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Original Research

Unforeseen ethical challenges for isotretinoin treatment in transgender patients

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Case scenario

A 28-year-old male-appearing patient comes into Dr. Miller's dermatology clinic for the first time. The patient reveals that he is here for the evaluation of severe acne. Dr. Miller soon learns that the patient is a transgender man and has been receiving hormone replacement therapy for the past year. He is on a regimen of weekly self-administered 100 mg intramuscular testosterone enthanate injections, and he has had no menses since shortly after beginning testosterone. His testosterone levels have remained in a normal male range. The patient is not on any other medications and has not had any procedural interventions for his transition. He is sexually active with a female partner. He has had his gender markers legally changed to male on his driver's license and in his medical record. After a long history of moderate acne, the patient states that his acne became severe shortly after initiating testosterone. Dr. Miller examines him and finds severe nodulocystic acne with areas of postinflammatory hyperpigmentation and scarring distributed over his face and back. The patient has been on a regimen of a topical retinoid and oral doxycycline for the past 3 months without any relief and is requesting oral isotretinoin. Dr. Miller is unsure of how to proceed because the patient's acne could possibly be improved if he stops taking his testosterone injections. She is also unsure of what sex to assign the patient when enrolling in iPLEDGE.

Dr. Miller should:

A. Agree to start the patient on oral isotretinoin only if the patient stops taking supplemental testosterone and his severe acne remains.
B. Agree to start the patient on oral isotretinoin and register the patient as a female of childbearing potential.
C. Agree to start the patient on oral isotretinoin and register the patient as a female of nonchildbearing potential.
D. Agree to start the patient on oral isotretinoin and register the patient as a male.

Discussion

Transgender medicine is an emerging field of health care that continues to make ground in public awareness, especially in the context of the recent media spotlight on many transgender individuals, such as the actress Laverne Cox and the athlete Caitlyn Jenner. Despite these gains, much work needs to be accomplished in order to provide transgender people with adequate access to care. Reports have shown that almost 90% of transgender patients feel that their health care professionals lack adequate knowledge and sensitivity to their medical needs. Additionally, a majority of patients feel that they have been discriminated against in the health care setting because

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of their transgender status (Lambda Legal, 2010). While taking care of transgender patients, physicians will be faced with many unforeseen challenges, one of which is presented in our case.

There are several ethical points to consider in this case scenario. With regard to the patient, the physician has an obligation to honor the patient's gender transition but also an obligation to act in a nonmaleficent way. iPLEDGE providers also have a contractual obligation with the iPLEDGE program and must honor this. If a physician decides to register a transgender male patient as female, the physician must determine whether the patient fits the definition of a female of childbearing potential, which iPLEDGE defines as "a nonmenopausal female who has not had a hysterectomy, bilateral oophorectomy, or medically documented ovarian failure" (iPLEDGE program, 2015). iPLEDGE recommends a particular panel of blood work for patients under age 54 to support a finding of hormonal deficiency (iPLEDGE program, 2015). Yet, the results they stipulate only apply to women with premature ovarian failure. These tests would have different results in a transgender man on testosterone therapy and could not reliably be used to determine if he is anovulatory. However, the potential for pregnancy for female-to-male transgender patients on testosterone is extremely low, as testosterone is known to suppress ovulation, in addition to impairing fertility in other ways (Hembree et al., 2009).

Currently, there is not a transgender male category in iPLEDGE, though perhaps an adjustment of the current categorizations is needed to more accurately serve transgender patients, while respecting iPLEDGE (Katz, 2016). We present the analysis of the case scenario later in the context of the current gender system in order to guide clinicians under present restrictions.

How should Dr. Miller proceed in order to respect the patient's wishes and transgender status yet honor her contractual obligation to iPLEDGE?

Analysis of case scenario

In option 1, the physician correctly identifies the patient's acne as most likely exacerbated by supplemental testosterone. The clinician provides the patient the option of initiating isotretinoin therapy but at the expense of discontinuing hormone replacement therapy. Some physicians might assume that this option would adhere to the tenet of nonmaleficence by avoiding treating a medication-exacerbated problem with another medication, which could cause potential harm to the patient. However, nonmaleficence is also important in the sense of avoiding psychological harm to the patient caused by stopping testosterone. Furthermore, since gender identity is a durable biological phenomenon (Saraswat et al., 2015), supplemental testosterone should be viewed as a necessary, vital medication for transgender men. Reports have shown that helping transgender patients transition, such as through hormone replacement therapy, dramatically improves quality of life and can significantly reduce attempts of suicide (Gorin-Lazard et al., 2012; Lambda Legal, 2010). Removing testosterone therefore would disrespect the dignity of the patient's medical needs to maintain his transition. Additionally, the patient should have the autonomy to choose to both stay on testosterone and begin isotretinoin, if the patient is well-informed of the risks and benefits of taking both medications simultaneously. Finally, under the tenet of beneficence, it is in the patient's best interest to both aggressively treat his acne and to continue hormone therapy.

For options 2, 3, and 4, there are two points to consider: the sex to assign the patient for the purposes of enrolling in iPLEDGE and, if female, whether to register as childbearing or nonchildbearing potential. Our patient has not undergone cross-gender genital surgery and so is still in possession of ovaries and a uterus. In the current system, he would need to be registered as female. Here the patient's dignity to be registered as a male is outweighed by his potential to become pregnant while on isotretinoin. While the patient is likely anovulatory as a result of testosterone, there is no way to be certain of this, and if he were to stop taking testosterone, his fertility could return. For these reasons, the tenet of nonmaleficence dictates that he should be registered as a female of childbearing potential in order to best protect against potential pregnancy. Thus, the current gender categorization in iPLEDGE necessitates an empathic discussion with the patient regarding system requirements and limitations, which can help preserve the dignity of the patient's identified gender.

The patient in our case scenario could claim abstinence as one of his contraceptive methods if he refrains from having intercourse with men. However, if he does begin to have intercourse with men while receiving treatment, an additional form of contraception should be considered since we are currently not equipped to determine whether a transgender man on testosterone therapy has zero potential to ovulate. This may compromise the patient's dignity at the expense of the tenet of beneficence, which dictates that the best interest of the patient is to legally adhere to iPLEDGE in order to be able to treat his severe acne with isotretinoin. In the future, though, if testosterone therapy is determined to have comparable pregnancy prevention effects to that of current hormonal contraception, testosterone therapy could be considered a method of contraception. Finally, the patient will also need to undergo monthly pregnancy tests, but this can be performed through blood tests, along with his other routine isotretinoin-related blood work in order to respect the patient's dignity and to minimize the potential negative psychological effects associated with taking a urine pregnancy test.

Conclusion

Transgender individuals have unique medical needs that will surely lead to many unforeseen medical and ethical dilemmas as these patients become more visible in the increasingly diverse medical environment. Many of these dilemmas center around the patient's stage with regard to his or her transition, such as is the case for our patient. Physicians must consider whether the patient has undergone transgender genital surgery, the sex of the patient's partner with regard to contraceptive recommendations, and the patient's hormone replacement therapy regimen.

Despite the aforementioned complexities, transgender patients' gender identities and autonomy to transition should be respected. For our patient, even though his current complaint is presumably exacerbated by a medication for his transition, there is no need for Dr. Miller to take him off testosterone. It is acceptable to start him on oral isotretinoin. Dr. Miller must register the patient as female of childbearing potential based on the current gender categorization scheme in iPLEDGE.

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