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# Pituitary Hyperplasia and Van Wyk Grumbach Syndrome: A Consequence of Chronic Untreated Congenital Hypothyroidism

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An eight-year, 4-month old Indian girl with low IQ and delayed milestones, presented with headache (4 years), breast development (4 months), and menstrual bleeding for 22 days. Examination revealed short stature [height: 91.5 cm; SD score: -5.59], coarse dry skin, umbilical hernia (arrow), delayed reflexes, Tanner's stage-3 breasts, absent pubic and axillary hair. Investigations revealed delayed bone age (3 years), enlarged ovaries with multiple follicles, free $T_4$ <0.35ng/dl (0.9-1.9), TSH 75μU/ml (0.4-4.2), prolactin 323ng/ml (2.5-17), LH <0.1U/L (1.14-5.75), FSH 3.2U/L (1.37-13.56), estradiol 28pg/ml (prepubertal<5pg/ml) and anti-thyroid peroxidase antibody 21U/L (<34). LH and FSH, 40 minutes post 100μg triptorelin were pre-pubertal (0.9U/L and 5.8U/L respectively). Brain MRI revealed diffuse pituitary enlargement. She showed clinical improvement with levothyroxine replacement with resolution of headache, cessation of menstrual bleed, mild decrease in breast size, normalization of TSH, prolactin and 15 cm height gain in 15 months since treatment initiation.

Van Wyk Grumbach syndrome (VWGS)[1] is GnRH independent precocious puberty, believed to be due to TSH mediated activation of gonadal FSH receptor (in the setting of chronic TSH elevation secondary to chronic untreated primary hypothyroidism) resulting in increased estrogen leading to breast development, ovarian follicular cysts and menstruation in the absence of pubic and axillary hair development which are dependent on adrenal androgens.[2] Hormonal overlap at the level of G-protein coupled receptors due to common $\alpha$-subunit between TSH and FSH is the underlying principle.[3] TRH mediated reversible thyrotroph and lactotroph hyperplasia explains the pituitary enlargement and headache in these children.[4]

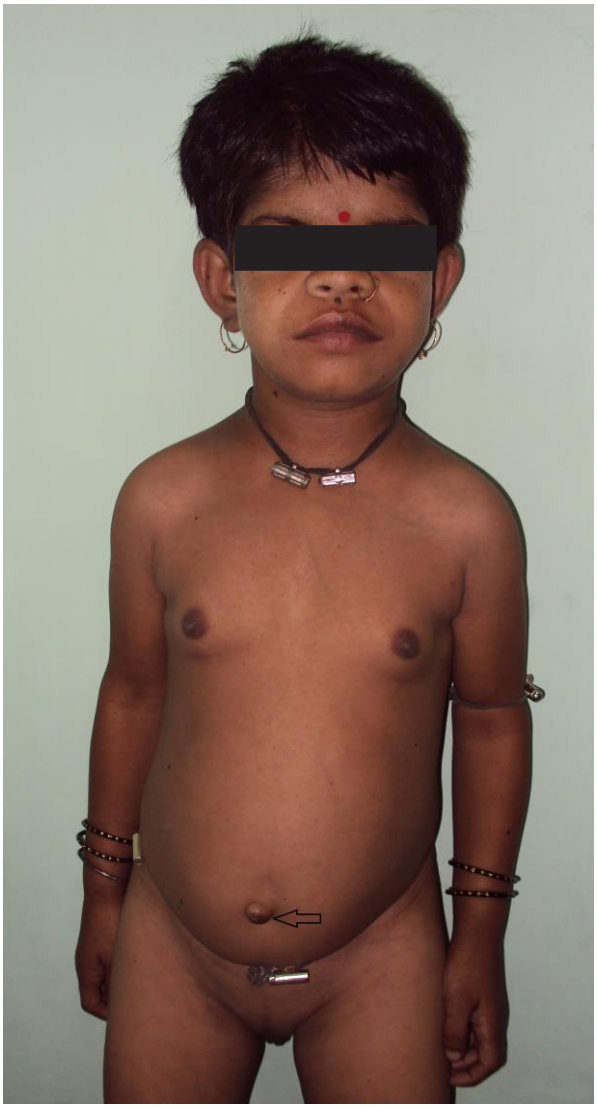

**Figure 1.** Profile of child with Van Wyk Grumbach syndrome

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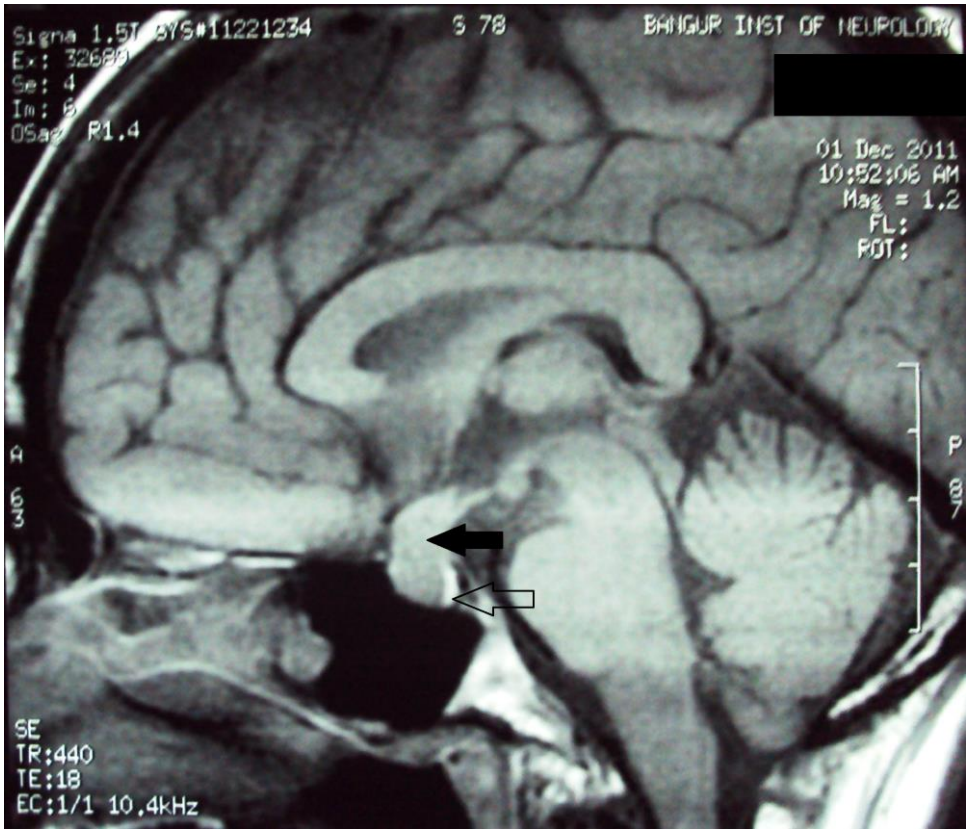


**Figure 2.** Brain MRI showing diffuse pituitary enlargement (solid black arrow) with intact posterior pituitary bright spot (hollow black arrow).

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