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Systemic Steroids, Clarithromycin and Metronidazole in the Treatment of Rosacea during Pregnancy

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Abstract

Rosacea is a common skin disease with a predilection for the face. Patients suffer from symptoms like flushing, redness of the face, telangiectasia, pustules, or papules. A more acute form is rosacea fulminans that occurs preferentially in women. Hormonal fluctuations as during a pregnancy can aggravate existent rosacea.

The case of a female patient is presented, who was in the 26th week of her pregnancy. She discontinued her usual rosacea medication when she became pregnant. The patient developed rosacea fulminans, which was treated with systemic corticosteroids as recommended. She responded well to clarithromycin 250 mg for three times a week in combination with topical treatment using metronidazole 0.75% creme, continuing this regimen until a stable result was obtained.

Based on the observations in this case study the therapy of rosacea fulminans with clarithromycin can help to reduce the symptoms, especially since treatment with systemic isotretinoin and doxycycline is contraindicated during pregnancy.

Keywords: Rosacea; Rosacea fulminans; Clarithromycin; Pregnancy

Introduction

Chronic skin diseases with a facial manifestation like rosacea significantly affect the patient's quality of life. Rosacea can appear similarly to acne with erythema, pustules, papules, and even nodules but without comedones. Fair-skinned individuals have a higher prevalence to develop rosacea. There are contradictory reports in the literature. For Germany a study in 2016 determined a prevalence of 12.3%. In the last years, the therapy has improved [1-4]. A successful treatment of rosacea should consider the individual course of disease. It includes behavioural modification regarding trigger factors like heat, alcohol, or spicy food [5]. An urgent and special form of rosacea, which predominantly affects women, is rosacea fulminans. Formerly, it was also described as pyoderma faciale [6] a misnomer as an infectious etiology is unlikely and an increased incidence during pregnancy is reported [7]. For the treatment of rosacea fulminans the German Guidelines for the therapy of rosacea recommend oral corticosteroids and isotretinoin [1]. This treatment regimen is untenable due to the teratogenicity of systemic retinoids. Newer findings confirm the effectiveness of macrolide antibiotics especially in pregnant patients [8,9].

Case Report

The 32-year-old female patient visited the clinic for dermatology of the LMU Munich with the initial diagnosis of exacerbation of her pre-existing acne. She had the imperative desire to have children and suffered from a polycystic ovarian syndrome, thus she was formerly treated with dexamethasone 0.5 mg and metformin 750 mg. When she sought advice, she was in the 26th week of pregnancy and took levothyroxine 50 µg, vitamin D3 1,000 IU, and folic acid 5 mg. The skin presented with infiltrated papules and pustules, fistulous ducts, and reddish, inflammatory nodes, but no comedones (Figure 1a). No other acneiform lesions were found on back or chest. The patient reported no other health problems and blood test parameters were normal. Bacterial cultures from the abscess-forming nodes revealed coagulase negative staphylococci. Rosacea fulminans was diagnosed. As recommended by the German Guidelines for the therapy of rosacea, she was treated with prednisolone 5 mg for one week and reduced the dose rate to 2.5 mg in the second week. This low-dose approach was chosen based on the patients experience with dexamethasone, the slightly increased

Figure 1: Rosacea fulminans. (a) Before treatment: Infiltrated papules and pustules, fistulous ducts, and reddish, inflammatory nodes. (b) After 3 weeks of prednisolone (1st week 5 mg, 2nd week 2.5 mg) and clarithromycin 250 mg (3 times a week), the lesions had reduced substantially. (c) Another month later with clarithromycin (3 times a week) and metronidazole creme 0.75 % (once daily) further improvement.

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equivalent prednisolone dose is a save medication during pregnancy. Additionally, a treatment with oral clarithromycin 250 mg three times a week was started. After 3 weeks, the skin lesions had reduced substantially (Figure 1b). In addition, metronidazole 0.75% creme once daily was prescribed. One month later the patient presented with good results compared to her first visit (Figure 1c). Due to the good toleration of the therapy, the patient wanted to continue the combined low-dose antibiotic treatment in case of recurrence of the skin lesions.

Discussion

The use of drugs during pregnancy requires consistent clinical surveillance and should be restricted to severe diseases. Rosacea fulminans or severe papulopustular rosacea may not be accompanied by systemic symptoms, though affected patients evidently suffer from the disturbing skin lesions. Rosacea fulminans is characterized by a sudden onset of facial skin lesions like reddish nodules, papules and pustules [1]. As it is often associated with pregnancy or oral contraception, hormonal factors could be a trigger [7]. Systemic corticosteroids and isotretinoin are recommended as first line treatment [1,10,11]. During pregnancy or in case of the desire to have children isotretinoin is contraindicated. The use of systemic corticosteroids during pregnancy should be carefully considered as they can cause maternal diabetes mellitus and hypertension as well as a retardation of fetal growth. Therapy of rosacea during pregnancy or for patients with a desire to have children has been discussed, especially macrolide antibiotics are a therapeutic option as they are classified as safe for the unborn child [8,9]. A common side effect of erythromycin is gastrointestinal discomfort. In the treatment of papulopustular rosacea its application should be restricted in case of intolerance to doxycycline. The only systemic medication, even though contraindicated during pregnancy, which is approved in the treatment of rosacea is slow-release doxycycline 40 mg, which is effective for papulopustular rosacea [1]. One study showed that clarithromycin was more effective in the reduction of erythema and papules than doxycycline [12-15]. As none of the mentioned drugs are approved for the treatment of rosacea during pregnancy a reasonable discussion prior to treatment is necessary. The patients gave informed consent for this off-label treatment due to their imperative desire for resolution of their skin lesions.

The combination of systemic corticosteroids with doxycycline is not indicated in pregnancy, for the combination with clarithromycin no severe side effects are reported [1]. At the first control visit after four weeks, the blood parameters were within normal limits, gastrointestinal problems were not reported. The systemic therapy was combined with a topical application of metronidazole 0.75% creme.

D'Erme et al. recently reported a similar case in a 59-year-old female patient [16]. Being treatment-naïve, the patient was prescribed prednisone 25 mg (tapering off over 15 days) once daily, oral clarithromycin 500 mg, and topical metronidazole twice daily, respectively. The patient's skin improved substantially, and the treatment was well tolerated. Treating an expecting patient, a low-dose corticosteroid regimen was chosen deliberately due to the only partial inactivation at the placenta and the preceding treatment with dexamethasone 0.5 mg. Furthermore, clarithromycin was prescribed in low doses, although it is safe during pregnancy. Clarithromycin and its 14-hydroxylated metabolite maintain high serum levels and tissue-to-serum concentrations as well as concentrate in macrophages and polymorphonuclear leukocytes [17]. As the patient responded well to the low-dose treatment, it can be reasoned that this regimen is sufficient in patients with rosacea fulminans.

Conclusion

Based on the observations made in this case study, it can be concluded that the application of clarithromycin in the treatment of rosacea fulminans during pregnancy is a viable treatment option. The sub-antimicrobial but anti-inflammatory therapy with 250 mg clarithromycin three days per week achieved a reduction of the skin lesions. In combination with a frequently used topical treatment with metronidazole creme 0.75% a nearly complete healing of the skin lesions can be accomplished. The therapy was tolerated well and is continued by the patient to maintain the good skin result.

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