

Van-Wyk Grumbach syndrome associated with trisomy 21: a case report

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Introduction:

Van-Wyk Grumbach syndrome (VWGS) described in 1960 combines primary hypothyroidism with precocious puberty, polycystic ovaries and a pituitary adenoma with or without hyperprolactinemia. It is a very rare cause of precocious puberty. The etiopathogenesis is still not very clear

Observation

We report the case of an 8-year-old girl known for Down syndrome, in whom the treating physician diagnosed primary hypothyroidism considered usual in Trisomy 21, treated with low-dose of Levothyrox. 6 months after treatment she presents a cyclic vaginal bleeding every month that lasts 3 months with a very high TSH above 1000 mui/ml and was then referred to our clinic.

Clinical examination:

the weight was 25kg (-0.53 SD), the height was 98cm (-6.2 SD), Tanner B2 (with adipomastia), P1 M, bone age: 4 years.

The association of cyclic vaginal bleeding with statural retardation and delayed bone age, primary hypothyroidism with a very high TSH suggested the Van-Wyk Grumbach syndrome,

Laboratory studies:

FSH: (3.5-12.5) mUI/m	LH: (1.7-8.6) mUI/ml	estradiol: (<20) pg/ml.	prolactinemia: (4.7-23) ng/ml
13.21	0.1	147.44	121.6
TSH: (0.27-4.2)microUI/ml	T4: (12-22) pmol/ml	TPO: (<35) UI/ml	TG: (<55) ng/ml
1000	0.88	278.7	0.65

Imaging studies:

abdominopelvic ultrasound(fig2) found an uterus measuring 63/20mm with regular contours with polycystic appearance of normal echostructure and 2 polycystic ovaries.

Brain MRI (fig3): shows an intra and suprasellar cystic formation with a very limited vertical wide axis measuring 16-16mm that enlarges the sella turcica in favor of a pituitary macro adenoma.

Treatment and evolution:

treatment with Levothyrox at 100 micro gr /day was started, the vaginal bleeding stopped after 24 hours, weight loss of 5 kg, improvement of psychomotor and emotional performance. On the follow up Brain MRI (fig4) there is a total disappearance of the pituitary macro adenoma after only 90 days of treatment.

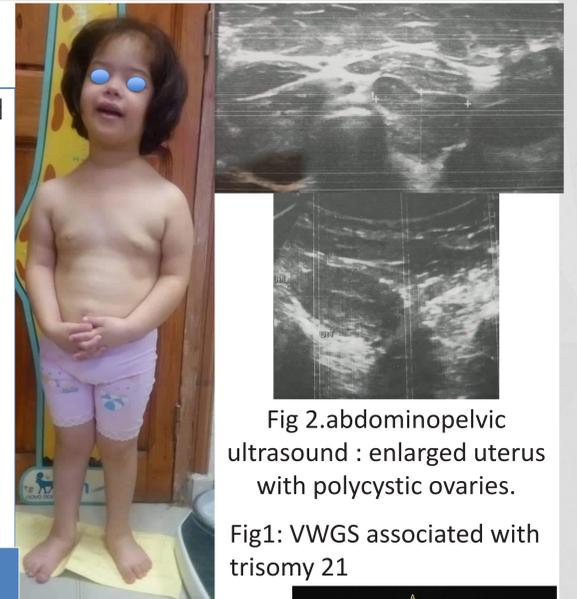


Fig 2.abdominopelvic ultrasound : enlarged uterus with polycystic ovaries.

Fig1: VWGS associated with trisomy 21

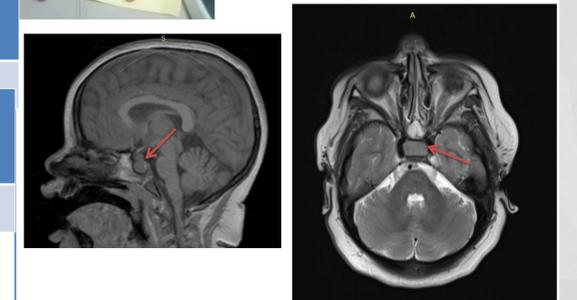


Fig 3. Brain MRI before treatment pituitary macro adenoma.



Fig 4.Brain MRI after 90 days of treatment disappearance of the pituitary macro adenoma

Discussion:

the pathophysiology of Van-Wyk Grumbach syndrome[1,2,3] involves a complex interaction between different hypothalamo-petuitary axes, autoimmune origin is the most likely cause of hypothyroidism, hyperplasia of thyreothropic cells is responsible for the petuitary macro adenoma itself responsible for the secretion of very high levels of TSH, it plays the role of FSH as the molecular similarities between the two hormones inducing the estrogenic secretion, polycystic ovaries and vaginal bleeding,hyperprolactinemia inhibits the secretion of LH, the delay in bone age contrasting with early puberty reflects the age of hypothyroidism, and the main triggering factor, this hormonal disorder being the loss of negative retrocontrol of thyroid hormones on the secretion of TSH.

Conclusion:

Van-Wyk Grumbach syndrome although very rare, but remains an important entity to know because is of good prognosis under medical treatment that avoids the need for unnecessary surgeries (polycystic ovaries) and risky (petuitary macro adenoma).

References:

1. Van Wyk J.J., Grumbach M.M. Syndrome of precocious menstruation and galactorrhea in juvenile hypothyroidism: an example of hormonal overlap in pituitary feedback J Pediatr 1960 ; 57 : 416-435
2. Kaci L., Durbin K., Diaz-Montes T., Loveless M., Van Wyk Grumbach: an unusual case and review of the literature. J Pediatr Adolesc Gynecol 2011 ; 24 : e93-e96
3. Hachicha M et coll. Van Wyk-Grumbach syndrome: A rare cause of precocious puberty. Presse Med 2018