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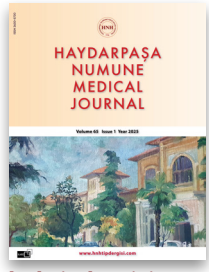

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CASE REPORT

Acute Urticaria and Angioedema Associated with the Use of Levonorgestrel-Releasing Intrauterine System: A Case Report and Literature Review

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Abstract

Levonorgestrel-containing intrauterine systems (LNG-IUS) are widely used for contraception and the treatment of abnormal uterine bleeding. However, they can rarely lead to serious allergic reactions. This study aims to present a case of a 38-year-old woman who developed acute urticaria and angioedema two months after the insertion of an LNG-IUS and to synthesize similar cases reported in the literature. The patient's clinical findings, laboratory results, and treatment process were examined in detail. Allergic reactions associated with LNG-IUS and similar intrauterine devices were reviewed in the literature. Two months after LNG-IUS insertion for abnormal uterine bleeding, the patient developed widespread urticaria and facial angioedema. The urticarial lesions on the patient's back and torso are presented in Figures 1 and 2. Despite daily treatment with 15 mg of oral methylprednisolone and 5 mg of desloratadine, her symptoms did not improve. The patient was evaluated by an allergist, and the removal of the LNG-IUS was recommended. Following the removal of the device, she responded to systemic therapy, and her symptoms completely disappeared within 15 days. Although acute urticaria and angioedema developing during LNG-IUS use are rare, clinicians should be aware of this potential adverse effect. In allergic reactions related to LNG-IUS, symptoms may resolve entirely with device removal and appropriate medical management.

Keywords: Acute urticaria; allergic reaction; angioedema; desloratadine; intrauterine device; levonorgestrel; methylprednisolone.

Levonorgestrel-releasing intrauterine systems (LNG-IUS) not only provide effective and long-term contraception but are also used in the treatment of gynecological conditions such as abnormal uterine bleeding, adenomyosis, and prevention of endometrial hyperplasia[1,2]. While these devices are generally well-tolerated, their side effects include menstrual irregularities, ovarian cysts, and pelvic pain. Serious allergic reactions are rarely reported[3,4].

Progesterone hypersensitivity, or "autoimmune progesterone dermatitis," is a rare hypersensitivity reaction developing against endogenous or exogenous progesterone, leading to cutaneous symptoms such as urticaria, angioedema, and dermatitis[5,6]. There are a limited number of cases in the literature reporting that levonorgestrel-containing intrauterine devices can cause allergic reactions due to progesterone hypersensitivity[7-10].

In this study, we aim to present a case of a patient who developed acute urticaria and angioedema two months after the insertion of LNG-IUS and did not respond to daily treatment with 15 mg of oral methylprednisolone and 5 mg of desloratadine, and to compare it with similar cases in the literature.

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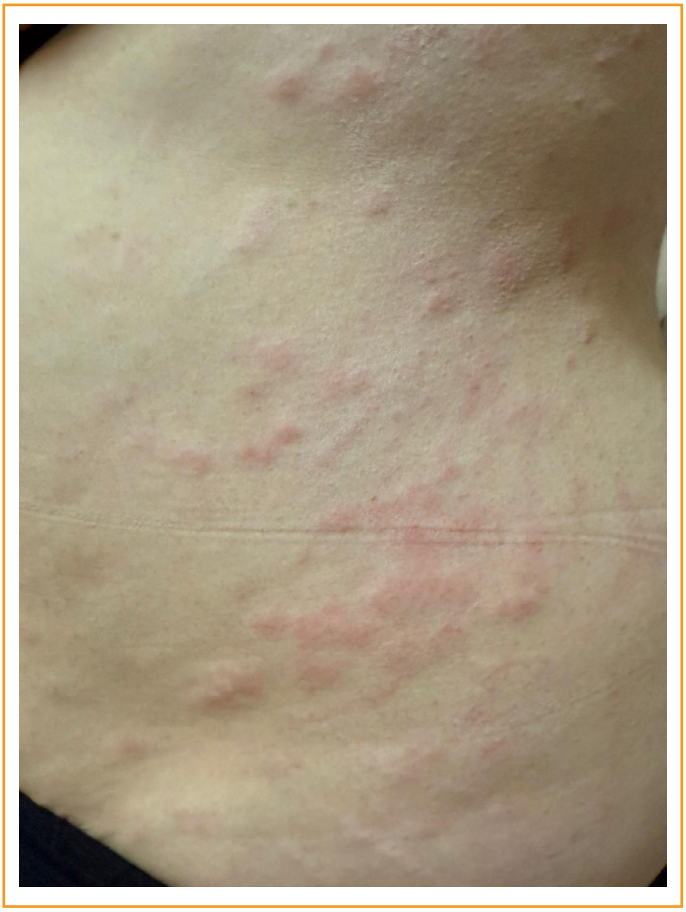

Figure 1. Widespread urticarial lesions on the patient's back.

Case Report

A 38-year-old woman with no known chronic diseases or history of allergies had LNG-IUS (levonorgestrel 52 mg-releasing intrauterine system) inserted for the treatment of abnormal uterine bleeding. Two months after the insertion of LNG-IUS, the patient began to experience widespread urticarial symptoms. The lesions were predominantly concentrated on her back and torso

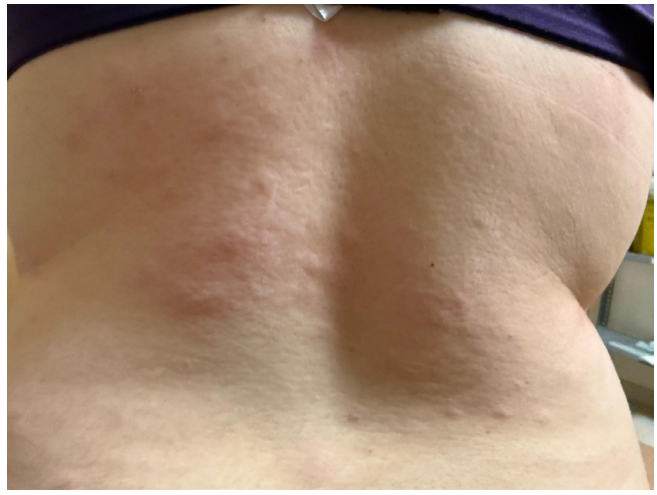

Figure 2. Urticarial lesions on the patient's torso and abdominal area.

(Figs. 1 and 2) and were accompanied by severe pruritus. She was treated with 15 mg of oral methylprednisolone and 5 mg of desloratadine daily, but her symptoms did not improve.

As her symptoms persisted and angioedema developed on her face, the patient was referred to the allergy and immunology department. Upon evaluation, it was determined that she had no prior history of reactions to any drugs, foods, or environmental allergens. Laboratory tests, including complete blood count, liver and kidney function tests, were within normal limits. Serum IgE levels were mildly elevated. Antinuclear antibody (ANA), anti-thyroid antibodies, and other autoimmune markers were negative.

The allergist considered a possible hypersensitivity reaction developing against levonorgestrel or other components of the intrauterine device and recommended the removal of LNG-IUS. After the device was removed, the patient continued systemic corticosteroid (15 mg

Table 1. Summary of previously reported cases of acute urticaria and/or angioedema associated with LNG-IUS use.

Author (Year)	Patient Age	Clinical Presentation	Onset After Insertion	Treatment	Outcome
Chen et al.[7]	42	Acute urticaria, severe itching	2 hours post-insertion	Oral methylprednisolone + desloratadine	Symptoms resolved within 3 days
Alheeh et al.[8]	29	Urticarial rash, pruritus	3 weeks post-insertion	Oral antihistamines; IUD removal	Symptoms resolved fully after device removal
Emeryk-Maksymiuk et al.[9]	NA	Acute urticaria (face & torso)	2 hours post-insertion	Not specified	Complete resolution after IUD removal
Ganguli & Dimov[11]	33	Persistent urticaria	Within weeks	Oral antihistamines; IUD removal	Complete resolution after device removal

of oral methylprednisolone) and antihistamine (5 mg of desloratadine) therapy. Significant improvement was observed in her symptoms, and by the end of 15 days, the urticaria and angioedema had completely disappeared. The patient was discharged, and during follow-up, it was observed that her symptoms did not recur.

Discussion

Allergic reactions developing due to the use of levonorgestrel-releasing intrauterine devices are quite rare but can be clinically significant. Similar cases have been reported in limited numbers in the literature. Chen et al.[7] reported a case where acute urticaria developed two hours after the implantation of LNG-IUS and responded to treatment with 10 mg of oral methylprednisolone and 5 mg of desloratadine. Similarly, Emeryk-Maksymiuk et al.[9] described a patient who developed acute urticaria two hours after the insertion of LNG-IUS, and symptoms resolved with the removal of the device and treatment with 20 mg of oral methylprednisolone and 180 mg of fexofenadine. A summary of previously reported cases, including clinical presentation, onset time, treatment, and outcomes, is presented in Table 1.

In our case, the onset of symptoms two months after the insertion of LNG-IUS and the lack of response to systemic therapy necessitated the removal of the device. The complete resolution of symptoms with the same treatment regimen after the removal of the device supports a hypersensitivity reaction related to levonorgestrel.

Urticaria (hives) is characterized by transient wheals on the skin accompanied by intense itching. The pathophysiology primarily involves mast cell degranulation and histamine release, which cause vasodilation, increased vascular permeability, and the resulting wheals. Urticaria may be immunoglobulin E (IgE)-mediated (Type I hypersensitivity), or it can have non-IgE-related mechanisms triggered by physical factors, infections, or autoimmune processes.

Treatment of urticaria typically begins with second-generation H1 antihistamines, such as cetirizine and fexofenadine, as first-line agents. When standard doses prove insufficient, increasing the dosage of antihistamines can be considered. In chronic or refractory cases, additional therapies like omalizumab (an anti-IgE monoclonal antibody) may be introduced. Systemic corticosteroids are sometimes used for short periods to control severe flares, but their long-term application is generally discouraged due to potential side effects. Equally important is identifying and avoiding any underlying triggers, such as certain foods, medications, or infections.

Progesterone hypersensitivity can manifest as Type I (IgE-mediated) or Type IV (delayed-type) hypersensitivity reactions[5,6]. In our patient, the slight elevation of serum IgE levels and the initial lack of response to systemic corticosteroid and antihistamine therapy suggest a more complex immunological mechanism.

Although skin prick tests and intradermal tests can be used in the diagnosis of progesterone hypersensitivity, standardized protocols are lacking[5,8]. These tests were not performed in our patient. In treatment, eliminating the source of progesterone is essential alongside symptomatic therapy[6,10]. In our patient, symptoms completely resolved after the removal of LNG-IUS.

An adverse drug reaction (ADR) is any undesired or harmful response to a medication used at normal doses, which can significantly impact healthcare systems worldwide by increasing costs, hospital stays, and patient morbidity and mortality. Various national and international reporting systems (such as WHO's VigiBase, FDA's MedWatch, and regional pharmacovigilance centers) collect and analyze ADR data, helping to identify high-risk medications, update clinical guidelines, and ultimately protect public health.

This case demonstrates that levonorgestrel-containing intrauterine devices can, albeit rarely, cause serious allergic reactions. In clinical practice, it is important to review medications and medical devices used in patients with unexplained and treatment-resistant urticaria and angioedema.

Most cases reported symptoms within hours to a few weeks after insertion of the levonorgestrel-releasing IUD. In contrast, our patient experienced symptoms two months later, suggesting a delayed or cumulative hypersensitivity process. While standard treatments (oral corticosteroids and antihistamines) were partially effective in other cases, our patient's symptoms resolved only after device removal. This highlights the importance of considering IUD removal when therapy-resistant urticaria or angioedema is suspected to be device-related[11].

Conclusion

Levonorgestrel-releasing intrauterine systems, although effective and reliable contraceptive methods, can rarely lead to serious allergic reactions. Clinicians should be aware of this potential side effect, especially in patients with unexplained and treatment-resistant urticaria and angioedema. Symptoms can completely resolve with the removal of the device and appropriate medical treatment.

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References

1. Lähteenmäki P, Rauramo I, Backman T. The levonorgestrel intrauterine system in contraception. Steroids 2000;65:693–7. [CrossRef]
2. Bahamondes L, Bahamondes MV, Monteiro I. Levonorgestrel-releasing intrauterine system: Uses and controversies. Expert Rev Med Devices 2008;5:437–45. [CrossRef]
3. Bahamondes L, Petta CA, Fernandes A, Monteiro I. Use of the levonorgestrel-releasing intrauterine system in women with endometriosis, chronic pelvic pain and dysmenorrhea. Contraception 2007;75(6 Suppl):S134–9. [CrossRef]
4. Kaunitz AM, Bissonnette F, Monteiro I, Lukkari-Lax E, Muysers C, Jensen JT. Levonorgestrel-releasing intrauterine system or medroxyprogesterone for heavy menstrual bleeding: A randomized controlled trial. Obstet Gynecol 2010;116:625–32. [CrossRef]
5. Snyder JL, Krishnaswamy G. Autoimmune progesterone dermatitis and its manifestation as anaphylaxis: A case report and literature review. Ann Allergy Asthma Immunol 2003;90:469–571. [CrossRef]
6. Ridehalgh C, Moore A, Hough A. Sciatic nerve excursion during a modified passive straight leg raise test in asymptomatic participants and participants with spinally referred leg pain. Man Ther 2015;20:564–9. [CrossRef]
7. Chen X, Wu X, Zhu H. Acute urticaria as a side effect of the Mirena® (levonorgestrel-releasing intrauterine system): A case report. BMC Res Notes 2014;7:209. [CrossRef]
8. Alheeh I, Shalalfeh N, Wajeeh S, Farah R, Farah R. A Case of Autoimmune progesterone dermatitis post-intrauterine device placement in rural occupied Palestine. SAGE Open Med Case Rep 2024;12:2050313X241283601. [CrossRef]
9. Emeryk-Maksymiuk J, Grzywa-Celińska A, Woźniak S, Szkodziak P, Szczyrek M. Acute urticaria: An extremely rare adverse effect of levonorgestrel-releasing intrauterine system as a possible manifestation of progestogen hypersensitivity syndrome. Postepy Dermatol Alergol 2018;35:530–1. [CrossRef]
10. Frieder J, Younus M. Autoimmune progesterone dermatitis with delayed intradermal skin reaction: A case report. Ann Allergy Asthma Immunol 2016;117:438–9. [CrossRef]
11. Ganguli MP, Dimov V. Chronic urticaria suspected to be caused by a 13.5 mg levonorgestrel ıntrauterine device (Skyla®). Cureus 2023;15:e42287. [CrossRef]