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Gynecomastia in a Young Male Caused by Isotretinoin : A Case Report

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Abstract

Isotretinoin has been used in the treatment of acne for decades.We report a young male at 17 years of age who developed gynecomastia after using isotretinoin after 2.5 months at dose of 20 mg bid. It resolved within 1.5 months after stopping isotretinoin.

Keywords: Gynecomastia • Acne • Isotretinoin

Introduction

Isotretinoin is used for acne for decades. The most common side effects are dryness of skin, eyes, mouth and nose mucosa, and increases of liver enzymes, cholesterol and triglycerides of serum [1]. According to the literature, there have been four case reports to cause gynecomastia during isotretinoin medication during 1992-2020 [2-5]. We report a young male at 17 years of age who developed gynecomastia after using isotretinoin after 2.5 months at a dose of 20 mg bid.

Case Presentation

A healthy male (184 cm, 80 kg) born in November 2004 used tetracyclinhydrochlorid (Oricyclin) 500 mg/day for one month together with topical Epiduo (0.3% adapalene-2.5% benzoyl peroxide) gel for his mild acne in March 2019. His acne thereafter again was treated 3 months later topically in Feb 2020 by clindamycin cream (Dalacin) with benzoyl peroxide with pH 3.5 liquid soap (Lactacyd) for 2 months. Six months later in Aug 2020 the acne condition was again exacerbated. Therefore, lymecycline (Tetralysal caps) 300 mg once a day was prescribed together with topical 5% clindamycin-1% benzoyl peroxide (Clindoxyl) gel in Aug 2020 for 3 months.

However, the acne was severely active in Aug 2021, and isotretinoin 20 mg bid with topical Lactacyd soap and 1% clindamycin-0.025% tretinoin (Acnatac) gel with the follow-up of laboratory values. After one month no clear response was noticed, and treatment was continued another month. The acne papules were getting smaller, but the skin was moderately inflamed. Therefore, 0.1% hydrocortisone-17-butyrate-1% chlorhexidine cream (Duocort) for 4 days followed by 1% hydrocortisone-1% chlorhexidine cream (Sibicort) for 2 weeks was additionally prescribed.

One week later a general practice doctor consulted because of signs and symptoms of gynecomastia in both breasts with some tenderness. Clinically there were palpable resistances in both mamillary areas. Isotretinoin had been used for 2.5 months (Figure 1).

Isotretinoin was stopped and after 2 weeks, lymecycline (Tetralysal) 300 mg/day was started, topically Clindoxyl gel and cream Duocort/Sibicort with Lactacyd soap. Ultrasound examination confirmed the findings for gynecomastia. Laboratory analysis for plasma LH (Luteinizing Hormone) was 3.6 U/L (1.7-8.6 U/L) and for serum SHBG 25 nmol/L (15-48 nmol/L). Serum testosterone was 17.9 nmol/L (10-838 nmol/L) and serum E2 Estradiol 0.08 nmol/L. All hormone levels were in the reference range.

The lymecycline dose was doubled to 600 mg/day for 2 weeks, and then decreased to 300 mg/day. One month later, i.e., 1.5 months after stopping isotretinoin, the breasts started to markedly soften and after another month, there were no longer signs or symptoms of gynecomastia.

1.5 months later the acne was getting better in the forehead, with less improvement in the cheeks. Lymecycline was increased to 300 mg and 600 mg on alternate days. After confirming the Alat value to be normal, lymecycline was again increased to 600 mg/day to obtain a faster response.

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At control 3 months later (end of June 2022), the skin condition was moderately better, with superficial small pustules and a few papules on cheeks. At control 1.5 months later in Aug 2022 there were about 10 small superficial and 10 deeper papules on each cheek. The lymecycline was continued at 600 mg/day with the previous topical treatment.

Two months later in Oct 2022 there were a few small superficial papules, and the oral and topical treatments were continued for two more months, and a hew superficial pustules were detected in the forehead, and topical and remaining lymecycline capsules were used for another month.

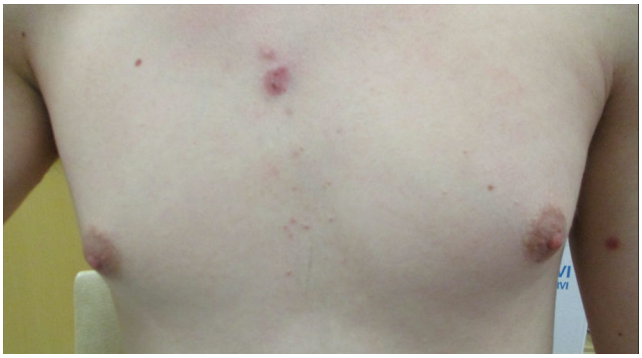

Figure 1. Our patient's clinical appearance after 2.5 months of isotretinoin treatment by 40 mg/day.

Source (ref.no)	Country	Year of publication	Age (years)	Weight (kg)	Localization	Dose and isotretinoin use (months) before onset
2	Switzerland	1992	39	69	Right breast	10 mg/day-6 months
3	Germany	2000	19	70	Both breasts	30 mg/day-2 months
4	Türkiye	2013	20	N.A.	Right breast	20 mg/day-3 months
5	Italy	2020	17	65	Both breasts	105 mg/kg*-6 months
our case	Finland	2023	17	80	Both breasts	40 mg/day-2.5months

Note: N.A., data not available, *Cumulative dose during treatment for 6 months by 0.5 mg/kg/day

Table 1. Published Gynecomastia cases.

Discussion

This gynecomastia side effect of isotretinoin in our patient is very rare. To our knowledge, the medical world literature has previously published only 4 case reports in males (Table 1). There looks to be a trend for shorter appearance time of gynecomastia with higher isotretinoin doses. Also, the time the patient contacts his doctor, may vary to report of gynecomastia symptoms. However, due to very small number of cases, a definite conclusion cannot be made. The reports are geographically from a limited area globally, thus, it may be possible that these cases are underreported.

Also, the pharmaceutical company's (Galderma) files did not reveal more cases. Lymecycline is usually clearly less effective in acne treatment than isotretinoin. The patient wanted his facial skin to improve quickly, but some scars had already developed.

The gynecomastia started to develop after 2.5 months with isotretinoin dose of 40 mg/day. After stopping the medication, the condition resolved in about 1.5-2.5 months. The development of gynecomastia after initiation of isotretinoin, ultrasound examination and the resolution after discontinuation, and the relatively short duration of symptoms and signs support isotretinoin as the cause.

A possible mechanism for isotretinoin-induced gynecomastia could be the reduction of testosterone. A few studies have shown that isotretinoin decreases LH and testosterone concentrations. A decrease in testosterone concentrations may also be the mechanism for erectile dysfunction and decreased libido that occasionally occurs with isotretinoin [6-8].

In our patient, both testosterone and estradiol concentrations were normal. In adolescence, gynecomastia occurs commonly. It may be that relatively small changes in the relative testosterone and estrogen concentrations after initiation of isotretinoin treatment could have been sufficient to cause gynecomastia, even though testosterone and estrogen concentrations remained clearly in the normal range. In one case report of gynecomastia in association with isotretinoin, estradiol concentrations were slightly elevated and testosterone concentrations normal during isotretinoin treatment [5]. In three other case reports, testosterone and estrogen concentrations were both within the normal range [2-4].

Many drugs have been associated with gynecomastia. Decreased androgen concentrations or an imbalance in the testosterone and estradiol concentrations are a common mechanism, but most often mechanism is unknown or uncertain. There may be other unknown mechanisms by which isotretinoin causes gynecomastia.

Conflict of Interest

Authors declare no conflicts of interests.

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