

## CASE REPORT

# Challenging Interpretation of Blistering Patch Test Reaction in Hair Dye Induced Allergic Contact Dermatitis with Cross-Reaction: A Case Report

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## ABSTRACT

Hair dye contact allergy is an emerging public health concern globally, including in Malaysia. Para-phenylenediamine (PPD), an aromatic amine commonly found in hair dyes and henna tattoos, is a well-known allergen contributing to these reactions. This report discusses a case of PPD-induced contact dermatitis, complicated by a blistering reaction following a patch test with PPD 1% in petrolatum. The case highlights the challenges dermatologists face in accurately interpreting patch test results, particularly in the presence of multiple cross-reactions involving PPD, also include the mechanism of cross reaction and novel hair dye compound investigated with lower cross reaction rate. *Malaysian Journal of Medicine and Health Sciences* (2025) 21(5): 435-437. doi:10.47836/mjmhs.21.5.50

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## INTRODUCTION

Para-phenylenediamine (PPD) is an aromatic amine commonly used in permanent hair dyes and henna tattoos. PPD contact allergy is diagnosed using an epicutaneous patch test with 1% PPD in petrolatum in clinically suspected patients. It ranks as the eighth most common contact allergen, affecting up to 6.7% (n=46) of patients patch-tested over a five-year period at Hospital Kuala Lumpur, Malaysia. (1) We would like to report an interesting case of PPD-induced hair dye contact dermatitis with blistering and cross-allergenic reactions, highlighting that blistering and cross-reactions can complicate patch testing and result interpretation.

## CASE REPORT

A 48-year-old gentleman presented with intermittent, itchy, erythematous, scaly patches around his entire hairline, posterior neck, periauricular area, and scalp over the past two months after using permanent hair

dye for the first time. Patch test with European Baseline Series (EBS) (Chemotechnique MB Diagnostics AB, Sweden) and additional p-aminophenol 1% in *pet*, n-aminophenol 1% in *pet*, and resorcinol 1% in *pet* was conducted. Readings, as per International Contact Dermatitis Research Group guideline showed positive reactions to the following haptens in Table I, Figure I and Figure II. PPD allergy was confirmed from patient's history, while other allergens showed cross-sensitization to PPD. The blister resolved with post-inflammatory hyperpigmentation within one month after using 0.1% betamethasone valerate ointment. There was no recurrence after hair dye avoidance within 6 months of follow-up.

**Table I: Patch Test Result**

Haptens	Concentration and Dilution	48 hours	96 hours	Interpretation
PPD	1% in <i>pet</i>	3+	Blistering	Contact Allergen
Textile dye mixed	6.6% in <i>pet</i>	3+	3+	Cross reaction
Fragrance mix II	14% in <i>pet</i>	-	1+	Co-sensitizer
p-Amino-phenol	1% in <i>pet</i>	1+	1+	Cross reaction
n-Amino-phenol	1% in <i>pet</i>	1+	1+	Cross reaction



Figure 1: Positive epicutaneous patch test to PPD showing a 3+ blistering reaction.



Figure 2: Positive epicutaneous patch test showing, A= Textile dye mixed 3+; B=fragrance mix II 1+; C= p-Aminophenol 1+; D = n-Aminophenol 1+

## DISCUSSION

Patients with a history of reactions to black henna tattoos or commercial hair dyes may develop severe blistering reactions when tested with PPD 1% pet, as recommended by EBS (2). Ho et al. reported that using lower concentrations of PPD significantly reduces the frequency of severe reactions, with 3+ reactions observed in 33%, 8%, and 0% of patients tested with PPD 1%, 0.3%, and 0.01% pet, respectively (2). Additionally, Geier et al. (2013) demonstrated that PPD 0.3% pet maintains good sensitivity with parameters of diagnostic selectivity, including a Relevance Index (RI)

of 0.29 and a Positive Rate (PR) of 49%. Despite a 26% reduction in positive reactions when compared with PPD 1% in pet (32/123), this reduction can be attributed to the inherent non-reproducibility of patch test results, as shown in the German Contact Dermatitis Research Group (Deutsche Kontaktallergie-Gruppe) study from the 1990s. Therefore, PPD 0.3% pet is the preferred and reliable concentration for patients with a history of reactions to black henna tattoos or hair dyes (3).

PPD can cross-react with structurally similar chemicals containing para-amino compounds, particularly in individuals prone to severe reactions. Table II summarizes common compounds and their respective cross-reaction rates. This case highlights a significant positive reaction to PPD, along with cross-reactions to substances such as textile dye mix, p-aminophenol, and n-aminophenol. The cross-reactivity of structurally similar compounds can occur through several mechanisms. Prohaptenic para-compounds may be metabolized into common reactive metabolites that act as haptens, leading to the formation of identical neoantigens. (4) Chemically related compounds may also bind to self-proteins in a similar way, resulting in the presentation of identical cryptic peptides to T cells. Alternatively, true cross-reactivity can arise when T cells are unable to distinguish between peptide adducts formed by different haptens, a phenomenon attributed to the limited discriminatory capacity of  $\alpha\beta$  TCR-carrying T cells, as demonstrated by Wulferink et al. (2002). (4)

Table II: Compounds that demonstrate cross-reactivity with PPD

Compounds	Common product	Cross reaction rate (%)
2,5-Toluenediamine sulfate	Hair dyes	31.3
p-Aminophenol		20.1
m-Aminophenol		19.4
Disperse orange 3	Textile Dye	14.2
Disperse Yellow 3		4.5
N-isopropyl-N'-phenyl-p-phenylenediamine	Rubber	6
Benzocaine	Local anesthetics	7.5
Sulfamides	Antibiotics	6.0
Para Aminobenzoic Acid	Sunscreen	1.5

(Adopted from Laberge et al., 2011)

In practice, clinicians should inform patients about the potential for cross-reactivity with other para-amino compounds, particularly those found in textile dyes, such as those used in synthetic fibers like nylon, polyester, or acetate (5). Even hair dyes that do not contain PPD may contain other para-amino compounds such as PTD, and p- and n-aminophenol, which frequently cross-react with PPD. Novel compounds in development, such as 2-Methoxymethyl-p-phenylenediamine (ME PPD), show a significantly lower degree of cross-elicitation under simulated hair coloring conditions, with only 30% cross-reactivity observed (4).

**CONCLUSION**

In summary, using a lower concentration of PPD (0.3% in petrolatum) for patients with a history of henna tattoo or hair dye allergies may help reduce the risk of severe blistering reactions. Given the multiple cross-reactive compounds and the various mechanisms of cross-reactivity, clinicians should remain vigilant and educate patients about these potential allergens. Additionally, the development of novel hair dye compounds such as ME PPD with low cross-reactivity is necessary.

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