

CASE REPORT

Case report: The long-term effects of anabolic steroids on the female voice over a 20-year period

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Key Clinical Message

Anabolic steroids and androgenic steroids (AAS) can have long-term effects on the female voice. These changes are clinically relevant since they are difficult to treat and therefore should be disclosed to patients using AAS or receiving androgenic steroid therapy.

KEYWORDS

anabolic steroids, androgenized voice, laryngology, testosterone insufficiency, voice

1 | INTRODUCTION

A 27-year-old female bodybuilder presented with an androgenized voice ($F_0 = 110$ Hz) after 6 weeks of androgenic anabolic steroid. She was followed for 20 years, requiring multiple surgical interventions to increase her pitch and presented with delayed severe vocal fold atrophy, with concurrent abnormal low testosterone levels.

Androgenic anabolic steroids (AAS) can have virilizing effect in women. The most common side effects include weight gain, acne, and increased libido, which are usually reversible. However, the masculinized voice change associated with AAS, including decreased pitch, reduced F_0 , and vocal fold thickening, has been reported as irreversible^{1,2} despite discontinued use.

A new entity, anabolic steroid-induced hypogonadism (ASIH), described by Jarow,⁴ suggests AAS can have an inhibitory effect on the hormonal axis long after discontinuing their use, including hypotestosteronism. Several authors have since described this condition in men,⁵ but there has been no reported case of ASIH in woman or description of vocal symptoms due to this condition.

This Case report was presented as a Poster presentation at the annual meeting of the Canadian Society of Otolaryngology—Head & Neck Surgery in June 2016, in Charlottetown, Prince-Edward-Island, Canada.

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This is a case report on the effect of AAS in a 27-year-old woman who ingested AAS when competing as a bodybuilder. This patient experienced disabling side effects due to androgenization of her voice and required surgery to increase vocal pitch in order to be identified as female. She has been followed for 20 years and experienced further unanticipated changes in vocal function many years after discontinuing anabolic steroid use, concurrently with abnormally low testosterone levels.

2 | CASE REPORT

K. A, a 27-year-old woman, formerly a bodybuilder, sought treatment at our tertiary voice center for “masculine” voice in 1998. The patient had developed a gradual husky and low-pitched voice change over a period of months, two years prior to presentation (at presentation— $VHI = 40$, $F_0 = 110$ Hz, Jitter = 0.64%, Shimmer = 2.6%, pitch range = 2 semitones). The patient was more often than not perceived as male, and the gender misidentification was disabling in her personal and professional life including the loss of employment due to her voice quality. The patient had taken nandrolone, 50 mg/wk for 6 weeks as part of a muscle enhancement bodybuilding program. The voice change developed within 8 weeks of starting the androgenic steroids, and despite discontinuing the drug, the voice did not improve. No other previous voice

issues or general health problems were reported. The patient was no longer bodybuilding and denied any other hormone replacement or medical therapy. She was fully evaluated by an endocrinologist (at presentation, normal female hormone profile) and was followed long-term by her specialist.

Videostroboscopy at initial evaluation showed thick vocal folds, with blunting of the free edge bilaterally. A dull pink color was noted throughout the full length of the membranous vocal folds. There was no glottis gap with mucosal wave present bilaterally (Figure 1). Mild aperiodicity was also noted, and the fundamental frequency (F_0) was 110 Hz, clearly in the lower range for a male and below the normal range for females.

A trial of 3 months of pitch increasing speech therapy (1998) and a type 4 thyroplasty⁶ (1999) resulted in very minimal improvement.

A novel endoscopic 1/3 anterior web creation procedure was then performed (2000)⁷ (Figure 2), resulting in an increased $F_0 = 215$ Hz with normal perturbation measures. The patient was able to return to normal premorbid vocal function and was perceived as a female with habitual voice use.

The patient had no voice complaints for ten years but returned 13 years later with new symptoms of pitch and phonation breaks, inconsistent and “weak” voice quality without change in pitch. A Voice Handicap Index-10 (VHI-10) questionnaire revealed a score of 40 (severe disability).

Videostroboscopy revealed an unchanged anterior web. However, both VF now showed marked bowing and significant spindle-shaped glottis gap with moderate aperiodicity (Figure 3).

The patient denied new medical treatment or surgery, hormone therapy, or irregular menses. Repeat hormonal serum profile ordered by her endocrinologist now showed low level of free testosterone (Table 1). At that time, she also reported symptoms of generalized fatigue. She was then started on

testosterone replacement therapy, which improved energy level without any impact on perceived voice handicap.

The patient underwent bilateral type 1 medialization thyroplasty (MT) under local anesthetic with silastic blocks to augment vocal fold mass (2015), which resulted in a significant improvement in vocal function reflected by an reduction in her VHI.

3 | DISCUSSION

The larynx and the vocal folds are often described as secondary sexual characteristic due to their distinctive role in puberty and gender identification.⁸ Many authors have studied this phenomenon by demonstrating the presence of hormonal receptors within the laryngeal tissue.^{9,10}

It is therefore not surprising that our patient developed an androgenized voice with the fundamental frequency and



FIGURE 2 Direct laryngoscopy showing an anterior web creation to create a 1/3 membranous vocal fold web using microlaryngoscopy, anterior vocal fold mucosal resection, and Gelfoam paste injection (Pfizer, Michigan)



FIGURE 1 Endoscopic evaluation of the larynx at initial presentation showing thickened, dull, pink vocal folds with blunting of the free edge bilaterally



FIGURE 3 Stroboscopic evaluation of the larynx 13 y after withdrawal from AAS showing marked bowing of the vocal fold bilaterally and spindle glottic gap

TABLE 1 Hormonal serum values for patient K.S from 2008 to 2016

Date	TSH (U/mL)	TT (nmol/L)	FT (pg/mL)	DHEA (nmol/L)	SHBG (nmol/L)	LH (U/L)	FSH (U/L)	PrL (ng/mL)
2008/02	2.71		11.0	1.8			<1	9.0
2012/06	3.52		<0.3					
2012/08			1.3					
2013/07	3.03		<0.3					
2014/01		<0.1	<0.3			6.0	6.0	5.0
2014/05		0.2						
2014/07		0.6	<0.3	4.1				
2014/08	2.87							
2014/12		0.8	<0.3					
2016/01	2.19	0.2	2.0		61.5			
2016/02		0.3	4.0		57.9			
2016/03			18					

DHEA, dehydroepiandrosterone (normal range: 1.8–7.7 nmol/L); FSH, follicular-stimulating hormone; FT, free testosterone (normal range: 0.3–6.9 pg/mL); LH, luteinizing hormone; SHBG, sex hormone-binding globulin (normal range for adult female: 20–180 nmol/L); PLC: prolactin (normal range for nonpregnant female: <26 ng/mL); TSH, thyroid-stimulating hormone (normal range: 0.3–5.0 U/mL); TT, total testosterone (normal range: <1.8 nmol/L). All values since 2008 were taken after more than 9 y of withdrawal from AAS. The year of 2012 coincides with the patient presenting back to our clinic 13 y later with vocal fold atrophy.

stroboscopic appearance of male vocal folds. Several authors have reported AAS associated dysphonia in woman but described it as irreversible changes, up to 4 years after discontinuing the drugs.^{1,2} To explain these irreversible changes, Amer and al. demonstrated structural and immunophysiological changes in an animal model after 2 months of systemic anabolic steroid treatment.³ The rat model vocal folds showed thicker epithelial layers with increased mitotic figures, thicker lamina propria, and thicker muscle fibers. Moreover, more recent evidence (2015) suggests a dose and concentration dependent decrease in vocal pitch in woman receiving androgenic steroid therapy after hysterectomy. Although the changes are thought to be permanent, the follow-up period in these studies does not exceed 1–4 years.¹¹

The findings that differ from the existing literature are the late changes in her voice 13 years later as well as the objective findings that correlate her symptoms on laryngoscopy. Instead of showing signs of androgenized vocal fold changes (thickening, edema, and shortening), she presented with thinned and atrophied vocal cords with significant impact on her voice. Although the previous literature describes androgenic effects of AAS to be permanent, no study has ever provided more than 2- to 4-year follow-up. There are a few hypotheses that should be mentioned to explain the late changes and others that should be excluded.

Firstly, the patient was 40 years of age at the time these late changes occurred and still had regular menses. Therefore, presbyphonia and menopause should not have contributed to the changes. The surgical interventions the patient underwent 10–15 years earlier are not known to cause drastic vocal cord atrophy. The superficial lamina propria of the cords and the body of the cords were never instrumented during these procedures.

One of the plausible hypotheses could be related to anabolic steroid-induced hypogonadism (ASIH), a recently described entity. Jarrow and Lipshultz first reported ASIH in 1990, by describing two cases of men with low testosterone levels 3 months and 2.5 years after discontinuing use of AAS.⁴ Rahnama et al⁵ published a comprehensive review of this phenomenon in 2014, describing the secondary hypogonadotropic hypogonadism by feedback suppression of the hypothalamic-pituitary-gonadal (HPG) axis via inhibition of pulsatile GnRH. Only male patients were described, and there was no mention of vocal symptoms. Interestingly, our patient did have low free testosterone levels as well as generalized fatigue which both improved after testosterone therapy by her endocrinologist. It is to be noted that she did not have complete suppression of her HPG axis since she did not suffer from amenorrhea.

Another explanation of these late changes could be that the effect of AAS are not permanent after all and wear off after several years leaving the vocal cords atrophied from the resorbed edema throughout the years. This hypothesis could not explain the low testosterone levels. Testosterone levels have been shown to have an impact of voice pitch and quality in recent literature studying transgender therapy.¹²

In both cases, late changes to the voice and larynx have not been described in the past due to lack of long-term follow-up in literature.

4 | CONCLUSION

To the best of our knowledge, this is the first report of the long-term effects of anabolic steroid on a female voice over a 20 years period. This challenging case suggests that effects of anabolic steroids on the female voice previously thought to be permanent could potentially change years after withdrawal. These changes are clinically relevant since they are difficult to treat and therefore should be disclosed to patient using AAS or receiving androgenic steroid therapy.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

Yael Bensoussan: performed the chart review and developed the manuscript. Jennifer Anderson: involved in the care of patient in this case report as a surgeon and reviewed the manuscript and literature.

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