

PSEUDOPRECOCIOUS PUBERTY IN A GIRL WITH UNTREATED ACQUIRED HYPOTHYROIDISM

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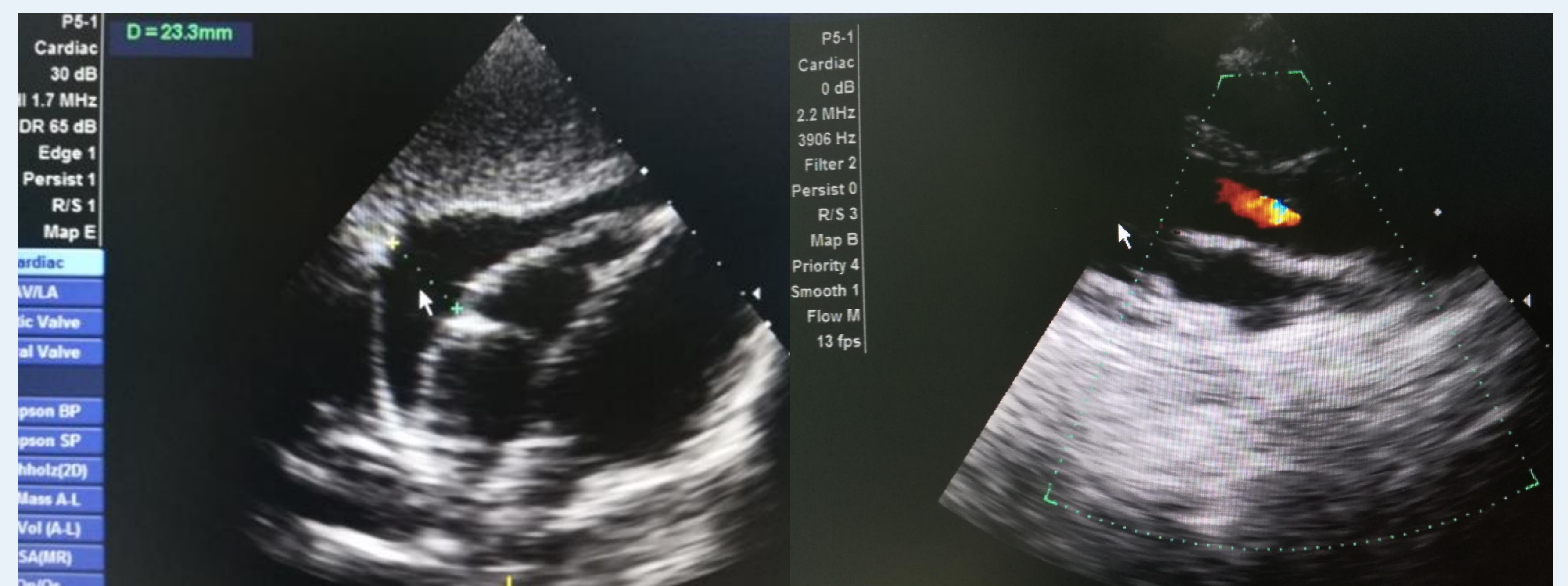
Background: Autoimmune thyroiditis (Hashimoto's thyroiditis, AT) is the most common thyroid disease causing childhood hypothyroidism. It is mainly diagnosed in adolescents but is also found in younger children. The main symptoms of hypothyroidism in children are: obesity, dry skin, brittle hair, facial puffiness, delayed teeth eruption, constipation, cold intolerance, lethargy, sluggishness, school difficulties, easy fatigue (1).

Hypothyroidism is associated with impaired growth and delayed bone maturation, leading to pubertal delay. However, there are patients with untreated acquired hypothyroidism and paradoxical precocious pubertal signs, which include breast development, galactorrhoea and vaginal bleeding in girls and testicular enlargement without virilization in boys (1). This presentation is also called Van Wyk Grumbach syndrome (2). There are several theories for the development of this pseudoprecocious puberty, but the exact mechanism is not clear. The most probable explanation is that high levels of TSH act through the FSH receptor and cause gonadal stimulation. Symptoms regress with thyroid hormone replacement (3).

The most common cardiovascular signs and symptoms of hypothyroidism are bradycardia, narrowed pulse pressure, mild diastolic hypertension, cold intolerance and fatigue. There are also changes in cardiac gene expression, causing diastolic dysfunction and development of protein-rich pericardial and/or pleural effusion (4). Pericardial effusions may present in 10 % do 30 % of adult patients and in pediatric cases with longstanding untreated hypothyroidism. Treatment with levothyroxine leads to complete resolution of the effusions in most patients (5).

Clinical Case: A 10-year old girl was admitted to Endocrinology department with complains of short stature, fatigue, loss of appetite, constipation and cold intolerance. Physical examination showed: pale and very dry skin, puffy masklike face, height 123 cm (<3th percentile), body weight 22 kg (<3th percentile), pulse 59 beats/ min, systolic murmur grade 2, blood pressure - 88/56 mmHg. Thyroid gland was not tender but the size was normal. Breast development was Tanner stage IV without galactorrhoea or other pubertal signs. Bone age was 7.8 years. Laboratory data showed: anemia with hemoglobin 10.5 g/dl, cholesterol 7.02 mmol/l (normal <4.40), triglycerides 1.5 mmol/l. Hormonal evaluation revealed: FT4- <4.50 pmol/l (normal 10.8 – 22.7), TSH 1261 mIU/l (normal 0.40-4.00), Anti-Thyroglobulin Ab 676 IU/ml (normal <35), Anti-Thyroid Peroxidase Ab 553 IU/ml (normal <40), pubertal levels of FSH and prepubertal levels of LH and prolactin. Ultrasound of the thyroid showed typical changes for autoimmune thyroiditis. Echocardiogram revealed moderate pericardial effusion and bicuspid aortic valve with insufficiency I grade (Picture 1). Initial treatment was with increasing doses of L-Thyroxin and decreasing doses of corticosteroids. The pericardial effusion resolved completely within 2 months after the initiation of the therapy. Follow up showed improvement of patient's physical condition, emotional status (Picture 2) and appetite. She gained 4 cm in height. Breasts are Tanner stage III, with no pubic hair development. Levels of TSH, FT4, hemoglobin and cholesterol are within the reference range.

Our patient had typical symptoms of Van Wyk Grumbach syndrome, which regressed with the reduction of TSH levels. This is similar to the other cases, described in literature.



Picture 1. Echocardiographic images of pericardial effusion (left) and aortic insufficiency (right).



Picture 2. Facial appearance before (left) and after (right) initiation of levothyroxine therapy.

Conclusion: The prevalence of autoimmune thyroiditis is increasing worldwide. Thus, we see more pediatric patients with acquired hypothyroidism. Early recognition of thyroid dysfunction is very important because untreated hypothyroidism has negative effect on growth and metabolism and may also cause pseudoprecocious puberty. Hormonal replacement with L-Thyroxin leads to a resolution of all these complications.

References:

1. Zdraveska N, Kocova M. Hashimoto thyroiditis in childhood-review of the epidemiology, genetic susceptibility and clinical aspects of the disease. *Maced J Med Sci.* 2012; 5(3):336–345
2. Van Wyk JJ, Grumbach MM. Syndrome of precocious menstruation and galactorrhea in juvenile hypothyroidism: an example of hormonal overlap in pituitary feedback. *J Pediatr.* 1960; 57:416
3. Anasti JN, Flack MR, Froehlich J, et al. A potential novel mechanism for precocious puberty in juvenile hypothyroidism. *The journal of clinical endocrinology and metabolism.* 1995; 80 (1): 276-9.
4. Levey GS, Klein I. Disorders of the thyroid. In: *Stein's Textbook of Medicine*, 2nd ed. Boston, Mass; Little Brown & Co: 1994; 1383.
5. Martinez-Soto T, Deal C, Stephure D, et al. Pericardial effusion in severe hypothyroidism in children. *J Pediatr Endocrinol Metab.* 2010;23(11):1165-8.