TPM Vol. 32, No. S2, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

HYPOTHALAMIC HAMARTOMA UNVEILED BY CENTRAL PRECOCIOUS PUBERTY: A CASE REPORT

PRIYA DARSNI MUTHUKRISHNAN[1], SHALINI PRIYA NANDAGOPAL[1], ARUNKUMAR MOHANAKRISHNAN[2], LAVANYA PANCHATCHARAM[1], SHAPNALAKSHMI THIRUMURUGESAN[1], DHANASANGARI MANIVANNAN[1], DR. SAJID .T HUSSAIN[3],

[1]PAEDIATRICS, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES (SIMATS) SAVEETHA UNIVERSITY, CHENNAI, INDIA
[2]RADIODIAGNOSIS, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES (SIMATS) SAVEETHA UNIVERSITY, CHENNAI, INDIA
[3]READER, DEPARTMENT OF PERIODONTOLOGY, SREE BALAJI DENTAL COLLEGE & HOSPITAL, CHENNAI, INDIA

Abstract

Introduction:

Hypothalamic hamartoma (HH) is a rare congenital malformation associated mainly with central precocious puberty (CPP) and gelastic seizures, often leading to progressive neurocognitive and behavioral issues. Early diagnosis facilitates timely treatment and improved outcomes.

Case Presentation:

We describe a 2-year-3-month-old female child from Kanchipuram, India, presenting with recurrent vaginal bleeding for one year, breast budding for 8 months, and sparse pubic and axillary hair for 5 months. She demonstrated accelerated growth and significant advancement of bone age. Hormonal assays indicated elevated luteinizing hormone and estradiol levels. MRI showed a well-defined hypothalamic hamartoma located in the suprasellar region. The patient was started on monthly intramuscular leuprolide acetate (a GnRH analogue) and managed for iron deficiency anemia.

Conclusion:

This case emphasizes the importance of considering a central cause like hypothalamic hamartoma in early-onset puberty and reinforces the role of MRI for diagnosis and GnRH analogue therapy to halt pubertal progression, optimize final adult height, and improve psychosocial outcomes.

INTRODUCTION

Hypothalamic hamartomas (HHs) are rare congenital, benign malformations arising chiefly in the tuber cinereum or mammillary bodies of the hypothalamus, with an approximate prevalence of 1 in 50,000 to 1 in 200,000 individuals. Histologically, these lesions consist of mature neurons, glia, and myelinated fibers in a disorganized fashion, resembling normal hypothalamic tissue but leading to pathological activation of hormone secretion and epileptogenesis.

Clinically, HHs present a heterogeneous spectrum primarily characterized by two phenotypes: central precocious puberty (CPP) due to ectopic secretion of GnRH resulting in premature activation of the hypothalamic-pituitary-gonadal axis, and gelastic seizures (GS) — distinct epileptic seizures marked by episodic inappropriate laughter. CPP is commonly associated with pedunculated or parahypothalamic HHs, whereas sessile or intrahypothalamic HHs typically provoke gelastic epilepsy with cognitive and behavioral sequelae.

Early recognition using high-resolution MRI and hormonal evaluation is essential for diagnosis, guiding treatment provisions including GnRH agonists for CPP and surgical or laser ablation procedures for refractory seizures. Genetic mutations, particularly in GLI3 (notably in Pallister-Hall syndrome), have been implicated in rare syndromic forms.

Case Presentation

Patient Information

- **Age/Gender:** 2 years 3 months, female
- **Location:** Kanchipuram, India
- **Informant:** Mother

Chief Complaints

- Vaginal bleeding every 28–34 days for one year (moderate flow, 3-4 days each episode)

- Breast budding started 8 months ago
- Sparse pubic and axillary hair for 5 months
- Growth acceleration compared to peers

Past Medical and Family History

- Non-consanguineous marriage, no seizure or chronic illnesses in family
- Mother with PCOS and history of infertility
- No antenatal or perinatal complications; uneventful birth

Developmental History

- Age-appropriate milestones achieved
- Up-to-date immunizations until 18 months

Examination

- **Vitals:** HR 102 bpm, BP 90/60 mmHg, RR 32/min, Temp 98.6°F, SpO_2 98% RA
- **Anthropometry:** Weight 18 kg (+3 Z-score), Height 93.5 cm (0 to +2 Z), Head circumference 48 cm (0 to +1 Z), MUAC 16 cm (0 to +1 Z)
- **Sexual Maturity:** Breasts Tanner stage 2, Pubic/axillary hair Tanner stage 2
- Pallor present
- No dysmorphic features or systemic abnormalities

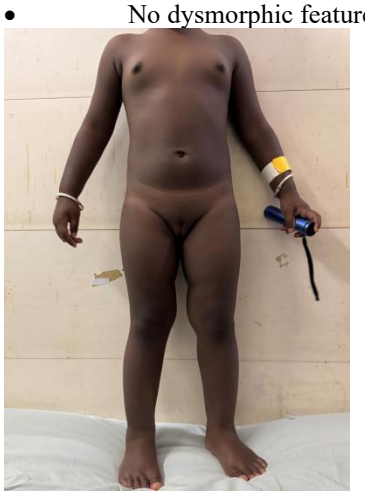


Figure 1. Child's Tanner staging

Growth charts:

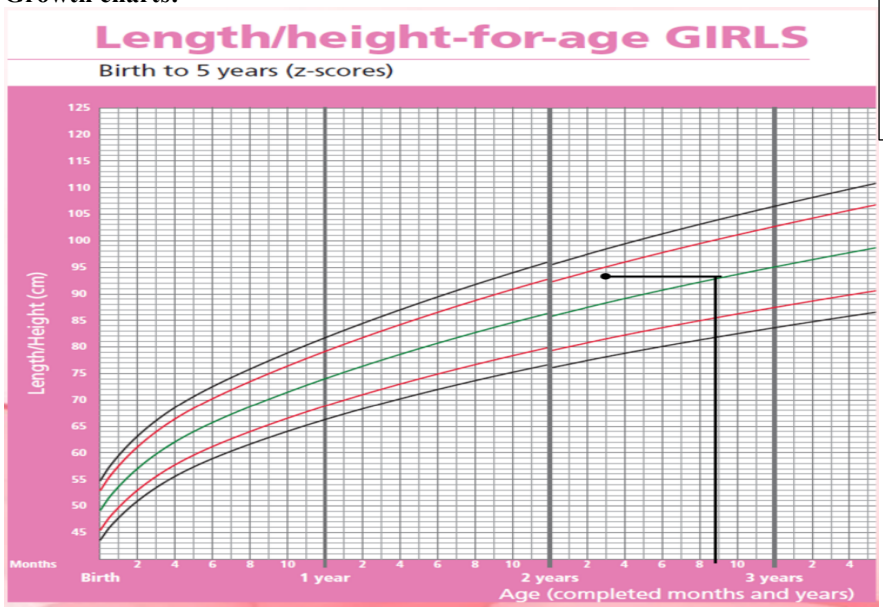


Figure 2. Length/height-for-age chart (girls) highlighting advanced linear growth

TPM Vol. 32, No. S2, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

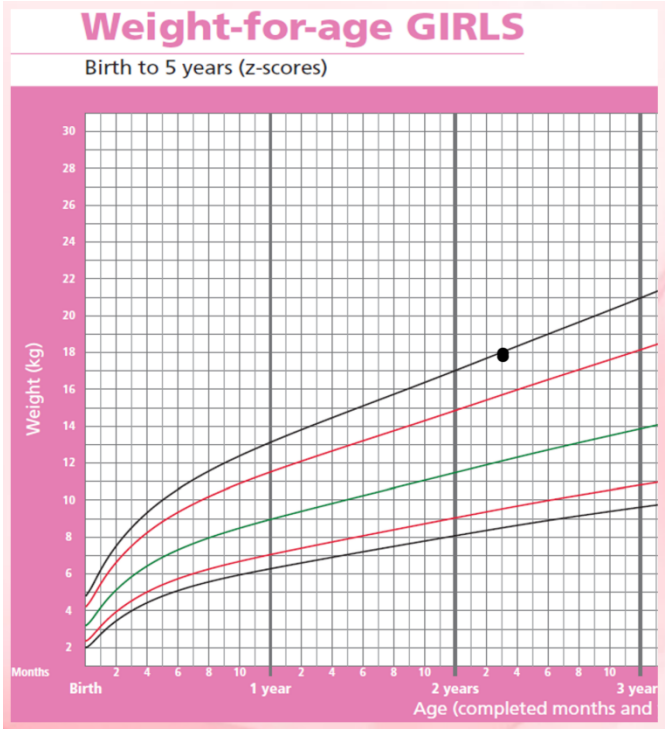


Figure 3. Weight-for-age chart (girls) showing weight above the normal percentile

Age Analysis

Parameter	**Value**
Chronological Age	2 y 3 m
Height Age	**2 y 9 m**
Bone Age	**7 y**
Pattern	**BA > HA > CA**

Investigations

Hormonal Profile

Hormones	**Result**	**Reference Range**
LH	**10.6 mIU/mL**	<0.26 mIU/mL
FSH	3.48 mIU/mL	0.72–5.33 mIU/mL
LH:FSH Ratio	**3:1**	—
Estradiol	**180.79 pg/mL**	<25 pg/mL (prepubertal)
Prolactin	**25.7 ng/mL**	3–18.6 ng/mL
T3	4.6 pg/mL	2.7–5.27 pg/mL
T4	0.93 ng/dL	0.85–1.75 ng/dL
TSH	2.138 mIU/mL	0.7–5.97 mIU/mL

Hematology and Iron Profile

Parameter	Result	Reference
Hemoglobin (Hb)	8.5 g/dL	11.5–13.5 g/dL
Peripheral smear	Microcytic hypochromic anemia	—
Serum Iron	67 µg/dL	60–160 µg/dL
Ferritin	4.56 ng/mL	6.24–137 ng/mL
TIBC	516 µg/dL	265–497 µg/dL

Imaging

- **Bone Age Imaging**

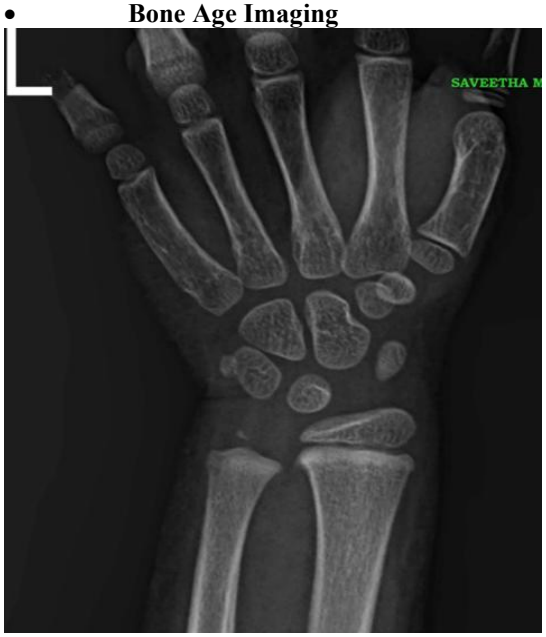


Figure 3. X-ray of left hand showing advanced bone age (~7 years) in this 2-year-old girl

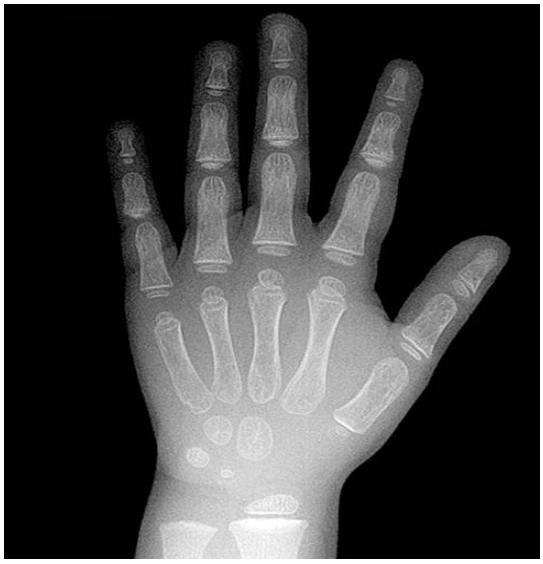


Figure 4. Comparative X-ray wrist and hand with prominent ossification centers for a normal 2 year old child .

- **Ultrasound Abdomen:** Left ovarian cyst 2.5 × 1.5 cm . No other significant abnormalities noted.
- **MRI Brain :** A relatively well defined solid suprasellar lesion measuring 11 × 10 × 10 mm seen epicentered in the tuber cinereum of hypothalamus appearing hypointense on T1, hyperintense on T2/FLAIR with no postcontrast enhancement - consistent with hypothalamic hamartoma.

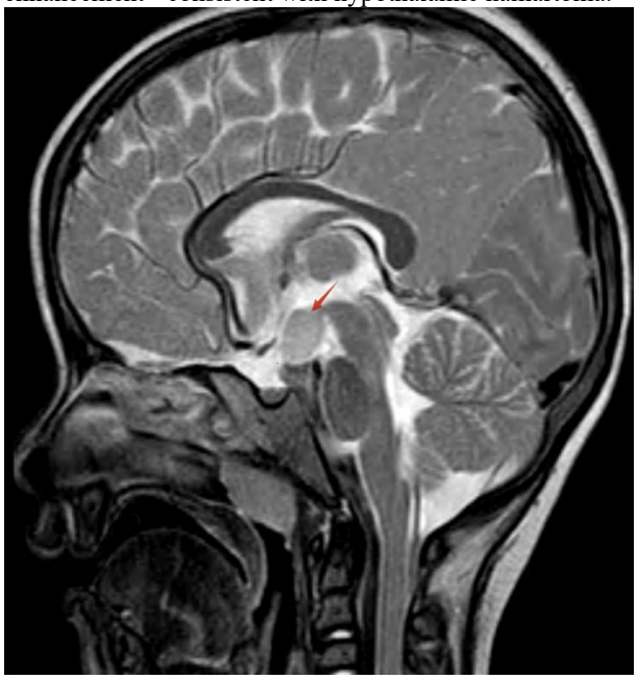


Figure 5 : T2 MRI showing suprasellar hypothalamic hamartoma (hyperintense lesion).

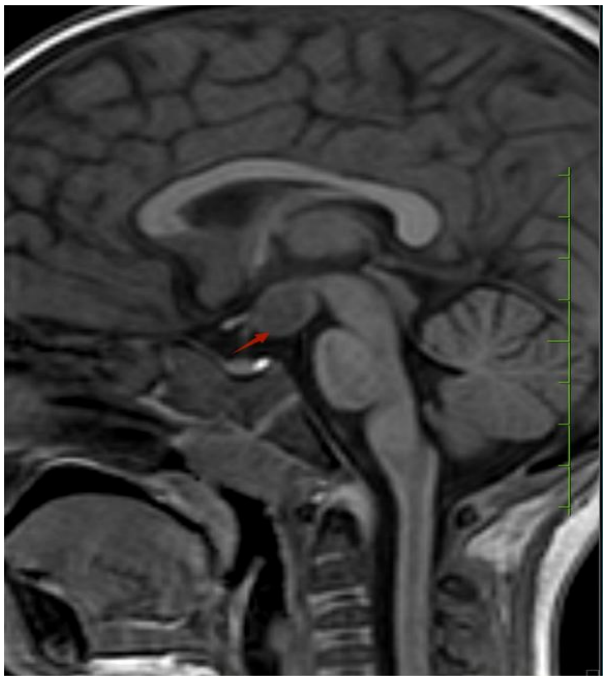


Figure 6: T1 MRI showing suprasellar hypothalamic hamartoma (isointense lesion).

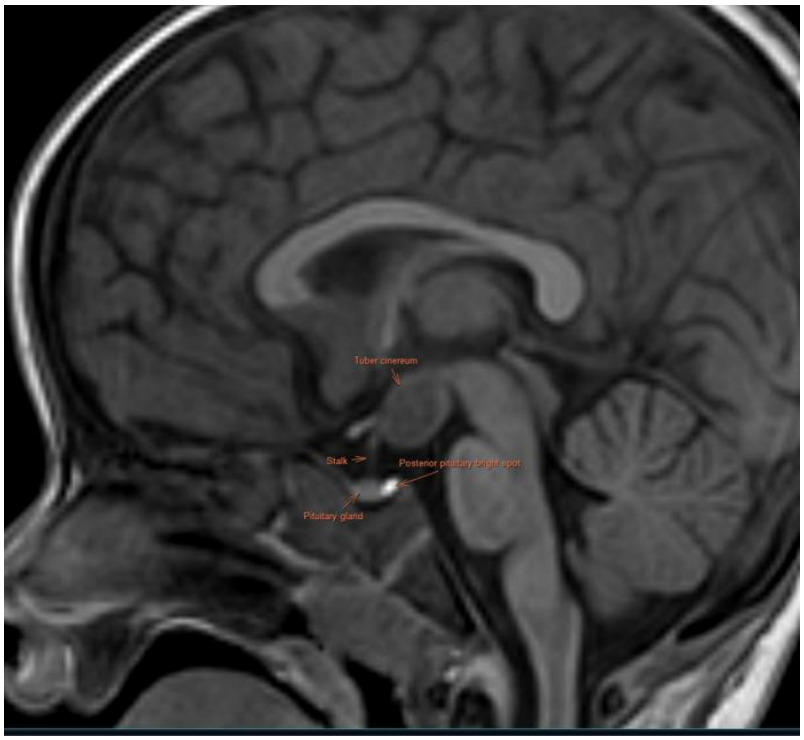


Figure 7: T1 MRI showing suprasellar hypothalamic hamartoma (isointense lesion) with anatomical parts labelled in the sella region and hypothalamus.

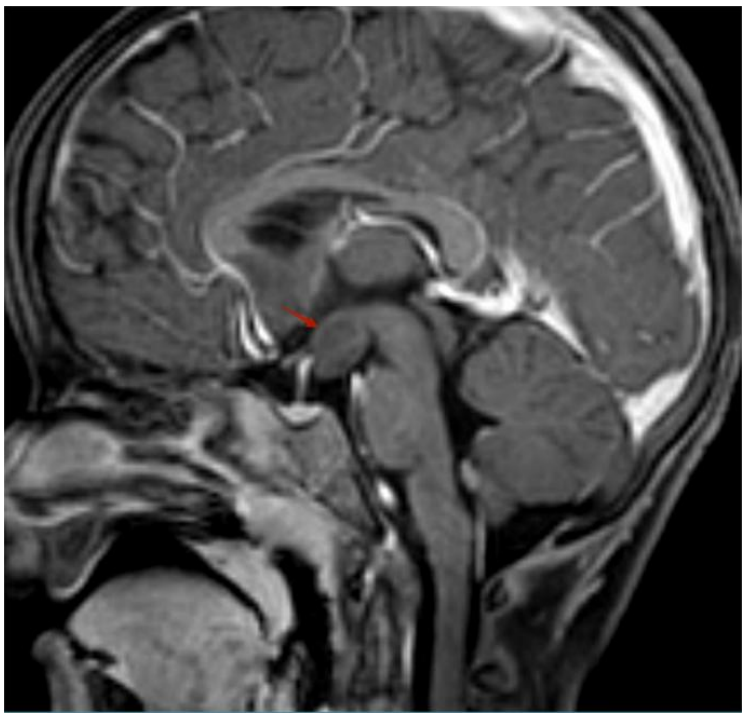


Figure 8: T1FS post contrast MRI showing isointense lesion without contrast enhancement.

Diagnosis

- Central Precocious Puberty secondary to hypothalamic hamartoma
- Associated Iron Deficiency Anemia

Management

- Intramuscular leuprolide acetate 3.75 mg monthly (GnRH analogue)
- Oral iron supplementation and nutritional counseling
- Counseling caregivers on diagnosis and treatment importance
- Planned regular follow-ups for clinical assessment, hormonal monitoring, growth, and skeletal maturity

DISCUSSION

Hypothalamic hamartomas are rare congenital malformations consisting of disorganized but mature neuronal and glial tissue, most commonly located near the tuber cinereum or mammillary bodies. The clinical presentation varies depending on the lesion's size, location, and involvement of adjacent structures. Parahypothalamic, pedunculated hamartomas primarily cause central precocious puberty via ectopic GnRH secretion, while intrahypothalamic, sessile lesions are often linked to gelastic seizures, developmental delay, and behavioral abnormalities.

Precocious puberty from HH results from premature pulsatile GnRH release, causing premature activation of the hypothalamic-pituitary-gonadal axis. This leads to elevated gonadotropin and sex steroid levels with advanced skeletal maturation, as observed in our patient. MRI remains the gold standard diagnostic tool, revealing lesions isointense to gray matter on T1 and hyperintense on T2-weighted images without contrast enhancement.

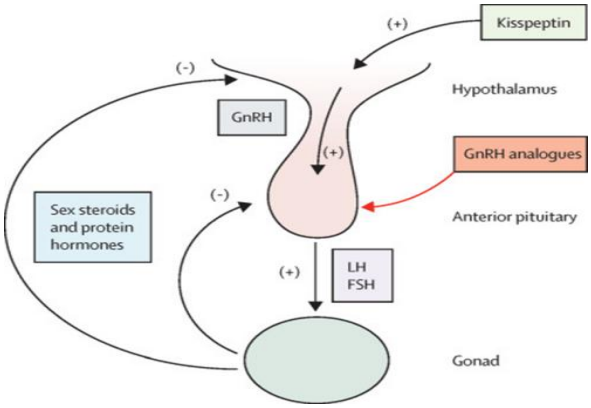
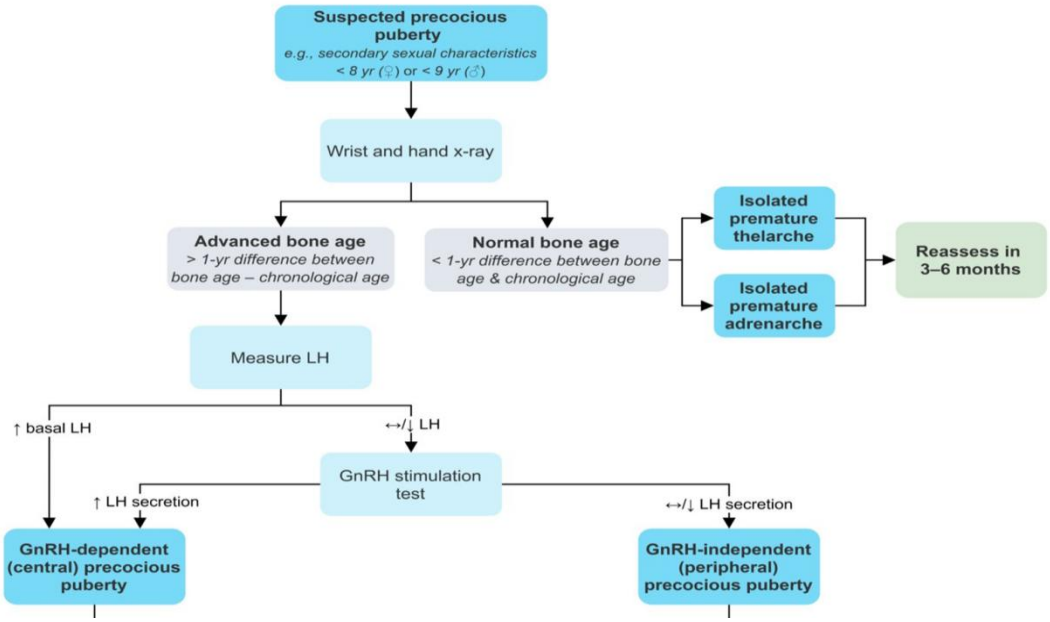


Figure 9. Pathophysiology of GnRH secretion and regulation in puberty.
[summarizes the key feedback mechanisms in normal and pathologic puberty including the role of GnRH analogues for treatment].



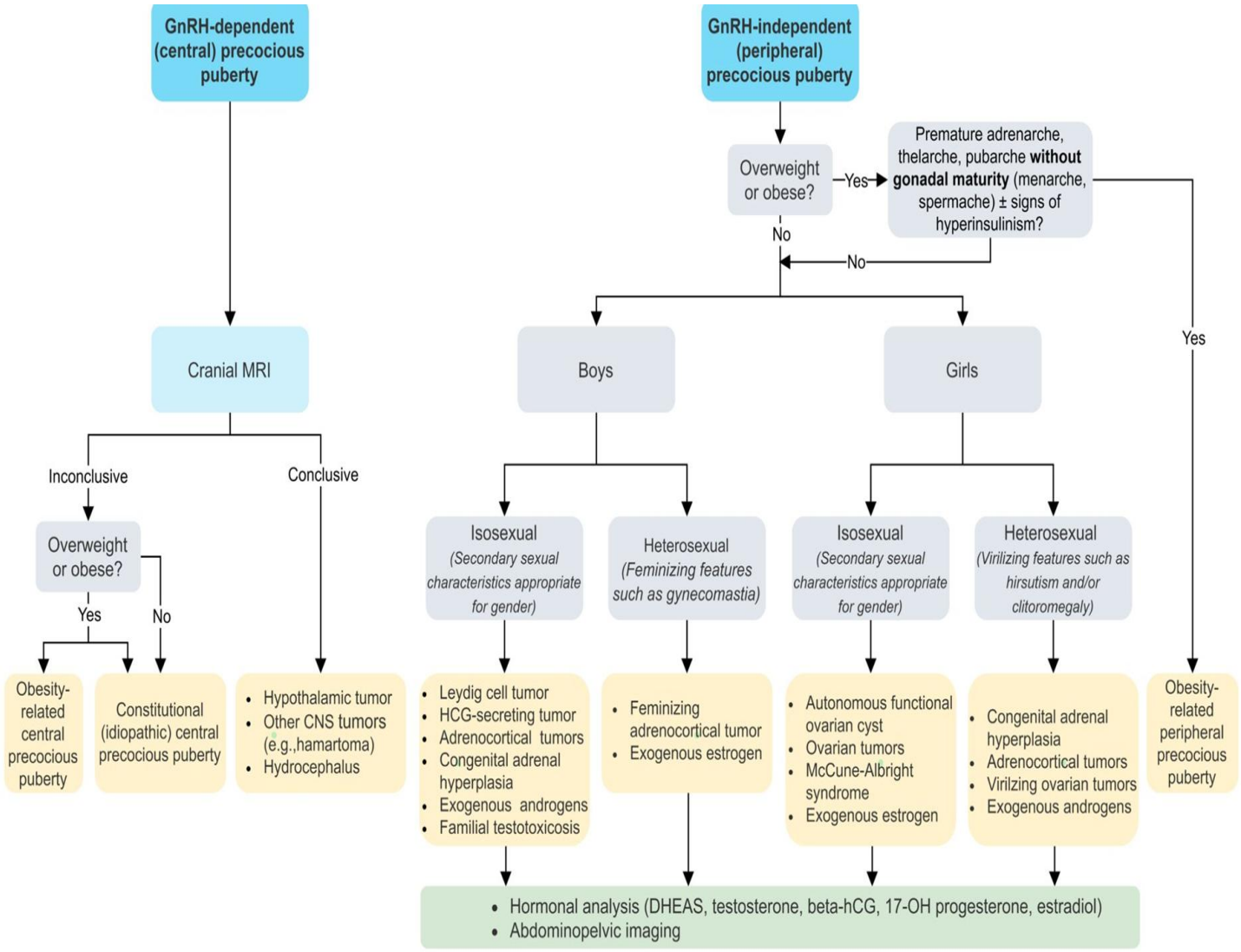


Figure 10. Schematic flowchart approach to suspected precocious puberty in child.

Classification of Central Precocious puberty and Peripheral precocious puberty is summarized in the following table.

Central Precocious Puberty	Peripheral Precocious Puberty
True precocious	Pseudo-precocious
Isosexual	Isosexual/heterosexual
Premature HPG axis activation	HPG axis not activated
Progressive sexual maturation in sequence observed in normal puberty	Sequence of pubertal changes is discordant
Gonads produce sex steroids	Many sources of sex steroids (gonads, adrenal, ectopic, exogenous)

Pubertal levels of LH & FSH	Pre pubertal levels of LH & FSH
More common in females	More common in males
The causes are similar in both the genders	Etiology differ in the two genders and may result in heterosexual development

Table 1: Central precocious puberty vs Peripheral precocious puberty

Central causes:

Acquired CNS insults	Trauma and perinatal insult, postinfectious meningitis, or encephalitis , low dose cranial irradiation
Tumors	Hypothalamic hamartoma, astrocytoma, and pineal tumor Ependymoma, optic pathway glioma, and craniopharyngioma
Structural defects	Hydrocephalous, subarachnoid cyst, and septo-optic dysplasia
Neurocutaneous syndromes	Tuberous sclerosis, Sturge–Weber syndrome, and neurofibromatosis
Other pathology	Cerebral palsy, IUGR, and prolonged untreated PPP
Genetic	Mutations in the MKRN-3, kisspeptin/kisspeptin receptor gene
Syndromes	Temple, Silver–Russell, and Williams–Beuren

Table 2: Causes for central precocious puberty

Peripheral causes:

- Ovarian disorders (Ovarian cyst, Ovarian tumors, Granulosa theca cell tumor, Gonadoblastoma, Teratoma, Choriocarcinoma)
- Adrenal disorders (CAH, tumor)
- Exogenous hormones (estrogen, androgen)
- Primary hypothyroidism
- McCune–Albright syndrome
- Peutz–Jeghers syndrome
- Tumors (Hormone secreting tumors, Hepatoblastoma, Pineal gland tumors, Cerebral tumors, Mediastinal tumors)
- Masculinizing adrenal or ovarian tumors , Feminizing adrenal or testicular tumors

Diagnostic Approach :

	Sequence of pubertal changes	*Growth*	*BA*	*Gonadal hormones*	*Gonadotropins*	*GnRH stimulation*
CPP	Concordant	+	+	↑	LH↑	LH predominant
PPP	Discordant	+	+	↑	Suppressed	No rise
PT	No progression	N	N	Prepubertal	Prepubertal	FSH predominant
PA	No progression	N	N	Prepubertal	Prepubertal	Prepubertal

(BA: bone age; CPP: central precocious puberty; FSH: follicle-stimulating hormone; LH: luteinizing hormone; PA: premature adrenarche; PPP: peripheral precocious puberty; PT: premature thelarche)

Medical management with GnRH analogues like leuprolide is effective in suppressing pubertal progression, preserving adult height, and mitigating psychosocial distress. In contrast, patients with seizures, especially refractory or gelastic seizures, often require surgical intervention, including endoscopic disconnection or laser ablation, although these treatments carry surgical risks.

Cognitive and behavioral comorbidities are often associated with seizures stemming from HH; however, in isolated CPP presentations, cognitive function is frequently normal. Our patient had no seizures or cognitive deficits noted, consistent with the typical presentation of pedunculated parahypothalamic hamartomas.

Early diagnosis and institution of treatment optimize outcomes, emphasizing a multidisciplinary approach involving pediatric neurology, endocrinology, neurosurgery, and psychology.

Conclusion

Hypothalamic hamartomas are rare lesions presenting variably as central precocious puberty, gelastic seizures, or neurobehavioral disorders. This case illustrates the classical presentation of isolated CPP from hypothalamic hamartoma in a young child, diagnosed by MRI and managed effectively with GnRH analogues. Vigilance for central causes in early puberty and proper imaging are crucial for timely diagnosis. Targeted therapy not only halts premature puberty progression but also supports better adult height prognosis and psychosocial well-being. Multidisciplinary care remains paramount, particularly for seizure control when present.

Conflict of interest

There are no conflicts of interest.The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Author's contributions

All the authors contributed equally to this article.

Acknowledgements

The authors acknowledge the patient as a great source of learning.

REFERENCES

1. Coons SW, Rekate HL, Prenger EC, Wang N, Drees C, Ng Y, et al. The Histopathology of Hypothalamic Hamartomas: Study of 57 Cases. J Neuropathol Exp Neurol. 2007;66(2):131–41.
2. Wang B, Ma J. The diagnosis and management of hypothalamic hamartomas in children. Chin Neurosurg J. 2016;2:29.
3. Zosangliani, Datta A, Thele R, Gurung B, Kambiakdik T. Hypothalamic hamartoma with gelastic seizures: a case report. Int J Contemp Pediatr. 2020;7:961–2.
4. Grech R, Looby S, Thornton J, Brennan P. Hypothalamic hamartoma. BMJ Case Rep. 2013;2012:bcr2012008273.

5. Kesavan TMA, Neethu KK, Rabiya A. Antenatally detected hypothalamic hamartoma–A case report. IP Indian J Neurosci. 2022;8(1):84–7.
6. Alves C, Barbosa V, Machado M. Giant hypothalamic hamartoma: case report and literature review. Childs Nerv Syst. 2013;29:513–6.
7. Badihian S, Bahrani S, Tabrizi N, Moein H, Zare M, Barekatain M, et al. An Undiagnosed Case of Hypothalamic Hamartoma with a Rare Presentation. Case Rep Med. 2017;2017:2432315.
8. Gosavi TD, Walker MC. A case of pure gelastic seizures due to hypothalamic hamartoma with a benign course. Epilepsy Behav Case Rep. 2017;8:34–7.
9. Wang B, Ma J. The diagnosis and management of hypothalamic hamartomas in children. Chin Neurosurg J. 2016;2:29.
10. Wilfong AA, Curry DJ. Hypothalamic hamartomas: optimal approach to clinical evaluation and diagnosis. Epilepsia. 2013;54 Suppl 9:109–14.
11. Cohen NT, Wilfong AA. Hypothalamic Hamartomas: Evolving Understanding and Therapeutic Approaches. Child Neurol Open. 2021;8:2329048X211028057.[1]
12. Kotwal N, Yanamandra U, Menon AS, Nair V. Central precocious puberty due to hypothalamic hamartoma in a six-month-old infant girl. Indian J Endocrinol Metab. 2012;16(Suppl2):S327-9.[2]
13. StatPearls Publishing. Hypothalamic Hamartoma [Internet]. Treasure Island (FL): StatPearls; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560663/[3]
14. Goel K, et al. Outcomes following surgical interventions for hypothalamic hamartomas: a systematic review and meta-analysis protocol. Syst Rev. 2024;13:53.[4]
15. Child Neurology Foundation. Hypothalamic Hamartoma. [Internet]. 2022 Nov 17. Available from: https://www.childneurologyfoundation.org/disorder/hypothalamic-hamartoma/[5]
16. Gelastic seizures and the hypothalamic hamartoma syndrome: new insights to clinical management. Epilepsy Behav. 2021;121(Pt A):106509.
17. Hope for Hypothalamic Hamartomas. What is precocious puberty? 2021 Apr 23. Available from: https://www.hopeforhh.org/endocrinologysept2011-1/[7]
18. Neurology.org. Hypothalamic hamartomas and gelastic epilepsy. Neurology. 1998;51(4):1046-1050.[8]
19. Antenatally detected hypothalamic hamartoma: a case report. Indian J Neurosci. 2022;8(1):84–87.[9]
20. International Journal of Contemporary Pediatrics. Hypothalamic hamartoma presenting as central precocious puberty: a rare case report. 2020;7(7):1634–1637.[10]