The American Journal of Medical Sciences and Pharmaceutical Research
ISSN 2689-1026 | Open Access

TYPE Original Research
PAGE NO. 48-54
DOI 10.37547/tajmspr/Volume07Issue06-05

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Precocious Puberty Induced by Chronic Rhinosinusitis

Laiba Razaq
International Centre of Medical Sciences Research (ICMSR), Islamabad PAKISTAN.
Akhtar Saeed Medical and Dental College, Lahore PAKISTAN

Muhammad Saqib Mian
Akhtar Saeed Medical and Dental College, Lahore PAKISTAN

Muhammad Faizan
International Centre of Medical Sciences Research (ICMSR), Islamabad PAKISTAN.

Muhammad Arsalaan Awais
International Centre of Medical Sciences Research (ICMSR), Islamabad PAKISTAN.
Atlanticare Regional Medical Center, Pomona, New Jersey, USA
Omar Hospital & Cardiac Centre Johar Town, Lahore PAKISTAN

Syed Shayan Gilani
International Centre of Medical Sciences Research (ICMSR), Islamabad PAKISTAN.
Omar Hospital & Cardiac Centre Johar Town, Lahore PAKISTAN
Sheikh Zayed Hospital Lahore PAKISTAN

Rizwan Uppal
Islamabad Diagnostic Center (IDC), F8 Markaz, Islamabad PAKISTAN

Muhammad Rehan Uppal
Islamabad Diagnostic Center (IDC), F8 Markaz, Islamabad PAKISTAN

Umar Saeed
Foundation University Islamabad (FUI), Islamabad PAKISTAN

Zahra Zahid Piracha
International Centre of Medical Sciences Research (ICMSR), Islamabad PAKISTAN.
International Center of Medical Sciences Research (ICMSR), Austin, TX, United States of America
International Center of Medical Sciences Research (ICMSR), Chadwell Heath, United Kingdom

Acknowledgement:
Muhammad Nouman Tariq
Akhtar Saeed trust hospital

Abstract: Background: Precocious puberty is the early

OPEN ACCESS

SUBMITED 17 April 2025
ACCEPTED 24 May 2025
PUBLISHED 24 June 2025
VOLUME Vol.07 Issue 06 2025

CITATION

Laiba Razaq, Muhammad Saqib Mian, Muhammad Faizan, Muhammad Arsalaan Awais, Syed Shayan Gilani, Rizwan Uppal, Muhammad Rehan Uppal, Umar Saeed, Zahra Zahid Piracha, & Muhammad Nouman Tariq Nouman Tariq. (2025). Precocious Puberty Induced by Chronic Rhinosinusitis. The American Journal of Medical Sciences and Pharmaceutical Research, 7(06), 48–54. https://doi.org/10.37547/tajmspr/Volume07Issue06-05

onset of secondary sexual characteristics before age 8 in girls and 9 in boys. It is classified into central precocious puberty (CPP), which is GnRH-dependent, and peripheral precocious puberty (PPP), which is GnRH-independent. Hypothalamic hamartomas are a well-documented cause of CPP, while chronic rhinosinusitis has not been commonly associated with early puberty.

Case Presentation: We report a 6.5-year-old boy who presented with increased penile length, deepened voice, and axillary and pubic hair growth for six months. Additionally, he had a history of nasal obstruction, rhinorrhea, blurred vision, and mild headaches. Examination revealed signs of precocious puberty, including Tanner stage III pubic and axillary hair and an advanced bone age of 12 years. MRI revealed a hypothalamic hamartoma, while a CT scan showed chronic rhinosinusitis. Histopathology confirmed chronic inflammatory changes without fungal infection. The patient was initially considered for neurosurgical intervention, but after ENT evaluation, he was treated with intravenous antibiotics for chronic sinusitis. He showed clinical improvement, and surgery was no longer required.

Discussion: This case highlights a rare association between chronic rhinosinusitis and CPP. While hypothalamic hamartoma is a recognized cause of early puberty, chronic inflammation might contribute to HPG axis activation. Persistent sinonasal inflammation could induce systemic inflammatory responses affecting neuroendocrine regulation. This raises questions about the potential role of chronic infections in puberty onset.

Conclusion: Chronic rhinosinusitis may be an underrecognized factor influencing early puberty. Multidisciplinary evaluation, including endocrinology, neurosurgery, and ENT, is crucial in such cases to ensure accurate diagnosis and management. Further research is needed to explore the possible link between chronic inflammation and hypothalamic activation leading to precocious puberty.

Keywords: Precocious puberty, chronic rhinosinusitis, hypothalamic hamartoma, invasive sinusitis

INTRODUCTION

Precocious puberty is defined as the early onset of puberty and secondary sexual characteristics before the age of 8 in girls and 9 in boys, with an estimated incidence of 1:5,000 to 1:10,000 children. The female-to-male ratio is approximately 10:1 (1).

Based on etiology, precocious puberty is classified into two major types:

1. Central Precocious Puberty (CPP) – GnRH-dependent
2. Peripheral Precocious Puberty (PPP) – GnRH-independent

CPP results from early activation of the hypothalamic-pituitary-gonadal (HPG) axis, commonly caused by CNS tumors such as hypothalamic hamartoma, optic glioma, and astrocytoma. Among these, hypothalamic hamartoma is the most frequent cause (3). Other contributing factors include CNS injury, cerebral palsy, tuberculosis, neurofibromatosis type 1, and genetic mutations, particularly loss-of-function mutations in the MKRN3 gene (2). The activation of the HPG axis leads to the development of secondary sexual characteristics, accelerated growth, and behavioral changes due to pulsatile GnRH secretion (6). Kisspeptin, a critical regulatory peptide, influences GnRH production through interactions with neurokinin B and dynorphin in the hypothalamus (7).

PPP, on the other hand, results from increased secretion of sex steroid hormones (androgens, estrogens, and progestogens) independent of GnRH stimulation. Conditions such as congenital adrenal hyperplasia (CAH), McCune-Albright syndrome, and gonadal or adrenal tumors are common causes. Clinical features include breast enlargement and early menarche (thelarche), accelerated growth (total height increase of 20–25 cm from the onset to completion of puberty), pubic and axillary hair growth, acne, adult body odor, deepened voice, and facial hair in boys (7). Neurological symptoms such as headaches, increased head circumference, seizures, and visual or cognitive changes may also occur.

Diagnostic evaluation includes bone age assessment, BMI measurement, serum LH, FSH, TFTs, and

testosterone levels. In PPP, pelvic ultrasonography is recommended for girls to detect ovarian cysts, and testicular ultrasonography for boys. MRI is essential in all cases of CPP to rule out hypothalamic lesions (5).

The primary goal of CPP treatment is to preserve adult height and alleviate psychological distress. GnRH agonists, available in intranasal, subcutaneous, and intramuscular forms, are the treatment of choice (8). In the United States, depot leuprolide acetate is the most commonly used option, effectively suppressing the GnRH axis (5). Treatment for PPP focuses on eliminating the source of sex steroids—CAH is managed with glucocorticoids, while McCune-Albright syndrome benefits from aromatase inhibitors such as anastrozole or tamoxifen. Early initiation of treatment improves outcomes, but long-term endocrine, metabolic, reproductive, and psychological consequences remain uncertain (4).

Case Report

A 6.5-year-old boy presented to the outpatient department of Farooq Hospital, Lahore, with a six-month history of increased penile length, deepened voice, and axillary and pubic hair growth. His parents also reported intermittent nasal obstruction, rhinorrhea, and blurred vision. The child occasionally experienced mild headaches, primarily during episodes of flu. There was no history of radiation therapy, trauma, polyuria, fever, gelastic seizures, cachexia, or medication use. The parents had a normal pubertal history.

Physical Examination

The child appeared thin and moody, measuring 112 cm in height and weighing 25 kg. He exhibited grade III pubic and axillary hair growth, with normal neurological findings. Testicular volume was 8–10 mL, and stretched penile length was 7 cm. The abdomen was soft and non-tender with no palpable masses. While there were no visual field defects, his visual acuity was reduced. Fundoscopy showed no evidence of papilledema. No café-au-lait spots, rashes, or pigmentation were observed.

Laboratory and Imaging Findings

- Hormonal analysis: Elevated FSH, LH, and testosterone within the upper normal range
- Renal function tests: Normal, excluding aldosterone deficiency
- Thyroid function tests: Normal, ruling out hypothyroidism
- Bone age assessment (X-ray wrist): Advanced bone age of approximately 12 years, showing complete ossification of carpal bones, including the pisiform, with an enlarged distal ulna and radius epiphysis (Figure 1)
- Ultrasound of the abdomen, pelvis, and testes: No abnormalities detected

MRI Brain with Contrast (Figure 2): A well-defined, midline rounded lesion was identified in the hypothalamic region, projecting inferiorly behind the infundibulum of the pituitary gland, measuring 11.7 × 9 × 8.3 mm (TR × AP × CC). The lesion demonstrated iso-signal intensity on T1-weighted images and heterogeneous high-signal intensity on T2-weighted and FLAIR images, with mild post-contrast enhancement, suggestive of a hypothalamic hamartoma. Other brain structures, including parenchyma, ventricular system, and extra-axial CSF spaces, were normal. However, fluid signals were observed in all sinuses and bilateral mastoid air cells.

Given the radiological diagnosis of hypothalamic hamartoma—a benign mass consisting of disorganized neurons and glial cells that may function as an accessory GnRH pulse generator—the patient was referred to a pediatric neurosurgeon. Surgical intervention was initially considered; however, an ENT consultation was sought to rule out fungal or invasive sinusitis before proceeding.

Further Evaluation and Diagnosis

Unenhanced CT Paranasal Sinuses (Figure 3): The FESS protocol CT scan showed polypoid mucosal thickening and soft tissue opacification of nearly all sinuses (maxillary, ethmoid, and sphenoid bilaterally). There was partial opacification of bilateral mastoid air cells, more pronounced on the right side, suggestive of

mastoiditis.

Endoscopic Nasal Biopsy and Histopathology: Biopsy from both nasal cavities revealed polypoidal masses covered by benign columnar epithelium with severe chronic inflammation, predominantly involving mononuclear eosinophils. No fungal elements, granulomas, dysplasia, or malignant cells were observed.

Treatment and Outcome

With a confirmed diagnosis of chronic sinusitis, the patient was started on:

- Injection Co-amoxiclav 750 mg IV TDS for 4 weeks
- Injection Ceftazidime 750 mg IV BD for 4 weeks

The patient showed significant improvement with antibiotics, negating the need for surgery.

DISCUSSION

Hypothalamic Hamartoma and Central Precocious Puberty (CPP)

The patient's clinical presentation, characterized by a deepened voice, increased penile length, and the development of axillary and pubic hair, strongly suggested central precocious puberty (CPP). The MRI findings confirmed the presence of a hypothalamic hamartoma, a well-documented cause of CPP (10). Hypothalamic hamartomas are benign congenital lesions composed of disorganized neurons and glial cells that can function as ectopic GnRH pulse generators. This results in the premature activation of the hypothalamic-pituitary-gonadal (HPG) axis, triggering early puberty (11).

Association with Chronic Rhinosinusitis

This case is unique due to the simultaneous diagnosis of chronic rhinosinusitis alongside CPP. The patient exhibited persistent nasal obstruction, rhinorrhea, intermittent headaches, and blurred vision, all of which suggested underlying chronic sinus inflammation. CT and histopathology confirmed chronic rhinosinusitis, which had not been previously associated with CPP in medical literature. While hypothalamic lesions are a well-known trigger for GnRH secretion and CPP, the potential contribution of chronic sinus inflammation to this process is less understood.

Inflammatory Factors and Endocrine Activation

Chronic rhinosinusitis is characterized by persistent mucosal inflammation, with tissue histology revealing severe eosinophilic infiltration. The prolonged inflammatory state could have influenced the neuroendocrine axis, potentially contributing to the early activation of GnRH-secreting neurons (12). Inflammatory mediators such as IL-6, TNF-α, and prostaglandins are known to impact the HPG axis, potentially leading to premature puberty (12,14). However, the exact mechanism linking chronic sinus inflammation and early puberty remains speculative, and further studies are needed.

Management and Handling

Initially, neurosurgical resection of the hypothalamic hamartoma was considered as the primary treatment option. However, given the unexpected MRI findings of extensive sinus inflammation, consultation with an ENT specialist was prioritized to rule out fungal or invasive sinusitis before proceeding with surgery. Further workup confirmed chronic bacterial sinusitis, leading to a shift in management toward aggressive antibiotic therapy with Co-amoxiclav and Ceftazidime for four weeks. Remarkably, the patient responded well to medical therapy alone, eliminating the need for immediate surgery. This highlights the importance of a multidisciplinary approach in managing atypical presentations of CPP (13).

Clinical Practice Implications

This case underscores the importance of considering chronic inflammatory conditions as potential contributors to endocrine dysfunction. It also reinforces the necessity of a multidisciplinary approach when dealing with complex cases of precocious puberty. Pediatric endocrinologists, neurosurgeons, and ENT specialists must collaborate to ensure a thorough diagnostic evaluation and an optimal, individualized treatment plan.

Limitations and Future Research

While this case presents a compelling clinical association, it does not establish a definitive causal link between chronic sinus inflammation and CPP. Future research should explore the potential mechanisms by which chronic inflammation affects GnRH secretion. Long-term follow-up studies on patients with chronic sinusitis and endocrine abnormalities may provide valuable insights into whether persistent inflammatory states influence pubertal timing (14).

CONCLUSION

This case highlights a novel association between chronic rhinosinusitis and precocious puberty, emphasizing the importance of considering underlying inflammatory conditions when evaluating early-onset puberty. The successful resolution of symptoms with antibiotic therapy suggests that chronic inflammation may play a role in endocrine dysregulation. Further studies are needed to explore the connection between persistent inflammation and early HPG axis activation. This case also stresses the importance of an interdisciplinary approach when managing atypical presentations of precocious puberty.

Consent

The patient's express written permission to publish this case report and the related photographs were acquired. The Editor-in-Chief of this journal can examine a copy of the written consent upon request.

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Figure 1

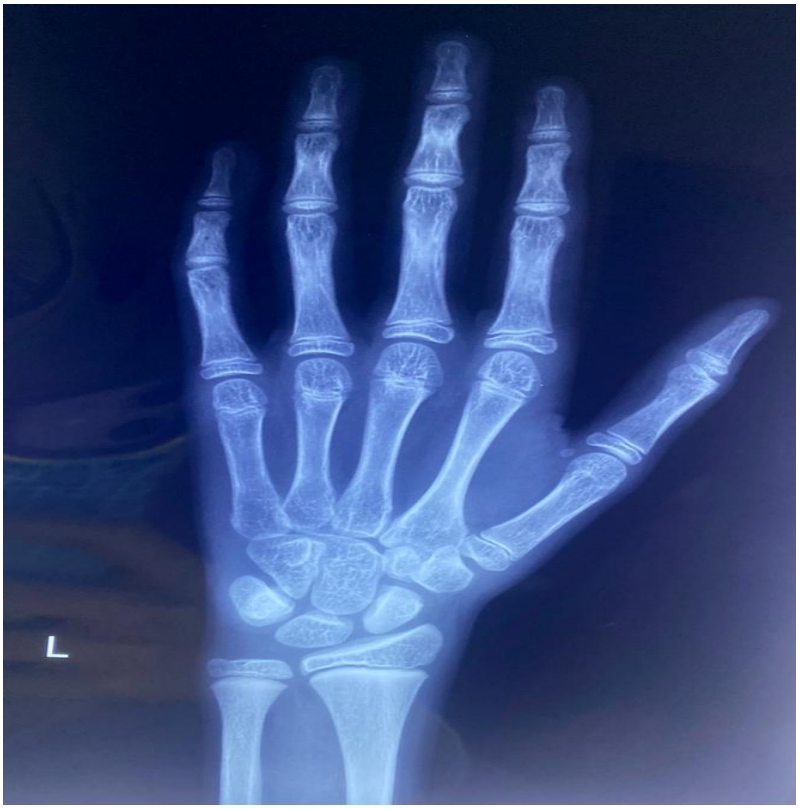

Figure 2

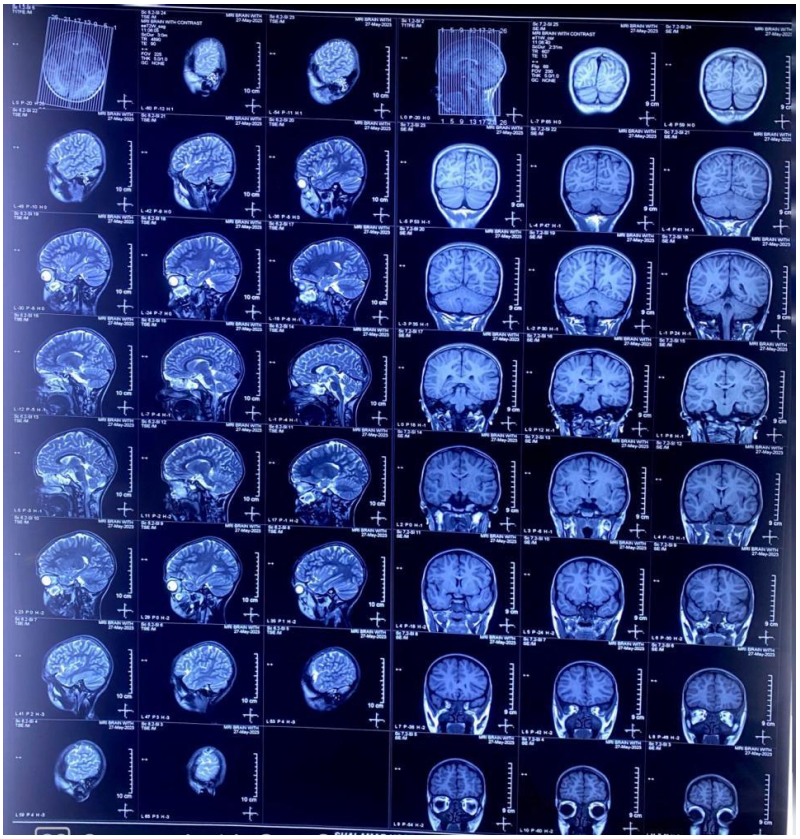

Figure 3