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Kumkum Dermatitis

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Introduction

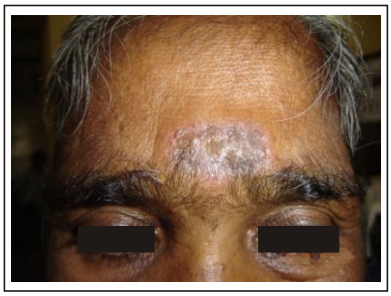
'Kumkum' is a coloured cosmetic used exclusively by the Hindus. In south Indian states 'kumkum' is prepared at home by alkalizing pure turmeric powder.[1] Kumkum can be prepared artificially, which contains starch or chalk powder colored with azodyes.[2] It is available as powders and liquids, and red is the most popular colour. Kumkum is used mainly for religious purpose. It is applied as a round patch or a linear streak on the forehead, front of neck, and sometimes on the abdomen. Some Hindu women use kumkum as Sindoor (vermilion), a red powder sprinkled along the parting of the scalp hair to denote their marital status.[1]

Composition of kumkum

The exact composition of commercial 'kumkum' formulation is unknown; known components include various dyes, fragrances, corn starch, ground-nut oil, tragacanth gum, tumeric powder, and parabens.[3] Now-a-days, several dyes are sold under the commercial name of kumkum. These include coal tar dyes, toluidine red, erythrosine, and lithol red calcium salt.[1,4] Several different colors in kumkum, including white and black, are available to match the color of clothes.[4] Thin-layer chromatography has also demonstrated the presence of other allergens such as sudan I, aminoazo-benzene and canaga oil.[5]

Dermatoses caused by kumkum

Kumkum has a tendency to produce various types of dermatoses. All the patients exposed to kumkum may not develop contact dermatitis; this may be due to inter-individual variations or prolonged constant use.[5]



Allergic contact dermatitis

Allergic contact dermatitis (ACD) due to kumkum manifests as erythema, papules and vesicles at the site of application.[5] Dermatitis may develop in the surrounding skin also due to spread to that area by trickle of sweat.[2] Several authors have reported ACD due to kumkum.[2,5,6] In our experience, kumkum was the cause of ACD in 45.8% of patients presenting with ACD

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Editorial

Non-Eczematous Contact Dermatitis (Reaction)

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Majority of contact dermatitis (reaction) is definitely eczematous. However, some of them are non-eczematous in nature.[1] Importance of detecting these entities lies in the facts : (a) these dermatoses can be detected by simple patch test, (b) other unnecessary costly and invasive investigations can be avoided, (c) treatment and avoidance of offending allergens are both required to cure the condition.[2] (d) before stamping certain dermatoses as 'idiopathic' we can declare the etiology of the disease to the patient.

Various types of non-eczematous contact dermatitis have been shown in Table 1.[2,3,4] Whatever may be the morphological response allergic patch test remains the cornerstone in the

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Prevention of Nickel Allergy

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Nickel is the commonest contact allergen in women.[1] These days with piercing of various body parts becoming more common, the incidence of nickel sensitivity in men is also on the rise.[2] The age of onset of sensitization has also fallen and most women are sensitized to nickel in their teens.[3] Pure nickel or nickel containing alloys that are in prolonged contact with the skin, can induce sensitization by releasing free nickel ions. Topical contact with nickel can cause a dermatitis in those already sensitized to nickel. Systemic exposure to nickel may cause systemic contact dermatitis in nickel sensitized individuals.[4] Exposure to nickel can occur from various sources :[5-10] (1) General exposure[5] (2) Orthopedic implants, Orthodontic appliances.[6,7] (3) Occupational exposure[8,9] (4) Dietary nickel.[10]

Nickel sensitivity is of a great nuisance value to a jewellery sufferer and can affect the livelihood of those exposed to it occupationally. Hence any measures that can reduce the incidence of nickel sensitivity in the general population as well as the chances of recurrence in an individual are of utmost importance. In prevention of nickel contact dermatitis, many statutory bodies like dermatologists, legislative bodies, government, corporate industry, media, surveillance and consumer bodies and patient support groups have a role to play. Measures to prevent nickel allergy can be taken on an individual or collective level. It may also happen incidentally or unintentionally.

Individual Prevention

1. Personal protection

A study that followed up nickel sensitive patients after 10 years, found a statistically significant association of dermatitis with exposure to metal objects. It was concluded that it is possible that the prognosis for nickel dermatitis could be improved if nickel sensitive patients would strictly avoid metal contact especially in clothing and jewellery.[11] Patients need to avoid all nickel containing articles such as jewellery, safety pins, hooks, snaps on undergarments, medals, ID tags, watch bands, blue jeans metallic buttons. They should be warned that since sweat readily dissolves nickel out of metal, they are especially susceptible to a rash in hot, sweaty weather.[5] Some of these articles should be substituted with plastic snaps, buttons or Velcro fasteners.

Every patient should be provided a list of all possible items that contain nickel. Patients need to be educated to think of their environment in terms of materials rather than objects. Coins, keys, needles, paper clips, drawer handles and thimbles are common household articles that can cause nickel dermatitis. Mobile phones have also been recently implicated as a source of nickel dermatitis.[12] Mascara and eye shadow are another source of nickel.[13] A dimethylglyoxime test kit may help to identify nickel containing objects at home and at work.

A simple remedy for preventing nickel from leaching onto the skin is to coat the metallic areas in contact with the skin with a coat of clear nail varnish. A study has shown that one coat of clear nail polish can prevent nickel release from metal buttons in blue jeans through 2 wash/dry cycles.[14] Water proof tape may also be used the cover the nickel plated objects, although nickel can leach out if the contact site is prone to sweating or friction.

2. Protection during Medical Intervention

Orthopedic Implants[6]

Nickel sensitivity was commonly seen with the metal to metal prosthesis used for joint replacements. However their replacement with metal to plastic prosthesis has resulted in a virtual disappearance of this problem.[15] Static stainless steel implants for e.g., those used for tibial implants, have been shown to produce a local dermatitis in nickel sensitive individuals, which has cleared up when the metal implant has been removed. In such patients titanium implants can be used as titanium allergy is practically unknown. However titanium may not be as long lasting as stainless steel.

Orthodontic Appliances

Orthodontic appliances have been rarely reported to cause either local or systemic allergic dermatitis, in which case removal of the appliance resulted in resolution of the rash. In spite of the widespread use of nickel containing stainless steel in orthodontics, dermatitis has been rarely reported. It has been postulated that exposure of the oral mucosa to nickel could actually lead to the development of immunological tolerance.[16]

3. Reduction of dietary nickel

The exact contribution of dietary nickel to nickel dermatitis is unclear.[4] Pompholyx may be due to nickel ingestion.[17] Oral provocation tests may be needed to confirm the same. Nickel is found in shellfish, dark chocolate, beans, lettuce, peas, bran, oatmeal, pineapple and green leafy vegetables. Some patients do experience a benefit by omitting intake of these items in their diet.[18,19]

4. Protection at work

Occupational nickel dermatitis usually manifests as a hand dermatitis. About a quarter of nickel sensitive patients, may have an occupational element to their dermatitis.[9] Occupational exposure is seen in nickel platers, metal workers, refinery workers, hairdressers, hospital cleaners and cashiers handling coins. It is believed that nickel sensitivity predates industrial exposure and the occupational nickel exposure may elicit a secondary dermatitis. Hence pre-employment patch testing and exclusion of nickel sensitive patients from employment in certain industrial occupations has been advocated.

The basic principle of prevention of occupational contact dermatitis is reduction of contact or preferably of avoidance. Barrier creams that chelate nickel have been advocated for use in the workplace.[20] One of the most effective ligands is 5-chloro-7-iodoquinolin-8-ol. Generally regarded as safe, it's usage in some situations may be limited by some concerns about its toxicity. Other ligands that have been used are ethylenediaminetetraacetic acid in various forms, diphenylglyoxime and dimethylglyoxime.[20] Propylene glycol, petrolatum and lanolin have been used to reduce the absorption of nickel through the skin.

Collective Prevention

1. Legislative Measures

Ear piercing and prolonged close contact with nickel releasing alloys are the mains reasons for primary sensitization. Hence legal restraints on the amount of nickel in such items could reduce the number of people sensitized to nickel and in turn reduce the incidence of hand eczema and contact dermatitis to nickel in an occupational setting. In Denmark such legislation passed in 1990 reduced the incidence of nickel sensitization from 24.8% in 1985-86 to 9.2% in 1997-98.[21] In 1994, the European Union passed regulations based on the Danish legislation. This is called the Nickel Directive. (See Table 1) Metallic items that are in relatively short term contact with the skin, for e.g., cutlery, coins and keys, have been excluded from the legislation.[22] The Nickel Directive came into full force in Sweden in 2001. By 2005, fewer items intended for direct and prolonged contact with the skin were found to contain nickel. However stricter implementation of the Nickel Directive would be need to make a significant difference in the long term.[23,24]

2. Corporate responsibility

Self regulation within the industry would go a long way in influencing the incidence of sensitization. Manufacturers of jewellery, etc should ensure that their products are safe to use. The potential for allergenicity should be assessed before a new product is placed on the market.

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Contact Dermatitis to Colors of Holi

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Dye mixtures and pigments containing henna, P-phenylenediamine (PPD), and indigo are applied to the skin in various parts of the world for religious purposes, social recognition or fun. "Holi" or the "festival of colors" is a popular Indian festival, in which pigment mixtures or dyes in powdered or paste forms are applied on each other's skin for the purpose of fun. Such pigment mixtures are considered non-hazardous by most. Although allergic contact dermatitis to some of these agents are a known side-effect, yet these go mostly unreported as these are mostly mild and transient in nature. However, severe irritant dermatitis is known to occur in some users and this can leave behind resultant intense post-inflammatory hyperpigmentation, which can be rather disturbing to the patient.[1] Elsewhere in the world, severe contact allergic dermatitis is known to occur mainly to PPD and henna and is associated with residual hyperpigmentation[2,3] but in India there is a paucity of literature on this common yet pertinent problem.

Contact dermatitis to dye mixtures, mostly remain confined to the site of application[2,3]. The colors used during Holi are dye mixtures which may be mixed with chemicals such as persulphate compounds, zinc salts, mercuric iodide and chromium iodide in addition to the commonly used colorants. The red dye mixture may contain lead chromate and mercuric iodide and the green contains melachite green and nickel sulphate. The blue dye contains cobalt nitrate, indigo and zinc salts. The agents in the red dye can cause eye irritation while those in green and blue dyes, mostly cause dermatitis. Other than these, the dye mixtures can also cause photosensitivity and carcinogenicity, rarely. The "shiny dust" in the pigment mixture are mica particles, which can also cause skin allergy. Several other contaminants can further aggravate the condition.

It may be difficult to determine the exact nature of the ingredients used in the pigment mixtures sold loosely in the streets. Hence, it may be difficult to carry out patch tests with individual ingredients. A chemical analysis may help to determine the nature and proportion of some ingredients, although some of the probable ingredients have been mentioned above. However, awareness of this common phenomenon which can cause cosmetic disfigurement is something that should be kept in mind by the common people, while purchasing inferior quality pigment mixtures for Holi.

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Prevention of Nickel Allergy

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3. Education

Education of public through the media, patient information sheets and lectures could result in an informed public who would demand products that are safer to use.

Incidental prevention

A Russian population exposed to emissions from 2 polluting local Russian nickel factories was found to have a lower incidence of nickel sensitivity compared to the population in the adjacent Norwegian border. It has been suggested that long-term exposure to nickel may have induced immunologic tolerance in the Russian population.[25]

Table 1. Summary of the European Union Nickel Directive[22]

1.	After piercing, post, rings or other items used during re-epithelialization shall not contain more than 0.05% nickel.
2.	Products intended to be used in direct and prolonged contact with the skin, such as earrings, wristwatches, watch straps, buttons and zips, should not release more than 0.5µg/cm^2/ week of nickel.
3.	Nickel should not be used in the abovementioned products in Part 2, unless the coating is sufficient to ensure that the release of nickel is not more than 0.5µg/cm^2/ week after 2 years of normal use.

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The Contact Urticaria Syndrome

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Introduction: The contact urticaria syndrome (CUS), first defined as a biological entity by Maibach and Johnson,[1] comprises a heterogeneous group of inflammatory reactions that usually appear within minutes after cutaneous or mucosal contact with the eliciting agent and disappear within 24 hours, usually within a few hours.[2,3] The term "syndrome" clearly illustrates the biological and clinical polymorphism of this entity, which may be either localized or generalized and may involve organs other than the skin, such as the respiratory, gastrointestinal tract, and vascular system, displaying a wide spectrum of clinical manifestation, ranging from mild erythema and/or itching, to death.

Clinical symptoms and stages of CUS : The symptoms can be classified according to morphology and severity. In the mildest cases, there are only subjective symptoms (invisible contact urticaria). These are reported as itching, tingling, or burning sensations, without any objective change, or just a discrete erythema occurs. Wheals and flare at the contact area is a prototype of contact urticaria, while generalized urticaria following a local contact is less common. Extracutaneous symptoms may also occur in severe reaction and may include rhinoconjunctivitis, asthmatic attack, and orolaryngeal or gastrointestinal manifestation. Finally, anaphylaxis may occur as the most severe manifestation of CUS. Urticarial lesions of CUS do not differ clinically from those observed in common urticaria. Size varies from few millimeters to large sizes, corresponding to the site of contact.

Etiology and Mechanisms of CUS : The mechanisms underlying immediate contact reactions are divided into two main types : immunological and non-immunological. However, there are substances that causes immediate contact reactions whose mechanisms (immunological or not) remains unknown.[4]

Immunological contact urticaria (ICU) is a type I hypersensitivity immunological reaction in individuals who have previously contacted the causative agent and synthesized specific immunoglobulin E (IgE) antibodies against this agent. IgE molecules react with IgE receptors on the most cells, basophils, eosinophils, Langerhan's cells and other cells. Eventually, allergen penetrating through the skin or mucosal membrane will react with two adjacent IgE molecules bound to the cell membranes of the mast cells. Within minutes, histamine, neutral proteases and proteoglycans are released from the mast cells, resulting in an immediate skin response. The allergen-IgE reaction also leads to synthesis of leucotrienes,

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Non-Eczematous Contact Dermatitis (Reaction)

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diagnosis of non-eczematous contact dermatitis. Interestingly, positive patch test reaction shows usually eczematous reaction like classic eczematous contact dermatitis.[3]

Lichen planus like CD or lichenoid CD clinically resemble classic LP except (i) larger papules (ii) Wickham's striae usually absent (iii) post-LP pigmentation more pronounced in lichenoid CD.[5] Common contributory agents of LP-like CD are color film processors, hair dyes (PPD from socks and shoes color),[6] parabens,[6] potassium dichromate, red ink/color,[7] temporary tattoos,[8] metals, chlorpheniramine maleate etc. Oral lichenoid contact dermatitis (OLCD) may mimick oral lichen planus. Contributory agents of OLCD are dental fillers/restorative devices like methacrylie acid ester, silver, gold, mercury, balsam or peru[6] and fragrances[6] (cinnamic aldchyde). Histopathologially lichenoid CD has unique features as compared with classic LP like (i) focal parakeratosis and hypogranulosis (ii) greater amount of spongiosis (iii) more number of necrotic kerotinocytes and cytoid bodies (iv) pleomorphic cellular infiltrales containing more plasma cells and eosinophils, (v) deeper perivascular infiltrates and (vi) less dense and 'not band-like' cellular infiltrates.[5,9]

Pigmented contact dermatitis denotes macular pigmentation of skin without preceding itch or eczema. These are more common in oriental populations. Some cases may mimic melasma. Patch test reactions show usually eczematous features and occasionally hyperpigmented patches.[2] Common contributory agents are fragrances jasmine oil, rose oil, black hair dyes (PPD), Kumkum (Sudan I) and parabens, textile dyes and topical minoxidil.[2,10] Histopathologically are

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Non-Eczematous Contact Dermatitis (reaction) : Commoner Types[2,3,4]

- Lichenoid contact dermatitis
- Pigmented contact dermatitis
- Contact leukoderma
- Contact urticaria
- Erythema multiforme like contact dermatitis
- Purpuric contact reaction
- Bullous contact reaction
- Granulomatous contact reaction

Non-Eczematous Contact Dermatitis (reaction) : rarer types[2,3]

- Pustular contact reaction
- Papular & nodular contact reaction
- Erythematous & exfoliative contact reaction
- Scleroderma-like contact reaction
- Lymphomatoid contact reaction
- Vascular occlusive contact dermatitis

Kumkum Dermatitis

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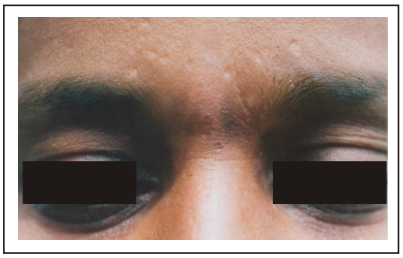
due to various cosmetics. All known components of kumkum have been implicated in contact dermatitis.



Pigmented contact dermatitis

The term 'pigmented contact dermatitis' was used by Osmundsen (1970)[7] to explain hyperpigmentation as a manifestation of contact dermatitis. Nakayama[8] later (1976) described 'pigmented cosmetic dermatitis', which was then common in Japanese women. Pigmented contact dermatitis is classified as non-eczematous contact dermatitis,[9] which occurs almost exclusively in dark complexioned individuals.[7,10] Tendency to hyperpigment may be due to idiosyncrasy of the patients, postinflammatory, or some peculiarity of the allergen itself.[7] Hyperpigmentation may follow an eczematous dermatitis or it may occur without any evidence of preceding inflammation.[7]

Kumkum is an important cause of pigmented contact dermatitis (in our experience, 76.1% of patients with kumkum dermatitis had PCD). It appears that only red 'kumkum' can sensitize and cause pigmented contact dermatitis.[3] The reason might be that red 'kumkums' are more commonly used as compared with other coloured 'kumkums' and that probably only red 'kumkums' contain the sensitizers that cause pigmented contact dermatitis.[3]

Depigmentation and hypopigmentation

Contact leucoderma, also called contact vitiligo or contact depigmentation, may be defined as a complete depigmentation without preceding inflammation, [11] and it is mainly due to direct melanocytotoxic effects of certain chemicals.[12] This is in contrast to postinflammatory hypopigmentation which must by definition be preceded by inflammation and which usually does not lead to total depigmentation.[11]

The exact mechanism of chemical induced depigmentation is not clear; several theories have been proposed for melanocyte destruction.[13] Chemicals capable of producing contact leucoderma are mainly alkyl phenols and catechols,[13] and there is a wide variety of consumer products like acrylates, adhesive tapes, bindi, cinnamic aldehyde in toothpaste, dyes like paraphenylenediamine, germicidal phenolic detergents, latex glues, rubber products and shoes that can produce contact leucoderma. Azo dye has also been reported to produce contact depigmentation.[14]

Koebner's phenomenon

Koebnerization can occur at the site of contact dermatitis. The Koebner phenomenon is known to occur at the site of positive patch test reaction.[15,16]

Photosensitivity

Photosensitivity in kumkum dermatitis has not been described in the literature. Pigmentation, which is a well defined phenomenon in kumkum dermatitis, may follow photocontact dermatitis.

Lichenification

In our experience, its occurrence is not uncommon in kumkum dermatitis. Most of such patients have kumkum dermatitis of prolonged duration.

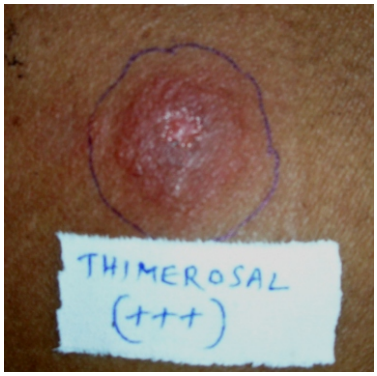
Diagnosis

PUT/ROAT: One practical way of confirming a contact dermatitis to kumkum is by Provocative Use Test (PUT) which is also known as Repeat Open Application Test (ROAT).[17] This involves twice daily application of a product over a 3 cm patch of skin below the antecubital fossa for one week.[18] A positive reaction manifests as itching, erythema, papules and vesicles. Some authors recommend a longer duration of application.

Patch test: Diagnosis of kumkum dermatitis should be confirmed by patch testing with the ingredients. But, since the exact composition of commercial 'kumkum' formulation is unknown,[3] the knowledge of the constituents of kumkum for patch testing is limited.[5] ed Hence, it is recommended that patch testing be done with the patient's kumkum as such where individual ingredient list cannot be obtained. The kumkum is applied as a closed patch test. Standard guidelines (e.g., North American Contact Dermatitis Group recommendations) for patch test reading can be followed for reading the results. Photopatch test may be carried out if required.

Usage test: If patch testing to a strongly suspected test substance is negative, the patients are asked to use the preparation again routinely as they would normally use it. This is particularly valuable in deciding whether the specific cosmetic, kumkum is the cause of contact dermatitis. [4]

Chemical analysis: Kumar et al[5] identified components of patient's kumkum by thin layer chromatography (TLC) and then performed patch testing with those components. Such an approach, if feasible, deemed ideal until further knowledge is gathered on this subject.



Treatment

Treatment of kumkum dermatitis can be divided into:[4] (i) preventive treatment; (ii) corrective treatment; and (iii) treatment of substitution.

Preventive treatment: While this is recommended in patients sensitive to multiple cosmetics or in patients with cosmetics intolerance syndrome, it may not be feasible for preventing kumkum dermatitis because prolonged exposure may be required for the dermatitis to develop.

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Non-Eczematous Contact Dermatitis (Reaction)

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basal cell degeneration and incontinence of pigment are seen.

Erythema multiforme like contact reaction are usually eczematous at the point of origin. Peripheral-most lesion are typically target. In between lesion are papules, plaques and urticarial in nature. Lesions are usually limited and histopathologically non-specific features are usually seen. Common contributory agents are mango, poison ivy, Brazilian rosewood, proflavine, vitamin E, topical corticosteroid, vioform, epoxy resin and nickel.[1,3,4]

Purpuric contact reactions are mostly allergic in nature; few may be irritant. These are common in lower legs and feet, sometimes may be associated with eczematous changes. Extravasation of RBCS are the basic pathomechanism. Offending agents are black rubber (Substituted PPD), textile dyes (navy blue uniform; disperse blue 85), topical drugs like topical NSAIDS, proflavine etc.[1,3]

Bullous contact reactions clinically and histologically simulate bullous pemphigoid but direct immunofluorescence shows negative result. Lesions are usually negative. Contributory allergens are cinnamon powder, cinnamaldelyde, cinnamic alcohol, nickel and potassium dichromate[1,4]

Granulomatous contact reaction may originate from zinconium contained in antiperspirants/ topical medicines producing allergic granuloma. Gold from ear or nose ring may cause sarcoidal gramuloma. Tattoo pigments (red, green, blue, yellow) may produce allergic gramuloma. Vaccination containing aluminium may also induce allergic granuloma.[1,2]

Contact or chemical leukoderma represents an acquired vitiligo-like hypomelanosis induced by repeated (multiple) exposure to specific chemical compounds. This chemical effect, independent of their sensitizing potential, is distinctly separate from post-inflammatory depigmentation and koebner phenomenon in vitiligo.[4] ials, Common sources are phenols/catechol derivative sulfhydryls, mercurials, arsenic, cinnamic aldehyde, PPD, azo dyes, corticosteroids, chloroquine, soyamilk and derived protein, ammoniated mercury, thiotaptepa.[11,12]

Contact urticaria may be immunologic and non-immulogic. Urticarial lesions develop instantly on direct exposure to the offending substance. Clinically the lesions are like classic urticaria having wheals and flare. In atopics, the existing eczematous patches are exacerbated without producing any wheals causing difficulty in diagnosis. Diagnosis can be done by detailed history, skin testing like open patch test, prick test, scratch test. Common agents are fragrances and flavouring agents, foods, hair cosmetics, medicines, metals, plants, preservatives etc.[4,13]

Management of non-eczematous contact dermatitis should be based not only on specific therapeutics but also to find out specific contact agents by relevant skin testing and counselling. Patients should be instructed to avoid the contact allergens out and out for long time persistently to get the desired therapeutic results.[14]

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Invitation

Articles are invited from dermatologists and other physicians regarding various facets of allergic and immunologic skin diseases for contribution in this bulletin.

– Editorial Team

Kumkum Dermatitis

From Page 5

Corrective treatment: Use of kumkum should be stopped. Symptomatic relief should be given according to the needs of the patient, e.g. topical treatment with corticosteroids in gel, lotion, or cream base, and systemic treatment in the form of antihistamines, and rarely oral corticosteroid if at all required. The avoidance of sun with sunscreen agents is necessary in patients with photo-sensitivity.

Patients with pigmented contact dermatitis can be prescribed demelanizing agents like hydroquinone, glycolic acid, kojic acid or arbutin along with sunscreens. Hypopigmentation tend to improve with time a mild potent topical steroid may be enough. Depigmentation can be treated by grafting procedures.

Treatment of substitution: Patients may not be able to completely stop using kumkum for socio-cultural reasons. Patient's kumkum can be substituted with a product to which patient is not sensitive. However, this is easily said than done as identification of the causative ingredient is often not possible and dermatitis may develop only after a prolonged use making it difficult to give any judgment based on routinely done tests, in which patient's kumkum is applied for a relatively short duration. One practical way of dealing with this problem is to apply vaseline on the skin before application of kumkum.

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The Contact Urticaria Syndrome

From Page 4

prostaglandin and platelet-activating factors in the cell membrane of the activated mast cells. Immunological-type agents are confirmed by specific positive radioallergo-sorbent tests (RASTs) and by negative tests on control subjects. Substances that have been reported to produce ICU is protein, both vegetal and animal origin. However, non-protein allergen are also able to provoke ICU. Among others, food derived and food associated materials such as preservatives, flavourings, stabilizers, emulsifiers and antioxidants also responsible for allergic contact dermatitis are often quoted.[3] Prick testing is the investigation tool to be used in order to trace etiological factors responsible for ICU.

Non-immunological contact urticaria (NICU) occurs in subjects not sensitized to the contactant, i.e. almost any normal subject. The mechanism of action is the result of a direct release of vasoactive substances, which causes a localized k response. Prostaglandines are media-tors in the reaction. The NICU is often limited to erythematous macules without oedema rather than a real wheal and flare reaction. The intensity of reactions depends mainly on the duration of exposure, the concentration of the contactant and other factors such as rubbing or scratching. The reaction usually remains localized, and systemic reaction are probably not evoked. Substances capable of producing NICU are not protein, but low-molecular weight molecules, that easily cross the skin barrier, like chemicals used as flavouring fragrances, preservative in cosmetic, pharmaceutical and food industries. Prick testing is not the investigation tool at tracing NICU contactants.

In some instances, the reaction resembles that of ICU, but no specific IgE can be demonstrated in the patients serum or in the tissue; this category is considered as contact urticaria of uncertain mechanism. It is possible that there are other immunological mechanisms in addition to the IgE-mediated ones. Specific IgG and IgM might activate the complement cascade through the classic pathway. Prick testing detects the etiological agent in cases of contact urticaria of uncertain mechanism.

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Localized Toxic Epidermolysis Necrolysis due to Temozolamide and Radiotherapy- a new form of EMPACT syndrome?

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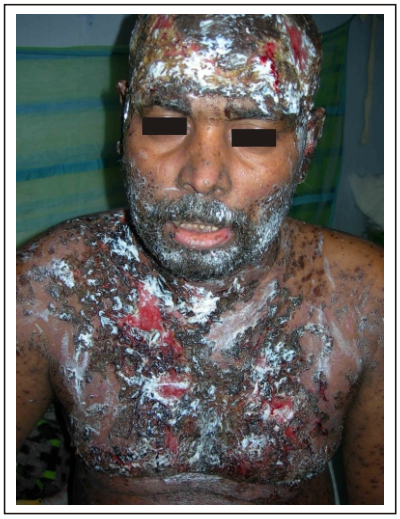
Introduction

Toxic Epidermolysis Necrolysis is a severe pattern of drug reaction in which there is extensive necrosis and denudation of skin. Usually there is generalized involvement of skin and mucosal areas like lips, oral mucosa, conjunctiva etc. Area of disease involvement or severity can be limited. However localization of disease to the area of external triggering factor is extremely rare and is obscure. Here I report a case of TEN mostly limited to the upper segment of body after cranial radiotherapy and systemic Temozoamide therapy for cranial metastasis from malignant fibrous histiocytoma of right thigh.

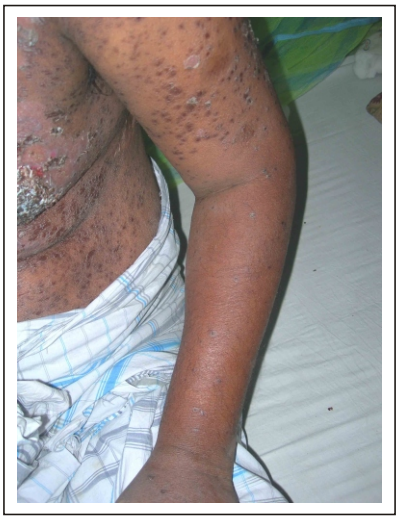
Case report

A 46 years old male presented with wide spread erythema, crusted lesion with oozing and large area of denuded skin limited to the scalp, face, ear, lips, eye lids, neck and chest. There were small-crusted erosions scattered over the abdomen and arm. Forearm and lower limbs were almost normal except very few scattered crusted lesions.



Nickolsky's sign was positive in the upper trunk. He complained of severe dysphagia. All these appeared suddenly 10 days back. Patient was diagnosed as suffering from toxic epidermal Necrolysis (TEN) localized predominantly in the upper half of body.

Patient suffered from right thigh swelling almost 5 years back. In histology of the mass, there were spindle cells with elongated hyperchromatic nuclei and mitotic figures. There was bony destruction by the tumor. It was diagnosed as malignant fibrous histiocytoma. His right lower limb was amputated at the upper thigh level.



Two month back he suffered from headache. In MRI examination (in January 2007) of the brain, multiple well-defined predominantly hypo-intense lesions were noted in the right cerebellar hemisphere, right high parietal region and left frontal region with malignant mass effect and peri-lesional edema. He was diagnosed as suffering from glioblastoma arising as metastasis from the primary malignancy over the thigh.

Patient was put on cranial radiotherapy (30 gray per day) along with oral temozolamide tablet (100mg tablet, 1 tablet OD). He was also started tab phenytoin sodium, paracetamol and NSAIDs. The skin lesion developed on 7-8th day of the therapy. Radiotherapy and temozolamide therapy was stopped after 10 day of treatment. Other medications were continued.

At this time dermatological opinion was sought. It was diagnosed as TEN. NSAIDs, phenytoin sodium and all the antibiotics were advised to stop. Patient was put on everyday dressing with sterile normal saline and covering the lesion with Gellonet along with topical supragent cream. Patient started improving rapidly and after 10 day he requested for discharge from hospital.

Phenytoin sodium was the suspected culprit. Role of radiotherapy in mediating or potentiating the pathogenic role of phenytoin was also suspected. At that moment, to our mere surprise patient disclosed that he used to take phenytoin sodium, NSAID everyday on his own against the direction with a false belief that those medicines would help early recovery.

Retrospectively the case was diagnosed as localized TEN due to systemic temozolamide along with cranial radiotherapy.

Discussion

Unlike EM, which is usually seen after viral or other infections like mycoplasma, radiation, drugs, contact dermatitis etc, most common and probably the only etiology of TEN is drugs. There are remarkably less inflammatory changes in the necrotic epidermis and dermis in TEN.

A cell surface death receptor called Fas, and its ligand (FasL) are involved in the apoptotic cell necrosis in TEN. Soluble FasL produced by peripheral blood monocytes are found in high level in TEN patients. It is easily assumed how the reactions rapidly become generalized after a trigger. It is very difficult to explain a localized reaction.

Temozolamie is an imidazotetrazine-alkylating agent with antitumor activity. The active component is monomethyl triazeno imidazole carboxamide (MTIC). The main indication for this compound is glioblastoma multiforme or anaplastic astrocytoma. In low dose it can acts as radiation sensitizer.

Cranial radiotherapy is given in the temporal area of the head. Direct damage of the skin to the radiation at the local areas is almost never reported due to very low dose of the radiation in causing damage to the skin. Allergic reaction manifesting as erythema multiforme (EM) however is rarely reported in the local areas. The incidence increases with phenytoin when used simultaneously. The mechanism of such synergistic pathogenicity is still elusive and is described with the acronym EMPACT (Erythema Multiforme associated with Phenytoin And Cranial radiation Therapy).[1] TEN in the vicinity of radiation field is recently reported after radiation therapy along with phenytoin.[2] However TEN limited in the upper segment of the body after cranial radiotherpapy and temozolamide was never reported.

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