Why did I stop growing? A case of halted puberty

Funmbi Babalola
Hospital for Sick Children University of Toronto, funmbi.babalola@lhsc.on.ca

Andrea Ens
London Health Sciences Centre

Follow this and additional works at: https://ir.lib.uwo.ca/paedpub

Citation of this paper:
https://ir.lib.uwo.ca/paedpub/731
Clinician’s Corner

Why did I stop growing? A case of halted puberty

Funmbi Babalola MD1, Andrea Ens MD MEd FRCPC2,3

1Division of Endocrinology, Department of Pediatrics, Hospital for Sick Children, Toronto Ontario; 2Division of Endocrinology, Department of Pediatrics, Children’s Hospital, London Health Sciences Centre, London, Ontario; 3Schulich School of Medicine and Dentistry, Western University, London, Ontario

Correspondence: Andrea Ens. Department of Pediatrics, Children’s Hospital, London Health Sciences Centre, 800 Commissioners Road East, PO Box 5010 London, Ontario N6A SW9. Telephone 519-685-8138, fax 519-685-8105, e-mail Andrea.Ens@lhsc.on.ca

Both authors have participated in drafting and revising the manuscript, and have approved the submitted manuscript.

CASE PRESENTATION

A 15-year-old boy presents with a 2 to 3 year history of minimal height and pubertal changes. He reported development of pubic and axillary hair starting at 12 years old with no recent progression. He had minimal facial hair. He seldomly had early morning erections. He denied galactorrhea. He described daily nonprogressive, dull headaches not associated with visual changes. He had a normal sense of smell. Energy level and appetite were fair. He had no significant weight change, abdominal pain, dry skin, hair changes, or cold intolerance. He denied sex steroid use, medication, or stimulant use. On past medical history, he had been healthy and developmentally appropriate. There was no history of head or testicular trauma or radiation. There was no family history of delayed puberty. Mid parental height was 179 cm (50 to 75%).

Height was 162 cm (14%), and weight was 69.9 kg (83%). Fundoscopy and visual fields were normal. The remainder of his neurological exam was normal. He had scant axillary hair. Pubic hair was Tanner stage 3. Testes were 2 to 3 mL bilaterally. There was no gynaecomastia. Thyroid, cardiac, respiratory, and abdominal exams were normal.

Bone age was 14 to 15 years. Luteinizing hormone (LH) was 0.2 IU/L (1.2 to 8.6), follicle-stimulating hormone (FSH) was 0.8 IU/L (1.3 to 19.8) and total testosterone was 1.2 nmol/L (8.4 to 28.8). Thyroid function tests, complete blood count, liver enzymes, and kidney function were normal. Further investigations confirmed the diagnosis.
DISCUSSION

Prolactin was 249 µg/L; 48% was macroprolactin indicating a substantial level of biologically active prolactin. Growth hormone was 0.1 µg/L (<3). IGF-1 was not available on the initial bloodwork. An MRI of his head with gadolinium revealed fullness in the right pituitary measuring 7.5mm, consistent with a microadenoma. The optic chiasm was not affected. These investigations confirmed a diagnosis of hyperprolactinemia secondary to a microprolactinoma.

Delayed puberty is defined as the absence of testicular enlargement in boys by 14 years or absence of breast development in girls by 13 years. A testicular volume of 4 mL in males indicates onset of central puberty. Breast budding is the first sign in females. Pubertal assessment also includes Tanner staging pubic hair and assessment of growth parameters.

An approach to delayed puberty is to divide etiologies into two categories based on the gonadotropic levels: hypergonadotropic hypogonadism or hypogonadotropic hypogonadism (Table 1). Hypergonadotropic hypogonadism is characterized by elevated FSH and LH with low testosterone or estrogen indicating gonadal dysfunction. Congenital etiologies in males include Klinefelter’s syndrome, cryptorchidism, and congenital anorchia. In females, Turner syndrome is one of the more common causes of gonadal dysgenesis. In both sexes, acquired etiologies of gonadal dysfunction include autoimmune destruction, infection, chemotherapy, and radiation treatment (1).

In contrast, hypogonadotropic hypogonadism is associated with low LH and FSH with low testosterone or estrogen. This may be secondary to a functional cause or may be permanent. In the case of our patient, his LH was 0.2 IU/L, which is low and aligns with his prepubertal testes. Etiologies of permanent hypogonadotropic hypogonadism include: isolated hypogonadotropic hypogonadism, Kallmann Syndrome, congenital multiple pituitary hormone deficiencies, CNS tumours, and injury secondary to chemotherapy or radiation therapy. Functional hypogonadotropic hypogonadism, which is usually transient, can be seen with inflammatory bowel disease, celiac disease, anorexia nervosa, hypothyroidism, excess exercise, and hyperprolactinemia. Another transient etiology is constitutional delay of growth and puberty. This is a variant of normal where growth velocity is normal for a prepubertal child (1).

Lactotroph cells in the anterior pituitary produce prolactin, where it is stored and released into the bloodstream. At baseline, dopamine delivered from the hypothalamus inhibits prolactin release by the pituitary. Physiologic etiologies for high prolactin include pregnancy, breastfeeding, chest wall injury, and psychological stress. A prolactinoma is a lactotroph adenoma. There are a number of other causes of increased prolactin release including elevated thyrotropin releasing hormone (TRH) as seen in primary hypothyroidism, adrenal insufficiency, and certain medications (neuroleptics such as haloperidol, methyl-dopa, TCA, opiates). Tumours and infiltrative diseases of the hypothalamus can also result in hyperprolactinemia. Decreased clearance of prolactin can be seen in chronic renal failure. Macroprolactin forms from aggregates of prolactin and antibodies, which is detected on prolactin assays. Macroprolactin is not biologically active and does not cause clinically significant hyperprolactinemia (2).

Macroprolactinomas can be symptomatic with headache and visual disturbances secondary to mass effect. Headaches have also been reported with hyperprolactinemia from other causes (3,4). Given that the presenting patient had a microprolactinoma, mass effect likely does not explain his headache. Males with hyperprolactinemia can also present with decreased libido, impotence, decreased sperm production, infertility, gynaecomastia, and rarely galactorrhea. Amenorrhea can be seen in females (2,3). First-line treatment of prolactinomas is Cabergoline, a dopamine agonist. When a patient does not have improvement of his/her symptoms or if there are visual disturbances, surgical treatment may be considered (2–4).

Our patient was started on Cabergoline treatment 0.25 mg twice weekly. His dose has been gradually increased to bring prolactin levels down. Resumption of the hypothalamic-pituitary axis can take several months after prolactin levels decrease.

<table>
<thead>
<tr>
<th>Table 1. Causes of delayed puberty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypergonadotropic hypogonadism</td>
</tr>
<tr>
<td>Congenital Males</td>
</tr>
<tr>
<td>Klinefelter’s Syndrome Cryptorchidism Congenital Anorchia</td>
</tr>
<tr>
<td>Females Turner’s Syndrome Acquired Autoimmune conditions Infection Chemotherapy Radiation</td>
</tr>
</tbody>
</table>

---

**Paediatrics & Child Health, 2021, Vol. 26, No. 4**

203
CLINICAL PEARLS

1) Pubertal assessment and sexual history is an essential component of adolescent care. The physical exam and questions about erectile function are important in the assessment of hypogonadism and should be conducted in a sensitive manner.

2) Determination of hypogonadotropic versus hypergonadotropic causes of hypogonadism is based on the findings from physical exam and assessment of gonadotropin levels.

3) Consider doing a prolactin level in patients presenting with delayed or halted puberty, particularly if gynecomastia, galactorrhea, headaches, or visual changes are present.

Informed consent: Informed consent was obtained from the family for publication of this case.

Funding: There are no funders to report for this submission.

Potential Conflicts of Interest: All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References