International Clinical and Medical Case Reports Journal
Case Report (ISSN: 2832-5788)

Beyond Para-phenylenediamine: Anaphylactic Reactions to Hair Dye and the Challenge of Cross-Reactivity

Bernaola Marta MD[1*], Bernaola Jaime MD[1], Bernaola Gonzalo MD[2]

[1]Allergy Department, Hospital Central de la Defensa Gómez Ulla, Madrid, Spain

[2]Allergy Department, Hospital Universitario de Galdácano, Vizcaya, Spain

Citation: *Bernaola Marta, Bernaola Jaime, Bernaola Gonzalo. Beyond Para-phenylenediamine: Anaphylactic Reactions to Hair Dye and the Challenge of Cross-Reactivity. Int Clinc Med Case Rep Jour. 2025;4(9):1-4.*

Received Date: 08 September 2025**; Accepted Date:** 10 September 2025**; Published Date:** 12 September 2025

***Corresponding author:** Bernaola Marta MD, Allergy Department, Hospital Central de la Defensa Gómez Ulla, Madrid, Spain

ABSTRACT

We report a rare case of severe anaphylaxis triggered by the application of a paraphenylenediamine (PPD)-containing hair dye, confirmed by a positive skin prick test. The reaction recurred following use of a commercially marketed "PPD-free" dye, most likely due to cross-reactivity with structurally related phenylenediamine derivatives, including toluene-2,5-diamine sulfate and m-aminophenol. This case underscores that, in type I hypersensitivity reactions to hair dye, avoidance of PPD alone is insufficient—derivatives must also be considered, in contrast to allergic contact dermatitis where selective avoidance may be adequate. Our findings highlight the importance of accurate ingredient labeling in hair dye products and the need to avoid forearm application as a tolerance assessment strategy, given the risk of inducing anaphylaxis in sensitized individuals. To our knowledge, this is the first reported case of life-threatening immediate hypersensitivity due to cross-reactivity between phenylenediamine derivatives.

Keywords: Anaphylaxis; Hair dye allergy; Paraphenylenediamine (PPD); Cross-reactivity; Allergic contact dermatitis

CASE REPORT

Currently, the use of hair dyes is a common trend among people of all ages. Consequently, an increase in the incidence of allergic contact dermatitis (type IV hypersensitivity reaction) due to these substances has been observed. Although IgE-mediated reactions (type I) have been reported less frequently, severe clinical manifestations such as systemic contact urticaria, asthma, and anaphylaxis have been described.[1]

The most commonly known causative agents, as noted in the recommendations made by GEIDAC members, include para-phenylenediamine (PPD) and its oxidation products. Other identified allergens include henna, para-aminophenol, meta-aminophenol, ortho-aminophenol, Basic Blue 99, and paratoluenediamine and/or their oxidation products.

Anaphylaxis is an acute, systemic, and potentially life-threatening reaction, for which the treatment of choice is intramuscular adrenaline. It is a type I hypersensitivity reaction in which immune system cells (especially mast

cells and basophils) rapidly release mediators that induce the characteristic clinical presentation of anaphylaxis. Symptoms may include bronchospasm, facial/glottic edema, urticaria, syncope, nausea, vomiting, palmoplantar or scalp pruritus, and in severe cases, respiratory failure or shock.[2]

We present the case of a 38-year-old woman with a history of rhinitis and mild intermittent bronchial asthma due to sensitization to dust mites. She sought medical attention for an episode of cutaneous pruritus accompanied by generalized erythematous hives and dyspnea occurring 10 minutes after applying a hair dye. She visited a hospital emergency department, where she received treatment with parenteral antihistamines followed by oral antihistamines, with rapid improvement.

An allergy workup was conducted using prick-prick tests with the components of the implicated hair dye (ADVANCE by Llongueras). Figure1. The tests yielded positive results for the coloring gel cream and for the mixture of the coloring gel cream with the developer cream, but negative results for the developer cream and the intensive color treatment. Ten control tests were performed on atopic and non-atopic subjects using the same compounds, all yielding negative results. A complete blood analysis was requested, revealing normal tryptase levels (3.7 mcg/L), a total IgE of 256 kU/L, and unremarkable hematological and basic biochemical findings. Given the positive results for the coloring gel cream, its components were reviewed, and the reaction was attributed to PPD. A controlled exposure test was performed with a PPD-free dye from Mahé laboratory (exclusively composed of plant-based products), which was well tolerated.

Figure 1: Results of skin tests with the components of the hair dye.

Several months later, the patient consulted again for a similar episode of pruritus, edema, and facial erythema, along with truncal pruritus with erythematous lesions on the abdomen and dyspnea occurring 10 minutes after applying a PPD-free hair dye (Natur Vital brand). Upon reviewing the packaging, it was found that the dye contained toluene-2,5-diamine sulfate and m-aminophenol, both derivatives of PPD, despite being labeled as "PPD-free."

Phenylenediamine is a chemical compound belonging to the class of aromatic amines. Its chemical formula is C6H8N2, and it appears as a crystalline solid. According to the Spanish Academy of Dermatology and

Venereology, there are two main isomers of phenylenediamine: ortho-phenylenediamine (1,2-phenylenediamine) and para-phenylenediamine (1,4-phenylenediamine), which differ in the position of the amino groups (-NH2) on the benzene ring.

Phenylenediamine is used in various industrial applications, including the manufacture of dyes, textile industry chemicals, and as an intermediate in the production of plastics and resins. However, it can also act as an allergen, causing adverse reactions in some individuals, particularly through exposure to cosmetic products such as hair dyes.

PPD is an azo organic chemical compound commonly used in hair dyes, industrial dyes, and tattoos. It is sometimes used as a henna substitute and is always present in black henna formulations. It is also used in other industries as an antioxidant. Its international INCI designation is 4-phenylenediamine, para-phenylenediamine, or PPD. Related or derivative compounds include 4-toluenediamine, 2,5-diaminetoluene sulfate, aminodiphenylamine, diaminoanisole, and aminophenols (4-aminophenol, 3-aminophenol, 2-aminophenol). These terms appear on product labels.

PPD is the most frequently implicated allergen in allergic contact dermatitis caused by hair dyes.[1,3,4,5,6,7] Less commonly, type I hypersensitivity reactions such as urticaria, angioedema, or anaphylaxis[4,5] have been reported, including a fatal case of anaphylaxis.[6] The simultaneous presence of immediate and delayed hypersensitivity to PPD in the same patient is rare.[7] In a review of contact urticaria syndrome conducted by Von Krogh et al., several cases of combined immediate and delayed hypersensitivity to various substances, including PPD, were described, leading the authors to propose the term "immediate and delayed-type contact dermatitis" for these patients.[1]

Furthermore, ingestion of PPD causes severe local irritation and edema of the face and neck. Systemic manifestations of PPD ingestion include rhabdomyolysis and acute renal failure, which can be fatal if not aggressively treated. Intentional PPD ingestion as a means of suicide is frequently reported in Africa and the Middle East. In most documented cases, symptom progression follows a consistent pattern with some variations. Although no specific laboratory test exists to aid in the diagnosis of PPD intoxication, recognizing its common clinical characteristics can help reduce morbidity and potential mortality. Physicians should be aware of the differential diagnosis of anaphylaxis in cases of ingestion or suspected exposure to PPD.[3]

We present a case of anaphylaxis caused by the application of a PPD-containing hair dye, confirmed by a positive prick test, which recurred with a "PPD-free" dye, likely due to cross-reactivity with phenylenediamine derivatives (toluene-2,5-diamine sulfate and m-aminophenol). Based on these findings, we conclude that, in cases of type I hypersensitivity reactions to hair dye, unlike allergic contact dermatitis, it is necessary to avoid not only PPD but also its derivatives.

This case highlights the need for accurate labeling of hair dyes, as in cases of immediate reactions due to allergy to phenylenediamine and its derivatives, avoiding PPD alone is insufficient. Additionally, we emphasize the risk

of potential anaphylactic reactions following forearm application of hair dye by hairdressing professionals as a tolerance assessment measure.

To the best of our knowledge, this is the first reported case of severe anaphylactic reaction due to cross-reactivity between phenylenediamine derivatives.

REFERENCES

1. Wong GAE, King CM. Immediate-type hypersensitivity and allergic contact dermatitis due to para-phenylenediamine in hair dye. Contact Dermatitis. 2003;48(3):166.
2. Grupo de trabajo de anafilaxia de la SEAIC. Guía de actuación en anafilaxia GALAXIA 2022. Available in: https://www.semg.es/index.php/consensos-guias-y-protocolos/407-guia-de-actuacion-en-anafilaxia-galaxia-2022
3. Elgassim M, Fadul KY, Abbas M, AlBakri F, Kamath R, Salem W. Paraphenylenediamine (PPD) poisoning mistaken for an anaphylactic reaction. Cureus. 2022;14(2):e22503.
4. Temesvári E. Contact urticaria from paraphenylenediamine. Contact Dermatitis. 1984;11:125.
5. Fukunaga T, Kawagoe R, Hozumi H, Kanzaki T. Contact anaphylaxis due to para-phenylenediamine. Contact Dermatitis. 1996;35:185–6.
6. Belton AL, Chira T. Fatal anaphylactic reaction to hair dye. Am J Forensic Med Pathol. 1997;18:290–2.
7. Edwards EK Jr. Contact urticaria and allergic contact dermatitis caused by paraphenylenediamine. Cutis. 1984;34:87–8.