Case Report

Sensitization and Clinically Relevant Allergy to Hair Dyes and Clothes from Black Henna Tattoos: Do People Know the Risk? An Uncommon Serious Case and a Review of the Literature

Paola A. Moro 1,*, Marco Morina 2, Fabrizia Milani 1, Marco Pandolfi 3, Francesca Guerriero 3 and Luca Bernardo 3

1 Poison Control Centre, Niguarda Great Metropolitan Hospital, Piazza dell’Ospedale Maggiore 3, 20162 Milano, Italy; fabrizia.milani@studenti.unimi.it
2 Postgraduate School of Clinical Pharmacology and Toxicology, University of Milan, Via Vanvitelli 32, 20129 Milano, Italy; marco.morina@unimi.it
3 Paediatric Department, Fatebenefratelli-Sacco Great Metropolitan Hospital, Corso di Porta Nuova 25, 20121 Milano, Italy; marco.pandolfi@ffs.milano.it (M.P.); francesca.guerriero@ffs.milano.it (F.G.); luca.bernardo@ffs.milano.it (L.B.)

* Correspondence: paolaangela.moro@ospedaleniguarda.it; Tel.: +39-02-6444-2523

Academic Editors: Lidia Sautebin and Immacolata Caputo
Received: 31 March 2016; Accepted: 2 July 2016; Published: 11 July 2016

Abstract: Henna (Lawsonia inermis L.) tattooing has been used in Egypt and India since ancient times. Today this temporary body art is becoming increasingly popular among young people. Various chemicals are added to henna to darken and enhance the definition of tattoos, especially para-phenylenediamine (PPD), which is a strong sensitizer known to cause cross sensitive reactions to azoic dyes and other para-amino compounds. We present the case of an 18-year-old girl who became clinically sensitive to textile dyes after having showed a serious reaction both to her first hair dying when she was 16 years old and following the application of a temporary henna tattoo when she was a kid. The evidence from our literature review showed 33 cases of manifest sensitization to hair dye and only one of observable contact allergy to both hair and textile dyes from henna tattoos. The sensitization of children may have long-life lasting consequences, because of cross-reaction to dyes and other chemicals contained in hair colourants, clothes and drugs. Since tattoos are very popular and globalization has increased the circulation of unauthorized products we point out the need for informative campaigns about the risk of sensitization caused by temporary tattoos.

Keywords: phenylenediamines; tattooing; henna; hair dyes; azoic compounds; textile dyes allergic contact dermatitis

1. Introduction

Henna is the common name of Lawsonia inermis L., a widely cultivated shrub of the Lythraceae family that originates from North Africa and the Middle East [1,2].

The crushed leaves of henna contain about 1% by weight of lawsone, a weak acid hydroxynaphthoquinone pigment (2-hydroxy-1,4-naphthoquinone; CI 75480; Natural Orange 6) that interacts with keratine and gives a reddish-brown colour when applied to the skin, hair or nails [3].

The plant also contains coumarin derivatives, gallic acid and tannin [4] and its fungicidal, anti-inflammatory and analgesic effects are well known [5].

The fine powder prepared from its dry leaves, mixed with oil or water, has been used since ancient time for medicinal, holistic and cosmetic purposes [3]. The primitive habit of painting feet, hands and
other parts of the body (named “mehindi” in the Hindi language), had the further benefit of preventing 
microbial and fungal infections [6] and accelerate wound healing [7].

Despite its millenary use, reports of sensitive reaction to pure henna are rare [8]. Although it is 
considered as a quite safe and very weak allergenic substance [9], percutaneous absorption of henna 
may induce oxidative injury and haemolysis in glucose-6-phosphate dehydrogenase (G6PD)-deficient 
subjects, especially newborns [10]. Henna colour is red to orange, so other pigments are added to 
achieve different nuances: they can be vegetal substances, such as powered leaves of Cassia obovata 
and/or Indigofera tinctoria (used to give a chestnut or black colouration, respectively), tea leaves, 
charcoal powder, metals or other chemicals [11,12].

Since the 1970s, tattoo artisans started adding para-phenylenediamine (PPD) to darken and 
enhance definition and prolong the duration of tattoos [13]. In that period “black henna” body art 
evolved from traditional “mehindi” and became popular, especially thanks to the fact that it was a 
self-limited, less invasive and cheaper alternative to permanent tattoos.

PPD is one of the five chemicals identified as “strong sensitizers” by the Scientific Committee on 
Consumer Safety since 1961 [14]. Reports of reactions started in the late 19th century and increased 
over the last two decades [15]. In the 28 States of the European Union, PPD is prohibited in cosmetics 
for cutaneous use and is restricted to a maximum of 2% (as free base) in hair dyes for general and 
professional use [16] and in eyelashes for professional use [17]. In the USA PPD is banned in topical 
cosmetics but allowed in hair dyes to a maximum concentration of 6% [14].

Moreover, the regulations established by the European Commission [18,19] require that warnings 
and conditions of use must be indicated on the packaging of hair dyes containing p-phenylenediamine, 
p-phenylenediamine HCl and p-phenylenediamine sulphate, with the following wording according to 
the European Cosmetic Regulation No 344/2013/EC [20]:

(a) General use. To be printed on the label: The mixing ratio.

“Hair colourants can cause severe allergic reactions. Read and follow instructions. This product 
is not intended for use on persons under the age of 16. Temporary ‘black henna’ tattoos may increase 
your risk of allergy. Do not colour your hair if: —you have a rash on your face or sensitive, irritated 
and damaged scalp; —you have ever experienced any reaction after colouring your hair; —you have 
experienced a reaction to a temporary ‘black henna’ tattoo in the past. Contains phenylenediamines. 
Do not use to dye eyelashes or eyebrows.”

(b) Professional use. To be printed on the label: The mixing ratio.

“For professional use only. Hair colourants can cause severe allergic reactions. Read and follow 
instructions. This product is not intended for use on persons under the age of 16. Temporary ‘black 
henna’ tattoos may increase your risk of allergy. Do not colour your hair if: —you have a rash on 
your face or sensitive, irritated and damaged scalp; —you have ever experienced any reaction after 
colouring your hair; —you have experienced a reaction to a temporary ‘black henna’ tattoo in the past. 
Contains phenylenediamines. Wear suitable gloves.”

Nowadays temporary black henna tattoos are widespread: they are available as do-it-yourself 
kits, or applied by street artists or beach hawkers in holyday resort areas [3].

Studies which aimed at identifying and quantifying ingredients of commercially available henna 
samples revealed that some products did not contain Lawsone at all, while variable amount of PPD, 
nickel, cobalt and other metals were detected [11,21].

Sensitization caused by PPD contained in temporary tattoos can lead to cross sensitive reactions 
with other para-amino compounds, such as para-aminobenzoic acid (used in sunscreen cosmetics), 
sulfonamides (antibiotics, diuretics, oral hypoglycaemic drugs), benzocaine (local anaesthetic) and azo 
dyes (used for textiles, foods and drugs colouring) [22–25].

The goal of this paper is to draw attention on the possible cross-reactions among black henna 
tattoos, hair dyes and textile dyes.
2. Materials and Methods

The evidence from the reported case was collected from patients admitted to the pediatric unit of the Fatebenefratelli-Sacco Great Metropolitan Hospital of Milan and analyzed with the toxicological advice of the Poison Control Centre of the Niguarda Great Metropolitan Hospital of Milan.

Afterwards, the authors carried out a review of the published cases of clinical reactions to hair dyes and/or clothing in patients previously sensitized by a temporary henna tattoo.

Embase, PubMed and MetaCrawler electronic databases were systematically queried using and matching the following Mesh terms [26]: henna, tattoo, tattooing, hair dyes, phenylendiamines, clothing, azo compounds. The authors did not apply any restrictions to the year of publication. Data extracted for each case included: age, sex, country, latency since the tattoo, presence of dermatitis after the tattoo, latency of the reaction since the hair dye application, name of the product, signs and symptoms, patch test results for para-phenylenediamine and for cross-reacting substances.

3. Results

3.1. Clinical Case

In January 2014, a previously healthy 16-year-old girl was admitted to the Emergency Department presenting itching vesicular eruptions on the scalp accompanied by hyperpyrexia and oedema extending from the scalp to the neck, the ears, the forehead and the periorbital region.

Her axillar temperature was 38.2 °C, pharynx was not oedematous and vital parameters were stable; pulse oximeter oxygen saturation was 99% in air and blood test showed a rise of inflammatory markers: White Blood Cell Count: $23.4 \times 10^9$/L (normal laboratory values: $4.0–10.0 \times 10^9$/L); C-reactive Protein: 98.6 mg/L (normal laboratory values: 0–5 mg/L).

The symptoms had suddenly started the previous day, one hour after the first application of a mix of two permanent hair dyes containing PPD and other chemicals (Table 1).

<table>
<thead>
<tr>
<th>Clady Colour Professional 1-Natura Black</th>
<th>Clady Colour Professional 6.38-Dark Blonde Chocolate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aqua</td>
<td>Cetearyl Alcohol</td>
</tr>
<tr>
<td>Cetearyl alcohol</td>
<td>Aqua</td>
</tr>
<tr>
<td>Ammonium hydroxide</td>
<td>Ammonium Hydroxide</td>
</tr>
<tr>
<td>$p$-Phenylenediamine</td>
<td>Stearic Acid</td>
</tr>
<tr>
<td>Stearic acid</td>
<td>Palmitic Acid</td>
</tr>
<tr>
<td>Palmitic acid</td>
<td>Polyquaternium-7</td>
</tr>
<tr>
<td>$m$-Aminophenol</td>
<td>Polyquartemium-7</td>
</tr>
<tr>
<td>Resorcinol</td>
<td>Polysorbate 80</td>
</tr>
<tr>
<td>Polysquartemium-7</td>
<td>$p$-Aminophenol</td>
</tr>
<tr>
<td>Polysorbate 80</td>
<td>Tetrasodium EDTA</td>
</tr>
<tr>
<td>Tetrasodium EDTA</td>
<td>Methylparaben</td>
</tr>
<tr>
<td>Methylparaben</td>
<td>$m$-Aminophenol</td>
</tr>
<tr>
<td>Ascorbic Acid</td>
<td>Ascorbic Acid</td>
</tr>
<tr>
<td>Hydrolyzed Silk</td>
<td>Hydrolyzed Silk</td>
</tr>
<tr>
<td>Sodium Sulfite</td>
<td>Sodium Sulphite</td>
</tr>
</tbody>
</table>

She had never used any kind of hair dye before. Her medical history was negative for drug, food or environmental allergies and atopy, but when she was 7 years old she developed a similar cutaneous reaction accompanied by high fever in a few hours from the application on her arm of a black henna tattoo made by a Chinese itinerant artisan.

At admission steroids (methylprednisolone 80 mg intravenous) and antihistamines (chlorpheniramine 10 mg intramuscular) were immediately administrated without any benefit: hence she was transferred to the paediatric unit where she received further medical treatments and slowly improved in 15 days.
During hospitalization IgE antibodies tested with ImmunoCAP Phadiatop resulted negative; a dermatologist diagnosed an allergic contact dermatitis and prescribed the continuation of steroid and antihistamine therapy.

In the first days, inflammatory markers decreased and oedema and urticaroid lesions slowly started healing, but they suddenly worsened on the fifth day when she was allowed to wash her hair using a soft detergent.

Oxatomide was promptly administered and steroid therapy, which was in de-escalation phase, was brought back to full dosage (methylprednisolone 80 mg/die). The next day an itching micropapular cutaneous eruption with macropapules and urticaroid elements appeared on the neck and the trunk. Her hair was pulled and tied very high on top of her head to prevent any contact with the neck and the face.

During the next days the cutaneous eruption and the oedema’s conditions improved on the neck but not on the face and the eyelids; an intense itching and some scratches were still present on the scalp and she started losing hair locks.

On the tenth day her hair was once again washed using a neutral shampoo and avoiding carefully any contact with the skin and she did not present any reaction.

On the 14th day inflammatory markers normalized and the patient was dismissed with a corticosteroid and antihistamine de-escalation scheduled home treatment. Moreover, the patient was instructed to wash her hair with shampoo once every 3–4 days maximum, preventing the contact of the hair with the skin and avoiding product containing \( p \)-phenylenediamine.

After this episode the patient started to suffer from pruriginous dermatitis when wearing coloured clothes especially during the warmest months.

In August 2014, the patient presented a severe local and systemic reaction triggered by a pair of snug black trousers. She developed itching vesicular eruptions on her legs and thighs accompanied by hyperpyrexia and was again treated with steroids and antihistamines.

Due to these recurrent allergic episodes, the scheduled patch test was delayed until October 2014. A standard series of 40 allergens in accordance with the Italian Society of Allergological Environmental and Professional Dermatology guidelines were tested. A few hours later she suffered from generalized malaise, sense of constriction (without bronchospasm or laryngospasm) and an intense itching in the area where the patches had been applied. She rapidly improved after a single administration of corticosteroids and antihistamines, therefore the patches were not removed.

Epicutaneous tests resulted negative for \( p \)-phenylenediamine, strongly positive for Benzocaine (++) and showed an extreme reaction to Disperse Dyes mix (+++), including Disperse Blue 124, Disperse Yellow 3, Disperse Orange 1 and 3, Disperse Red 1 and 17, Disperse Black 1.

The girl still suffers from dermatitis when wearing new clothes and alopecia persists on three little areas of her scalp; the patch test has not been repeated yet.

3.2. Case Series Review

In Table 2, 34 cases published between 2002 and 2014 are reported. All the selected subjects had been previously sensitized to henna tattoos before presenting clinical reactions to hair dyes.
Table 2. Case-series.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17</td>
<td>F</td>
<td>Canada</td>
<td>8 months</td>
<td>yes</td>
<td>12 h</td>
<td>Nice and easy 120 Clairol</td>
<td>Itchy eruption over the ears, temples and scalp. Severe edema of periorbital, perimandibular, anterocervical soft tissue. 3 cm patch of hair loss.</td>
<td>3+</td>
<td>Para-toluenediamine, 0-nitro-paraphenylenediamine, 3-aminophenol, 4-aminophenol, N-isopropyl-N'-phenyl-p-phenylenediamine (IPPD) , Benzocaine, Nickel sulphate</td>
<td>[27]</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>F</td>
<td>Australia</td>
<td>30 months</td>
<td>yes</td>
<td>–</td>
<td>–</td>
<td>Severe scalp swelling. In the previous ten months, the patients presented also an erythematous and pruritic rash on her feet and ankles due to dark coloured socks.</td>
<td>2+</td>
<td>Nickel, cobalt, 4-aminooazobenzene, disperse yellow 3, disperse red 1, disperse red 17, disperse orange 1, direct orange 34, maroon brassiere</td>
<td>[28]</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>M</td>
<td>UK</td>
<td>12 months</td>
<td>yes</td>
<td>24 h</td>
<td>–</td>
<td>Erythema and edema of the neck and face; fever; increased neutrophils</td>
<td>Strong positive (3+)</td>
<td>Ammonium persulfate, 3-aminophenol, 4-aminophenol, hydrogen peroxide, cocamidopropylbetaine, caine mix, methylchloroisothiazoline</td>
<td>[29]</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>F</td>
<td>UK</td>
<td>24 months</td>
<td>yes</td>
<td>few hours</td>
<td>–</td>
<td>Erythema and edema of the face</td>
<td>Strong positive (3+)</td>
<td>Neomycin, formaldehyde, colophony, balsam of peru, methylchloroisothiazoline, 2,5-diaminotoluene sulfate, 3-aminophenol, 4-aminophenol, hydrogen peroxide</td>
<td>[29]</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>M</td>
<td>Denmark</td>
<td>–</td>
<td>yes</td>
<td>24 h</td>
<td>Live, Schwartzkopf, Black</td>
<td>Within 24 h: edema of the ears and eczema. Facial edema lasted for 1 week</td>
<td>3+</td>
<td>Disperse orange 3, 2,5-diaminotoluene, p-aminophenol, hydro-quinone, black rubber, m-aminophenol, N-p-phenylenediamine, caine</td>
<td>[30]</td>
</tr>
<tr>
<td>6</td>
<td>14</td>
<td>F</td>
<td>Denmark</td>
<td>36 months</td>
<td>yes</td>
<td>48 h</td>
<td>Dark red, professional dye</td>
<td>Eczema of the forehead, eczema lasted for 10 days</td>
<td>2+</td>
<td>Disperse orange 3, 2,5-diaminotoluene, p-aminophenol, hydro-quinone, black rubber, m-aminophenol, N-p-phenylenediamine, caine</td>
<td>[30]</td>
</tr>
<tr>
<td>7</td>
<td>15</td>
<td>F</td>
<td>Denmark</td>
<td>24 months</td>
<td>yes</td>
<td>24 h</td>
<td>Evolution 564R, Alfa-Parfsrl</td>
<td>Eczema, edema of the forehead, eyes and face lasted for 2 weeks</td>
<td>3+</td>
<td>2,5-diaminotoluene, p-aminophenol, hydro-quinone, black rubber, m-aminophenol, N-p-phenylenediamine, caine</td>
<td>[30]</td>
</tr>
</tbody>
</table>
Table 2. Cont.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>14</td>
<td>M</td>
<td>Denmark</td>
<td>12 months</td>
<td>yes</td>
<td>72 h</td>
<td>Garnier Nutrisse Natae 2.10 Bilberry</td>
<td>Severe edema of the neck and face lasted for 1 week</td>
<td>3+</td>
<td>Disperse orange 3, 2,5-diamintoluene, 3,4-aminophenol, hydro-quinone, black rubber, N-p-phenylenediamine</td>
</tr>
<tr>
<td>9</td>
<td>15</td>
<td>M</td>
<td>Denmark</td>
<td>48 months</td>
<td>yes</td>
<td>24 h</td>
<td>Garnier Nutrisse Natae Blue black</td>
<td>Fainting, severe facial edema, with eyes completely closed</td>
<td>2+</td>
<td>Disperse orange 3, 2,5-diamintoluene, 3,4-aminophenol (uncertain), black rubber, m-aminoanisol (uncertain), caine (uncertain)</td>
</tr>
<tr>
<td>10</td>
<td>14</td>
<td>F</td>
<td>Denmark</td>
<td>72 months</td>
<td>yes</td>
<td>48 h</td>
<td>L’Oreal new casting 37 Mangue</td>
<td>Edema of the forehead and face. Oozing scalp dermatitis. The patient needed to cut off all her hair.</td>
<td>2+</td>
<td>3,4-aminophenol, m-aminoanisol, caine (uncertain)</td>
</tr>
<tr>
<td>11</td>
<td>14–38</td>
<td>F</td>
<td>Canada</td>
<td>–</td>
<td>yes</td>
<td>24–48 h</td>
<td>–</td>
<td>Erythema, edema, pruritus of the scalp and face</td>
<td>Strong positive (3+)</td>
<td>Paratoluenediamine, aminoanisol, 2-nitro-4-phenylenediamine</td>
</tr>
<tr>
<td>12</td>
<td>14–38</td>
<td>F</td>
<td>Canada</td>
<td>–</td>
<td>yes</td>
<td>24–48 h</td>
<td>–</td>
<td>Erythema, edema, pruritus of the scalp and face</td>
<td>Strong positive (3+)</td>
<td>Paratoluenediamine, aminoanisol, 2-nitro-4-phenylenediamine</td>
</tr>
<tr>
<td>13</td>
<td>14–38</td>
<td>F</td>
<td>Canada</td>
<td>–</td>
<td>yes</td>
<td>24–48 h</td>
<td>–</td>
<td>Erythema, edema, pruritus of the scalp and face</td>
<td>Strong positive (3+)</td>
<td>Paratoluenediamine, aminoanisol, 2-nitro-4-phenylenediamine</td>
</tr>
<tr>
<td>14</td>
<td>14–38</td>
<td>F</td>
<td>Canada</td>
<td>–</td>
<td>yes</td>
<td>24–48 h</td>
<td>–</td>
<td>Erythema, edema, pruritus of the scalp and face</td>
<td>Strong positive (3+)</td>
<td>Paratoluenediamine, aminoanisol, 2-nitro-4-phenylenediamine</td>
</tr>
<tr>
<td>15</td>
<td>14–38</td>
<td>F</td>
<td>Canada</td>
<td>–</td>
<td>yes</td>
<td>24–48 h</td>
<td>–</td>
<td>Erythema, edema, pruritus of the scalp and face</td>
<td>Strong positive (3+)</td>
<td>Paratoluenediamine, aminoanisol, 2-nitro-4-phenylenediamine</td>
</tr>
<tr>
<td>16</td>
<td>14–38</td>
<td>F</td>
<td>Canada</td>
<td>–</td>
<td>yes</td>
<td>24–48 h</td>
<td>–</td>
<td>Erythema, edema, pruritus of the scalp and face</td>
<td>Strong positive (3+)</td>
<td>Paratoluenediamine, aminoanisol, 2-nitro-4-phenylenediamine</td>
</tr>
<tr>
<td>17</td>
<td>14</td>
<td>M</td>
<td>Israel</td>
<td>12 months</td>
<td>yes</td>
<td>72 h</td>
<td>Oxidative dye</td>
<td>Facial and scalp edema</td>
<td>Positive</td>
<td>Unknown</td>
</tr>
<tr>
<td>Patient No</td>
<td>Age</td>
<td>Sex</td>
<td>Country of Origin</td>
<td>Time Elapsed Since Tattoo</td>
<td>Tattoo-Associated Dermatitis</td>
<td>Latency Since Dyeing</td>
<td>Product</td>
<td>Signs and Symptoms</td>
<td>Patch Test</td>
<td>Other Positive Patch Tests</td>
</tr>
<tr>
<td>------------</td>
<td>-----</td>
<td>-----</td>
<td>-------------------</td>
<td>--------------------------</td>
<td>-----------------------------</td>
<td>----------------------</td>
<td>---------</td>
<td>-------------------</td>
<td>------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>18</td>
<td>15–60</td>
<td>F</td>
<td>Switzerland</td>
<td>24–108 months</td>
<td>yes</td>
<td>–</td>
<td>–</td>
<td>Severe contact dermatitis</td>
<td>Positive</td>
<td>Some of the patients were positive to other dyes: disperse orange, disperse yellow, para-toluylendiamine, aminophenol</td>
</tr>
<tr>
<td>19</td>
<td>15–60</td>
<td>F</td>
<td>Switzerland</td>
<td>24–108 months</td>
<td>yes</td>
<td>–</td>
<td>–</td>
<td>Severe contact dermatitis</td>
<td>Positive</td>
<td>Some of the patients were positive to other dyes: disperse orange, disperse yellow, para-toluylendiamine, aminophenol</td>
</tr>
<tr>
<td>20</td>
<td>15–60</td>
<td>F</td>
<td>Switzerland</td>
<td>24–108 months</td>
<td>yes</td>
<td>–</td>
<td>–</td>
<td>Severe contact dermatitis</td>
<td>Positive</td>
<td>Some of the patients were positive to other dyes: disperse orange, disperse yellow, para-toluylendiamine, aminophenol</td>
</tr>
<tr>
<td>21</td>
<td>15–60</td>
<td>F</td>
<td>Switzerland</td>
<td>24–108 months</td>
<td>yes</td>
<td>–</td>
<td>–</td>
<td>Severe contact dermatitis</td>
<td>Positive</td>
<td>Some of the patients were positive to other dyes: disperse orange, disperse yellow, para-toluylendiamine, aminophenol</td>
</tr>
<tr>
<td>22</td>
<td>15–60</td>
<td>M</td>
<td>Switzerland</td>
<td>24–108 months</td>
<td>yes</td>
<td>–</td>
<td>–</td>
<td>Severe contact dermatitis</td>
<td>Positive</td>
<td>Some of the patients were positive to other dyes: disperse orange, disperse yellow, para-toluylendiamine, aminophenol</td>
</tr>
<tr>
<td>23</td>
<td>15–60</td>
<td>M</td>
<td>Switzerland</td>
<td>24–108 months</td>
<td>yes</td>
<td>–</td>
<td>–</td>
<td>Severe contact dermatitis</td>
<td>Positive</td>
<td>Some of the patients were positive to other dyes: disperse orange, disperse yellow, para-toluylendiamine, aminophenol</td>
</tr>
<tr>
<td>24</td>
<td>14</td>
<td>M</td>
<td>UK</td>
<td>18 months</td>
<td>yes</td>
<td>96 h</td>
<td>–</td>
<td>Life threatening allergic reaction</td>
<td>–</td>
<td>Allergic reaction to sunscreen</td>
</tr>
<tr>
<td>25</td>
<td>27</td>
<td>F</td>
<td>Turkey</td>
<td>24 months</td>
<td>yes</td>
<td>48 h</td>
<td>–</td>
<td>Severe edema of the eyelids, forehead and face. Erythema of the forehead</td>
<td>Positive</td>
<td>Unknown cross-reacting substances</td>
</tr>
<tr>
<td>26</td>
<td>14</td>
<td>M</td>
<td>Switzerland</td>
<td>12 months</td>
<td>yes</td>
<td>–</td>
<td>L'Oreal Garnier Nutrisse Cream</td>
<td>Edema of the scalp, facial angioedema</td>
<td>3+</td>
<td>Benzocaine, thiram mix, 3-aminophenol, p-aminophenol, p-toluylendiamine, hydroquinone, disperse orange 3, disperse yellow 3, disperse red 17 (uncertain)</td>
</tr>
</tbody>
</table>
Table 2. Cont.

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Age</th>
<th>Sex</th>
<th>Country of Origin</th>
<th>Time Elapsed Since Tattoo</th>
<th>Tattoo-Associated Dermatitis</th>
<th>Latency Since Dyeing</th>
<th>Product</th>
<th>Signs and Symptoms</th>
<th>Patch Test</th>
<th>Other Positive Patch Tests</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>-</td>
<td>F</td>
<td>Switzerland</td>
<td>Unknown (years)</td>
<td>yes</td>
<td>–</td>
<td>–</td>
<td>Contact dermatitis</td>
<td>3+</td>
<td>Sodium benzoate, cinchocaine HCl</td>
<td>[36]</td>
</tr>
<tr>
<td>28</td>
<td>14</td>
<td>F</td>
<td>Switzerland</td>
<td>36 months</td>
<td>yes</td>
<td>few hours</td>
<td>L’Oreal Casting Cream Gloss</td>
<td>Pruritus and vesicular dermatitis of the scalp, Edema of the eyelids, fever</td>
<td>3+</td>
<td>Benzocaine, fragrance mix, fragrance mix II (uncertain), turpentine (uncertain), 3-aminophenol, p-aminophenol, p-toluylenediamin, disperse orange 3, disperse yellow 3, disperse yellow 9</td>
<td>[36]</td>
</tr>
<tr>
<td>29</td>
<td>15</td>
<td>F</td>
<td>Switzerland</td>
<td>72 months</td>
<td>yes</td>
<td>–</td>
<td>–</td>
<td>Severe facial edema and scalp contact dermatitis</td>
<td>4+</td>
<td>Benzocaine, 3-aminophenol, p-aminophenol, p-toluylenediamin, disperse orange 3, disperse yellow 3, disperse yellow 9</td>
<td>[36]</td>
</tr>
<tr>
<td>30</td>
<td>43</td>
<td>M</td>
<td>Switzerland</td>
<td>120 months</td>
<td>yes</td>
<td>within 24 h</td>
<td>RefectoCil</td>
<td>Vesicular dermatitis after dyeing his eyebrows</td>
<td>3+</td>
<td>3-aminophenol, p-aminophenol, p-toluylenediamin, disperse orange 3, disperse yellow 3</td>
<td>[36]</td>
</tr>
<tr>
<td>31</td>
<td>59</td>
<td>F</td>
<td>Switzerland</td>
<td>–</td>
<td>yes</td>
<td>–</td>
<td>–</td>
<td>Contact dermatitis</td>
<td>2+</td>
<td>Sodium thiosulfatosaurate</td>
<td>[36]</td>
</tr>
<tr>
<td>32</td>
<td>40</td>
<td>F</td>
<td>Switzerland</td>
<td>132 months</td>
<td>yes</td>
<td>few hours</td>
<td>–</td>
<td>Itching, extreme swelling of the scalp and oozing eczema</td>
<td>4+</td>
<td>Benzocaine, textile mix, 3-aminophenol, p-aminophenol, p-toluylenediamin, disperse orange 1, disperse orange 3, disperse yellow 3</td>
<td>[36]</td>
</tr>
<tr>
<td>33</td>
<td>15</td>
<td>F</td>
<td>Turkey</td>
<td>36 months</td>
<td>yes</td>
<td>72 h</td>
<td>–</td>
<td>Severe edema of the neck, ears, eyelids, forehead, scalp</td>
<td>3+</td>
<td>Unknown</td>
<td>[37]</td>
</tr>
<tr>
<td>34</td>
<td>15</td>
<td>F</td>
<td>Turkey</td>
<td>12 months</td>
<td>yes</td>
<td>1 h</td>
<td>–</td>
<td>Pruritus of the forehead, scalp and face. After 2 days severe edema of the face, forehead and eyelids</td>
<td>Positive</td>
<td>Unknown cross-reacting substances</td>
<td>[38]</td>
</tr>
</tbody>
</table>
Only one patient (No. 2 in the Table 2) developed reactions to all three products: the tattoo ink, hair and textile dyes.

Ten patients were males and 24 were females, their age ranged between 12 and 59 years old. Considering the provenience of the reports, the majority came from occidental countries, respectively Switzerland (13 cases), Canada (seven cases) Denmark (six cases) the United Kingdom (three cases), Turkey (three cases), Australia (one case), Israel (one case).

The totality of the patients had presented a contact dermatitis after the application of the tattoo.

The time elapsed between the tattoo and the hair dyeing was reported in 25 cases and ranged from eight to 132 months.

In 22 patients the time lapse between the hair dye and the onset of clinical signs was less than 72 h and 96 h in one case.

In general, all patients suffering from contact allergy to PPD experienced erythema and oedema over the forehead, the face and/or the neck. Eyelids oedema was also common and explicitly reported in 7 cases (20.6%), itching/eczema in 14 (41.2%) and vesicular eruption in 2 (5.9%). Fever was reported only in two cases (5.9%) and alopecia only in one patient (2.9%). In one case (patient No. 24) the subject developed a life threatening allergic reaction.

A positive patch-test reaction to para-phenylenediamine was reported in all the cases but one who, anyway, had a history of allergy to known cross-reacting products such as sunscreens. Moreover, the results revealed an extremely frequent coexistence of sensitization to other allergens. In particular, a positivity to para-aminophenol and/or to disperse textile dyes was ascertained respectively in at least 13 and 9 cases.

4. Discussion

Pure henna (Lawsonia inermis L.) seems to have a low allergenic potential and reports of contact dermatitis are negligible [9] despite its millenary and increasing worldwide use.

On the other hand, contact dermatitis and sensitization from black henna temporary tattoos, known for containing PPD and/or various additives and chemicals, seems to be an ongoing problem.

In the same way, several cases of contact allergy from hair colourants [39] and textile dyes [40,41] are described in medical literature.

Nevertheless, only 34 clinical cases of sensitive reactions to hair dyes possibly caused by the previous application of a henna tattoo, could be found (Table 2); among these, only one patient manifested symptoms of contact allergy to both hair and clothing after the application of a henna tattoo [28], as in the case we observed. The actual scope of the problem is probably underestimated and the number of cases matching the one we analysed in this study is probably higher than the one reported by the published case reports.

Some of the patients included in our case-series were patch test positive to azoic dyes [28,30,33,36], but the majority were patch test positive to PPD, therefore it was supposed that this specific allergen was contained in the black henna tattoo.

In the light of what the literature says, it seems odd that in our case the PPD test was negative, while the other para-compounds resulted strongly positive.

We do not know the exact composition of the black henna used by the street artisan, therefore the causative relationship between the tattoo and the symptoms shown by the patient when dyeing her hair and wearing coloured clothes is mainly based on the clinical history and on the evidences available from scientific literature [3].

Since, as reported in Table 1, the hair dye contained PPD and other para amino compounds, but no azoic dyes, we could also suppose that the contact allergy was a cross reaction caused by a primitive sensitization to azoic dyes frequently contained in permanent tattoo inks [42]; however in this case the girl should have been suffering from clothes contact allergy from the time of the tattooing and not only after the hair dying.

Anyway, the result of the epicutaneous tests is questionable for several reasons.
First of all the test has been done nine months after she showed reaction to the hair dying: in this period she had avoided PDD containing products, while she had developed progressive intense sensitization to clothes confirmed by the strong positive patch reaction to Disperse mix.

Moreover, the administration of corticosteroids and antihistamines few hours after the application of the patches could have altered the test.

Eventually, we cannot exclude a false negative result of the test, as described in the literature [43,44].

It is to be noted that the cosmetics used for colouring our patient’s hair were correctly labelled with a specific warning about possible allergic reaction in subjects that have experienced a reaction to a temporary “black henna” tattoo in the past, but the professional hair stylist had not investigated about this occurrence before applying the hair dyes.

Until now the girl has been suffering from recurrent contact dermatitis caused by clothing.

In our opinion this case highlights the risk of developing contact allergy from the application of temporary tattoos not only to hair colourants but also to textile dyes.

This evidence seems to be very dangerous because people wear clothes coloured with unidentified dyes every day.

Cosmetics surveillance and vigilance systems can help to monitor the safety of cosmetic products used by large populations of consumers. Appropriate preventive measures and informative campaigns should be undertaken when serious adverse reactions are detected [45,46].

We point out that in the Europe Union (EU), tattoos are not considered cosmetics and consequently are not under Regulation 1223/2009 CE [17]. A resolution on requirements and criteria for the safety of tattoos and permanent make-up has been published in 2008 [47].

5. Conclusions

In Europe, as in many other countries, temporary tattoos and also permanent tattoos are an increasing fashionable habit among adolescents, but they are not sufficiently regulated yet because they are not considered cosmetics.

The case we presented highlights the potential hazard of developing direct and cross-sensitization to PPD, azoic dyes and other chemicals from the application on the skin of preparations designed for temporary body art.

The patients sensitized from henna tattoos may experience serious allergic reactions to many different types of products, since cross reacting compounds can be found in cosmetics, medicines, clothes and foods.

If regulatory dispositions about the composition and labelling of cosmetic can help consumers avoiding products containing PPD or other chemicals they are sensible to, a dermal contact with unidentifiable allergenic textile dyes seems to be a more frequent, poorly preventable and not less hazardous event.

Cosmetic dispositions are the same in EU countries, but they are different in respect to the USA and to the other parts of the world.

For this reason and due to the globalization phenomenon, people can be unknowingly exposed to dangerous legal or illegal products marketed as ‘natural’ preparations.

Cosmetovigilance is very important for improving the safety of cosmetic products on the market; therefore, health professionals and end users should be encouraged to report undesirable events associated with their use.

Medical and scientific attention is mainly drawn to the safety assessment of PPD, because of its involvement in several published cases of sensitization from tattooing and hair dyeing but various other allergenic substances could be contained in black henna batches.

In our opinion, considering the demonstrated risk of life-long sensitization caused by temporary tattoos and the increasing difficulty in controlling and monitoring the flow of merchandise, Health
Authorities should regulate any kind of body art and promote informative campaigns to prevent the use of henna and other cosmetic paints in children.

**Author Contributions:** Paola Angela Moro gave toxicological medical advice, conceived and designed the study; Marco Morina and Fabrizia Milani carried out the review and analyzed published cases; Marco Pandolfi, Francesca Guerriero, and Luca Bernardo handled the case and collected clinical data; All the Authors contributed to the writing and revision of the manuscript.

**Conflicts of Interest:** The authors declare no conflict of interest.

**References**

15. Goldenberg, A.; Jacob, S. Paraphenylenediamine in black henna temporary tattoos: 12-year Food and Drug Administration data on incidence, symptoms, and outcomes. *J. Am. Acad. Dermatol.* 2015, 72, 724–726. [CrossRef]


29. Jasim, Z.; Darling, J.; Handley, J. Severe allergic contact dermatitis to paraphenylenediamine in hair dye following sensitization to black henna tattoos. Contact Dermat. 2005, 52, 116–117. [CrossRef] [PubMed]


33. Kind, F.; Scherer, K.; Bircher, A. Allergic contact dermatitis to paraphenylenediamine in hair dye after sensitization from a black henna tattoo: Report of six cases. Contact Dermat. 2010, 63, 74.


