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Letter to the Editor

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Pemphigus Vulgaris Developing During IVF (*In Vitro* Fertilization) Treatment: A Case Report

IVF (In vitro Fertilizasyon) Tedavisi Sırasında Gelişen Pemfigus Vulgaris: Bir Olgu Raporu

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Dear Editor,

A 24-year-old female patient presented to our outpatient clinic with progressively worsening painful erosions affecting the oral, genital, and cutaneous regions. She had no prior history of pemphigus and was 10 weeks pregnant, receiving progesterone treatment (vaginal suppository and intramuscular injection). It was noted that her lesions had started approximately three months earlier, coinciding with her *in vitro* fertilization (IVF) treatment for primary infertility. During the onset of the lesions, she underwent ovarian stimulation with follitropin alfa and estradiol as part of the IVF protocol, but embryo transfer was not performed. Nevertheless, she subsequently achieved a successful pregnancy and presented to our clinic at 10 weeks of gestation.

Dermatological examination revealed widespread erosions and remnants of bullae on the oral, genital, and anal mucosa; hemorrhagic crusted erosions on the lips; and scattered bullae with crusted erosions on the skin (Figures 1, 2, and 3). The Nikolsky sign was positive. Based on clinical findings, pemphigus vulgaris was suspected. Histopathological and direct immunofluorescence analyses confirmed the diagnosis. Indirect immunofluorescence revealed high titers of anti-desmoglein 1 and 3 antibodies (>200 RU/mL). Following consultation with obstetrics and gynecology, topical corticosteroids and systemic methylprednisolone (0.5 mg/kg/day) were initiated, and progesterone therapy was discontinued. After the consolidation phase, systemic corticosteroids were gradually tapered by 20% every two weeks and discontinued within approximately four months. The patient showed a favorable response to treatment, with regression of existing lesions and no emergence of new ones. Routine antenatal evaluations revealed no

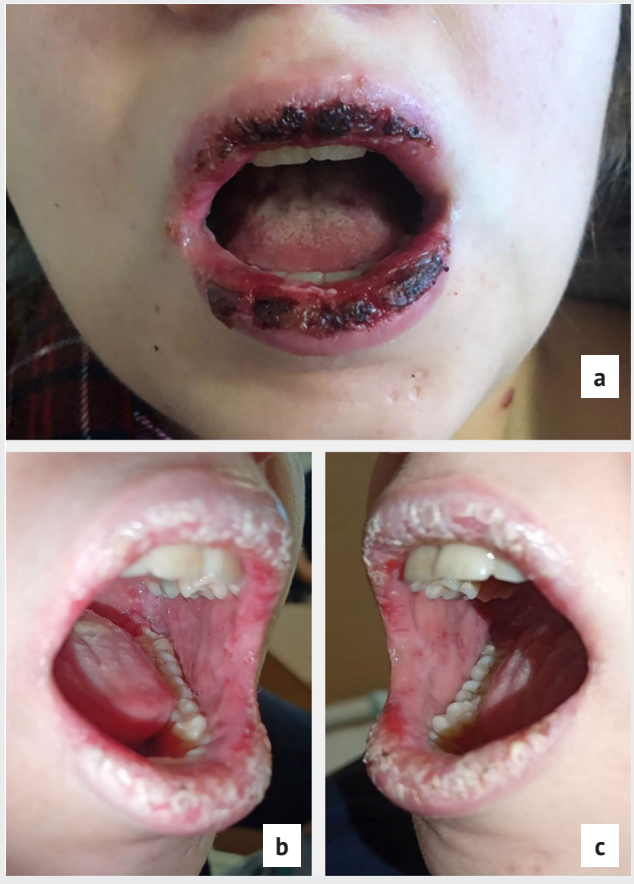

Figure 1. Clinical findings of the oral mucosa and lips. (a) Hemorrhagic crusty erosions on the lips, (b) erosions on the oral mucosa (right buccal region), (c) erosions on the oral mucosa (left buccal region)

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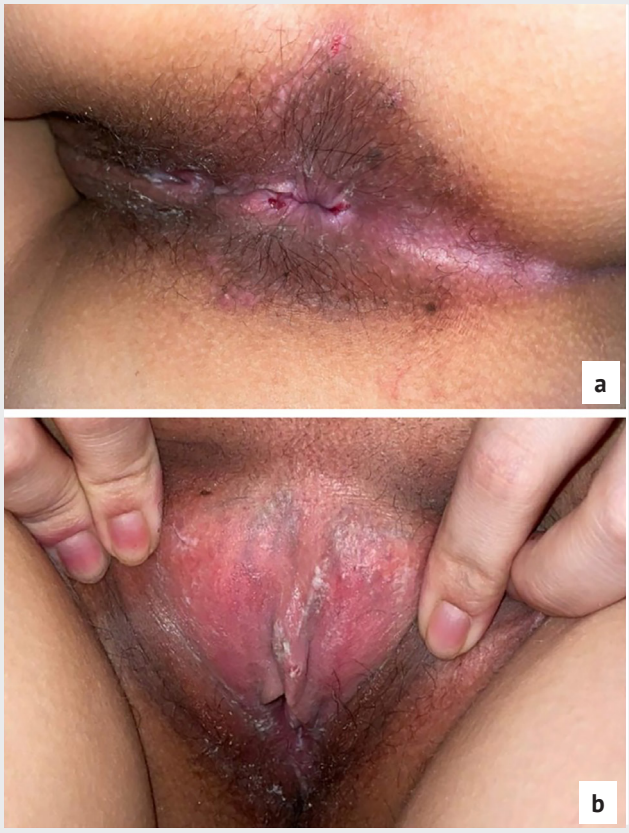

Figure 2. Mucosal erosions involving the anogenital region. (a) Erosions on the anal and perianal mucosa, (b) erosions on the genital mucosa

abnormalities. However, immediately postpartum, widespread mucocutaneous erosions recurred, which were effectively controlled with a moderate dose of systemic steroids (0.5 mg/kg/day). No neonatal pemphigus was observed.

Pemphigus vulgaris is a Th2-mediated autoimmune bullous disease, primarily driven by anti-desmoglein autoantibodies. Although the association between pregnancy and pemphigus vulgaris remains incompletely understood, hormone-induced immune modulation has been implicated in its pathogenesis. Elevated levels of estrogen and progesterone during pregnancy shift the immune response from a Th1- to a Th2-dominant profile. While this physiological shift promotes fetal tolerance, it may also predispose individuals to autoantibody-mediated diseases such as pemphigus vulgaris (1,2). Similarly, the hormonal agents used in IVF treatment may contribute to this immunological imbalance.

Following delivery, the abrupt decline in estrogen and progesterone levels induces a reversion to a Th1-dominant immune response. This transition leads to immune remodeling and can facilitate postpartum exacerbations of autoimmune diseases (1,2). Furthermore, the withdrawal of endogenous corticosteroids, previously produced by the chorion, may also contribute to postpartum flare-ups (3).

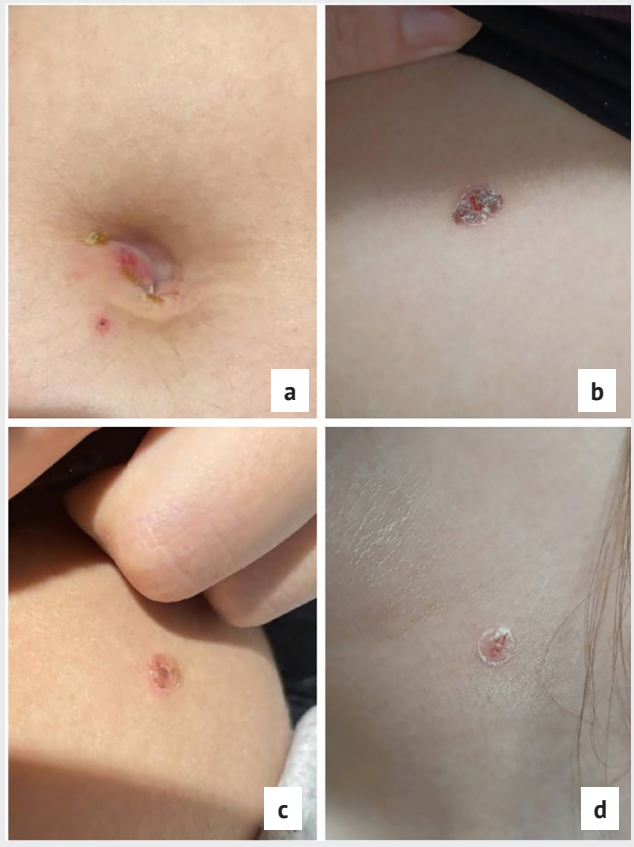

Figure 3. Cutaneous lesions on different body sites. (a) Bullae and erosions on the abdomen, (b) crusted erosions on the back, (c) erosions with bullae on the abdomen, (d) crust formation and healing erosions on the neck

To date, only one similar case has been reported in the literature. In the case presented by Gayathri Devi et al. (4), a 28-year-old woman developed pemphigus vulgaris following IVF-confirmed pregnancy. Exogenous hormone therapy was considered the likely trigger, and the patient responded well to systemic corticosteroids.

Both cases suggest that pemphigus vulgaris is a rare but possible complication of IVF treatment. Our case differs from the previously reported one in that the lesions developed before embryo transfer, during the hormonal stimulation phase alone. This supports the hypothesis that exogenous hormones may trigger pemphigus vulgaris independently of pregnancy. Additionally, our case is notable due to its postpartum relapse, which presents uncommon characteristics in the context of the patient's medical history.

Pemphigus vulgaris during pregnancy may lead to serious maternal and fetal complications (3,5). The condition complicates clinical management and may affect treatment decisions and prognosis. Systemic corticosteroids remain the first-line treatment during pregnancy owing to their relatively favorable safety profile and classification as

pregnancy category C. In corticosteroid-resistant cases, intravenous immunoglobulin is the preferred second-line option. Plasmapheresis has also been reported to be effective and safe in refractory cases. However, further studies are required to validate the safety and efficacy of these alternative therapies. Azathioprine, classified as category D, is associated with congenital anomalies and preterm birth. Methotrexate, cyclophosphamide, and mycophenolate mofetil are teratogenic and contraindicated during pregnancy. Rituximab is classified as pregnancy category C, with limited data on safety, and poses a risk of B-cell depletion in neonates. (1,6,7). Management should be individualized through a multidisciplinary approach, considering factors such as gestational age, maternal condition, fetal development, and potential treatment-related risks.

In conclusion, our case highlights that hormonal changes related to IVF treatment may trigger pemphigus vulgaris. Both endogenous and exogenous hormonal stimulation may contribute to the initiation or exacerbation of autoimmune processes. Particular attention should be paid to individuals undergoing infertility treatments. Timely diagnosis and carefully tailored treatment strategies are essential in managing pemphigus vulgaris during pregnancy. This case demonstrates that systemic steroid therapy can elicit a positive response, and appropriately individualized treatment plans may lead to successful outcomes for both the mother and the fetus. Early recognition and appropriate intervention are crucial to prevent complications in both the mother and fetus.

Informed Consent: Patient consent was obtained.

Footnotes

Authorship Contributions

Concept: K.K., S.Y., S.A.T., Design: K.K., S.Y., S.A.T., Literature Search: K.K., S.Y., S.A.T., Writing: K.K., S.Y., S.A.T., İ.Ö., M.D., R.D.

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