

An unusual case of erectile dysfunction with high total testosterone levels

A Sharma¹, M Siddiqui¹, K Steer¹, A Qureshi¹

¹Department of Endocrinology, Northwick Park Hospital, London North West Healthcare NHS Trust

INTRODUCTION

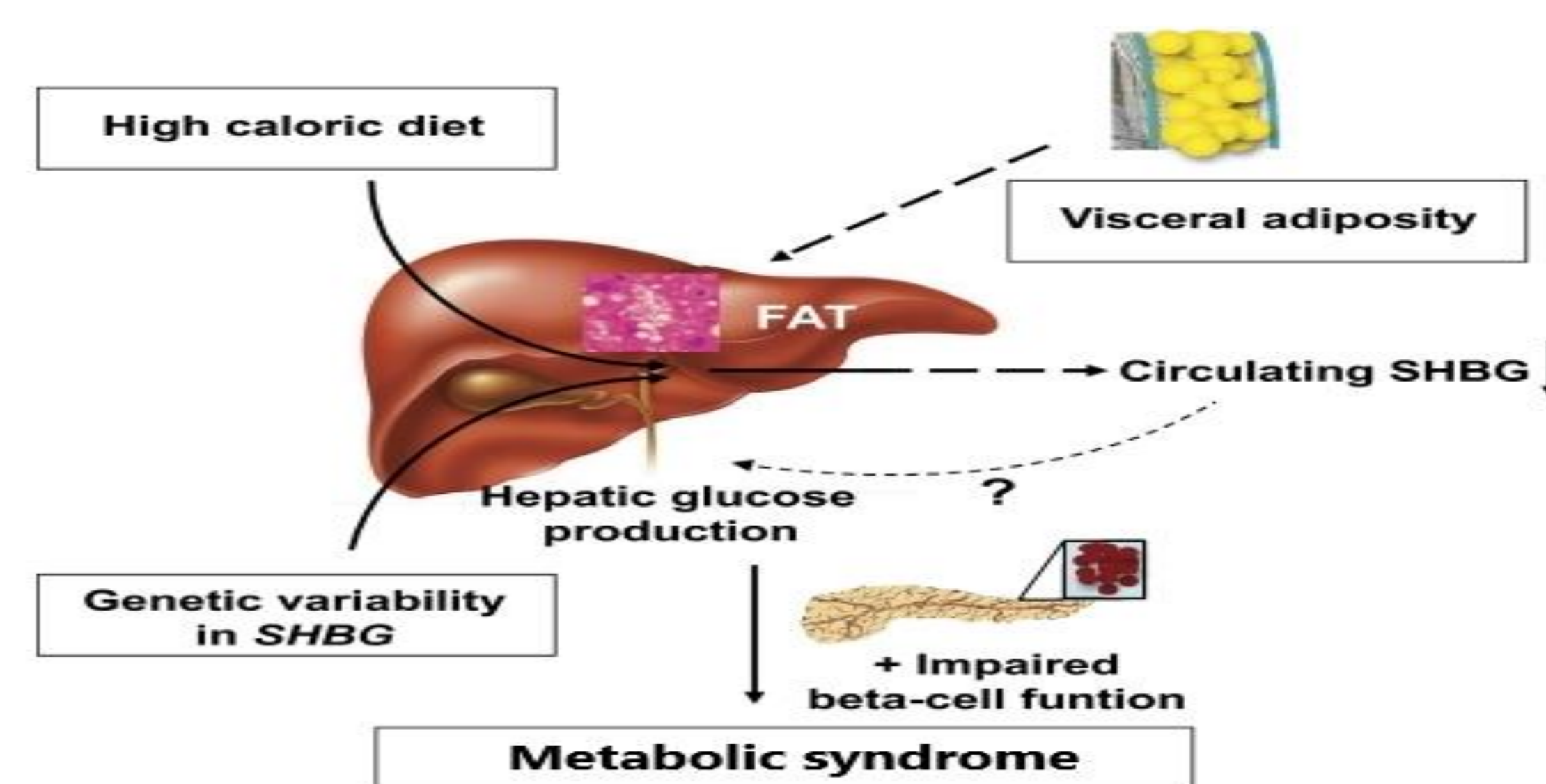
- 1 in 10 men in the world are thought to suffer from erectile dysfunction (ED).
- ED is common among men with an elevated body mass index (BMI).
- The pathophysiology of ED in high BMI is not fully understood, and is considered to be a result of vascular dysfunction and infrequently low bioavailable testosterone.
- Sex hormone binding globulin (SHBG) is expressed in the human liver under the control of hormones and nutritional factors.
- Obesity is characterized by a reduction in serum total testosterone concentration but a normal serum free testosterone concentration due to decreased SHBG.
- Non-alcoholic fatty liver disease and dysmetabolic iron overload syndrome have been shown to be associated with raised SHBG levels¹.

CASE PRESENTATION

- 56 year old Caucasian gentleman was referred to our endocrine clinic with erectile dysfunction and markedly raised testosterone levels.
 - He was noted to be hypertensive with a high BMI of 30 kg/m².
 - He denied using anabolic steroids or other supplements.
 - There were no other features of hypogonadism or pituitary disease. There was no history of diabetes. His recent HbA1c was normal.
 - He was drinking 20 - 25 units of alcohol per week and was a nonsmoker. Interestingly he also appeared to be a bit tanned having last been on holidays a few months ago.
 - In view of elevated hemoglobin level, iron indices and deranged liver functions, he was investigated by haematologists for hereditary haemochromatosis.
 - HFE genetic screen and JAK-2 mutation were negative.
 - He had one unit of venesection.
 - Ultrasound of the abdomen organised by gastroenterologists showed fatty liver and mild splenomegaly.
 - The viral serology, chronic liver disease and autoimmune screens were all negative.
 - Repeat endocrine testing showed similar results.
- **The elevated sex hormone binding globulin is thought to be secondary to nonalcoholic fatty liver disease which in turn, is responsible for raised total testosterone levels. This may also explain the elevated iron indices and deranged liver function tests.**

INVESTIGATIONS

Endocrine testing		
Testosterone (MS) 62.5 nmol/L (9.2 – 55.8)	Sex hormone binding globulin 193 nmol/L (16 – 55)	Free Testosterone 0.387 nmol/L Bioavailable Testosterone 9.08 nmol/L
FSH 6.4 IU/L (1.5 – 12.4)	LH 10.0 IU/L (1.7 – 8.6)	Prolactin 298 mIU/L (86 – 324)
TSH 1.68 mIU/L (0.27 – 4.20)	Free T4 11.2 pmol/L (12.0 – 22.0)	IGF-1 7.4 nmol/L (11.8 – 29.3)
Short Synacthen Test : normal		MRI Pituitary: normal
Iron studies		
Ferritin 1128 ug/L (30 – 400)	Transferrin Sat 86% (20 – 45)	Iron 44 umol/L (6 – 35)
Other results		
Hb 176 g/L (130 – 170)	Gamma GT 167 IU/L (10 – 71)	Bilirubin 27 umol/L (0 – 21)
PCV 49% (37 – 50%)		



Hypothetical picture regarding cause and metabolic consequences of circulating SHBG in humans

DISCUSSION

- Considering our patient's high BMI and features of metabolic syndrome, the elevated SHBG levels with high total testosterone levels are **unusual**.
- We think the hyperferritinemia and raised SHBG could be due to the underlying fatty liver disease and alcohol excess.
- Both metabolic syndrome and liver iron overload have been implicated in moderate hypogonadotropic hypogonadism. However the high total and normal free testosterone levels with normal gonadotrophins in our patient precludes it as the cause of his erectile dysfunction.
- Emerging evidence suggests that liver fat content rather than BMI is a strong determinant of circulating SHBG.
- The effect of mild to moderate iron overload on gonadal axis and sexual function has not been studied thoroughly at cellular level.

References:

- [1] Gautier A, et al. Liver iron overload is associated with elevated SHBG concentration and moderate hypogonadotropic hypogonadism in dysmetabolic men without genetic haemochromatosis. *Eur J Endocrinol.* 2011 Aug;165(2):339-43.
- [2] Peter A, et al. Relationships of circulating sex hormone-binding globulin with metabolic traits in humans. *Diabetes.* 2010 Dec;59(12):3167-73.
- [3] Simó R, et al. Novel insights in SHBG regulation and clinical implications. *Trends Endocrinol Metab.* 2015 Jul;26(7):376-83.