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Letter to the Editor

Androgen Deprivation Therapy: Parallels in the Treatment of Prostate Cancer and Pedophilia

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DEAR EDITOR,

Chemical castration has been used to treat male pedophiliacs in conjunction with psychotherapy with some success [1-5]. The underlying neuroendocrine mechanism for this treatment is to lower testosterone or it's efficacy on the higher behavioral centers that drive sexual behaviors [3]. The recent discoveries in the chemotherapy of prostate cancer may allow us to be able to utilize these paradigms in treating male pedophiliacs. A review of these agents and their mechanism of action will possibly pave the way for future treatment of pedophiliacs.

There are three possible mechanisms for lowering testosterone and/or its efficacy in the treatment of prostate cancer: surgical castration, agonists or antagonists of testosterone, or receptor blockade of testosterone. These treatments have been referred to as androgen deprivation therapy (ADT). In this paper the parallels between treating prostate cancer and treating male pedophiliacs will be pointed out and hopefully will direct the future use of these agents as ADT for pedophilia.

Surgical castration was the first attempt at ADT and was the only treatment for prostate cancer for years [6]. Leuprolide has been the gold standard for chemically reducing testosterone levels to castration levels. Chemical castration is effectively achieved by Leuprolide for both prostate cancer and male pedophilia [1,5]. Leuprolide has the deleterious effect of an initial rise in testosterone and delayed suppression of testosterone of up to weeks [7]. This initial rise in testosterone could have negative effects on sexual behavior in pedophiliacs by increasing sexual drive. Leuprolide suppresses testosterone by an ultimate decrease in pituitary luteinizing hormone (LH) release via a decrease in hypothalamic gonadotropic-releasing hormone (GnRH). Leuprolide does not fully decrease pituitary follicle stimulating hormone (FSH). The role of lowered FSH in chemical castration is unclear. To date, Leuprolide is a common ADT agent used to treat sexual offenders including pedophiles.

Degarelix is becoming the gold standard for antagonistic treatment for prostate cancer [8]. Degarelix was first theorized to be effective in paraphilias by Sorrentino in 2011 [9] and subsequently proven to be effective by Landgren et al in 2020 [10]. Degarelix antagonizes GnRH at the pituitary level resulting in a prompt decrease in LH and subsequent gonadal testosterone without a surge in testosterone. Degarelix also inhibits pituitary FSH [10]. A drawback to Degarelix is that it must be administered subcutaneously. Relugolix is a new oral anti-GnRH that has shown early promise in the treatment of advanced prostate cancer with the added benefit of a reduction in major adverse cardiovascular effects [11]. Relugolix acts similarly to Degarelix at the hypothalamic-pituitary-gonadal axis but has not yet been studied as a chemical castration treatment in pedophiliacs. Oral Relugolix may very well be the next ADT for pedophiliacs given its effectiveness in lowering both LH and FSH and subsequent testosterone, oral administration, and its reduction in cardiovascular morbidity.

Androgen receptor blockade has now been shown to be an effective ADT in the treatment of castration-resistant prostate cancer (CRPC). Many prostate cancers become resistant over time to lowered testosterone levels and progress as CRPC. Much like antibiotic resistant bacteria the prostate cancer cells adapt their receptors to survive in an androgen deprived environment [12]. Consequently, ADT with lowering testosterone over time, usually two to three years, loses its effectiveness in treating prostate cancer and subsequently androgen receptor blockade is added to the chemotherapy regimen. Biclutamide and flutamide, both androgen receptor blockers, have been used with some success to help solve this problem in CRPC [13]. Aplutamide and enzalutamide are newer blockers that show some promise in combating CRPC [14]. These are added to androgen suppression therapy in CRCP.

Drug repurposing is using a drug that has been proven effective for one disease, e.g. prostate cancer, for another, e.g. pedophilia. A common denominator for prostate cancer growth and pedophilic behavior is testosterone. The goal of treatment between prostate cancer and pedophilia is to lower testosterone or it's efficacy. A prominent side effect of ADT treatment in males is a diminution of sex drive which speaks to the ability of these agents to cross the blood brain barrier [15,16]. Presumably receptors in the brain which modulate sexual behavior can also be down regulated in the same manner that prostate cancer cells can be with ADT. The importance of this is that it is tempting to speculate that the regrowth of prostate cancer cells after two

or three years of lowered testosterone efficacy may mimic the recidivism seen in some pedophiliacs after ADT over time. If this is true, and it certainly seems plausible, then addition of androgen receptor blockade may help prevent or reduce this recidivism in pedophiliacs as it does in prostate cancer.

There is very little new research addressing the treatment of pedophilia with chemical castration for a number of socioeconomic and ethical reasons especially in the United States. Drug repurposing might allow psychiatrists to benefit from the burgeoning research that is being carried out in the prevention or reduction of prostate cancer. This has already been shown with Degarelix that successfully has been used to treat prostate cancer [17] and also shown to reduce or delay the sexual behavior of pedophiliacs [10]. ADT combined with psychotherapy may well be the future of treating this very difficult group of patients known as pedophiliacs. Treatment of prostate cancers may give physicians who treat pedophiliacs a ray of hope that this treatment may add to our scant armamentarium in treating pedophiliacs in the very near future.

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