FERTILITY AND STERILITY®
VOL. 79, SUPPL. 3, JUNE 2003

Published by Elsevier Inc.
Printed on acid-free paper in U.S.A.

Successful treatment of anabolic steroid–induced azoospermia with human chorionic gonadotropin and human menopausal gonadotropin

Dev Kumar Menon, M.D.

Department of Obstetrics and Gynecology, University Malaya Medical Centre, Kuala Lumpur, Malaysia

Objective: To document for the first time the successful treatment using human chorionic gonadotropin (hCG) and human menopausal gonadotropins (hMG) of anabolic steroid–induced azoospermia that was persistent despite 1 year of cessation from steroid use.

Design: Clinical case report.

Setting: Tertiary referral center for infertility.

Patient(s): A married couple with primary subfertility secondary to azoospermia and male hypogonadotropic hypogonadism. The husband was a bodybuilder who admitted to have used the anabolic steroids testosterone cypionate, methandrostenolone, oxandrolone, testosterone propionate, oxymetholone, nandrolone decanoate, and methenolone enanthate.

Intervention(s): Twice-weekly injections of 10,000 IU of hCG (Profasi; Serono) and daily injections of 75 IU of hMG (Humegon; Organon) for 3 months.

Main Outcome Measure(s): Semen analyses, pregnancy.

Result(s): Semen analyses returned to normal after 3 months of treatment. The couple conceived spontaneously 7 months later.

Conclusion(s): Steroid-induced azoospermia that is persistent after cessation of steroid use can be treated successfully with hCG and hMG. (Fertil Steril® 2003;79(Suppl 3):1659–61. ©2003 by American Society for Reproductive Medicine.)

Key Words: Anabolic steroid, azoospermia, human chorionic gonadotropin, human menopausal gonadotropin

Anabolic steroid abuse among professional athletes is especially common among body builders and power lifters. Anabolic steroids have been shown to increase lean muscle mass while suppressing the hypothalamic-pituitary-gonadal axis (1). Hypogonadotropic hypogonadism and oligospermia or azoospermia are common consequences of this suppression (2).

The exact drug combinations and dosages employed by such athletes have not been recorded in the medical literature. We were fortunate to encounter a patient who could describe his drug usage in detail. His endocrine suppression was atypical because it did not resolve spontaneously after stopping the steroids. We successfully treated him using an aggressive combination of both human chorionic gonadotropin (hCG) and human menopausal gonadotropin (hMG).

This is the first report to document the use of hCG and hMG to treat a patient in whom endocrine function failed to return despite 1 year of abstinence from steroid use.

CASE REPORT

A 27-year-old woman was referred by her general practitioner because of a 1-year history of primary subfertility. Her 37-year-old husband, who worked as a security guard, was an amateur bodybuilder and had been lifting weights regularly for the past 20 years. He had taken part in several regional level bodybuilding competitions. He admitted starting to use anabolic steroids to enhance his muscle mass

Received June 25, 2001; revised and accepted January 3, 2003.
Reprint requests: Dev Kumar Menon, M.D., Department of Obstetrics and Gynecology, University Malaya Medical Center, 50603, Kuala Lumpur, Malaysia (FAX: 603-79551747; E-mail: drmenon2000@yahoo.co.uk).

0015-0282/03/$30.00
doi:10.1016/S0015-0282(03)00365-0

and strength 10 years previously. In this time he had used more than seven different types of steroid, all of which he obtained illegally.

He explained that he used steroid combinations for usually a few months before taking a short break and then commencing another course of steroids. The longest sustained course he took was for 8 months when he took twice weekly injections of testosterone cypionate (amounting to 1 gram per week) combined with both daily Dianabol tablets (methandrostenolone; he started on 10 mg/day and then increased the dose to 60 mg/day) and daily Anavar tablets (oxandrolone at 20 mg/day). He admitted to also using Sustanon injections (testosterone propionate), Anadrol tablets (oxymetholone), Deca-Durabolin injections (nandrolone decanoate), and Primobolan Depot injections (methenolone enanthate).

During this period of time he had noticed a marked testicular atrophy as well as some erectile dysfunction (he described only partial erections which were difficult to maintain). He had not been on any medication in the past 1 year, had no other past medical history of note, and did not smoke or drink alcohol. On examination his skeletal muscle mass was found to be greatly increased. His secondary sexual characteristics were normal, although he had demonstrable gynecomastia. His testicles were of a low volume (2 to 3 mL) but were firm and nontender. There were no varicoceles present.

His serum gonadotropin and testosterone levels were low (FSH 0.5 U/L, LH 0.9 U/L, testosterone: 7 nmol/L). His serum prolactin level was normal. A urinary drug screen failed to identify any illicit substances; this was consistent with his story of having stopped taking the anabolic steroids 1 year previously when the couple decided to start a family. Three semen analyses (the third repeated 3 months after the second) showed a complete azoospermia with normal ejaculate volumes and liquefaction times.

His wife's periods were regular and she had no other significant medical history of note. Her investigations included a day-2 follicle stimulating hormone, luteinizing hormone, estradiol, prolactin and thyroid function test, a day-21 progesterone level, a hysterosalpingogram, and a transvaginal ultrasound scan; all were normal. A diagnosis was made of anabolic steroid–induced hypogonadotropic hypogonadism resulting in persistent azoospermia despite cessation of the steroids.

We provided him with injections of human chorionic gonadotropins (hCG; Profasi; Serono) three times a week at a dose of 10,000 IU together with daily injections of human menopausal gonadotropin (hMG, Humegon; Organon) at a dose of 75 IU per day. After just 1 month of this treatment there was a dramatic improvement in his semen analyses, which showed a count of 8 million sperm/mL, motility of 48%, and 60% with normal morphology. His serum gonadotropin and androgen levels were normal at this time (FSH 5 U/L, LH 8 U/L, testosterone: 21 nmol/L). We continued this regimen for 2 months more and then rechecked his semen analyses. The sperm count was 23 million sperm/mL; motility was 45%, and 50% had normal morphology. We stopped the drug regimen and rechecked his semen analyses and serum testosterone levels 3 months later. The semen analysis was normal, as were the testosterone levels.

He also described a spontaneous resolution of his erectile difficulties 2 months after commencing the treatment. There was no discernible improvement in his testicular volumes on examination. Four months later (10 months since we had begun the treatment) his partner conceived spontaneously. She then went on to deliver a healthy baby girl.

Institutional review board approval was obtained for this study.

DISCUSSION

Hypogonadism and azoospermia secondary to anabolic-androgenic steroid abuse in bodybuilders has been described as being reversible on stopping steroid use (3, 4). This case report demonstrates that exceptions do occur, and this patient in fact showed no signs of reversal of the hypogonadism despite a full 1-year of abstinence from the steroids. Tapering off the drug by using a gradual stepwise decrease in steroid dose is common practice in corticosteroid therapy. It is possible that the abrupt cessation of anabolic steroids in this patient may have contributed to the failure of normal endocrine function to return within 1 year.

The goal of treating anabolic steroid–induced azoospermia is to restore endocrine function. Endocrine medications that are targeted specifically to ameliorate hypothalamic-pituitary-gonadal function have been well described and include testosterone esters, hCG, synthetic analogues of GnRH, and antiestrogens (5). Human chorionic gonadotropin used alone has been reported to be successful in treating this group of patients (6, 7). In these cases, testicular function, once back to normal, continued even after the hCG was stopped. Although administering hMG seems appropriate given the hypogonadotropic results in this patient, it is not clear if exactly the same response could not have been achieved using hCG alone. Indeed the speed of recovery of endocrine function in our patient did not seem to be any faster than in reported cases using hCG alone (6).

There is no consensus on the ideal dosage of hCG or hMG in the treatment of this condition. We choose this dosage regimen empirically, with a mind to increase the dose further if subsequent semen analyses failed to show a response. Further study is needed to identify the optimal treatment in these patients.

Typically, bodybuilders are very reticent about the exact types and dosages of steroids used. This patient was exceptional in his willingness to provide exact details of his steroid

usage. The dosages of steroids routinely exceeded the recommended dosage maximums as described by the relevant pharmaceutical companies (e.g., Ciba recommends a maximum dose of 10 mg/day of Dianabol, but Mr. AL was consuming six times this amount). The degree of steroid usage by professional athletes (both in terms of numbers of different drugs employed as well as dosages used) is underreported in medical literature.

The patient's gynecomastia is most likely due to the aromatization of the excess androgens in his body to estrogen. This phenomenon has been described before in bodybuilders taking anabolic steroids (8). Testicular atrophy has been described in other cases of hypogonadotropic hypogonadism (9). It is interesting to note that, although appropriate functioning of the testicles resumed after 3 months of treatment, the testicular volumes did not return to a normal size.

CONCLUSION

Very little literature exists on the treatment of steroid-induced azoospermia following the cessation of abuse. It is hoped that this case report highlights the treatable nature of this condition.

References

1. Inigo MA, Arrimadas E, Arroyo D. 43 cycles of anabolic steroid treatment studied in athletes: the uses and secondary effects. Rev Clin Esp 2000;2000:133–8.
2. Torres-Calleja J, Gonzalez-Unzaga M, DeCelis-Carrillo R, Calzada-Sanchez L, Pedron N. Effect of androgenic anabolic steroids on sperm quality and serum hormone levels in adult male bodybuilders. Life Sci 2001;68:1769–74.
3. Boyadjiev NP, Georgieva KN, Massaldjieva RJ, Gueorguiev SI. Reversible hypogonadism and azoospermia as a result of anabolic-androgenic steroid use in a bodybuilder with personality disorder. A case report. J Sports Med Phys Fitness 2000;40:271–4.
4. Gazvani MR, Buckett W, Luckas MJ, Aird IA, Hipkin LJ, Lewis-Jones DI. Conservative management of azoospermia following steroid abuse. Hum Reprod 1997;12:1706–8.
5. Medras M, Tworowska U. Treatment strategies of withdrawal from long-term use of anabolic-androgenic steroids. Pol Merkuriusz Lek 2001;11:535–8.
6. Gill GV. Anabolic steroid induced hypogonadism treated with human chorionic gonadotropin. Postgrad Med J 1998;74:45–6.
7. Martikainen H, Alen M, Rahkila P, Vihko R. Testicular responsiveness to human chorionic gonadotropin during transient hypogonadotropic hypogonadism induced by androgenic/anabolic steroids in power athletes. J Steroid Biochem 1986;25:109–12.
8. Spiga L, Gorrini G, Ferraris L, Odaglia G, Frassetto G. Unilateral gynaecomastia induced by the use of anabolic steroids. A clinical case report. Minerva Med 1992;83:575–80.
9. Rodriguez de Ledesma JM, Cozar Olmo JM, Nistal Martin N, Cisneros J, Cuervo E, Martinez-Pineiro JA. Klinefelter syndrome with hypogonadotropic hypogonadism and absence of Leydig cells. Arch Esp Urol 1994;47:618–20.