Original Research Article

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Endocrine Ramifications of Anatomical Lesions of the Pituitary Gland

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Abstract

Context: The pituitary gland or hypophysis cerebri is a neuroglandular body regulating the secretory activity of a host of other endocrine glands and tissues of the body. It lodges in the hypophyseal fossa of the sella turcica in the body of the sphenoid bone of the skull and is easily identified radiologically. To comprehend the functional disturbances caused by pituitary gland it becomes imperative to correlate it anatomically. *Aims:* In this study we aim to highlight through case vignettes how an early recognition of anatomical lesions in the pituitary can influence the treatment plan in a patient presenting with a plethora of endocrine disturbances. *Methods and Material:* Interesting and illustrative cases were chosen from the endocrine clinic of a tertiary care centre. Both outpatient and inpatient cases were included for the study. *Results:* In this article through illustrative cases we demonstrate how anatomical lesions in the pituitary gland can affect other essential hormones and electrolytes namely sodium. The case vignettes will help the physician to interpret the not so common abnormalities of the thyroid function tests and also take early corrective measures to prevent mortality and morbidity in patients. *Conclusions:* The cases will impress upon the physician that all pituitary masses need not be operated and hence will prevent unnecessary surgical intervention. It will also help the anatomist to teach applied anatomy to students who will then relate to the endocrine emergencies and severe electrolyte abnormalities as a result of anatomical abnormalities in the pituitary gland.

Keywords: Pituitary Gland; Hyponatremia; Panhypopituitarism; Pituitary Adenoma; Pituitary Lesions; Hypothalamic Hamartoma.

Introduction

The pituitary gland, or hypophysis cerebri, is a reddish-grey, ovoid body, about 12 mm in transverse and 8 mm in anteroposterior diameter, and with an average adult weight of 500 mg. It is continuous with the infundibulum, a hollow, conical, inferior process from the tuber cinereum of the hypothalamus. It lies within the pituitary fossa of the sphenoid bone, where it is covered superiorly by a circular diaphragma sellae of dura mater [1]. The endocrine glands and the hormones they release are essential for the normal body homeostasis. The hormones released by these glands help in the brain development, attaining puberty, achieving target height, child bearing, maintaining the fluid and electrolyte homeostasis of the body and participate in almost all bodily functions. Developmentally the pituitary gland consists of a cellular portion derived from Rathke's pouch known as Anterior pituitary/ Adenohypophysis and a neural portion derived from a downgrowth from the diencephalon known as Posterior pituitary/Neurohypophysis. Adenohypophysis has two types of acidophils namely somatotrophs and mammotrophs along with three types of basophils namely gonadotrophs, thyrotrophs and corticotrophs [2]. The neurohypophysis contains unmyelinated nerve fibres, fenestrated plexus of blood capillaries and pituicytes. The hypophysiotropic area of hypothalamus via tubero-infundibular tract conveys releasing or inhibiting hormones to the adenohypophysis which is further regulated by a feedback mechanism in response to the level of circulating hormones from the target endocrine organs.

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The neurohypophysis supplied by hypothalamo-hypophyseal tract, acts as storage and releasing centre for vasopressin and oxytocin synthesized by supra-optic and paraventricular nuclei of hypothalamus respectively [3].

The sellar region is an anatomically complex area bounded by sphenoid sinus anteroinferiorly, the paired cavernous sinuses laterally, the suprasellar cistern and its contents, diaphragma sellae and hypothalamus superiorly, and the dorsum sella and brainstem posteriorly [4].

Anatomical defects in these glands have far reaching and sometimes life threatening consequences. In this article through illustrative cases we demonstrate how anatomical lesions in the pituitary gland can affect other essential hormones and the electrolytes such as sodium.

The case vignettes will help the physician to interpret the not so common abnormalities of the thyroid function tests and also take early corrective measures to prevent mortality and morbidity in patients.

Thus we aim to highlight that we need to expand our assessment of endocrine disturbances in the background of anatomical defects in the pituitary which is reflected in varied forms necessitating intervention which may not be surgical always.

Materials and Methods

Interesting and illustrative cases were chosen from the endocrine clinic of a tertiary care centre. Both outpatient and inpatient cases were included for the study. Informed consent was taken in preformed consent format to ensure that individuals understand the purpose, risk and benefits of research studies. Out of a myriad of cases presenting in the endocrine clinic of a tertiary care hospital in central India we are exclusively presenting those rare cases in which mere treatment of symptomatology arising from hormonal imbalance at the time of admission alone does not suffice. The final selection of these cases was made only after identifying pituitary lesion as the underlying etiology.

Results

Selected cases with case history, examination and investigation findings with final diagnosis is discussed subsequently with its anatomical correlation.

Case 1

History:

A 70 yrs female presented with recurrent admissions for hyponatremia in August 2017. With each admission she was managed with hypertonic saline and discharged on Tolvaptan (a selective vasopressin receptor 2 antagonist). On reviewing the previous years' papers we came across a thyroid function report dated July 2015 which suggested secondary hypothyroidism i.e. low thyroid hormones with a low or normal TSH.

A Thyroid function test was repeated and an 8 am cortisol was done. The 8 am cortisol was low (Fig. 1) suggesting hypocortisolism and the thyroid functions again suggested secondary hypothyroidism. The results suggested Panhypopituitarism. A MRI of the pituitary was advised.

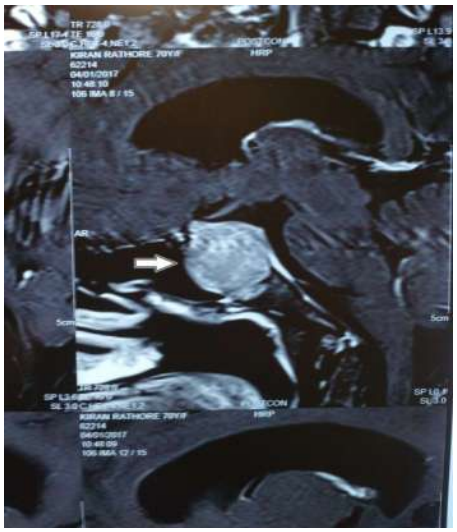

Fig. 1: A MRI of the pituitary was advised

The MRI revealed a pituitary macroadenoma. This was the reason for the secondary hypothyroidism and hypocortisolism.

The patient subsequently underwent a transphenoidal pituitary surgery. She is on steroid and thyroid hormone replacement and is doing well.

We must look out for abnormal thyroid function tests as they may just give you the clues to the aetiology of hyponatremia and also prevent life threatening complications. In the present case the hyponatremia was due to panhypopituitarism due to pituitary mass.

Case 2

History:

A 68 year old male presented with seizures and hyponatremia. The patient had recurrent admissions for the same over the past 2 years.

We were called to investigate the cause of hyponatremia. The thyroid function tests done again showed a picture suggestive of secondary hypothyroidism. Low serum sodium and thyroid function tests suggestive of secondary hypothyroidism i.e. low TSH and low free T4.

An X ray of the sella was advised to look for the sellar size. Fig. 2.

The X ray revealed a deep and large sella suggestive of a pituitary mass.

The MRI revealed an empty sella leading to

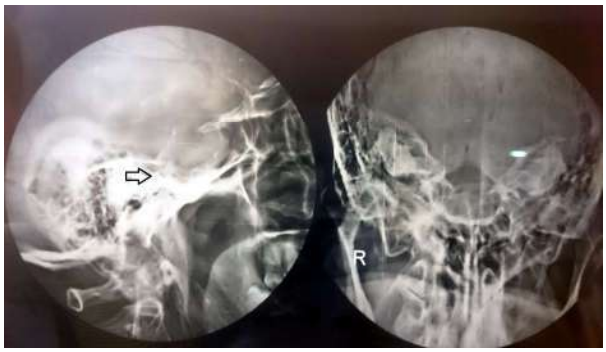

Fig. 2:

secondary hypothyroidism and the resultant hyponatremia.

Case 3

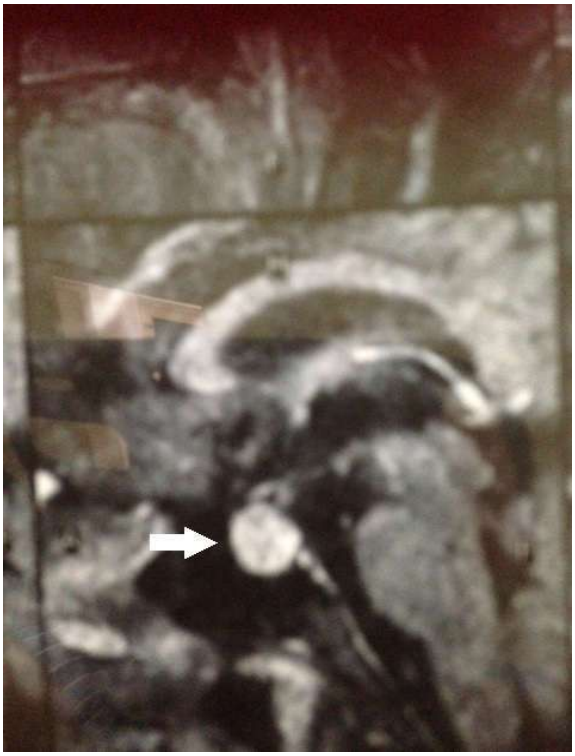

Fig. 3:

History:

A 32 year old male presented to us with infertility, loss of libido and lethargy.

He was investigated to have a high prolactin, low testosterone and a TSH of more than 150 mIU/ml.

A physician looking at the high prolactin got an MRI done which revealed a pituitary macroadenoma.

The patient was referred to us for the pituitary mass and the high prolactin. Fig. 3.

Now the interesting thing is the interplay the hormones have and their effect on the other hormones. The TRH has a molecular mimicry with the prolactin; so once TSH rises the prolactin witnesses a moderate rise too. Also in severe primary hypothyroidism there is a hypertrophy of the pituitary thyrotrophs leading to a pituitary hyperplasia and may be misinterpreted for a pituitary macro or a microadenoma. These patients don't require surgery but only an appropriate thyroid hormone replacement. The hyperplasia just melts away, just as in our patient. Fig. 4.

With the resolution of the hyperplasia, the libido improved, the testosterone level normalised and subsequently the patient fathered a child.

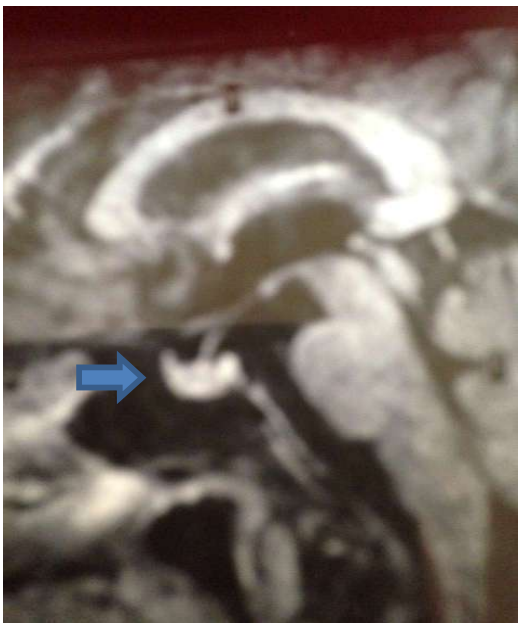

Fig. 4:

Case 4

History:

A 2 year old male child presented with history of early development of secondary sexual characters. The child was a product of full term normal vaginal delivery with normal psychomotor milestones.

Examination: Testicular volume of 8 ml bilaterally Stretched penile length of 6.5 cm (both high for his age).

Investigations: X–Rays of both hands for bone age determination (Fig. 5). The bone age of the child as determined by Greulich– Pyle atlas was 7 years as against the chronological age of 2 years. The advanced bone age signifies the rapidly progressive maturation of skeletal system due to systemic exposure to gonadal steroids.

GnRH analogue stimulation test confirmed central sexual precocity.

MRI scan of the brain revealed a hypothalamic hamartoma. (Fig. 6)

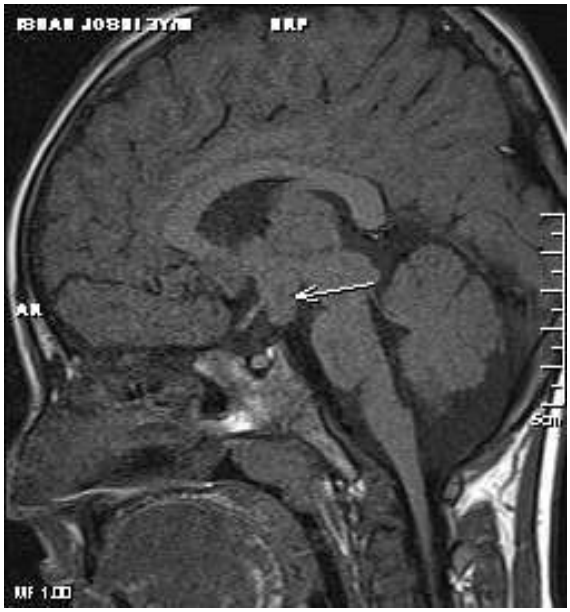

Fig. 5: Hypothalamic hamartoma

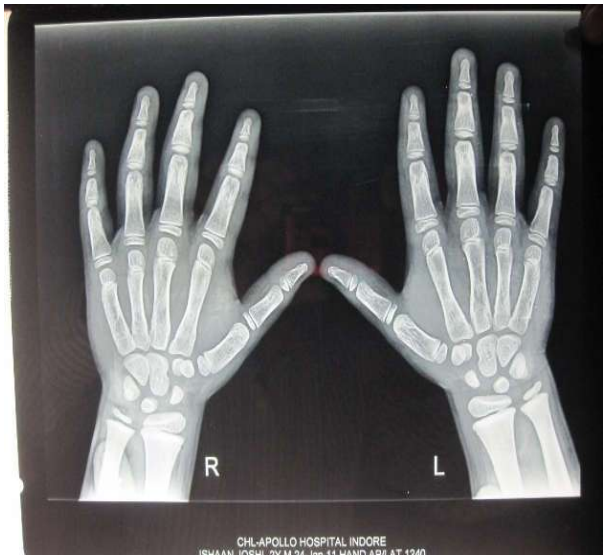

Fig. 6:

Diagnosis: Hypothalamic Hamartoma causing central sexual precocity.

Case 5

History:

A 14 year boy was referred to us with short stature, nystagmus,headache, poor scholastic performance.

The child had previously been investigated by the neurologist and an MRI of the brain had been done which revealed a pituitary mass.

The child was investigated and was found to have a TSH of more than 150 mIU/ml.

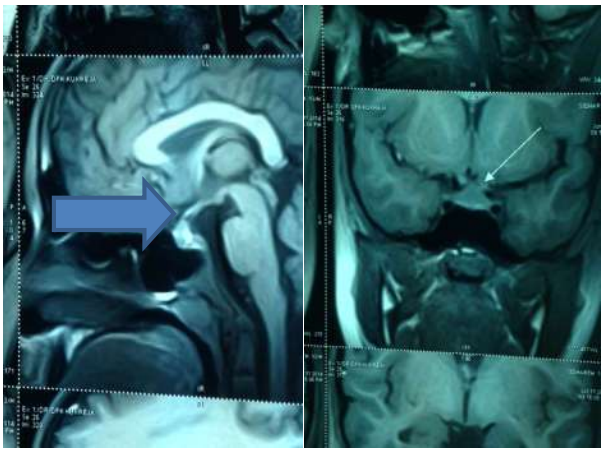

Fig. 7: Pituitary Mass in sagittal and coronal sections of the MRI

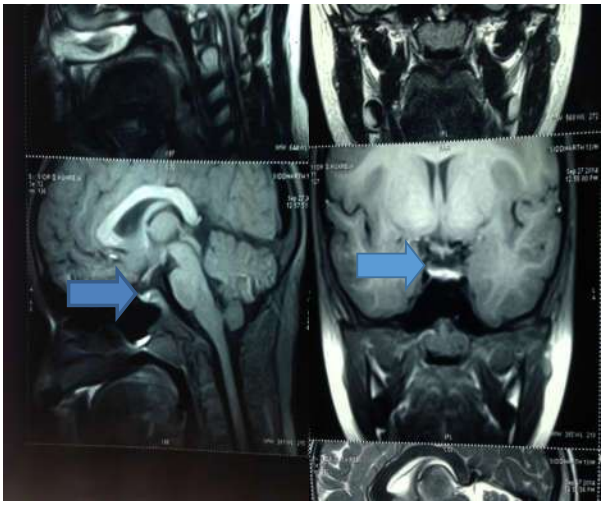

Fig. 8: Coronal and sagittal MRI sections showing complete resolution of the pituitary mass in the second MRI

Levothyroxine replacement therapy was started in appropriate doses.

A repeat MRI was performed 5 months after the treatment.

Discussion

The above cases illustrate how an alert physician can diagnose early the life threatening consequences of anatomic lesions of the pituitary. Hyponatremia is a common finding both in the inpatient and outpatient departments and results in significant morbidity and mortality [5]. Correcting the low sodium merely by hypertonic saline and giving tolvaptan for a few days and not interpreting the thyroid function tests and consequently not correcting the underlying etiology of hyponatremia can lead to poor outcomes for the patient as in our first two illustrative cases [6,7]. Both the cases had hyponatremia and thyroid function tests suggestive of secondary hypothyroidism but were initially not picked up for almost a year and a half as in the first case. They both were symptomatically treated for hyponatremia resulting in recurrent admissions and seizures. Once the cause was evaluated and treated by transphenoidal surgery in the first case (pituitary macroadenoma) and appropriate hormone replacement in the second case (empty sella), they have been totally asymptomatic and carrying on with their activities of daily living.

Not all pituitary masses need surgery and in fact surgery in cases of pituitary hyperplasia due to severe hypothyroidism can be catastrophic. The (Cases 3 and 5) [8] demonstrate how simple levothyroxine replacement can lead to complete resolution not only of the pituitary masses but also the associated endocrine abnormalities. The case 3 showed how the enlarged pituitary due to thyrotroph hypertrophy led to infertility, low libido, low serum testosterone and a high prolactin. The high prolactin was due to the molecular mimicry of TRH and prolactin [9]. Once the adequate levothyroxine replacement was done, the patient not only had normal sperm count and libido but even fathered a child after a year. Case 5 illustrates the need to evaluate short stature methodically and not to rush into surgical intervention of the pituitary. There have been cases where the hyperplasia of the pituitary has been operated upon with disastrous consequences. The child was referred to us and again appropriate thyroid hormone replacement led to complete resolution of the pituitary mass and rapid height gain and normal scholastic performance of the child.

The 4th case is a rare case of isosexual precocity in a 2 year old male child. The child had hypothalamic hamartoma leading to precocity. These tumors may or may not be operated upon depending upon the size and mass effects of the tumor. The hamartoma is a developmental malformation in the region of the tuber cinereum and mamillary bodies [10]. Children present with precocity and gelastic seizures. GnRH therapy can regress the precocity and occasionally they may require surgical removal.

MRI techniques in diagnosing pituitary lesions have witnessed a rapid evolution, ranging from non-contrast MRI in late 1980s to contrast-enhanced MRI in mid-1990s. Introduction of dynamic contrast-enhanced MRI has further refined this technique in diagnosing pituitary microadenomas [11].

Conclusion

The interplay of endocrinology and anatomy is essential to understand for the appropriate management of disorders of electrolyte imbalances and hormone disorders. Hyponatremia is one of the commonest electrolyte disorders and results in significant mortality and morbidity. It is multifactorial in origin and one important cause is endocrine abnormalities. Early diagnosis and treatment saves lives and recurrent hospital admissions. The physician and the endocrinologist have to work in tandem to manage cases as has been shown in the above examples. The applied anatomy of the pituitary and sella is important and must be taught to students which then forms the basis for future learning in clinics.

Key Messages

Anatomical lesions of pituitary have varied clinical outcomes that need to be taught and identified by medical professionals in an extensive manner as they are crucial in planning the appropriate treatment strategy.

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