

Original Article

Autoimmune thyroiditis associated with Sanjad-Sakati syndrome: A call for regular thyroid screening

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ABSTRACT

Sanjad-Sakati Syndrome (SSS) is a rare autosomal recessive disorder characterized by congenital hypoparathyroidism, growth retardation and dysmorphism. Thyroid status of patients with SSS has not been widely explored. Therefore, we aimed to review the occurrence of autoimmune thyroiditis, which is commonly associated with other genetic disorders, in SSS. A retrospective hospital based study was conducted at King Khalid University Hospital, Riyadh, Saudi Arabia, to determine the thyroid status of patients with SSS attending the hospital between 1990 and 2015. Data were extracted from the medical records of patients diagnosed with Sanjad-Sakati syndrome with special emphasis on the clinical features, thyroid function, thyroid antibodies, molecular studies and other relevant investigations. A total of 18 patients with a diagnosis of Sanjad-Sakati

Syndrome based on typical clinical features and low parathyroid hormone, were evaluated. Furthermore, molecular study was available on 15 patients; all had homozygous deletion of 12 bp (155-166) in exon 3 of the TCBE gene. In 6 patients the thyroid functions were abnormal (one patient with overt hypothyroidism and five patients with sub clinical hypothyroidism). Thyroid autoantibodies were positive in 4 patients. In conclusion, one third of this cohort with SSS had abnormal thyroid function test attributed mainly to autoimmune thyroiditis. Therefore, we recommend routine screening of patients with SSS for thyroid function and autoimmune antibodies during follow up.

Keywords:

Autoimmune; Children; Thyroiditis; Sanjad Sakati Syndrome; Saudi Arabia

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INTRODUCTION

Sanjad-Sakati Syndrome (SSS) or hypoparathyroidism-retardation-dysmorphism syndrome is a rare autosomal recessive disorder that typically presents with intrauterine growth retardation (IUGR), distinct dysmorphic features, early hypocalcaemia, and developmental delay [1-4].

Hashimoto's thyroiditis is the most common cause of hypothyroidism in children and adolescents. It is more common in females. Although the disease can be seen before three years, usually it peaks at 10-12 years of age. The prevalence of Hashimoto's thyroiditis in children between 6-18 years old is 3% in Japan. Up to 30 to 40 % of the cases have familial history of thyroid disease. Autoimmune thyroid disease has two clinical forms, a goiterous form and an atrophic one often called atrophic thyroiditis. Both are associated with circulating thyroid autoantibodies [5,6].

This work is an attempt to describe an observed association of autoimmune thyroiditis and Sanjad-Sakati syndrome in the cohort of these patients we saw at our institute over the last twenty-five years.

METHODS

The study population consisted of all patients with the diagnosis of Sanjad-Sakati syndrome referred to or born at King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia over a 25 years period (January 1990 - December 2015). King Khalid University Hospital is the main teaching hospital of King Saud University, and considered as one of the major referral hospitals in the central province of Saudi Arabia. Data included age, sex, clinical demographic data, and relevant biochemical investigations were collected from medical records and the hospital electronic laboratory system.

In our hospital, patients are usually screened for thyroid dysfunction by thyroid stimulation hormone (TSH), and free thyroxine (FT4). Antithyroid microsomal or also called thyroid peroxidase antibodies (Tpo Ab) and thyroglobulin antibodies (Tg Ab) were also estimated using haemagglutination method and a titer of 1:100 or more was considered positive. Thyroid function tests (TSH and FT4) were measured by methods using commercially available kits. The Middle East Extended Quality Assessment Scheme (MEEQAS) in Riyadh monitored the quality control of the assay.

Diagnosis of subclinical autoimmune thyroiditis (Hashimoto's) was based on high levels of TSH, more than 5 mu/l associated with the presence of at least one elevated thyroid autoantibody on two or more consecutive occasions. While clinical hypothyroidism (overt hypothyroidism) was associated in addition to the above with low FT4 levels [5].

RESULTS

A total of 18 patients with Sanjad-Sakati Syndrome (SSS) were reviewed with special emphasis on evidence of hypothyroidism and autoimmune thyroiditis. Six patients (33.3%) (N=4 Males and 2 Females), aged 2-11 years, were found to have high TSH. Five of these patients had subclinical hypothyroidism, while one had overt hypothyroidism. Four of the patients (22.2%) had positive thyroid antibodies (Table 1). All patients had low parathyroid hormone levels. Molecular study results were available in 15 patients; all of them had homozygous deletion of 12 bp (155-166) in exon 3 of the *TCBE* gene.

Table 1 - Characteristics of patients with Sanjad-Sakati Syndrome and abnormal thyroid function

Patient no.	Age	Sex	TSH	FT4	Thyroid antibodies
			Normal less than 5 mU/l	Normal =10-25 Pmol/L	Normal TPO < 35 IU/ml TgAb < 20 IU/ml
1	2 years	Male	10	14.5	TPO Ab- 1:330 Tg Ab- 1:152
2	2 years	Male	9.8	14.3	TPO Ab- 1:232 Tg Ab- 1:120
3	11 years	Male	12	13	TPO Ab- 1:412 Tg Ab- 1:202
4	5 years	Female	13	10	TPO Ab- 1:376 Tg Ab- 1:115
5	6 years	Male	7	13.5	TPO Ab- Normal Tg Ab- Normal
6	3 years	Female	8	13	TPO Ab- Normal Tg Ab- Normal

FT4- Free thyroxine, Tg Ab- Thyroglobulin antibodies, TPO- Thyroid peroxidase antibodies, TSH- Thyroid stimulating hormone

DISCUSSION

Sanjad-Sakati Syndrome (SSS) or hypoparathyroidism-retardation-dysmorphism syndrome is an autosomal recessive disorder first reported in 1988 and confirmed by a definitive report in 1991 [7-9]. It has been reported initially, almost exclusively in the Middle Eastern population [7,8]. However, it is later reported from other Arab and non-Arab populations [9-13]. The prevalence of SSS is unknown; however, the incidence in Saudi Arabia varies from 1 in 40,000- 1 in 600,000 live birth [3], probably due to high consanguineous mating [14].

SSS is characterized by congenital hypoparathyroidism with growth retardation and mental impairment associated with seizure. The molecular pathology of this syndrome was shown to be due to mutations in the TBCE gene in chromosomal area 1q42-q43 [2,4,10]. All patients reported so far from the Middle East had a founder homozygous deletion of 12 bp (155-166) in exon 3 of the *TCBE* gene.

The pathogenesis of many aspects of this disease is still

not well understood especially the growth retardation and the tendency of recurrent infections. Marsden et al [15] reported the use of growth hormone for a child with SSS with good outcome, while others failed to show so [7]. Severe Intrauterine growth retardation (IUGR), and growth hormone unresponsiveness could be the contributing factors. Al-Jurayyan, the senior author in this paper, demonstrated normal growth hormone secretion from studying five patients from this series in unpublished data.

In our cohort, we found that one third of our patients with SSS had abnormal thyroid function associated mainly with autoimmune thyroiditis. To our knowledge, this association has not been previously recognized. Likewise, the severe growth retardation associated with SSS, the pathogenesis of autoimmune thyroiditis is not clear. However, autoimmune thyroiditis has been reported with increased prevalence in other genetic disorders like Turner syndrome [5,6]. It is of interest that most of our patients with SSS and autoimmune thyroiditis had subclinical hypothyroidism. Yet, it is

not clear whether these patients will progress to overt hypothyroidism or not. Though the only patient with overt hypothyroidism in this cohort was younger in age than those with subclinical hypothyroidism.

Thyroid hormone is critical for physical and mental development of infants and young children. As patients with SSS have significant delay in both physical and mental developments, thyroid function should be monitored on regular basis and adjusted accordingly. This will enable physicians to detect early any dysfunction of the thyroid function and therefore prevent further deterioration of growth and development of these patients.

CONCLUSION

In this Study, one third of patients with SSS had abnormal thyroid function tests attributed mainly to autoimmune thyroiditis. Therefore, routine screening of thyroid function and autoimmune antibodies in these patients is recommended to prevent further neurological, growth and development consequences.

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