Full Length Research Article

Growth hormone “GH “profile in Sanjad Sakati Syndrome

Nasir A Al-Jurayyan¹, Hala G Omer², Huda A Osman³, Reem A Alkhalifah⁴, Abdulmajeed A Alsabaihin⁴, Hessah M Al-Otaibi⁵ and Sharifah T. Alissa⁵

¹Professor And Consultant Pediatric Endocrinologist, Endocrine Division, Department of Pediatrics, King Saud University, Riyadh, Saudi Arabia
²Fellow, Endocrine Division, Department of Pediatrics, King Saud University, Riyadh, Saudi Arabia
³Senior registrar, Endocrine Division, Department of Pediatrics, King Saud University, Riyadh, Saudi Arabia
⁴Assistant professor and consultant pediatric endocrinologist, endocrine division, department of pediatrics, King Saud University, Riyadh, Saudi Arabia.
⁵Consultant pediatric endocrinologist, endocrine division, Department of Pediatrics, King Saud University, Riyadh, Saudi Arabia

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Sanjad Sakati Syndrome (SSS) or congenital hypoparathyroidism growth retardation, and dysmorphism is rare autosomal recessive disease that typically present with intrauterine growth retardation (IUGR). Distinct dysmorphic feature early hypocalcaemia and developmental delay. This study was to assess growth hormone (GH) status in patients with Sanjad Sakati Syndrome. During the period March 2010 and July 2018, six Saudi children with clinical feature of SSS who were confirmed to have mutations in TBCE were investigated with physiological (sleep), and pharmacological (arginine, L dopa and clonoidine) growth hormone tests, at the endocrine services, King Khalid University Hospital (KKUH), Riyadh ,Saudi Arabia. Six patients with SSS were studied, four males and two females. Their ages ranged 6–16 years (mean 9.2 yrs). Five out of six patients (83.3%) had normal growth results. Our results indicate that the majority (83.3.%) of patients were not growth hormone deficiency (GH), However neuroendocrine assessment, Insulin like growth factor (IGF-1) growth hormone (GH) axis and neuro_radiological Imaging studies should be carried out to delineate the nature of disorder.

Keywords: Growth hormone, Neuro endocrine radiological imaging, Sanjad _Sakati__syndrome

INTRODUCTION

Sanjad Sakati Syndrome or hypoparathyroidism, retardation in growth, and dysmorphism (HRD) is a rare autosomal recessive genetic congenital disorder with equal distribution in both sexes. It is often severe and has fatal consequences. It was first described from Saudi Arabia but has been reported form other Arab centuries from Asia and Africa (Sanjad et al., 1991; Teebi, 1997). The condition is caused by mutations or deletions in the gene encoding tubulin –specific chaperone E (TBCE) gene, the locus for which is on chromosome 1q42-43 (Padidilia et al., 2009; Praven et al., 2002).

*Corresponding Author E-mail: njurayyan@gmail.com; Telephone No: 00966505400592
Table 1. Demographic Characteristics

<table>
<thead>
<tr>
<th>Serial No</th>
<th>Age in year</th>
<th>Sex</th>
<th>GA</th>
<th>BW (g)</th>
<th>IUGR</th>
<th>Hypoparathyridism</th>
<th>Growth retardation</th>
<th>Dysmorphi sm</th>
<th>Consanguinity</th>
<th>TBCE Gene Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9 M</td>
<td>32</td>
<td>1530</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>6 M</td>
<td>38</td>
<td>1670</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>8 F</td>
<td>40</td>
<td>1430</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>16 M</td>
<td>40</td>
<td>1640</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>N.D</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>6 F</td>
<td>39</td>
<td>1948</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>10 M</td>
<td>38</td>
<td>2160</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

N.= number, M = male, F =female, GA = gestational age, BW = birth weight, g = gram

Table 2. Post- Provocative Tests results

<table>
<thead>
<tr>
<th>Serial N.</th>
<th>Age year</th>
<th>sex</th>
<th>Sleep (6) patients</th>
<th>Arginine (6) patients</th>
<th>L .dopa (4) patients</th>
<th>Clonidine (2) patients</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9 M</td>
<td>11.3</td>
<td>15.6</td>
<td>1.6</td>
<td>ND</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>6 M</td>
<td>3.8</td>
<td>10.6</td>
<td>13.6</td>
<td>N</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>8 F</td>
<td>17.7</td>
<td>3.8</td>
<td>10.7</td>
<td>ND</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>16 M</td>
<td>1.1</td>
<td>11.1</td>
<td>ND</td>
<td>2.5</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>5 F</td>
<td>3.7</td>
<td>4.5</td>
<td>ND</td>
<td>3.5</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>10 M</td>
<td>16.5</td>
<td>12.6</td>
<td>5.6</td>
<td>ND</td>
<td>ND</td>
<td></td>
</tr>
</tbody>
</table>

Based on literature review, fostered by the clinical expiriance and to the best of our knowledge there were conflicted results of growth hormone secretion in such patients.

Richardson and Kirk (1990) found growth hormone deficiency in three children in their cohort of eight, while Sanjad et al (1991) reported normal growth hormone concentration in eight of eight tested subject.

In this study we assess growth hormone (GH) secretion in six patients with Sanjad Sakati Syndrome (SSS) or congenital hypoparathyridism growth retardation, and dysmorphism.

MATERIALS AND METHODS

During the period March 2010 and July 2018, six Saudi patients were tested to know growth hormone status due to sever growth retardation. Growth velocities of these children were subnormal (more than 3SD below the mean).

They were diagnosed with Sanjad-Sakati-syndrome (SSS) .They were four males, and two females. Their ages ranged from 6-16 years (mean 10 years).

After detailed history and physical examinations, an initial screening investigation, including Complete blood count, renal function, Bone profile and Thyroid function tests were performed.

After taking performed consents from the parents, all were subjected to growth hormone studies. One physiological test, namely night sampling at 60 and 90 mins after onset of sleep, and at 4:0AM .while the patient was asleep were done .The following morning, two biochemical growth hormone provocation test utilizing (arginine ,L dopa and clonidine) were performed as suggested (Tillmann et al., 1996).

Radioimmunoassay was used for growth hormone measurement using pharmacies kits.

RESULTS

Patients were of Saudi origin, consanguinity was present in four, However homozygous mutation in tubulin co factor E (TBCE), which confirm the diagnosis. The demographic data were shown in table 1. Six patients were included. Four males and two females their ages ranged between 6 and 16 years (mean 9.2 years). They were found to have clinical features of SSS, with congenital hypoparathyridism, sever growth retardation and variable dysmorphic features.

The patients were not anemic, mean hemoglobin was 11.2 g/dl (mean 10.4-14.1). Renal and bone profile were normal, on therapy (one alpha cholecalciferol, and calcium supplement). All patients were biochemically euthyriod. Peak plasma growth hormone concentration, post sleep ranged from 1.1 to 17.7 µg/l (mean 9.01). Table 2, which also showed the results of arginine (six patients) L-dopa (four patients) and clonidine (two patients). No single provocative test for growth hormone was diagnostic, However combining the result of one post sleep provocative test and two pharmacological test showed normal results in five of our patients.
DISCUSSIONS

Sanjad-Sakati-syndrome (SSS) is a rare autosomal recessive genetic congenital disorder with equal distribution in both sex, and the gene of the syndrome is on chromosome 1q42-43 and have sever and often fatal consequences. It is characteristic by congenital hypoparathyroidism, sever prenatal and postnatal growth retardation as well as mild to severe mental retardation, and dysmorphism. The common dysmorphic features of the syndrome are microcephaly with prominent forehead, deep set eyes, thin lips, depressed nasal bridge with peaking of the nose, large floppy ear lobe and small hands and feet. It is commonly described in the Middle East population of Arab origin (Sanjad et al., 1991; Teebi, 1997).

Sanjad et al (1991) reported a normal growth hormone secretion, in consist to our results. Richardson and Kirk (Richardson and Kirk,1990) found growth hormone deficiency (GHD) in the three children their cohort of eight. Two other patients of clinically diagnosed SSS have also been reputed with GHD (Marsden et al., 1994; Soliman et al., 1996). Hershkovitz (2007) observed postnatal growth failure in children with SSS in infancy with delay and attenuated childhood growth. It was suggested that mutation in TBCE affected microtubule assembly and chondrocyte maturation, which could be the cause. Longitudinal bone growth as has been previously demonstrated in chick (Hunziker and Schenk,1989; Farquharson et al., 1999). It was also stated that GH secretion and the GH –IGF1 axis were important (Smith et al., 1993). Growth hormone stimulation test no longer routinely be used for the diagnosis of growth hormone deficiency (GHD) in children as these tests lack precision, accuracy and have little concordance with the disease. The tests are poor predictors of response and can have side effects (Gandrud and Wilson, 2004).

CONCLUSION

Our results indicate that the majority (83.3%) of patients were not growth hormone deficient (GHD).However appropriate neuro-endocrine evaluations, including the gonadotrophins is essential. Neuro-radiological imaging by Magnetic Resonance (MRI) should be performed to exclude any structural abnormalities.

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REFERENCES


