INTRODUCTION

Hypogonadism is considered as an integral component of pathology leading to the Metabolic Syndrome (MetS) with insulin resistance (IR) at its core. In recent years a close association between hypogonadism and MetS has received more attention. This is because the prevalence of hypogonadism has been shown to be higher than previously thought, both in epidemiological studies and survey of clinical practice. Both MetS and hypogonadism have been shown to have an independent association with age, geography, ethnicity, lifestyle issues and obesity.

CASE REPORT

A 19 years old boy presented with bilateral marked gynaecomastia, absence of secondary sexual characteristics and weight gain. He had four siblings in all, with no one having a similar problem. His maternal grandmother and paternal uncle had type 2 diabetes mellitus (DM). There was no history of headache or anosmia and vision was intact. He had febrile fits in early childhood till the age of 5 years, which were managed with antipyretics. He remained fit-free thereafter. Rapid weight gain was noticed at age 6, with change in dietary habits.

On examination, his weight was 76 kg, height was 150 cm, BMI was 33.77 kg/m² and blood pressure was 130/80 mmHg. Paternal height was 160 cm and maternal height was 152.5 cm. Marked acanthosis nigricans was present over knuckles, flexures and neck (Figure 1). He had bilateral marked gynaecomastia with dark raised nipple-areolar complex and absent axillary hair. His genital examination revealed stage II pubic hair, micropenis and bilateral firm testes of 12 mls size with well-developed scrotum. Clinical impression of hypogonadism with MetS was made.

His laboratory results are shown in Table I. The laboratory tests suggested hypogonadotrophic hypogonadism, MetS and Vitamin D deficiency. His bone age was 18 years and had a normal pituitary MRI. In view of marked gynaecomastia, even though there was no genital ambiguity, karyotyping was also done which was normal. Dietary control, physical exercise, metformin therapy and Vitamin D replacement was advised alongwith monthly intramuscular injection of testosterone enanthate 250 mg. Reduction mammo-plasty was planned for the future. He was continued on metformin and Vitamin D replacement.
### Table I: Laboratory profile of the case: values within parenthesis indicating the normal range.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting blood sugar (70-125 mg/dl)</td>
<td>93.0</td>
<td>Cortisol (4.6-31.1 µg/dl)</td>
<td>9.00 am</td>
</tr>
<tr>
<td>Serum insulin (0.7-9 µU/L)</td>
<td>10.7</td>
<td>Testosterone (280-800 nmol/l)</td>
<td>106.2</td>
</tr>
<tr>
<td>Cholesterol (180-200 mg/dl)</td>
<td>183.0</td>
<td>SHBG (14.5-48.4 nmol/L)</td>
<td>17.87</td>
</tr>
<tr>
<td>HDL (45-65 mg/dl)</td>
<td>37.0</td>
<td>FAI (15.5-102)</td>
<td>47.69</td>
</tr>
<tr>
<td>LDL (&lt; 130 mg/dl)</td>
<td>111.0</td>
<td>FSH (0.7-11 mIU/ml)</td>
<td>2.8</td>
</tr>
<tr>
<td>TG (&lt;150 mg/dl)</td>
<td>199.0</td>
<td>LH (0.8-2.9 mIU/ml)</td>
<td>1.7</td>
</tr>
<tr>
<td>CRP (&lt; 1.1-1.5 mg/L)</td>
<td>1.4</td>
<td>DHEAS (8-560 pg/ml)</td>
<td>226.0</td>
</tr>
<tr>
<td>Calcium (8.5-10.5 mg/dl)</td>
<td>9.1</td>
<td>Estradiol (0-56 pg/ml)</td>
<td>30.50</td>
</tr>
<tr>
<td>Phosphate (2.7-4.5 mg/dl)</td>
<td>4.0</td>
<td>FT4 (0.85-2.8 ng/ml)</td>
<td>1.19</td>
</tr>
<tr>
<td>Vitamin D levels (&gt; 30 ng/ml)</td>
<td>16.44</td>
<td>Prolactin (2.5-17 ng/ml)</td>
<td>50.04</td>
</tr>
</tbody>
</table>

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**DISCUSSION**

MetS refers to a clustering of various medical conditions, with a number of pathological components that contribute to the development of early onset type 2 diabetes and cardiovascular disease. This syndrome is variously defined leading to much confusion. Increasing prevalence is being reported from all over the world, no matter what definition is used.

This patient had truncal obesity with marked acanthosis nigricans which is a marker of IR. According to IDF, any person who has central obesity and 2 out of 4 parameters, meets the criteria of MetS. In this case increased waist circumference with systolic blood pressure of 130 mmHg, TG levels of 199 mg/dl and HDL levels of 37 mg/dl, fulfilled the criteria of MetS.

Epidemiological studies show a prevalence of hypogonadism of 10-12% in the general population, which has only been found to be slightly lower, at 6%, when men with symptomatic androgen deficiency are considered. Data from physician's clinical practices, however, revealed a higher prevalence of hypogonadism, in the range of 36-39%.

Using strict criteria for hypogonadism, a total testosterone (T) < 8 nmol/L (< 230 ng/dl), the incidence of hypogonadism in men with MetS was 11.9% versus 3.8% in people without MetS. MetS and sexual dysfunction are inter-related with each other as the risk factors are similar in both entities. The exact pathophysiologial link is still unclear and needs further research to understand the mechanism. Both conditions not only lead to medical related consequences/morbidity but also have their psychosocial impact. MetS has been shown to have a negative impact on male sexual function through its relationship with cardiovascular disease risk, its association with hypogonadism and psychosocial factors.

The association between hypogonadism and MetS is beyond any reasonable doubt now. However, the cause and effect relation remains a subject of further study. It is becoming clear that the relationship in both ways i.e. low levels of T predispose to visceral obesity and IR and visceral adiposity suppresses the production of T, therefore, establishing a vicious cycle.

Micropenis in this case suggests intra-uterine onset of hypogonadism, in all probability due to inappropriately low levels of gonadotrophins or hypothalamic dysfunction. This may have set him up for future obesity/MetS as he grew older. Low T and low sex hormone binding globulin (SHBG) levels are risk factors for MetS, as evident in the study showing remarkable increase in visceral obesity after inducing experimental hypogonadotrophic hypogonadism.

Moreover, the adipocyte functions as an endocrine cell, producing and secreting adipocytokines/adipokines of which leptin is a prominent member. Hyperinsulinaemia as encountered in IR, might impair T secretion by the Leydig cells directly, as there are insulin receptors on the Leydig cells.

Extreme gynaecomastia with activated areolar nipple complex to the state of pregnant female defied explanation. It can be postulated that the combined effect of low androgen level and relatively high estrogen levels, as a consequence of the huge adipose pool, which is a factory for synthesis of estrogenic steroids, may be responsible for his gross gynaecomastia.

It may be postulated that partial hypogonadotrophic hypogonadism in this patient may be because of hypothalamic dysfunction/ pituitary gonadotroph inadequacy starting during intrauterine life. Morbid obesity may also be due to hypothalamic dysfunction in addition to hypogonadism and the positive family history of type 2 DM, which predisposes him to MetS. Profound gynaecomastia with pregnancy-like state of Nipple-areolar complex is perplexing.

**REFERENCES**


