Words of Wisdom Re: the relationship between premature ejaculation and hyperthyroidism.

Re: The Relationship Between Premature Ejaculation and Hyperthyroidism

Cihan A, Demir O, Demir T, Aslan G, Comlekci A, Esen A.

J Urol. 2009;181:1273–80

Expert's summary:

Cihan and coworkers studied the prevalence and characteristics of premature ejaculation (PE) in a single-center prospective study in a small Turkish population of hyperthyroid subjects ($n = 43$; 40% with Graves-Basedow disease, the rest of the sample with toxic nodules). PE was defined according to *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* criteria along with patient-reported outcome and stopwatch measurement of intravaginal ejaculation latency time (IELT; PE: IELT of <1 min). PE was observed in 31 (72%) hyperthyroid subjects. There was a positive correlation between thyroid-stimulating hormone (TSH) and IELT. After 2 mo of high-dose medical therapy, subjects were enrolled in continuing medical therapy ($n = 10$) or had definitive treatment with surgery ($n = 7$) or radioactive iodine ($n = 7$). Achieving euthyroidism at follow-up (24 patients), regardless of therapeutic intervention, increased mean IELT by a factor of 2 in the total population or by a factor of 3 in the PE population. Beck anxiety scores and International Index of Erectile Function also significantly improved in the euthyroid state. The authors conclude that hyperthyroidism should be considered a novel and reversible etiological risk factor for PE.

Expert's comments:

Although both PE and hyperthyroidism are relatively common conditions, their association has not been systematically studied until recently. In a consecutive series of 755 men presenting with sexual dysfunction, a 2-fold greater prevalence of hyperthyroidism was evident among men with PE [1]. According to this finding, Carani et al [2] demonstrated in a small, multicenter, prospective study that most (50%) hyperthyroid patients have PE. This prevalence was substantially reduced (15%) by treating the underlying disease, with a consequent doubling of ejaculatory latency. In Cihan et al as well as in Corona et al [1], a role for hyperthyroidism-induced anxiety was also suggested as a cause for PE; however, at multivariate analysis, even after adjusting for anxiety, low TSH was independently predictive of PE [1]. Inducing an experimental hyperthyroidism in male rats was associated with enhanced seminal vesicle contraction and activity of bulbospongious muscle [3]. These findings suggest a direct role for thyroid hormones in decreasing ejaculation latency that is independent from hyperthyroidism-induced anxiety. Furthermore, Carani et al [2] showed that medical treatment of the opposite state, hypothyroidism, resulted in a 2-fold decrease in ejaculatory latency and a reduction in delayed ejaculation. Hence, the view that thyroid hormones regulate not only the ankle reflex but also the ejaculatory reflex is consistently emerging [4].

Conflicts of interest: The author has nothing to disclose.

References

[1] Corona G, et al. Eur Urol 2004;46:615–22.
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[4] Donatucci CF. J Sex Med 2006;3(Suppl 4):303–8.

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Re: Aberrant ERG Expression Cooperates with Loss of PTEN to Promote Cancer Progression in the Prostate

Carver BS, Tran J, Gopalan A, et al.

Nat Genet 2009;41:619–24

Expert's summary:

The authors investigated the functional consequences of Ets-related gene (ERG) rearrangement and overexpression and its association with phosphatase and tensin homolog (PTEN) loss in prostate cancer (PCa). *PTEN* was lost in 14 of 15 *ERG*-rearranged samples but was lost in only 13 of 25 nonrearranged samples, suggesting that *PTEN* loss and *ERG* genetic rearrangements are concomitant events in PCa. Mouse experiments showed that combined *ERG* overexpression and *PTEN* haploinsufficiency lead to accelerated development of high-grade prostatic intraepithelial neoplasia (HGPIN) and subsequent progression to multifocal, invasive PCa. In contrast, *ERG* overexpression alone had no effect in mice with normal *PTEN* status. Functional experiments revealed that *ERG* overexpression increases cell migration through upregulation of the two genes chemokine (C-X-C motif) receptor 4 (CXCR4) and ADAM metallopeptidase with thrombospondin type 1 motif, 1 (ADAMTS1), while *PTEN* haploinsufficiency is known to promote cell proliferation through activation of protein kinase B (Akt). The authors concluded that *ERG* rearrangements and *PTEN* loss are frequent concomitant events in PCa, and that this cooperation promotes progression of HGPIN to invasive cancer.

Expert's comments:

This work continues the exciting story of transmembrane protease, serine 2 (TMPRSS2)–*ERG* rearrangement in PCa [1]. The *TMPRSS2-ERG* gene fusion prevails in almost 50% of PCa and leads to *ERG* overexpression through activation of the androgen receptor–regulated gene promoter of *TMPRSS2*. Despite the high prevalence of *TMPRSS2-ERG* rearrangement, its biological role has remained unclear. In accordance with