

## Case Report

# The Case of Symptomatic Hypogonadism-Myth or Reality

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John Foster, a 59 year old Caucasian male and highly successful businessman, was sitting in his home office one afternoon in late September 2012 when he developed a rapid heartbeat. Waiting to see if it would stop, he noted it to be in the range of 150 beats per minute. He decided to go to the emergency room in his local town but the tachycardia abated prior to his getting out of his car. He also at the same time began having increased anxiety. While shopping at the local grocery store, he had his blood pressure checked via an automated machine. It was noted to be in the 160/100 range. His average pressure had been in the 130-140/85-90 range in the past. Being stunned by the very high blood pressure but also having a history of Hypertension and taking Amlodipine 10 mg and Losartan Potassium 100 mg daily, he saw his Cardiologist and had an Echocardiogram and Treadmill evaluation. He was told that his evaluation was within normal limits. Incidentally, he mentioned that he had been having palpitations and the Cardiologist inquired about whether he had had a recent testosterone level, indicating that a low testosterone level might precipitate Atrial Fibrillation. Dr. Foster also told his Cardiologist about the tachycardia. His Cardiologist advised him that if it happened again, to seek emergency room evaluation and return for Holter monitoring.

About a month later, Mr. Foster began having symptoms of anorexia and then developed weight loss of 25 lbs over the several month periods through Dec 2012. He also began to experience palpitations on a daily and hourly basis. Mr. Foster began to experience severe insomnia in late December and severe agitation and anxiety during the day. Mr. Foster sought the help of a Psychiatrist and was diagnosed as having Major Depression. He developed severe anhedonia and would not leave the house. Mr. Foster had to take several months of annual leave as he became gravely disabled. During this period, he had a trial of several antidepressants, including the combination of Cymbalta (duloxetine) 90 mg, Trazadone 150 mg and Remeron (mirtazepine) 45 mg, and of which none of them relieved his symptoms.

Mr. Foster's other past history included BPH and Hyperlipidemia for which he took Tamulsin .4 mg in the am, Lipitor 10 mg (atorvastatin) at bedtime, and Niacin 500 mg slow release with a baby aspirin at bedtime

When asked about any stressors by his psychiatrist, he indicated that he had "significantly slowed down" his business

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activities in May 2012, as the business had become unmanageable, especially with not being able to "get good help".

Mr. Foster saw his Urologist in October of 2012 for a routine visit and was told that his prostate was relatively small (40 grams) and a post void residual performed in the office yielded only 63 cc of urine. His testes were noted to be small in the range of 10 ml. Mr. Foster shared his recent laboratory tests which had been ordered by his family physician with the urologist at that time which included a free and total testosterone and PSA level. The total and free testosterone levels were noted to be 259 (range of 348-1197) and 4.7 (normal range of 6.6-18.1). He asked the Urologist if the low testosterone levels could be associated with Depression and the "Male Menopause" as he had researched the topic online extensively. The Urologist indicated that low levels of that degree were not unusual and that he had treated hundreds of patients with low T levels with various forms of testosterone but he had not encountered the Syndrome of the Male Menopause or Severe Depression in any of his patients.

Mr. Foster's depressive symptoms continued through mid-2013. During this time, his psychiatrist continued to prescribe various anti-depressants including Lithium 600 mg at bedtime and Bupropion 300 mg in the am (May 1-June 30).

Desperate for additional help for relief of his symptoms in mid-June, he was referred by his family physician to an Endocrinologist who performed additional testing including an FSH (follicle stimulating hormone), LH (luteinizing hormone) and Prolactin level. Mr. Foster's FSH and LH were noted to be very high while his Prolactin level was noted to be normal. The urologist prescribed Testosterone injection, starting at 100 mg weekly. Over the next several weeks and months, Mr. Foster began to notice improvement in his appetite and had significant weight gain. His free and total testosterone levels normalized as well. He also developed improvement in his symptoms of Depression and Anxiety and sleep patterns. Mr. Foster returned to work and his blood pressure also normalized to the 130/70 range.

It is noteworthy to mention that various studies, though not conclusive, have indicated that statin use, especially those lipophilic (that cross the blood brain barrier) may be associated with Depression as well as cognitive deficits. Lipophilic statins include atorvastatin while those relatively lipophilic include simvastatin, lovastatin and fluvastatin. Those considered to be highly hydrophilic include pravastatin and rosuvastatin. As an added precaution, Mr. Foster's family physician switched his atorvastatin (Lipitor 10 mg) to Pravastatin 20 mg at bedtime [1,2].

It is important to differentiate low T Syndrome from symptomatic Hypogonadism in clinical practice. There has been a recent barrage of topical testosterone preparations that have entered the market in the last several years and through direct consumer advertising for low T Syndrome, touting their indication for fatigue and decreased well-being and libido and with the recommendation that testosterone levels be checked prior to administration and during therapy. Thus, physicians have seen a significant number of men requesting these agents. This becomes complicated by the fact that these agents are controlled drugs [3].

There is significantly controversy about whether the Male Menopause or Andropause is myth or reality. In contrast to the female perimenopause or menopause, the signs and symptoms may be less well defined and vague especially since men do not go through a defined phase like women. Rather than referring to it as the Male Menopause, some doctors refer to the problem as a decline in testosterone with aging. With aging, some men do report symptoms of fatigue, weakness, depression and sexual problems [4].

Whether the Male Menopause or Andropause is myth or reality, Metabolic Syndrome, associated with insulin resistance, hyperglycemia, hypertension, low high-density lipoprotein cholesterol, increased very low-density-lipoprotein and triglyceride levels has been shown to be associated with low testosterone levels according to several studies. In addition, testosterone replacement therapy improves various metabolic and anthropometric parameters of Metabolic Syndrome. Patients with various cancers treated with androgen deprivation therapy have also been shown to have a higher incidence of Metabolic Syndrome [5].

There are conflicting studies regarding the use of testosterone in older men and cardiovascular outcomes. One study involving 3690 community-dwelling men aged 70-89 years indicated that those with mid-range testosterone and dihydrotestosterone (DHT) levels had the lowest all-cause mortality and those with higher DHT levels had lower mortality from ischemic heart disease [6]. However, another study indicated that testosterone therapy was associated with a greater risk of cardiovascular outcomes (stroke or myocardial infarction) than non-users in a large observational study [7]. Yet another study indicates that low free testosterone predicts mortality from cardiovascular disease but is not associated with death from other causes and that prevention of androgen deficiency might improve cardiovascular outcomes but is unlikely to affect longevity otherwise [8]. Low

testosterone levels may also be associated with narcotic use, obesity or hyperinsulinemia as well as with Sleep Apnea [3].

In males with symptoms of Hypogonadism associated with a low testosterone level, an adequate workup is essential. This workup should include distinguishing secondary from primary hypogonadism starting with a history and physical examination documenting small gonads as well as performance of additional laboratory testing to include FSH, LH, Prolactin and free and serum testosterone levels. With a low free and total testosterone level, primary testicular failure or primary hypogonadism would be associated with a high FSH and LH. Secondary hypogonadism is associated with a low or inappropriately normal LH and FSH and may be due to a pituitary tumor associated with a high Prolactin level. In the latter case, pituitary magnetic resonance image and referral to an Endocrinologist should be performed [3].

Administration of testosterone (TRT-testosterone replacement therapy) may be associated with significant elevations of the serum prostate specific antigen level, for which evaluation including prostate biopsy with guided ultrasound may be necessary to rule out prostate carcinoma though PSA elevations may also be due to prostatitis or Benign Prostatic Hyperplasia. Therefore, regular monitoring of the testosterone level and PSA are recommended while on testosterone replacement therapy [9]. Though TRT is an absolute contraindication in the presence of prostate cancer, there is no definite correlation between testosterone administration and the initiation of prostate cancer [10]. Regardless of myth or reality, testosterone administration is associated with well documented benefits to bone, sexual health and well-being. Serious side effects include gynecomastia, abnormal liver function, hepatic tumors, and polycythemia (especially the parental formulation) [3].

Though Depression has been associated with the Male Menopause, significant stressors play a role in the development as do other factors such as increasing age and a family history or history of depression. Attention to proper diet, exercise, social activities, and even meditation are essential to management of Depression [11].

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