumor holds the minimal incidence of 100 per million adults[10,11]. Based upon morphology microprolactinomas do not encroach the parasellar region and macroprolactinomas, which are generally found to be locally invading characteristic resulting compression of surrounding structures. Its been noted that the size of the tumor is directly proportional to the level of serum prolactin, and in our case, the measured level of prolactin was 2860 ng/ml, the finding

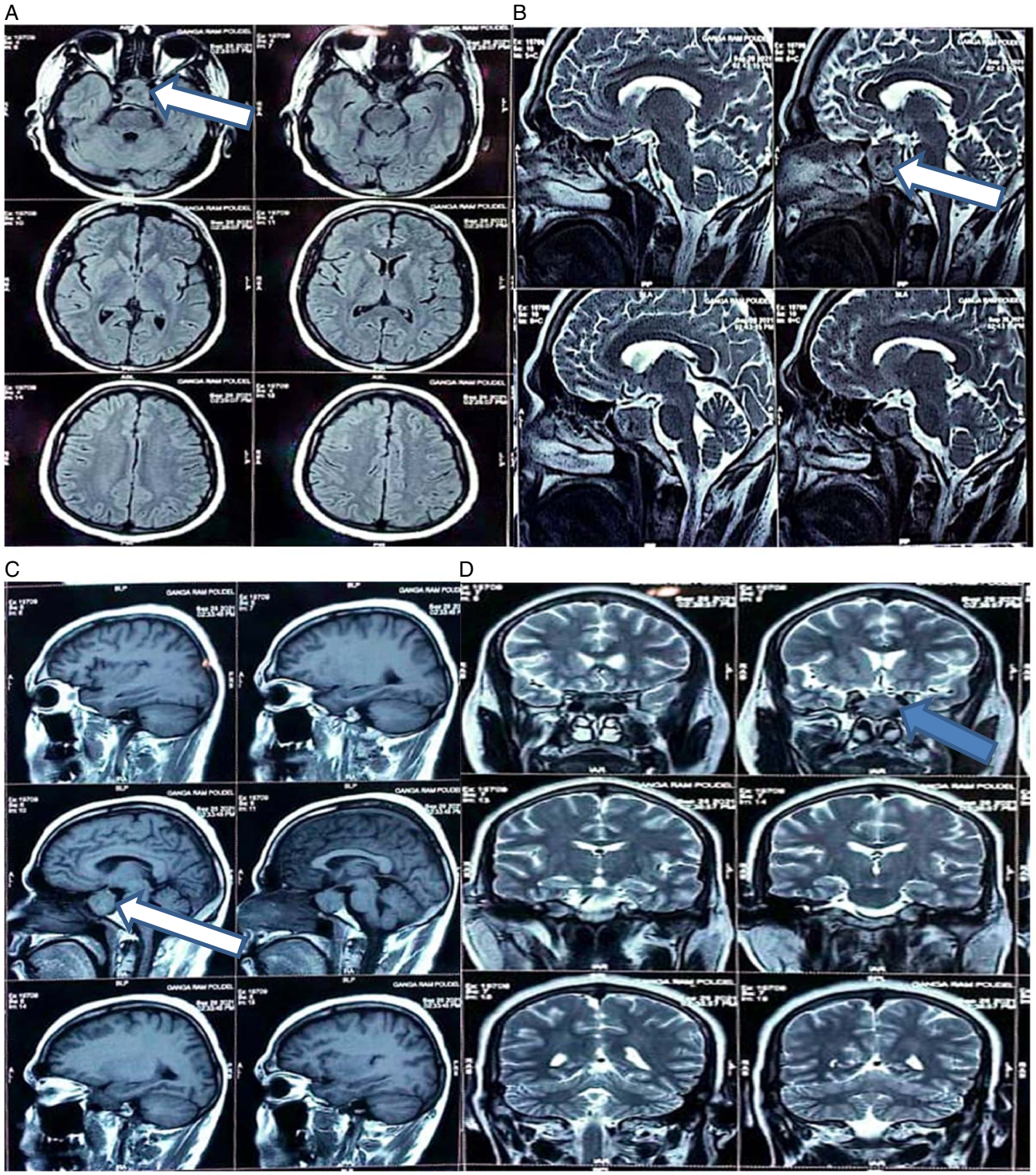

Figure 1. Laboratory investigations suggestive of panhypopituitarism. (A,B) Axial and Sagittal T2 and T2 flair images demonstrating sellar mass with suprasellar extension with erosion of floor of sella. (C,D) Sagittal FLAIR and T2 images demonstrating encasement of left cavernous sinus and internal carotid artery by pituitary macroadenoma without reduction in caliber of internal carotid artey.

of which is consistent macroadenoma[3]. Regarding the clinical presentation such patients usually presents with features of adrenal insufficiency, hypogonadotrophic hypogonadism, and symptoms secondary to hormonal imbalance such as hypothyroidism[3]. Along with it in some case patient also present with features of mass effect and local compression of vicinity structures from a prolactinoma, such as visual hallucinations, olfactory hallucinations, episodes of 'losing time', and apathy[9]. The physiological effect of hyperprolactinemia results from the effects on tissues upon which prolactin directly acts; and the effects due to the 'downstream' hypogonadism caused by hyperprolactinemia. In our case, the patients symptoms persisted

Table 1
Lab values.

Date	Lab type	Lab value [reference range]
01/10/2021	Free T4 (free thyroxine)	0.35 ng/dl [0.6–1.24 ng/ml]
01/10/2021	Free T3 (free triidodothyronine)	1.66 pg/ml [2.3–4.2 pg/ml]
01/10/2021	TSH (thyroid stimulating hormone)	5.38 ulU/ml [0.300–4.000 ulU/ml]
17/10/2021	Free T4	0.80 ng/dl [0.6–1.24 ng/ml]
17/10/2021	Free T3	1.48 pg/ml [2.3–4.2 pg/ml]
17/10/2021	TSH (thyroid stimulating hormone)	2.14 ulU/ml [0.300–4.000 ulU/ml]
01/10/2021	Prolactin	2860 ng/ml [4.04–15.2 ng/ml]
01/10/2021	GH (growth hormone)	0.07 ng/ml [0.4–10 ng/ml]
01/10/2021	Cortisol	0.37 mcg/dl [5–25 mcg/dl]
01/10/2021	LH (luteinizing hormone)	1.67 IU/l [5–25 IU/l]
01/10/2021	FSH (follicular stimulating hormone)	1.30 IU/l [1.5–12.4 IU/l]
21/10/2021	ACTH (adrenocorticotropic hormone)	53.4 pg/ml [10–60 pg/ml]

even after the continuous use of antipsychotic drugs suggesting that intracranial mass, rather than the psychiatric disorder, was a more likely cause of his symptoms. Also, psychiatric features and symptoms of psychosis are associated with prolcatinomas through idiopathic mechanism and the basic casualty has not been established[12,13].

Another of the robust mechanism by which panhypopituitarism comes into play in pituitary macroadenoma is through HPA-gonadal axis dysregulation, due to which the raised levels of prolactin down regulates gonadotropin-releasing hormone, which then inhibits luteinizing hormone and follicle-stimulating hormone production by the pituitary gland. This further suppresses ovarian and testicular function and results in reduced production of the sex hormones testosterone in men and estrogen and progesterone in women[3]. Similar laboratory findings is consistent in our case, where there was decrease in LH (Luteinizing hormone) and FSH (Follicular stimulating hormone) level. In macroadenomas serial MRIs are necessary to assess tumor growth and to determine the need of whether to intervene with surgical or medical therapy. Trans-sphenoidal resection of the mass can be undertaken in case where mass effects is present but long-term remission and prognosis is found not to be fruitful and furthermore hyperprolactinemia have been seen to recur in ~50% of patients with macroadenomas who have undergone trans-sphenoidal resection[3]. Surgery as the mainstay treatment is recommended in those cases where dopamine agonist therapy is contraindicated, in patients who cannot tolerate dopamine agonist therapy, and those with invasive macroadenomas resulting changes in their vision and poor response to dopamine agonist therapy[14].

For the management of combined clinicopathological lesions multidisciplinary approach is considered best for providing optimal benefit to the patient. In our case, psychiatrist, endocrinologist, and neurosurgeon decided together about the management of patients prolactinoma based upon tumor location, extension, mass effect, endocrine side effects of tumor. Usually, dopamine agonists in patients of psychiatric disorders are not recommended due to the risk of psychiatric decompensation[15]. In cases where the tumor is not exerting a mass effect another treatment method is gonadal steroid replacement with conjoint monitoring of tumor size without surgery or dopamine agonist, which is mostly carried out in patients with nongrowing microadenomas[16,17]. In our case, cabergoline as dopamine agonist therapy was attempted in a setting of close psychiatric monitoring, which showed complete recovery of symptoms within a short period of time. Furthermore, the growth of prolactinoma should be assessed regularly in yearly basis with an MRI with or without gadolinium contrast. Along with it serum prolactin levels should also be monitored[18]. In our case, in yearly radiological follow-up there was a reduction in the size of the adenoma by 50% with dopamine agonist therapy.

Conclusion

Various neurosurgery related disease presents as neuropsychiatry symptoms but pituitary macroadenoma very rarely presents as symptoms of psychosis and schizophrenia. Detailed hormonal analysis and neuroradiology is utmost in patients presenting with multiple psychiatric symptoms. Although surgical intervention is considered as breakthrough treatment modality in such cases, conservative treatment also plays a potential role in bringing out the best outcome in patient care.

Ethical approval

Ethical approval is exempted in our institution KIST medical college and teaching hospital where as written informed consent was taken from patient himself.

Consent

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

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Author contribution

S.G.: study concept, informed consent, and manuscript draft formulation; S.S.: study concept, patient management, and manuscript review; S.S.: patient management, patient counseling, and introduction writing; A.S.: radiological diagnosis, patient management, and MRI labellings.

Conflicts of interest disclosures

No any conflict of interest noted.

Research registration unique identifying number (UIN)

As this paper is a case report where only gathering of information which was the part of patient treatment was carried out hence register into clinical trial registry is not needed.

Guarantor

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