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(RESEARCH ARTICLE)

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Thyroid dysfunction in patients with Down Syndrome: Beyond hypothyroidism

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Abstract

Down Syndrome (DS) is the most common chromosomal disorder among live-born infants. Its' prevalence varies world-wide, from one in 700 to 1500 live-births. This is even higher in Saudi Arabia which was reported as 18 per 10,000 live-births. The majority of patients is due to non-dysjunction of chromosome 21, while the remaining are either due to translocation or mosaicion. DS is associated with an increased risk of various endocrine disorders, of which thyroid dysfunction is the commonest. The spectrum of thyroidal dysfunctions in patients with DS, include congenital hypothyroidism (CH), subclinical hypothyroidism (SH), acquired hypothyroidism, autoimmune and non autoimmune. and hyperthyroidism, including graves disease.

In this report, we present our experience with the various thyroid dysfunction in different patients with DS. The need for an annual evaluation of the thyroid function to detect early abnormalities, hence, an early intervention.

Keyword: Acquired hypothyroidism; autoimmune; non autoimmune; Congenital hypothyroidism; Down Syndrome; Graves disease; Hyperthyroidism; Thyroid disorders; Saudi Arabia; Subclinical hypothyroidism.

1. Introduction

Down Syndrome (DS) is the commonest chromosomal disorder among live-born infants. Its prevalence various world-wide, from one to 700 to 1500 live-births. The majority of patients are due to non dysjunction of chromosome 21, while the remaining patients are either due to translocation Or mosaicism (1-5) In Saudi Arabia the prevalence have been reported to be one 544 live- births (18 per 10000) (6-7). The rising proportion of older mothers is likely to have contributed to the high trends of DS. It is associated with increased risk of endocrine abnormalities (8,9). Among the endocrine abnormalities, the thyroid dysfunction is the commonest. If is estimated to account for 4-8 percent of children with DS (10,11). The spectrum of thyroid dysfunction in patients with DS, include congenital hypothyroidism, subclinical hypothyroidism, acquired hypothyroidism (autoimmune and non autoimmune), and hyperthyroidism, including Graves disease.(12 -19)

Here in, we report on different Patients with DS who were diagnosed to have variable thyroid abnormalities.

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2. Materials and Results

2.1. Patient

Over the last six years, many patients with Down Syndrome (DS) were diagnosed with variable thyroid disorders. Two neonates with congenital hypothyroidism and four patients were diagnosed to have acquired hypothyroidism.

Results —///S.A.Q, who was born with features suggestive of DS. He was the product of full-term normal preqnancy and delivery. No family history of thyroid disorders, or maternal drug ingestion. Neonatal screening for thyroid diseases suggested primary hypothyroidism, Serum thyroid-stimulating hormone (TSH) was 409 mIU/L, which was confirmed upoun repeat. The TSH was high, 630 mIU/L, and low thyroxine of 4.6ug/dl (Normal: 5-12). The Thyroid Scan, 99 m Tc pertechnetate thyroid scintigraphy (fig 1) suggestive of thyroid gland aplasia. Chromosomal study confirmed the diagnosis of Down Syndrome (DS), 47XY-21.

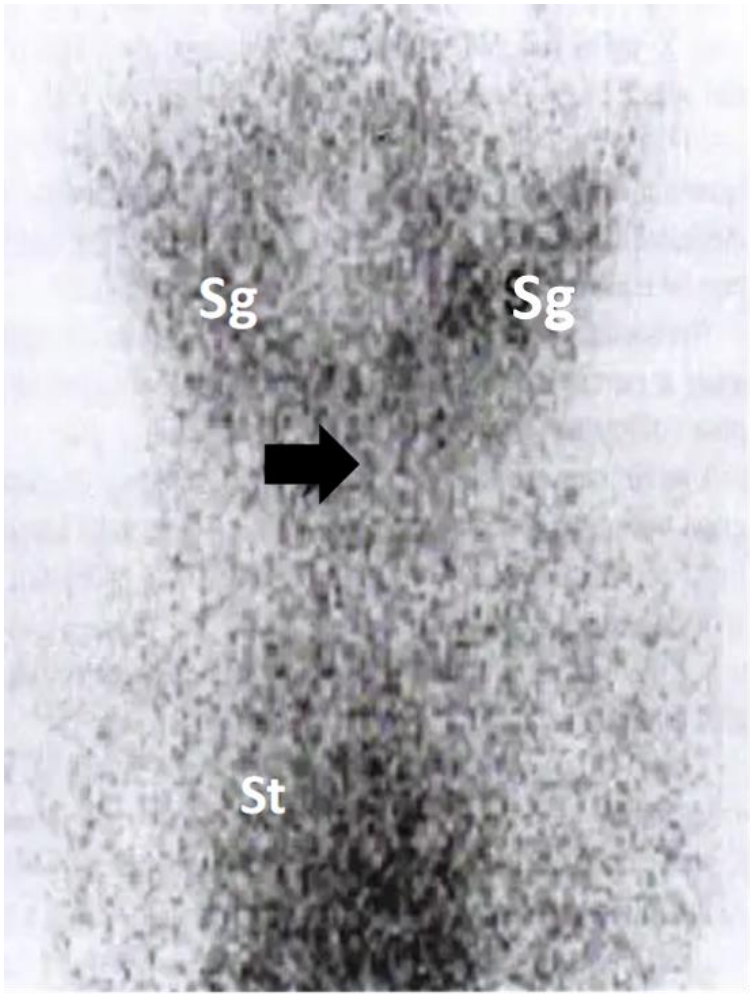

Figure 1 99mTc pertechnetate thyroid scintigraphy, showing no tracer Uptake (arrow) suggesting Thyroid gland aplasia. Tracer uptake is seen in (Sg) salivary glands, and (St) stomach

—///A. A. S, a three year old boy ,who was known to have DS (47,XY-21) was evaluated for thyroid swelling and chronic constipation. The thyroid gland was diffusely enlarged, measuring 4 by 3, on physical examination. Thyroid function tests revealed an abnormal TSH of 96 mIU/L (Normal: Less than 5) and free thyroxine (FT4) of 10.2. Thyroid autoantibodies were strongly positive (TPO autoantibodies of 1665 Unites, and Thyroglobulin autoantibodies of 160 Units). Thyroid ultrasound (US), (Fig 2) examination demonstrated diffuse heterogenous enlarged thyroid gland with multiple hypoechoic nodules (pseudo nodules) with normal thyroid gland vascularity. The 99m Tc scintigraphy (fig 3), showed diffusely enlarged with multiple hypoechoic areas, with markedly reduced uptake of 1.4%. The diagnosis of Hashimotos' thyroiditis was entertained with hypothyroidism.

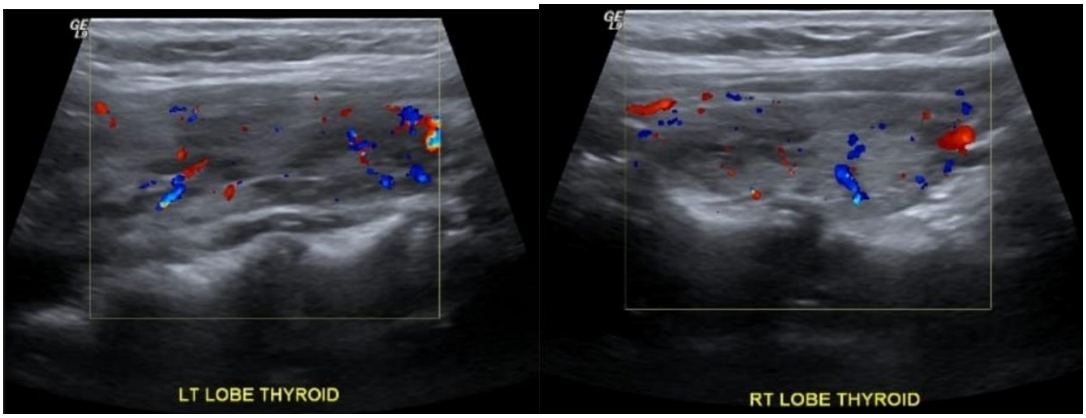

Figure 2 Thyroid Sonogram, showing diffuse heterogenous enlarged thyroid gland with multiple hypoechoic nodules (pseudo nodules) with normal thyroid gland vascularity

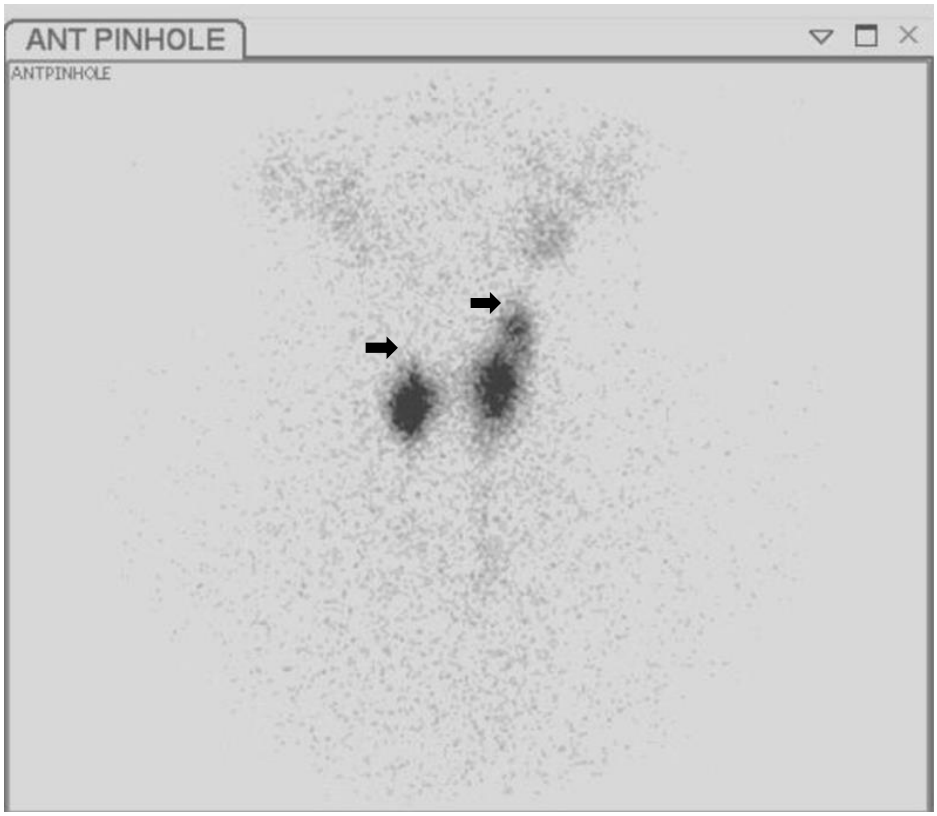

Figure 3 99m Tc pertechnetate thyroid scintigraphy, showing diffusely enlarged gland with multiple hypo echoic areas (arrows). The tracer uptake is markedly reduced (1.4 percent).

On the other hand,five patients with Down Syndrome with different gender and age ranging from two to eight years were presented with hyperthyroid function. The glands were varing in size from normal to diffusely enlarge at physical examination. Thyroid function tests were compatible with hyperthyroidism. Throid-stimulating-hormone (TSH) was persistently suppresed, TSH of less than 0.001mIU/L, and free thyroxine (FT4) was high in the range of 29-48 Pmol/L Thyroid peroxidase auto-antibodies(anti-TPO) and thyroglobulin autoantibodies (anti-Tg) were variably positive. Thyroid Ultrasound (US) (Fig 4), showed hyperechoic diffusely enlarged gland. Technetium 99m scintigraphy (Fig 5) showed diffusely enlarged thyroid gland with increased homogenous tracer uptake in all patients, suggesting the diagnosis of Graves disease.

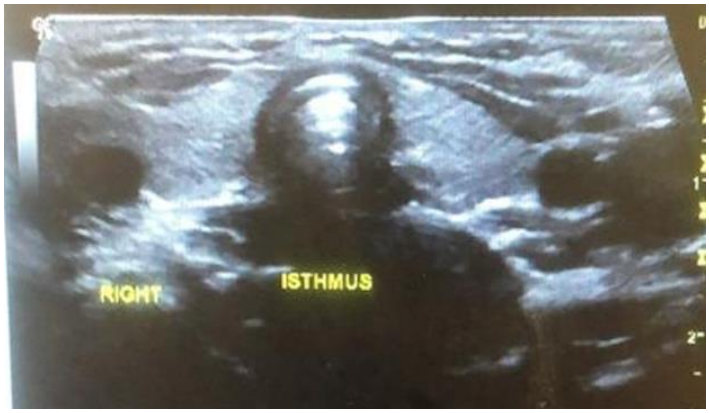

Figure 4 Thyroid Ultrasound of an eight-year-old with goiter showing diffusely enlarged hyperechoic thyroid

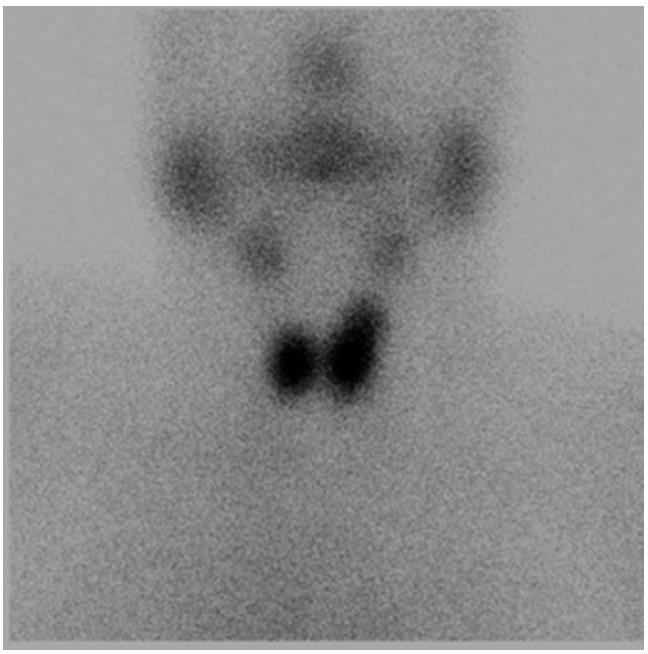

Figure 5 99m Tc pertechnetate scintigraphy, showing diffusely enlarged thyroid with homogeneous increased uptake (36 percent).

3. Discussion

Down Syndrome (DS) is the most common genetic disorder in human. Its prevalence varies world-wide, between one in 700 to 1500 live births (1-5). It is associated with an increased risk of thyroidal dysfunction which was estimated to be (4-8 percent) compared to general population. Thyroidal dysfunction is almost 25-40 percent folds more likely in patients with DS. The spectrum of such disorders is so wide and might include congenital hypothyroidism, acquired hypothyroidism that caused by different etiologies, either autoimmune or non autoimmune and hyperthyroidism that Include Grave's disease. (10-20)

The reported incidence of congenital hypothyroidism (CH) in DS is much higher compared with that of normal population, estimated to be thirty times higher. (10 - 14) Most of patients were due to thyroid aplasia or hypoplasia. (10–14,21,22) Acquired causes were also prevalent (10–26). Subclinical hypothyroidism is themost common thyroidal dysfunction reported in almost 50 percent of patients with DS. (11,12,27–29). Autoimmunity is among the important causes of subclinical hypothyroidism. Thyroid peroxidase (TPO) anti-bodies were detected frequently in patients with such disorder. The natural course is not consistent, and the debate is still not resolved (27–29). Hashimoto thyroiditis is strongly associated with positive autoantibodies being present in one third of the patients affected with the disease,

(30-33). Hyperthyroidism though rare, is more prevalent in patients with DS than in general population, and has no genderpredominance. Hyperthyroidism due to Grave disease usually has a more prevalence than expected. (34—36)

4. Conclusion

The increased frequency of thyroid dysfunction and pattern in patients with DS suggest the need and importance of continuosly and longitudinal screening of thyroid function annually to detect early changes and, hence, proper advice and management. Expert specialists should develop a practical and easy guidelines to adhere wifh and follow in the care of DS patients.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors have no conflicts of interest to declare.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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