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CASE STUDY - ALLERGIC CONTACT DERMATITIS IN RELATION TO TATTOOS

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რეზიუმე

ტატუირების პოპულარიზაციის პარალელურად, სამედიცინო პრაქტიკაში მატულობს ტატუირების შედეგად კანზე განვითარებული რეაქციების შემთხვევათა რიცხვი. ჩვენს ნაშრომში აღწერილია ტატუთი გამოწვეული კანის ალერგიული რეაქციის შემთხვევა და განხილულია მისი იმუნოლოგიური მექანიზმი. ასევე აღწერილია ტატუს მელნის შემადგენელი კომპონენტები, მათი ალერგენული პოტენციალი და განვითარებული ალერგიული რეაქციების მკურნალობის შესაძლო ვარიანტები.

ტატუს მელანი შესაძლოა შეიცავდეს სხვადასხვა ტიპის ალერგენს. გამოყოფენ ბიოდეგრადირებად და არაბიოდეგრადირებად კომპონენტებს. პირველ ჯგუფში შემავალი ნივთიერებები, როგორებიცაა ბუნებრივი საღებავები და კონსერვანტები, განაპირობებენ კანზე ისეთი ალერგიული პროცესის განვითარებას, რომელიც კარგად ემორჩილება კონსერვატიულ თერაპიას. რაც შეეხება არაბიოდეგრადირებად კომპონენტებს, მათ მიერ განვითარებული ალერგიული რეაქციები, როგორც წესი, საჭიროებენ ინვაზიური მეთოდების გამოყენებას, როგორებიცაა ქირურგიული ჩარევა, დერმის ე.წ. "გაპარსვა" და ლაზერული თერაპია, რომელიც ყველაზე ხშირად გამოიყენება პრაქტიკაში. ამ მხრივ ყველაზე საყურადღებოა წითელი ფერის პიგმენტი.

ტატუს შემადგენელ ნივთიერებებთან დაკავშირებით მოქმედი რეგულაციები არ არსებობს, რაც უფრო მეტად ზრდის გვერდითი მოვლენების განვითარების რისკს. არსებობს ალერგიული რეაქციების თავიდან აცილების გარკვეული პრევენციული საშუალებები, როგორებიცაა კანის ალერგიული სინჯები. მსგავსი ტესტების სპეციფიკურობა საეჭვოა, რამდენადაც უარყოფითი პასუხი სრულებით არ გამორიცხავს ალერგიული რეაქციის განვითარების შესაძლებლობას მოგვიანებით, რამოდენიმე კვირის და თვის შემდეგ. აღსანიშნავია, რომ არ არსებობს მკურნალობის მკაცრად განსაზღვრული გაიდლაინი, ამიტომ თითოეული შემთხვევა ფასდება ინდივიდუალურად და ამავე პრინციპით ხდება მკურნალობის შერჩევაც. ჩვენი პაციენტი იყო ახალგაზრდა ქალი, რომელსაც ტატუს არეში, კერძოდ, წითელი პიგმენტის ადგილას, განუვითარდა მწვავე ალერგიული რეაქცია. ამ კონკრეტულ შემთხვევაში, საწყისი მკურნალობა მიზნად ისახავდა ანთებითი რეაქციის შემცირებას, რათა შემდგომში შესაძლებელი ყოფილიყო ალერგენის, წითელი პიგმენტის, სრულად მოცილება დერმიდან. როგორც ცნობილია, სწორედ ეს უკანასკნელი წარმოადგენს ალერგიული კონტაქტური დერმატიტის ალაგების აუცილებელ პირობას. პაციენტს ჩაუტარდა ადგილობრივი, ანთების საწინააღმდეგო თერაპია. ირიტაციისა და ანთებითი მოვლენების უკუგანვითარების შემდეგ, ჩატარდა ლაზეროთერაპია Q-switched Nd 532 nm ლაზერით. პირველი პროცედურის შემდეგ ტატუს არეში განვითარდა ირიტაცია და ექსუდაცია, რის გამოც ჩატარდა ადგილობრივად ანთების საწინააღმდეგო მკურნალობა. ლოკალური და ლაზერული თერაპიის უშედეგობის გამო, პაციენტს დაენიშნა სისტემური კორტიკოსტეროიდი კლებადი დოზით და დაავადების კონტროლით. ორთვიანი მკურნალობის ფონზე პაციენტის მდგომარეობა გაუმჯობესდა. ივი კვლავ ავრძელებს სისტემურ სტეროიდულ თერაპიას.

Introduction. With the growing popularity of tattooing, allergic reactions caused by inks are becoming a serious health concern. This paper, along with a single case study, gives a general overview of causes, results and treatment options for such allergic reactions. It is known from several investigations that tattoo inks may contain contact allergens such as metals, colorants and preservatives [6]. Cutaneous

injection of these agents can elicit different types of immunological reactions. Reactions from inks can range from mild local symptoms to systemic ones affecting patient's quality of life. The situation is complicated since there are no strict regulations on dyes used in inks. More new products are appearing in tattoo shops, the quality of which may be questionable and in certain cases may be contaminated with different carcinogenic agents [21]. This, along with already present dangers from dyes themselves, puts tattoo enthusiasts at a higher risk of immunological complications. Most notable in this regard are red inks with the highest overall incidence. Unfortunately, research in this field is lacking and there are no set guidelines for treatment or prevention. Topical or intralesional corticosteroids can be used as the first line of treatment. However, their effectiveness varies and may be temporary or insufficient. It is well understood that allergic reactions will persist as long as an irritant is present. Thus, more drastic measures must be taken. This includes surgical interventions and laser therapy. The effectiveness and safety of laser removal have been disputed in the past [2]. However, a recent study (in regard to red ink) [1] has shown that complications such as anaphylactic reactions are unlikely and all outcomes in this study have been positive. Regarding prevention, professional tattoo artists do perform patch and dot tests prior to tattooing. Unfortunately, such measures are insufficient [1] since allergic reactions may occur weeks or months later.

Case report. We present a case of a 25-year-old woman with severe tattoo irritation and itching on the flexor surface of her right forearm. The patient got a multicolored tattoo (black, yellow, green and red) (Fig. 1) with permanent ink 6 months ago with skin irritation forming 10 days after and worsening ever since. Itching and pain were very severe. The patient had one other old permanent colored tattoo (black and blue) on the same hand, on the extensor surface, more proximally. Information regarding this tattoo is limited due to them not causing allergic reactions.

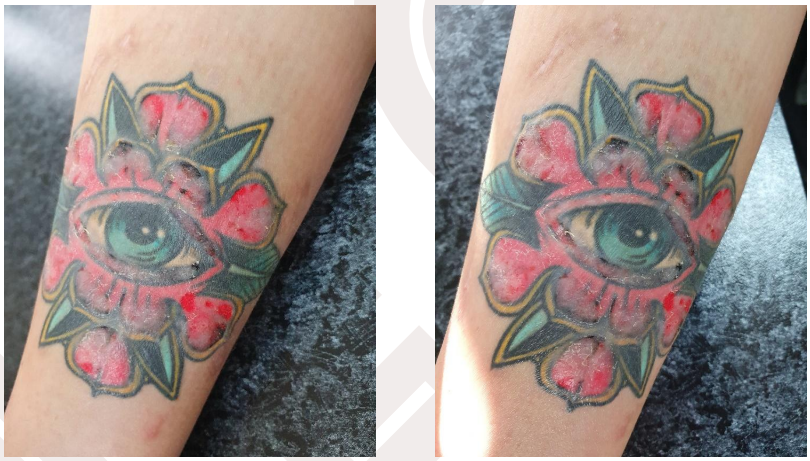

Fig. 1. Flexor surface of right forearm. Erosions, exudation, infiltration and scaling on red-colored parts.

She has previously visited a dermatologist and was prescribed: for local application - Betamethasone dipropionate, Zn-hyaluronate, Terbinafine, Triamcinolone, Tetracycline, Ethacridine lactate; and per os – Chloropyramine, Ceftriaxone, Dexamethasone, Fexofenadine. The treatment slightly improved symptoms, but the patient still had recurrent episodes of strong itching and pain. On examination skin over the tattoo was hyperemic with slight erosions on red-colored parts (Fig. 1). Scaling, exudation, infiltration and multiple crusts were also present.

Diagnosis of allergic contact dermatitis was made. The patient was prescribed oral Bilastine - 1 tab. BID, for local application - Mometasone furoate - in the evenings; Microdacyn hydrogel - BID, in the morning and afternoon. The patient was advised to undergo laser tattoo removal therapy once inflammation would subside. One month later the patient returned with decreased swelling, infiltration and erosions (Fig.2). Because of this, laser therapy removal session was arranged.

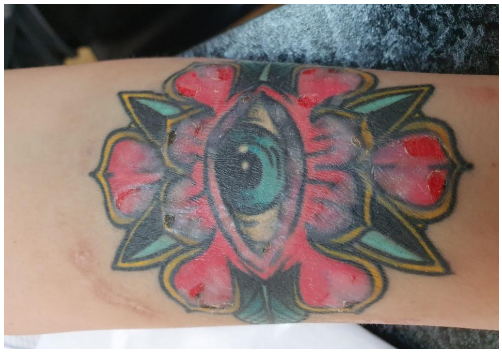

Fig. 2. One month after treatment. Decreased swelling, infiltration and erosions.

Three days after the first sessions of laser tattoo removal therapy with Q-switched neodymium (Nd) 532 nm laser, the patient consulted with us regarding pain in the tattooed area. Skin irritation was present with exudation (Fig.3) Ethacridine lactate pads and Microdacyn hydrogel were prescribed for local application; to alleviate pain Ibuprofen was added.

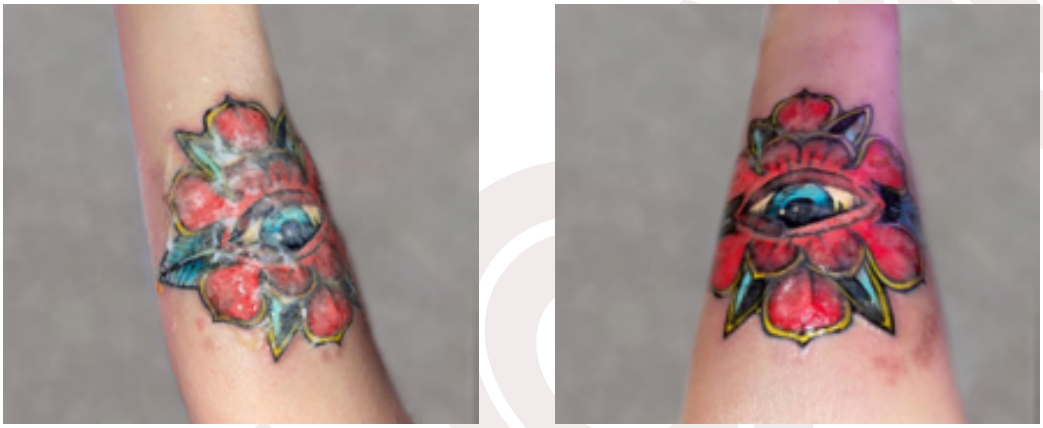

Fig. 3. After laser removal treatment. Skin irritation with exudation. Erosions over the tattooed skin.

After one week patient visited us again. Acute inflammation and exudation had subsided. On examination parts of the skin treated with laser removal had developed deep erosions and hypertrophic scarring (Fig. 4). The itchiness remained while the pain was slightly reduced.

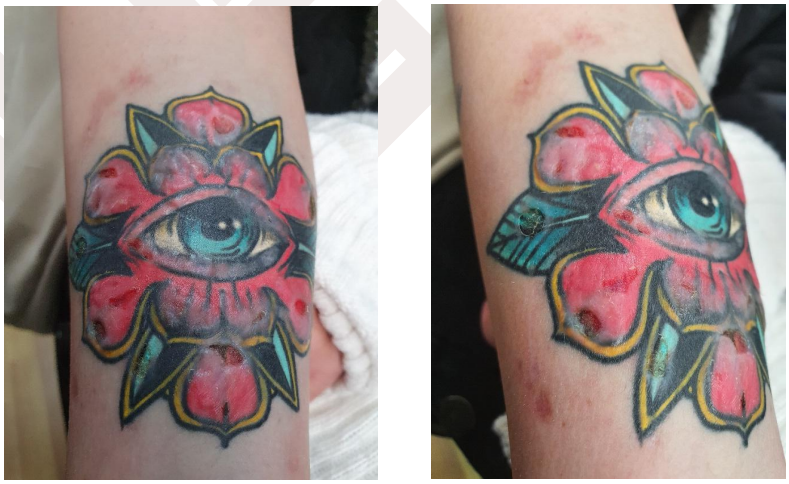

Fig. 4. One week after treatment (and laser removal therapy). Deep erosions and hypertrophic scarring.

The patient was prescribed Mometasone furoate and Dexpanthenol/Chlorhexidine for topical application. To reduce the pain, Meloxicam per os QD was prescribed. Due to the ineffectiveness of topical and laser removal therapy, patient was prescribed systemic treatment with Methylprednisolone (16mg) with an indication to gradually decrease the dosage. After two months of systemic therapy, patient's condition improved (Fig.5). She still continues the treatment.

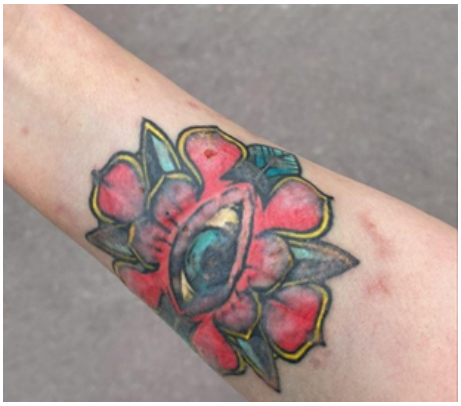

Fig. 5. Two months after treatment with systemic corticosteroids.

Discussion. Complications of tattooing are not a novel problem. Different types of reactions have been recorded throughout the history. With the growing prevalence of tattooing, more research and regulations are required to eliminate possible adverse reactions. These effects include acute allergy directly after tattooing or delayed hypersensitivity after long-term exposure to the chemicals in the inks [18,19,31]. According to the literature, the most frequent tattoo reactions concern allergic contact dermatitis due to delayed hypersensitivity reaction to different pigments contained in the tattoos [29]. There are two types of contact dermatitis: Irritant contact dermatitis (ICD) and allergic contact dermatitis (ACD). ICD arises in response to the obligate irritant, while ACD is caused by a facultative agent (also called contact allergens). ICD accounts for ~80% of all contact dermatitis, with the rest being ACD [5]. These processes cause inflammation of the skin manifested by varying degrees of erythema, edema and vesiculation [10].

Mechanism of Allergic contact dermatitis. In ACD, a distinction should be made between induction (sensitization) and effector (elicitation) phases [20]. The induction phase includes the events following first contact with the allergen. This is also called contact allergy [20].

Contact allergy is a T-cell mediated reaction induced by haptens. These are low molecular weight (<500 Daltons) chemicals (such as metal salts, dyes, preservatives and fragrances), which are not immunogenic by themselves but can be efficiently recognized by the immune system after binding to the skin components and penetrate the stratum corneum barrier of the skin. The allergen penetrating the skin readily associates with all kinds of skin components, including major histocompatibility complex (MHC) proteins. These molecules, in humans encoded for by histocompatibility antigen (HLA) genes, are abundantly present on epidermal Langerhans cells (LC) [6,15]. Hapten-Protein binding is the initial step in the development of allergic contact dermatitis [6]. During the induction phase, skin contact with a hapten triggers the migration of epidermal Langerhans cells (LC) via the afferent lymphatic vessels to the skin-draining lymph nodes. Haptenized LC home into the T-cell-rich paracortical areas. Here, conditions are optimal for encountering naive T cells ($CD8^+$ and $CD4^+$) that specifically recognize allergen–MHC molecule complexes. Hapten-specific T-cells now expand abundantly and generate effector and memory cells, which are released via the efferent lymphatics into the circulation. With their newly acquired homing receptors, these cells can easily extravasate peripheral tissues. The induction phase ends here and begins the second, effector phase [6,17,21,30].

The second phase is also called the elicitation or provocation phase [6] and results in the clinical manifestation of ACD. It occurs after re-exposure to the allergen and is mediated by CD8+ T cells, which are primed in lymphoid organs during the sensitization phase and are recruited in the skin upon re-exposure to the haptens. By renewed allergen contact, the effector phase is initiated, which depends not only on the increased frequency of specific T-cells, and their altered migratory capacities, but also on their low activation threshold. Due to their lowered activation threshold, hapten-specific effector T-cells are triggered by various haptenized cells, including LC and keratinocytes (KC), to produce proinflammatory cytokines and chemokines. Thereby, more inflammatory cells are recruited further amplifying local inflammatory mediator release. This leads to a gradually developing eczematous reaction.

Tattoos as allergens. Tattooing involves injection of tattoo ink into the dermis to a depth of 1-2 mm using a tattoo machine. Tattoo inks are complex formulations containing several ingredients, both organic and inorganic, by-products and impurities. The inks are usually ready-to-use-products, which

consist of insoluble pigments (responsible for the color) in a liquid made of binder(s) and solvent(s). Preservatives are often added to the mixture to avoid microbiological contamination of the often water-based mixture. Besides intentional ingredients, other substances may be present as impurities such as metals from inorganic and organometallic pigments. Colorants are by far the major ingredient of tattoo inks and may reach high concentrations. The colorants can be classified into dyes and pigments. Dyes along with other biological ingredients and preservatives are soluble and biodegradable. In case of adverse immunological reactions, no long-term treatment will be needed since they will be metabolized and cleared naturally. Pigments, on the other hand, are insoluble, chemically resistant and the preferred choice of tattoo inks. Therefore, sensitization caused by them will be last as long as pigment remains in the dermis [6]. Allergic contact dermatitis in tattoos has been reported regularly since the 1950s [6]. The severity of allergic reaction is mainly determined by the composition of tattoo ink. The components of tattoo ink are difficult to determine and undergo changes with time. There are also no regulations for tattoo inks or color additives, which contain potentially allergic substances and in some cases these pigments used in the formulation of tattoo inks are not even produced for this purpose [28]. The main pigment causing allergic reactions historically is the red one, due to the presence of mercury and its sulfides. Other common etiological factors include chrome and cobalt representing the different dyes (Table 1). However, not all reactions are due to the traditional presence of mercury sulfides and other metal-derived colors, but due to new organic pigments (e.g., Pigment Red 181 and Pigment Red 170) [3,6]. Studies have shown, that people with different colors in their tattoos are at higher risk of developing chronic reactions than the ones with single-colored tattoos. The two ink colors most commonly involved in chronic color-associated reactions were red (8/18) and black (6/18), although other colors were also reported [7]. Red tattoo pigment can be either organic or inorganic. Inorganic red pigment includes mercury, cadmium selenide and sienna (ferric hydrate - iron oxide and manganese oxide) [13]. Organic red pigment includes sandalwood and brazilwood, both organic vegetable dyes [8]. The red pigment can also be made with cinnabar (a mercury derivative) and this is the one that is thought to cause the cell-mediated delayed hypersensitivity reaction [13].

Table 1. Types of dyes and their composition

Color	Composition
Red	• Mercury sulfide (cinnabar) • Ferric hydrate (sienna) • Sandalwood • Brazilwood • Iron oxide
Black	• Carbon (India ink) • Iron oxide • Logwood
Brown	• Ferric oxide
Blue	• Cobalt aluminate • Azure blue • Cobalt blue
Green	• Chromic oxide • Lead chromate • Phthalocyanine dyes • Ferrocyanides and ferricyanides
Yellow	• Cadmium sulfide
Purple	• Manganese • Aluminum
White	• Titanium oxide • Zinc oxide • Lead carbonate

Prevention. We've made it abundantly clear that tattooing comes with its risks which should not be underestimated. Unfortunately, things are not quite clear in terms of harm reduction and allergy prevention. In general, contact allergy can be demonstrated by an allergy test, called a patch test, which is an internationally accepted tool to diagnose contact allergy. The methodology has been in use for over 100 years and is in use worldwide. At patch testing, small amounts of the suspected allergens are applied in aluminum chambers to the upper back of the person under investigation. The patches are left in place for two days and then removed. The skin is inspected for allergic reactions several times over the following days. The diagnosis of allergic contact dermatitis requires typical clinical symptoms, as described, and positive results from patch testing to substances, to which the person is exposed to. Alternatively, in professional tattoo shops, dot tests are performed. This means that a section of skin is tattooed with a single dot of ink. This area is monitored over the course of 24 hours to see what happens. Any swelling or redness could indicate an allergic reaction. These methods however don't guarantee anything. For example, studies [1] have shown that patch and dot testing do not correlate to tattoo reactions caused by mercury (red ink) and understanding of the mechanisms behind the reactions observed in red tattoos is still lacking with type I–III hypersensitivity reactions playing a role [2]. There is no conclusive evidence to date. In light of all these new steps are being taken by world healthcare organizations to prevent unnecessary harm from tattooing. New bills have passed this year in EU that will limit and regulate ingredients in inks. The consequences of such actions remain to be seen. Since outright banning some colors might force tattoo enthusiasts to seek their desired designs from unlicensed professionals further increasing their risks [2].

Treatment. Treatment of allergic reactions to tattoos is difficult, as tattoo pigments are permanently stored in the dermis. Topical, oral and/or intralesional corticosteroids are indicated as first-line treatment. Conservative therapy options also include calcineurin inhibitors and oral antihistamines, but these methods are often insufficient [4,12]. The best treatment option to remove the responsible allergen is unknown. Surgical excision, dermatome shaving or lasers (Q-switched nanosecond laser, ablative CO_2 lasers, picosecond laser) are reported as treatment options with permanent results [12,23]. Though, each treatment option has its disadvantages, such as possible scarring, infection, risk of generalized allergic reactions and treatment imprecision [4]. Laser removal of tattoos has been reported to stimulate an allergic response itself, as it causes fragmentation of the pigment-containing cells, exposing the pigment to the extracellular environment, where it can be recognized as foreign by the immune system [12].

Dermatome shaving is the surgical removal of pigment (hapten) concentrated in the outer dermis. This method is proposed as a first-line treatment of chronic tattoo reactions.

A study from 2015 examined the treatment of 50 patients, with chronic tattoos reactions, with dermatome shaving. Tattoos with red/red nuances dominated the study material. Shaving was performed to the level of the dermis which was free of tattoo pigment as assessed visually by the surgeon. After surgery severity rating of patient's symptoms declined from 3,2 pre-operatively to 1,0, 0,8 and 0,7 after 3,6 and 12 months, respectively [9,24]. With Q-switched laser technology, tattoo removal can be achieved through permanent pigmentary alteration. They are considered the standard method for removing both regular and traumatic tattoos [22]. There are three types of Q-switched nanosecond lasers, that are currently used for tattoo removal: Q-switched ruby laser (694 nm), Q-switched Nd:YAG laser (532 nm,1064 nm) and Q-switched alexandrite laser (755 nm). The Q-switched ruby and alexandrite lasers are useful for removing black, blue and green pigments. The Q-switched 532 nm Nd:YAG laser can be used to remove red, brown and green pigments and the 1064 nm Nd:YAG laser is used for the removal of black and blue pigment. The most common adverse effects following laser tattoo treatment with the Q-switched ruby laser include textural change, scarring, and pigmentary alteration. Other types of Q-switched nanosecond lasers have less risk of scarring or hyperpigmentation [16]. Ultra-pulse CO_2 lasers remain a second-line treatment option. This is a microsurgical laser beam, which removes both the ink and the skin, layer by layer. Complete removal of a tattoo is determined by the size, ink pigment and localization of the tattoo. Several sessions may be needed to reach the desired goal. With this method, entire tattoo can be removed but is replaced by scar tissue. According to studies, in the initial stages of traumatic tattoo removal, the ablative fractional laser treatment appears to be as effective as the standard ruby laser therapy. However, from the 6th session onwards, ruby laser therapy becomes more effective [22].

Picosecond laser, associated with minimal risk of scarring, was recently introduced. It selectively destroys the target pigment without damaging healthy, normal tissue. These lasers use pulse durations of less than 1 nanosecond, which causes predominantly photoacoustic, rather than photothermal destruction of pigment or ink particles (in the case of Q-switched nanosecond lasers). This allows rapid clearing of the abnormal pigmentation with minimal collateral damage to surrounding tissue. Although potential side effects from picosecond laser treatment include pain, erythema, edema, pinpoint bleeding, crusting, blistering, scarring and post-inflammatory hyperpigmentation. [14]

Conclusion. The case presented in this paper is one of the most common ways patients may present with a tattoo caused allergic reaction. As was described, the allergic reaction was severe enough to affect the quality of life of the patient. A diagnosis of ACD was made. Topical treatment with corticosteroids was initiated. Allergic reaction couldn't be fully cleared, since pigments of ink remained in the skin. The patient underwent one session of tattoo removal therapy with Q-switched Nd 532 nm laser. This, however, caused local irritation, for which she was prescribed topical anti-inflammatory medications. Due to the ineffectiveness of topical and laser removal therapy, the patient was prescribed systemic treatment with corticosteroids. After two months of this therapy, the patient's condition improved. She is still undergoing this treatment.

ACD, the most common reaction caused by tattoos, is a delayed-type hypersensitivity reaction. This process may be broken down into two parts. First being sensitization and second, caused by re-exposure, immune reaction. In cases of ACD's caused by tattoos, we have continued exposure to such allergens. Since most dyes used in inks are not bio-degradable, patient's condition won't be resolved unless pigments are fully removed. Due to their components, red and black inks are the most common cause of tattoo-induced allergic reactions. Modern prevention methods that are widely used in tattoo shops are patch and dot allergy tests. They are performed 24 hours before the actual tattoo is applied to check for possible allergies. Such measures may not be enough, since allergic reactions may not appear acutely. Topical or intralesional corticosteroids can be used as conservative therapy. If the allergen is bio-degradable material and can be easily cleared, this may be enough. In cases where it's not, laser-assisted tattoo removal remains the gold standard for treatment. Since many wavelengths are needed to treat multicolored tattoos, not single laser will be enough to remove all variety of inks and their combinations [16]. In case laser removal therapy proves to be ineffective, systemic treatment with corticosteroids may be initiated with scheduled monitoring of patient's condition.

New measures are just now being put in place to regulate the quality and content of inks to reduce the incidence of such allergic reactions.

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CASE STUDY - ALLERGIC CONTACT DERMATITIS IN RELATION TO TATTOOS

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SUMMARY

As tattooing becomes more and more popular, growing numbers of skin reactions caused by tattoos are also becoming frequently encountered by medical professionals. We present a generic case of a tattoo-induced allergic reaction and explore its' immunological mechanism. This paper also highlights components of tattoo inks, their allergenic potential, and possible options for treatment. There can be different types of allergens in tattoo inks. Some are biodegradable, while others are not. Examples of biodegradable components include natural dyes and preservatives. Allergic reactions caused by such agents may resolve with simple therapy since after a short period they will be cleared from the skin. On the other hand, synthetic molecules and other non-degradable dyes will need invasive therapy, such as surgery, dermatome shaving and most commonly used - laser removal therapy. Most notable in this regard is red ink with the highest incidence. There are no current regulations on tattoo inks, which puts tattoo enthusiasts at a higher risk of developing allergic reactions. There are certain preventive measures, such as patch and dot tests. Because the specificity of these tests is mediocre, despite negative results, an allergic reaction may develop weeks or months later. There are no strict treatment guidelines and each case must be assessed individually. Our patient was a young woman, who developed a local allergic reaction due to the red pigment used in her tattoo. Initial treatment, in this case, was anti-inflammatory to reduce inflammation. The only way to get full resolution in such cases is to remove the allergen (red pigment) from the dermis. The patient was prescribed topical treatment with corticosteroids. Once irritation subsided tattoo removal therapy with Q-switched Nd 532 nm laser was initiated. The inflammation returned after the first session, for which local anti-inflammatory medications were started. Due to the ineffectiveness of laser removal and local treatments systemic therapy with corticosteroids was prescribed with gradually decreasing the dosage and controlling the disease. After two months of this treatment, the patient's condition improved. She is still undergoing therapy with systemic corticosteroids.

Keywords: Allergic contact dermatitis, Tattoo ink, red pigment, Laser removal therapy, Q-switched Nd laser, Treatment with systemic corticosteroids.