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Interesting Cases of Pituitary Adenoma with Varied Presentations

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Abstract

Pediatric pituitary adenomas (PPAs) are rare neoplasms sometimes with unusualpresentations and varied clinical course. We describe 2 atypical PPAs to highlight the clinical examination, radiological, hormonal and management aspects.

A 6-year-old girl presented with bleeding per vagina with difficulty in walking with breast enlargement without visual disturbances. MRI revealed an enlarged anterior pituitary gland showing intense enhancement on contrast of size 11mm x 16mm without invasion of 3rd ventricle or parasellar extension into cavernous sinuswith USG Abdomen and pelvis revealing complex ovarian cyst with reduced TSH levels suggesting Primary Hypothyroidism.

Another 30-year-old male presented with blurring of vision in both eyes with bilateral temporal field defects with absence of secondary sexual characters and decreased libido with decreased testosterone levels and MRI Brain showing non diffusion restricting T1 iso T2 hyperintense lesion in sellarsuprasellar region suggestive of Cystic pituitary macroadenoma with haemorrhage,which was managed surgically.

Keywords: Adenoma; Medical; Pituitary; Surgery.

Introduction

Pediatric Pituitary adenomas (PPAs) are rare neoplasms that account for 2% of all pediatric brain tumors.[17] Typical clinical presentation depends on the extent of mass effect and, for secreting tumors, which trophic hormones are dysregulated. In addition to headaches, children frequently come to medical attention because of visual disturbances, growth failure, or abnormal pubertal onset.[15,16] Interestingly, PPA appears to have unusual presentations, atypical symptomatologies, or extremes of severity. When these tendencies are combined with the lesion's relative rarity, frequent misdiagnosis occurs with management challenges. We report two such cases with particularly striking presentations and/or extraordinary challenges in both diagnosis and

treatment of atypical PPA. This study was approved by our institutional review board, including a consent obtained from patients and their family members.

Case 1

A 6 year old female presented to the Neurosurgery outpatient department with progressive breast enlargement and episodes of irregular vaginal bleeding for past 3 months with gait disturbance in the form of left side high stepping gait since1 year. She was full-term delivered vaginally, was born of non-consanguineous marriage and was first in the birth order. Her birth weight was 2.5 kg (between 3rd and 15th centiles; WHO growth charts). She has not joined school because of her declining socialistic performances. There was no history of headache, vomiting, or visual symptoms. There was no other significant past history. There was no history of autoimmune disorder in the family.

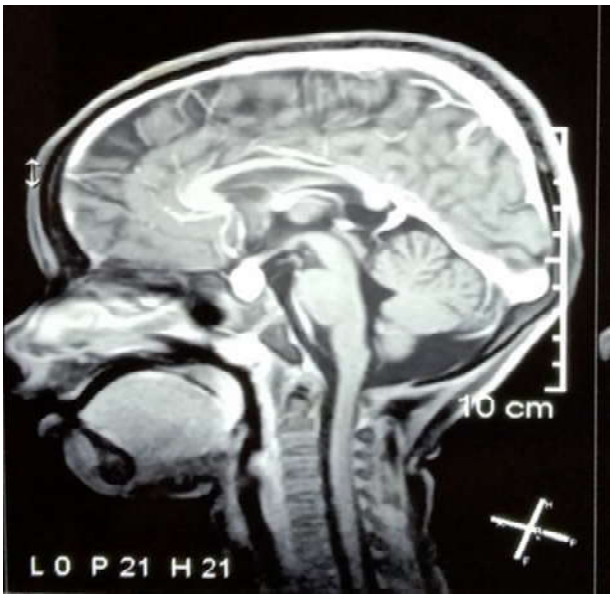
Her height was 114 cm (<3rd percentile, IAP chart), Her weight was 11 kg (between 25th and 50th centiles; IAP growth chart). Her pulse rate was 74/min and blood pressure was 100/62 mmHg (50th centile) She had dry skin, pallor and there were no café au lait spots. Child was having gait disturbances in the form of left high stepping gait with lateral deviation of left toes.

There was no goitre on palpation. She was having Tanner's staging II Breast enlargement, and there were no axillary or pubic hairs. Visual acuity and fields were normal.

Her hormonal profile is evaluated which showed TSH - > 1000 microIU/ml, Serum prolactin -75 ng/ml, Inhibin B level is 439.5 ng/l,LDH – 394 u/l and others hormonal values are normal.

Ultrasonography (USG) of the Abdomen and pelvis suggested multi-septated right ovarian cyst measuring around 4.9x 2.5 cm with bulky left ovary for the age with large follicles with mildly bulky left adrenal gland. USG screening of both breast shows prominent retroglandular areolar tissue, Screening of thyroid gland shows diffuse altered with increased vascularity.Skeletal survey was done of hands and feet which showed left deviation of toes.

Magnetic resonance imaging (MRI) scan of the brain revealed an enlarged anterior pituitary gland showing intense enhancement on contrast of size 11mm x 16mm without invasion of 3rd ventricle suprasellarextension into cavernous sinus.



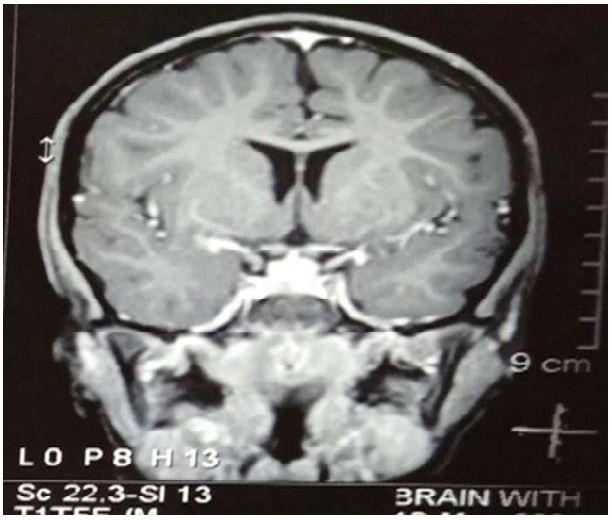


Fig. 1 and 2: MRI Brain contrast sagittal and coronal view showed enlarged anterior pituitary gland showing intense enhancement on contrast.

The child was managed with thyroid replacement therapy and was started on tablet L- thyroxine at a dose of 25 µg, which was escalated weekly to a daily dose of 50 µg, given in the early morning on an empty stomach and within a month of starting the therapy, her bleeding cycles stopped. She was referred to Pediatric surgery.

Department ICH Chennai for further treatment of ovarian mass.

Case 2

A 30 year old male presented to the Neurosurgery outpatient department with blurring of vision in both the eyes with bilateral temporal field defect since 3

months with lack of secondary sexual characters like absence of axillary and pubic hairs, h/o decreased ejaculation and loss of early morning tumescent. There was no history of headache, vomiting. There was no other significant past history. There was no history of autoimmune disorder in the family.

His height was 163 cm and absence of axillary and pubic hairs with long hands and feet with fingers and toes and Bilateral testicular atrophy.

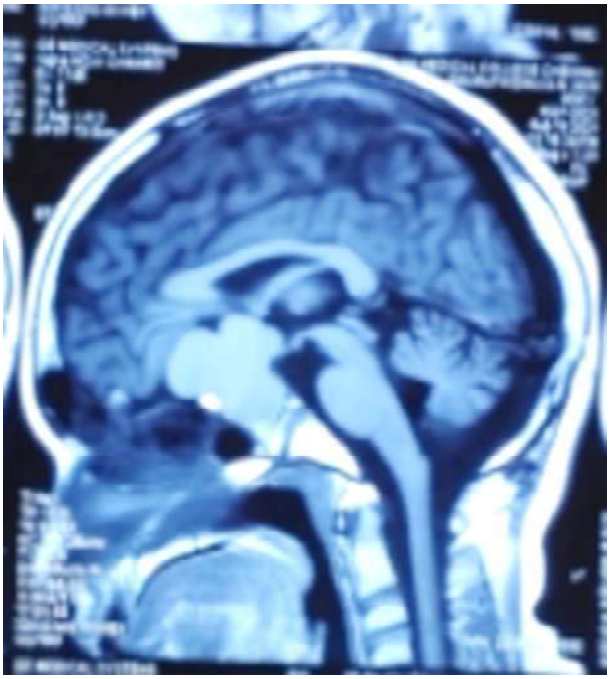
Fig. 3: Showed absence of axillary and pubic hairs with long hands.

His pulse rate was 74/min and blood pressure was 120/82mmHg. Visual field testing showed bitemporalhemianopia.

His hormonal profile is evaluated which showed serum Testosterone is <0.025, serum cortisol is 4.74 and FSH is 0.64 and LH is 0.320and other hormones are in normal limits.

Ultrasonography (USG) of the Abdomen does not reveal any abnormality.

Magnetic resonance imaging (MRI) scan of the brain shows non diffusion restricting T1 iso and T2 hyperintense lesion not suppressing on FLAIR measuring 3.6x2.7x3.9 mm with blood fluid levels noted within the sellar and suprasellar region with lesion extending anteriorly upto anterior cranial fossa exerting mass effect over basifrontal region with erosion of dorsum sella and widening of sella without cavernous sinus invasion without involvement of internal carotid artery suggestive of cystic pituitary macroadenoma with haemorrhage.



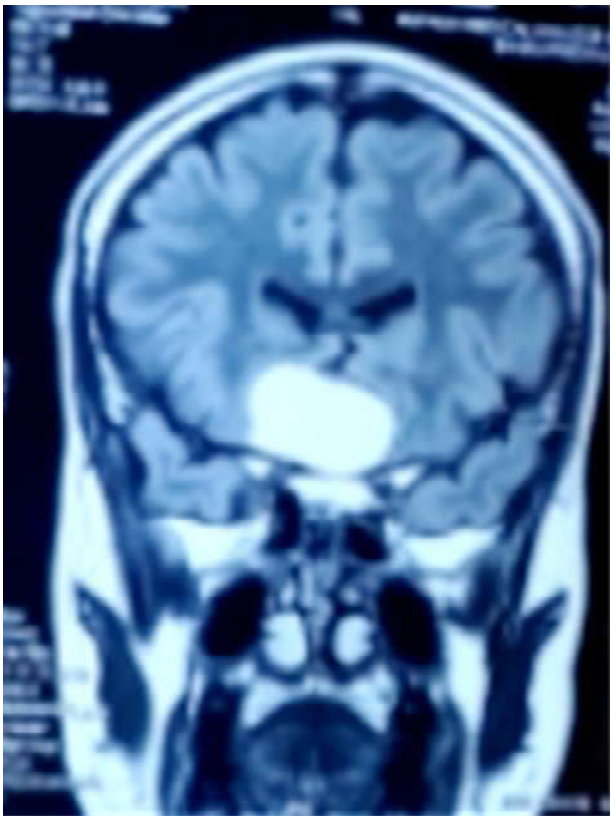


Fig. 4 and 5: MRI brain showsT1 iso and T2 hyperintense lesion with blood fluid levels noted within the sellar and suprasellar region.

The patient was managed medically and surgically with Transnasal microscopic excision of tumor and histopathology turned out to be pituitary

macroadenoma features and postoperatively patient recovered vision partially and discharged to be followed up in neurosurgery and endocrinology opd.

Discussion

Case 1

Our patient presented with features of growth retardation and a delayed bone age with iso-sexual peripheral precocious puberty. The most common differentials of growth failure were juvenile hypothyroidism, Cushing's disease and panhypopituitarism. Short stature without obesity initially pointed towards juvenile hypothyroidism as the diagnosis.

Precocious puberty with adnexal masses is always associated with an advanced bone age with an elevated basal cortisol level, which was not seen in the index case. Severe growth retardation is also observed in patients with panhypopituitarism (due to the combined deficiency of growth hormone and TSH). It is associated with secondary hypothyroidism and delayed puberty, which was not seen in this patient. Hence, we came to the diagnosis as primary hypothyroidism in view of the linear growth failure with a delayed bone age and features of thyroid hormone insufficiency with pituitary lesion. The association of long-standing thyroid insufficiency with sexual precocity has been described in literature as Van Wyk and Grumbach syndrome (VWGS).

The exact mechanism of the development of precocious puberty in VWGS remains undefined and has been explained with several theories.[1] The most widely accepted of which is hormonal overlap in the pituitary feedback mechanism due to molecular mimicry between TSH and follicle-stimulating hormone (FSH) receptors. TSH in high concentrations leads to stimulation of gonadal FSH, as they share the common alpha subunit, which, in turn, increases the oestrogen levels, thereby manifesting as peripheral sexual precocity in females and macroorchidism in males. Pubic and axillary hairs are characteristically absent as there is no effect on adrenal hormone synthesis, thus it is also known as incomplete sexual precocity.[2]

Multiple cysts in the ovaries develop secondary to the enhanced production and decreased clearance of FSH due to hyperstimulation of its receptors by elevated thyrotropin-releasing hormone (TRH). In addition, high circulating TSH acts on the FSH receptors present on the ovarian follicle due to specificity spillover, resulting in the follicular cyst formation.[3]

Pituitary adenoma reported on imaging is basically thyro-lactotrope hyperplasia, which is an indication of a long-standing, severe thyroid deficiency state. High circulating levels of TRH due to lack of thyroxine-mediated feedback inhibition result in hyperstimulation of thyro-lactotropes in the pituitary gland, thus presenting as a macroadenoma on imaging studies. The similar mechanism is also responsible for the stimulation ofprolactin secretion, thereby leading to hyperprolactinaemia.[4] Hyperplastic pituitary causes compression of the pituitary stalk that disrupts the hypothalamic inhibition of prolactin secretion, which further explains the presence of high prolactin levels with long-standing hypothyroidism.

The most common cause of thyroid insufficiency in an iodine sufficient area in young females has been attributed to immune-mediated destruction of the thyroid gland (Hashimoto's thyroiditis)[5] which is not the case in our patients as anti-TPO antibody titre was normal and screening of thyroid gland showed diffuse altered echopattern with increased vascularity. Hypothyroidism in our patient could have been due to severe iodine deficiency or a delayed onset dyshormogenesis. Several methods have been devised for the estimation of bone age in children, of which the most frequently used and practically feasible is through Greulich and Pyle atlas. In females aged 3 years and above, assessment of the bone age is done through comparison between ossification centres of the epiphysis and metaphysis of proximal and intermediate phalangeal joints, in an X-ray of hand. This can also be done by comparison with age-matched standards derived from healthy children, published in the atlas.[6-8]

Our patient at presentation had a bone age of 4 years, which was delayed by 2 years from the chronological age. Thyroxine is needed for the secretion and action of growth hormone. It acts directly on the growth plate and promotes differentiation of chondrocytes to hypertrophic chondrocytes, which is required for the growth of long bones.[9] Deficiency states as seen in primary hypothyroidism lead to growth failure and a delayed bone age, as was seen in our patient. Thyroid replacement therapy in VWGS will lead to complete resolution of all the symptoms along with complete regression of ovarian cyst and pituitary hyperplasia without any need of surgical management.

Case 2

In the evaluation of our patient with erectile dysfunction in pituitary macroadenoma, an endocrinopathy is the rarest of causes.[9,10] However, when an endocrinopathy does affect erectile function, it is almost always caused by hypogonadism.[9-11] Obtaining a serum testosterone (T) level is the most

costeffectiveway of screening for an endocrinopathy as the cause of erectile dysfunction.[10,11] Then additional evaluation should include obtaining serum luteinizing hormone, free T, and prolactin levels.[10] If the serum T is elevated, then a thyroid evaluation may be indicated.[10] In our patient, hypogonadism as well as an elevated prolactin level (prolactin was emanating from the lesion within the pituitary gland) were found. Hyperprolactinemia induces hypogonadism by interfering with the secretion of gonadotropinreleasing hormone (GnRH) from the hypothalamus.[12,13]

However, when the serum prolactin is corrected in patients with an elevated prolactin level, erectile function is usually restored (if erectile dysfunction was present).[10] Hyperprolactinemia is a very rare cause of impotence in a general population of men with impotence.[14] However, men who have hyperprolactinemia have a high incidence of sexual dysfunction, and the erectile dysfunction appears more likely to resolve in patients with the most severe hyperprolactinemiawith dopaminergic agonist like bromocriptine, cabergoline and after surgical excision of pituitary lesion.

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