

An Unusual side effect of Clomiphene Citrate (Clomid)

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Abstract: Clomiphene citrate (Clomid) is a Selective Estrogen Modulator used to induce ovulation.¹ Many side effects of Clomiphene citrate were reported including mood swings and hot flashes.² Stimulation of multiple follicles and consequently multiple gestation is a complication of Clomid. Skin rash is a reported non-serious and un common side effect of Clomid.³ We report a case of a 31-year-old female who developed thinning and whitening of the vulvar area after taking clomid.

KeyWords: Clomiphene citrate (Clomid), Lichensclerosus like lesion, Thinning of skin, Side effect

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I. Introduction

Clomiphene citrate is a widely used drug for ovulation induction in women desiring pregnancy.⁴ It is mainly used to increase follicular number and fertility.⁵ It primarily acts at the hypothalamus to block the negative feedback effect of circulating estradiol by binding and depleting hypothalamic estrogen receptors^{6,7}. Clomiphene thereby causes a hypoestrogenic effect. This in turn leads to an increase in hypothalamic gonadotropin-releasing hormone (GnRH) pulse frequency, thereby leading to increased concentrations of follicle-stimulating hormone (FSH) and luteinizing hormone (LH)⁸. The dose of clomiphene to be administered is titrated based on the response of the patient.³ Clomid is reported to have produced a 70%-80% ovulatory rate in patients receiving the drug.³

II. Case Report

A 31-year-old female, P0A1L0 presents with severe vaginal itching and excoriation since 2 months. She first noticed the itching 3 days after finishing a cycle of Clomid (Clomiphene Citrate). She was prescribed Clomiphene Citrate 50mg for the first cycle, 100 mg for the second cycle and 150 mg for the third cycle from day 5 to day 7. She first developed itching 3 days after finishing the first cycle of Clomid. The itching gradually became severe with excoriations. The itching initially started around the vulva and spread to the perianal area. She developed a dull lower abdominal pain 2 days after the itching started. The pain was diffuse, over the pelvic region, 4/10 in intensity, non-radiating with no aggravating and relieving factors. She denied the presence of any vaginal discharge. Past and family history insignificant. No history of previous STIs.

On Physical examination, there was mild erythema over the vulvar and perianal region, but there was no vaginal discharge. There was no cervical motion tenderness. Abdomen was soft, non-tender, non-distended and bowel sounds were heard in all four quadrants. Cervical swab taken at that time was negative for Chlamydia and Gonorrhea. The pain subsided after two days but the itching persisted. She was advised to keep the area dry and to avoid the use of soaps and detergents. As she was trying to conceive, steroids were not prescribed.

The itching reduced in intensity over the next 2 weeks but did not completely resolve. The itching worsened immediately after the second cycle of clomid. She also noticed bleeding PR but denied abdominal or pelvic pain. She also noticed that her menstrual flow turned black after the first cycle of Clomid. The itching became so severe as to affect her daily functioning. On physical examination the vulvar and perianal regions were erythematous and edematous. There were excoriations all around the perineal area. The labia majora appeared thinner, whitish and wrinkled, resembling lichen sclerosus. There was no vaginal discharge. There were no hemorrhoids or fissures around the anal area. There was no active bleeding per rectum.

Patient was advised to stop Clomid and was prescribed topical steroid. The symptoms gradually improved, and the steroid was tapered off after a week of application. During follow-up visit one month later, the patient was symptom free. On physical examination, there was no erythema or edema. The labia majora and perianal area looked normal. The majora no longer looked thinner nor whitish. There were

thickened healed excoriations around vulva. The patient came in for regular follow ups and was symptom free with normal examination findings.

III. Discussion

Clomiphene citrate is a drug used for ovulatory dysfunction in women desiring pregnancy. The well-known adverse effects of Clomid include nausea, vomiting, breast discomfort, visual disturbances, headaches, abnormal uterine bleeding, dizziness, vertigo, insomnia, fatigue, depression, increased frequency and amount of urination, skin rash, hair loss, constipation, diarrhea, and dry vaginal mucosa.³ The other common side effects are ovary enlargement, hot flashes, abdominal distension or abdominal distress and bloating. Dermatological side effects are very rare with clomiphene citrate and there are hardly any cases published recently. It can cause erythema, erythema multiforme and erythema nodosum in less than 1%. This patient developed itching in the genital area followed by excoriations and erythema over the vulvar and perianal region. The labia majora appeared thinner, whitish and wrinkled. The lesions resembled lichen sclerosus, which is a chronic progressive dermatologic condition characterized by marked inflammation and epithelial thinning, associated with symptoms of pruritus and pain⁹. Classic vulvar lichen sclerosus appears as whitish papules that can form plaques and later can transform into hemorrhagic or ulcerated lesions¹⁰.

Once the patient was asked to stop clomid, the itching gradually subsided and the lesions resolved. The patient became completely symptom free with normal examination findings during subsequent visits. The notable finding was that the labia majora returned to normal thickness after stopping clomid which goes against the diagnosis of Lichen sclerosus in this case. This suggests that the lesion could be a side effect of clomid resembling Lichen sclerosus, a "Lichen Sclerosus Like Lesion".

Development of lichen sclerosus like lesions after intake of clomid and resolution of symptoms following discontinuation of clomid further suggests that the lesions possibly developed as a side effect of clomid. This is a rarely reported side effect which stresses the importance of this case report. This also shows that physicians must be cautious while prescribing this drug and regular monitoring can identify the side effect at an early stage.

IV. Conclusion

Clomiphene citrate (Clomid) is a widely prescribed drug for the treatment of infertility. Skin manifestations as a side effect of Clomid is rare and a Lichen sclerosus like manifestation following Clomid ingestion is never reported. Careful monitoring for the incidence of similar cases is required to establish the causative relationship between clomid in this specific manifestation.

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