

Case Report

An unusual cross reactivity between hydrochlorothiazide and para-phenylenediamine: a case report

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ABSTRACT

Over the last decade, the usage of hair color is gradually increasing from adolescents to the geriatric population. In the elderly population, more use of hair color due to graying of hairs exposes them to chemicals such as para-phenylenediamine (PPD). Many cases are reported regarding various manifestations of allergic contact dermatitis due to PPD compound present in hair color. It is noteworthy that, in the elderly the use of antidiabetics and antihypertensives, makes them vulnerable to cross-reaction or interaction with drugs and chemicals. We report a case that highlights the adverse reaction to hydrochlorothiazide in a PPD sensitive individual.

Keywords: Cross-reaction, Para-phenylenediamine, Hydrochlorothiazide, Hair dye, Contact dermatitis

INTRODUCTION

Hair dyes include a variety of coloring agents such as 2,7-naphthalenediol, 2-aminomethyl-p-aminophenol hydrochloride, 2-chloro-p-phenylenediamine, *N*-phenyl-p-phenylenediamine, and o-aminophenol, *p*-aminophenol.¹ Among all, p-phenylene diamine (PPD) is a potent sensitizer and there is a strong possibility of cross-reaction with other chemicals as well.² Over the last decade, many cases are reported regarding various manifestations of allergic contact dermatitis due to para-phenylenediamine compound present in hair color.³ In the elderly, there is more use of hair color. It is noteworthy that, in this population antidiabetics and antihypertensives makes them vulnerable to cross-reaction or interaction with drugs and chemicals. We report a case that highlights the adverse reactions to hydrochlorothiazide in a PPD sensitive individual.

CASE REPORT

A 70-year-old female, presented to dermatology outpatient department with rashes on the extremities on 4th

day following administration of tablet telmisartan (40 mg) and hydrochlorothiazide (12.5 mg). She gives a history of working in the garden for a day in the afternoon. The same evening rashes appeared on the extensors of the forearm and later spread to the lower limbs. The rashes were associated with itching and burning sensation. On examination there were maculopapular rashes on the extremities (Figure 1a-d). Palms, soles, and oro-genital mucosa were normal. She was clinically diagnosed as photodermatitis and prescribed topical clobetasol propionate 0.05% and photoprotection. She was a known case of hypertensive and on telmisartan 40 mg for 14 years. Five days before the development of this rash, her medication had been changed to a combination of telmisartan (40 mg) and hydrochlorothiazide (12.5 mg) due to uncontrolled blood pressure parameters. Also, the patient's previous history revealed that she had no drug allergies except that she had developed severe allergy to permanent hair color (two episodes) a month back. These two episodes were associated with severe itching and oozing on the scalp, the next day of application of hair color suggesting features of allergic contact dermatitis. The patch test performed at that time showed +++ (3+) positive

result. There was neither any history of drug allergy nor atopic diathesis. Despite topical steroid application, the rashes were persistent and soon became purpuric (Figure 1e and f). There was associated burning rather than itching. Palms and soles showed few erythematous macules. Skin biopsy was not done as patient did not give consent for the same. Then the patient was started on oral prednisolone 30 mg in tapering doses over 10 days. Also, considering the photosensitive effect of hydrochlorothiazide, the drug was stopped. Later, the rashes gradually subsided over 2 weeks. According to the Naranjo scale of causality assessment, the adverse drug reaction falls under 'probable' category as the score was found to be 7 and as per Hartwig's severity assessment scale, the reaction belongs to category of moderate- level 3.^{4,5}



Figure 1: (A), (B), (C), and (D) Erythematous rashes present on extensors aspect of both hands; and (E) and (F) persistent purpuric rashes on both the hands even after topical steroid treatment.

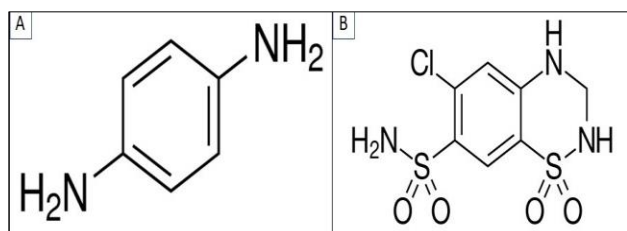


Figure 2: (A) Structure of para phenylenediamine hydrochloride and (B) hydrochlorothiazide.

DISCUSSION

Many elderly individuals on polypharmacy medications are often exposed to external chemical compounds in their day-to-day activities. Among them, PPD is a strong sensitizing chemical used in hair dye and textiles. PPD is an aromatic amine and shows cross sensitization to other

chemicals belonging to paragroup which contains an amine group on a benzene ring at the para position.⁶ The chemical structure of PPD and hydrochlorothiazide (Figure 2) has an aromatic ring with one amino group at para position depicting structure similarity. The chemicals of the para group include N-isopropyl-N-phenyl-4-phenylenediamine (IPPD), toluene-2,5-diamine (TDA), ethylenediamine (EDA), paraben mix and benzocaine. LaBerge et al conducted a study on 134 PPD sensitive patients showed that 6% of them had cross reactivity with sulpha drugs.⁷

According to "prehapten" concept, autoxidation of PPD by atmosphere is quite rapid and is responsible for its immunogenicity. This autoxidized product on the skin, bind to different proteins forming hapten-protein complexes which are potent sensitizers.^{3,8} PPD increases the production of thymic stromal lymphopoietin (TSLP) in the keratinocytes and its repeated exposure leads to eczematous reaction in a sensitized individual.⁹ In PPD sensitized individuals, the clinical presentation may vary from acute urticaria to delayed type hypersensitivity reactions such as allergic contact dermatitis, photocontact dermatitis.^{3,6,10} It may also induce chemical leukoderma, prurigo like lesions, lichenoid eruption and lymphomatoid contact dermatitis.^{3,10} It was also observed in a study conducted by Han et al, that increase in exposure time and duration to PPD causes more wide spread lesions including both direct and indirect contact area.¹¹ A strong contact sensitivity to PPD increases the risk of allergies to other compounds of the para group.⁶ Cross reactivity is defined as an allergy to a chemical with a related structure. The compounds which cross react with PPD are para-amino benzoic acid and its derivatives, azodyes, sulfonamide, benzocaine, and para- amino salicylic acid, thiazides, and celecoxib (COX-2 inhibitors).^{3,6,12,13} According to the study by Chew et al, more positive patch test was seen to PPD than sesquiterpene mix in chronic actinic dermatitis. Although, there is no structural similarity between these compounds, cross reactivity was observed in PPD and sesquiterpene mix.¹⁰

Hydrochlorothiazide is the most common photosensitizer among antihypertensive drugs. The photosensitivity is elicited by both UVA and UVB light.¹⁴ Hydrochlorothiazide undergoes photolysis to form ethoxy hydrochlorothiazide, which is a photodegraded product, plays an important role in photo allergy by acting on cell membrane.¹⁵

CONCLUSION

It is therefore concluded that, due to photosensitizing property of these chemicals and cross sensitivity between PPD and hydrochlorothiazide, caution should be taken while prescribing medications for PPD sensitized individual. The chances of these individuals developing hypersensitivity reaction can be predicted. This case report is presented to create awareness of adverse drug reactions to hydrochlorothiazide in PPD sensitized individuals.

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