Facial Hirsutism Following Danazol Therapy

Vijay Zawar, MD; Chandrakant Sankalecha, MD

We describe a 32-year-old woman who presented with excessive facial hair growth of sudden onset that disturbed her psychologically. She had been treated for fibrocystic breast disease with danazol for 6 months. Two months after discontinuation of the drug, the patient had complete reversal of the hair abnormality.

Cutis. 2004;74:301-303.

Fibrocystic breast disease is a benign disease that presents as one or more lumps in the breast that are often associated with cyclical mastalgia, which can be incapacitating at times. The disease usually occurs in the early reproductive years and is clinically obvious in most instances. It rarely needs to be investigated to rule out malignancy. Treatment modalities include reassurance, evening primrose oil, analgesics, and danazol; in rare instances, the disease may be treated with tamoxifen and luteinizing hormone–releasing hormone agonists.[1]

Danazol is an attenuated androgen and has weak androgenic properties. It is a useful drug for treating hormonally mediated perimenstrual benign breast pain and/or lumps of significant severity, as well as for treating demanding patients.[2]

Case Report

A 32-year-old woman presented with sudden onset of increased facial hair for 3 months' duration. The color of her hair changed, and its density increased remarkably, which had never happened previously. The patient was grossly anxious and psychologically disturbed.

Accepted for publication January 5, 2004.

Dr. Zawar is from Skin Disease Centre, Maharashtra, India. Dr. Sankalecha is from Sankalecha Hospital and Maternity Home, Nashik.

The authors report no conflict of interest.

Reprints: Vijay Zawar, MD, Shreeram Sankul Opp Hotel Panchavati, Vakilwadi Nashik -422002, Maharashtra, India (e-mail: vijayzawar@yahoo.com).

Eight months prior to the hair growth, the patient was evaluated for a lump in the upper outer quadrant of the left breast that became tender perimenstrually. The woman was being treated with assurance and analgesics by a general surgeon. Due to her persistent fear of malignancy, the patient was reexamined by radiologic investigations and an excision biopsy of the lump. Results of the biopsy revealed no malignancy and confirmed fibrocystic disease of the breast.

During the following 2-month observation period, a lump formed again at the same site and another lump formed in the upper outer quadrant of the right breast. The patient experienced increasing discomfort and intensity of pain around the time of menses. She was started on danazol 600 mg daily for 2 months, which greatly reduced the mastalgia, as well as the size of the breast lump. She continued on the drug at a dose of 400 mg daily for another 4 months, at which time she visited our clinic for the appearance of facial hair growth.

Her past health was remarkably good. She had normal menses and had 3 full-term normal deliveries. Tubal ligation was performed 9 years earlier. There was no family history of menstrual irregularity, breast disease, or hirsutism. There was no history of weight gain, voice change, libido alteration, or muscular symptoms. There also was no history of topical applications to the face, including cosmetics, in the past few months.

On examination, the patient had many coarse dark terminal hairs on both sides of the face that were more prominent between the mouth and ears. Faint brown macules of melasma also were seen on the malar aspect of the cheeks. Her facial skin was oily and had a few tiny acne lesions (Figure 1). The rest of the patient's body hair showed no abnormality.

The patient's systemic examination results were normal. An endocrine workup was not conducted; however, the workup had been done earlier when she was being examined for the breast lump and included testing of the follicle-stimulating hormone, luteinizing hormone, prolactin, cortisol, and

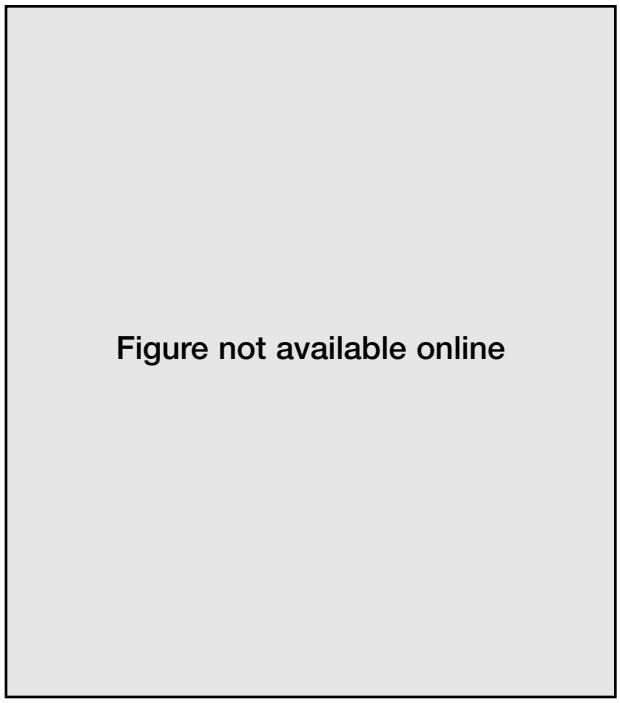

Figure 1. Facial skin is oily and has excessive coarse, dark terminal hair with a few acne lesions on the left cheek.

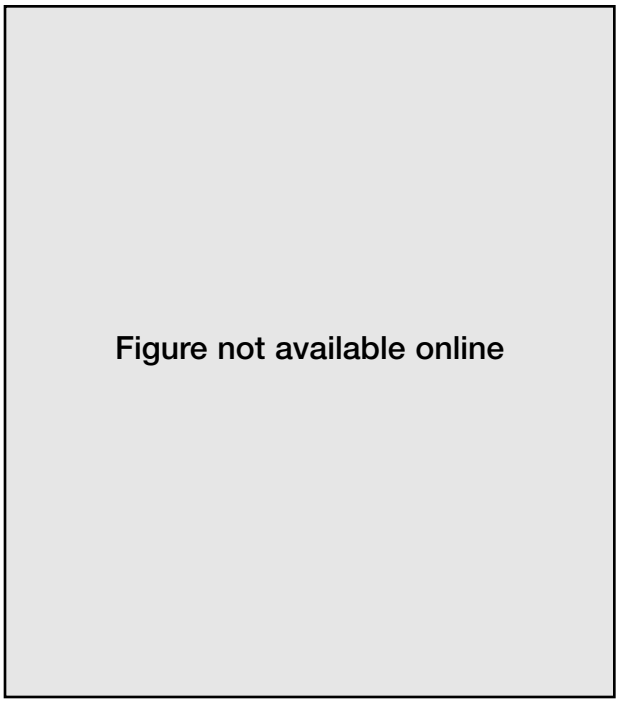

Figure 2. Significant reversal of the condition is seen 2 months after discontinuing treatment with danazol.

thyroid-stimulating hormone. The test results all were within reference range, as were the results of a complete blood cell count, a glucose test, and a urinalysis. An ultrasound of the abdomen and pelvis did not reveal any abnormality. The patient was asked to discontinue danazol and to return for follow-up. After one month, there was remarkable lightening of newly grown hair, many of which had started becoming notably inconspicuous. At the end of 2 months, the condition further improved, and the patient was satisfied with the cosmetic result of the hair on her face (Figure 2). She was referred back to the surgeon for alternative treatment of the breast lump and cyclical mastalgia.

Comment

Danazol acts by suppressing the hypothalamic-pituitary-ovarian axis by inhibiting the release of gonadotrophins from the pituitary.[2] Danazol is frequently used in gynecologic practice to treat endometriosis,[3] premenstrual syndrome,[4] benign breast diseases,[5] primary menorrhagia,[6] preoperative thinning of the endometrium before hysteroscopic endometrial ablation, and primary constitutional precocious puberty when other treatments do not help or are not indicated.[7] In dermatologic practice, it is used for the prevention and treatment of hereditary angioedema,[8] cholinergic pruritus or urticaria,[9] chronic actinic dermatitis,[10] and autoimmune progesterone dermatitis.[11]

Various side effects of danazol therapy include hot flashes, alteration in libido, amenorrhea and emotional disturbances, oily skin, acne, excessive hair growth of androgen-dependent hair, alteration in the voice, edema, increase in weight, and reduction in breast size. Other recognized side effects are gastrointestinal symptoms, headache, dizziness, tremors, depression, fatigue, sleep disorders, muscular cramps, alopecia, skin rash, abnormal glucose tolerance, disturbed lipid profile, and rarely cholestatic jaundice.[2]

Drugs that induce hirsutism include glucocorticoids, corticotrophin, testosterone, danazol, metyrapone, and anabolic steroids. Hypertrichosis is a recognized adverse effect of cyclosporine, minoxidil, and diazoxide.[12]

Our patient had excessive hair growth only on the face. It remains speculative why the other androgen-dependent hair-bearing areas were normal. It could be that her hirsutism had just begun on the face or that a slight change in the color or the thickness of hair at other areas was not appreciable when she presented to us.

Excessive hair growth could be alarming to the patient and may result in profound psychological distress, as in our case. Patients requiring long-term

treatment with danazol therefore should be educated about this side effect before starting therapy. Patients who have unacceptable hair growth during the course of treatment may be evaluated for possible alternative therapeutic regimens.

Early recognition of this reversible side effect of danazol is important in clinical practice. It not only helps to alleviate the anxiety of the patient but also negates the need for a costly and exhaustive endocrinal workup for hirsutism.

REFERENCES

1. Saunders CM, Baum M. The breast. In: Russell RCG, Williams NS, Bulstrode CJK, eds. *Bailey and Love's Short Practice of Surgery*. 23rd ed. London, England: Arnold Publications; 2000:749-772.
2. Reynolds JEF, Parfitt K, Parsons AV, et al, eds. *Martindale: The Extra Pharmacopoeia*. 30th ed. London, England: Pharmaceutical Press; 1993:1166-1198.
3. Fedele L, Arcaini L, Bianchi S, et al. Comparison of cyproterone acetate and danazol in the treatment of pelvic pain associated with endometriosis. *Obstet Gynecol*. 1989;73:1000-1004.
4. Deeny M, Hawthorn R, McKay Hart D. Low dose danazol in the treatment of premenstrual syndrome. *Postgrad Med J*. 1991;67:450-454.
5. Gateley CA, Mansel RE. Management of the painful and nodular breast. *Br Med Bull*. 1991;47:284-294.
6. Chimbira TH, Anderson AB, Naish C, et al. Reduction of menstrual blood loss by danazol in unexplained menorrhagia: lack of effect of placebo. *Br J Obstet Gynaecol*. 1980;87:1152-1158.
7. Smith CS, Harris F. The role of danazol in the management of precocious puberty. *Postgrad Med J*. 1979;55:81-86.
8. Gelfand JA, Sherins RJ, Alling DW, et al. Treatment of hereditary angioedema with danazol: reversal of clinical and biochemical abnormalities. *N Engl J Med*. 1976;295:1444-1448.
9. Berth-Jones J, Graham-Brown RAC. Cholinergic pruritus, erythema and urticaria: a disease spectrum responding to danazol. *Br J Dermatol*. 1989;121:235-237.
10. Humbert P, Drobacheff C, Vigan M, et al. Chronic actinic dermatitis responding to danazol. *Br J Dermatol*. 1991;124:195-197.
11. Shahar E, Bergman R, Pollack S. Autoimmune progesterone dermatitis: effective prophylactic treatment with danazol. *Int J Dermatol*. 1997;36:708-709.
12. Tosi A, Misciali C, Piraccini BM, et al. Drug-induced hair loss and hair growth. incidence, management and avoidance. *Drug Saf*. 1994;10:310-317.