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EYELID DERMATITIS: A MULTIFACTORIAL DERMATITIS

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ABSTRACT:
Dermatitis means inflammation of the skin that is very frequently used as synonymous with eczema. On the basis of aetiology, it is classified as exogenous and endogenous dermatitis/eczema. There are overlaps in etiological factors for both exogenous and endogenous dermatitis. A detailed history, meticulous cutaneous examination, and specific investigations play a significant role in diagnosing the aetiology. Patients with dermatitis/eczema typically report symptoms like pruritus, burning, and irritation at specific sites. Local cutaneous findings align with the clinical stage. Eyelid dermatitis is the most common dermatological complaint and is often cosmetically very concerning for many patients, especially very young aged female patients, as it is a very concerning and distressing cosmetic problem. As the use of cosmetic agents in and around the eye is quite common in the everyday world like various creams, ointments, eyedrops. Identifying the cause is the most important factor in treating the management. The management of the eyelid dermatitis differs from the eczema/dermatitis on the other anatomical sites because skin of eyelids is thinnest leading to increased penetration of allergens and is a cosmetically concerned site. It is very much essential to timely diagnose and manage the eyelid dermatitis to avoid complications. Here we tried to compile the possible causes varying from exogenous exposure to endogenous causes, its pathophysiology and treatment in detail to meticulously understand and treat for the same. The evaluation of patients presenting with eyelid dermatitis remains a relatively complex strategy but is very rewarding when great results are achieved and improves patients' quality of life significantly.

Keywords: Dermatitis, Eczema, Eyelid dermatitis.

INTRODUCTION

Dermatitis means inflammation of the skin that is very frequently used as an identical with eczema by non-dermatologist and it is related with Grecian word – Ekzem and sense of the same is "boil out". It is an inflammatory skin disease to various stimuli which means every eczema is dermatitis but not every dermatitis is eczema. There are many classifications mentioned in the literature for the dermatitis/eczema. On the basis of aetiology, it is classified as exogenous and endogenous dermatitis/eczema. Exogenous dermatitis occurred due to external factors that induce skin inflammation. It includes: 1) Allergic contact dermatitis (ACD): due to an allergen, often at even low concentration such as nickel, hair dye, rubber, or perfumes that can be identified by patch testing. 2) Irritant contact dermatitis (ICD): due to through damage to the skin by an irritant such as soap or detergent. 3) Microbial eczema: due to bacteria or fungi. 4) Dermatophytide: that is due to a fungal infection elsewhere in the body. Endogenous dermatitis occurs because of internal factors and most frequently observed in the outpatient department, they are: 1) Atopic dermatitis: dermatitis occurring in children and adults with history positive for atopy and similar complain in family. 2) Nummular eczema: characterized by coin-shaped eczematous plaques of irritated skin. 3) Pompholyx: characterized by small deep-seated vesicles on the hands and feet. 4) Asteatotic eczema: characterized by dry, fissured skin. 5) Stasis eczema: due to long standing and poor vascular circulation.

There are overlaps in etiological factors for both exogenous and endogenous dermatitis. A detailed history, meticulous cutaneous

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examination, and specific investigations have a substantial role in diagnosing the aetiology. The effected subject with dermatitis/eczema typically reports symptoms like pruritus, burning, and irritation at specific sites (Beltrani, 2001). Local cutaneous findings align with the clinical stage.

Recognizing the significance of the eyes as a facial beauty organ, any changes, both subjective and visible, cause serious concern. The skin of the eyelids, being the thinnest anatomical site, allows greater allergen penetration, making it more sensitive (Huang et al., 2021a). Eyelids may appear inflamed due to immunologic reactions, irritation, infection, tumors, or systemic illnesses (Beltrani, 2001). This condition, known as eyelid dermatitis or periocular/periorbital dermatitis, requires timely diagnosis and treatment. Delay can lead to complications such as ptosis, ectropion, tearing, and worsening dermatochalasis due to persistent inflammation of the eyelids (Chisholm et al., 2017).

Epidemiology and Etiology

Eyelid dermatitis is observed across all age groups and genders, with literature indicating a female predominance. The 40 years or above age has been recognized as a responsible factor for periocular dermatitis (Feser & Mahler, 2010; de F. S. H. M et al., 2023).

Eyelid dermatitis is often associated clinical findings of diseases such as atopic dermatitis, seborrheic dermatitis, allergic contact dermatitis, airborne contact dermatitis, rosacea, psoriasis, and others (Wolf et al., 2014). Due to the thin skin and increased penetration, various allergens can come into contact with the eyelids, including through digits (e.g., nail varnish), airborne droplets (e.g., herbal allergens, plant antigens, wood allergens, plastics, rubber, glues, metals, industrial and agricultural dusts, pesticides, and drugs (Wolf et al., 2014), fragrance sprays), or volatile substances (e.g., epoxy resin), leading to eyelid dermatitis (G. M et al., 2018).

Cosmetic products such as eye creams, shadows, mascara, and makeup removers are also identified in existing literature as culprits for eyelid dermatitis, either as allergic or irritant contact dermatitis. Eyelash rollers and makeup appliers may contain nickel and/or rubber, potentially causing contact allergies at this site (Huang et al., 2021a; Landeck et al., 2014; Rietschel et al., 2007; Warshaw et al., 2021).

Common medicament sensitizers in eye drops and ointments, including neomycin, framycetin, gentamicin, tobramycin, chloramphenicol, sulphonamides, local anesthetics, antihistamines, β-blockers, anticholinergics, and sympathomimetics, have been identified as responsible for eyelid dermatitis. Eye drops and contact lens solutions containing preservatives (benzalkonium chloride, EDTA, mercurials) may also sensitize individuals. Medicaments are associated with "non-allergic periocular dermatitis," commonly occurred in elderly population as ophthalmic diseases are more prevalent in this age group (Huang et al., 2021b; Landeck et al., 2014).

The growing acceptance of natural cosmetic products has contributed to the rise in allergic contact dermatitis cases, particularly due to herbal products like aloe vera. There is a need to explore these allergens further (Huang et al., 2021b; G. M et al., 2018).

Pathophysiology

On histopathology of eyelid dermatitis there is variations as per etiology. If the cause is allergic contact dermatitis there will be spongiosis and exocytosis and epidermal necrosis due to irritant contact dermatitis. The eyelid dermatitis occurred because of disruption of epidermal barrier. The damaged barrier could be due to abnormal cutaneous microbial flora and an immune dysregulation, making skin prone to bacterial and fungal superinfection.

Clinical manifestations

The clinical appearance of eyelid dermatitis is alike to any dermatitis at each clinical stage (Table 1).

Table-1: Sign and Symptoms According to Stage of Presentation

Stage	Clinical Presentation
Acute stage	Erythema, edema, vesicles, oozing, crusting
Subacute stage	Oozing, erythema, serosanguinous, scaling, fissuring
Chronic stage	Scaling, fissured, lichenified

The involvement of the eyes can be unilateral or bilateral, directly related to the aetiology of causation. Eyelid dermatitis can be an isolated diagnosis or one of the associated findings with other exogenous or endogenous dermatitis. In a retrospective study on eyelid dermatitis, ACD was identified as the key source of unilateral eyelid dermatitis. The study also observed that metal allergy resulted in bilateral eyelid involvement, while components in cosmetic and medicaments were responsible for in both unilateral and bilateral eyelid involvement (Blanc et al., 2015; Crouse et al., 2018) (Table 2).

Table-2: Aetiology and Clinical Involvement

Clinical Diagnosis	Aetiology
Eyelid dermatitis as an Isolated diagnosis	ACD most commonly (10) or ICD
Eyelid dermatitis as an associated finding	Atopic dermatitis, Seborrheic dermatitis, Psoriasis, ACD, Autoimmune Connective tissue diseases, and dermatomyositis

Differential Diagnosis

Psoriasis, atopic dermatitis, contact urticaria, dermatitis secondary to conjunctivitis, blepharitis, irritant reactions, allergic contact dermatitis (ACD), collagen-vascular disease, streptococcal infection, photodermatitis, lichen simplex chronicus, and idiopathic disease are among the conditions included in the differential of upper eyelid dermatitis syndrome (Beltrani, 2001; Wolf et al., 2014).

Clues from the History/Clinical examination can be Helpful in Diagnosis and Identifying the Etiological Agent

1. Past History of Treatment Taken: The history of previous treatment is crucial for evaluation, as it helps in identifying the causative allergen. Patients often try various treatments in rapid succession to alleviate their eyelid condition. While older prescriptions may easily reveal the drugs used, thorough inquiry may be necessary to assess a range of over-the-counter "wonder" drugs. Herbal medicines from friends and family, as well as other at-home treatments, should also be considered. The clinician should be taken in consideration the oral drugs patient has taken two to three weeks prior to the onset of changes in the skin of eyelids (Beltrani, 2001).
2. Repetitive: Factors such as the frequency of skin cleaning with the cleansers, and cosmetics used, materials used in contact lenses and eyeglasses, and occupational exposures are frequently overlooked. Each remedy's outcome, especially the cause of discontinuance, may indicate a secondary or superimposed ICD or ACD. Adverse reactions to applied agents are more likely to occur on compromised, inflammatory eyelid skin.
3. History of Occupation: The occupation history is also crucial (de F. S. H. M et al., 2023). Common

occupations among males directly associated with eyelid dermatitis include mechanics/repairers, precision manufacturing workers, and machine operators/assemblers/inspectors (Warshaw et al., 2020).

Image-1: Approach towards Patient with Eyelid Dermatitis.

Management - Investigations

A detailed and proper history can aid clinicians in diagnosing eyelid dermatitis as it is a clinical diagnosis. Sometimes, despite a diagnosis, it is necessary to conduct certain investigations to confirm the allergen responsible for it. The recommended investigations include patch testing, skin biopsy for histopathology to rule out autoimmune connective tissue diseases and dermatomyositis. Additionally, an ophthalmologist's referral is required to check for associated ocular findings such as keratitis, conjunctivitis, and keratoconus (Thyssen et al., 2017).

Patch testing is particularly beneficial for patients with persistent, recurrent, or unyielding eczematous or lichenified dermatitis that responds temporarily to adequate medication. When conducted accurately, patch testing consistently provides valuable information, whether positive or negative, regardless of the outcome (Beltrani, 2001; Sam et al., 2017).

Most of the time it is clinical diagnosis and routine histopathology is avoided because of sensitive anatomical site but if required and performed then findings will be observed- infiltrate of non-specific inflammatory cells as lymphocytes and if the cause is allergic contact dermatitis there will be spongiosis and exocytosis and epidermal necrosis due to irritant contact dermatitis.

Treatment (Beltrani, 2001; Daniel & Orchard, 2015; E et al., 2007; Freeman et al., 2004)

A. General Measures - General Management:

- Avoidance of contact with the suspected allergen.
- Avoid rubbing, masking cosmetics, and all previously used treatments.
- Patient counselling and awareness are crucial for effective management.

B. Topical Treatment - Topical:

1. Corticosteroid: These are used as a first line treatment and because of thin skin low potency topical steroid for a short time period is recommended.

Mechanism of action: 1] Anti-inflammatory effect: It inhibits the pro-inflammatory cytokines from immune cells thus reduces the overall inflammatory response in skin. It inhibits the activation and proliferation of various immune cells, including T-lymphocytes and macrophages and play a crucial role in the inflammatory process leading to suppression of immune cell activity.

2] Immunosuppressive effects: Corticosteroids by reducing the presentation of immune cells to present antigens decreases the immune response to allergens or irritants that trigger inflammation of the skin. The hypersensitivity response decreased by inhibiting the production of immunoglobulins, involved in allergic reactions.

3] Vasoconstriction: The cutaneous vasoconstriction induced in the superficial blood vessels, which reduces erythema and oedema.

4] Inhibition of DNA Synthesis: They also inhibit the synthesis of DNA in certain cells, that reduces the proliferation of skin cells and preventing the lichenification.

5] Stabilization of Lysosomal Membranes: By stabilizing the lysosomal membranes within cells, the release of enzymes prevented that contribute to inflammation and tissue damage.

2. Calcineurin Inhibitors: For long term utilization as beyond four weeks these

topical drugs can be used as an alternative to minimise the side effects due to topical corticosteroids.

Mechanism of action: 1] Inhibition of Calcineurin: These drugs inhibit the enzyme calcineurin that have a critical role in activating T-cells, involved in immune responses. Calcineurin inhibitors bind to intracellular proteins (FKBP-12 for tacrolimus and macrophilin-12 for pimecrolimus) to form a complex.

2] Barrier Function Improvement: Calcineurin inhibitors help in maintaining and restoring the skin barrier function by reducing inflammation and preventing further damage to the skin. This is particularly important in areas like the eyelids, where the skin is thin and delicate.

3. Emollient: Petrolatum and similar emollient which are fragrance free and band can be applied on the eyelids.

Mechanism of action: 1] Restoration of Skin Barrier Function: Occlusive Effect: Emollients contain lipids that mimic the natural lipids in the skin. These emollients prevent the trans epidermal water loss and maintain the hydration which helps in making protective barrier on the skin surface. By maintaining the hydration of the skin, penetration of the allergens and irritants prevented.

2] Hydration: Humectants: Many emollients contain humectants (e.g., glycerin, urea, hyaluronic acid) that attract and retain moisture in the skin and help to maintain skin hydration and improve its texture

3] Reduction of Inflammation: Anti-inflammatory Ingredients: Some emollients contain anti-inflammatory ingredients (e.g., oatmeal, ceramides) that help to reduce inflammation and soothe irritated skin. Barrier Restoration: By repairing the skin barrier, emollients reduce the contact to external irritants and allergens, thereby decreasing the inflammatory response.

4] Soothing and Calming Effects: Reduction of Itching and Discomfort: Emollients help to soothe and calm the skin, reducing itching, redness, and discomfort associated with eyelid dermatitis. Softening of Skin: They soften and smooth the skin, improving its overall appearance and feel.

5] Improvement of Skin Elasticity: Enhanced Skin Flexibility: By maintaining proper hydration and barrier function, emollients improve the elasticity and flexibility of the skin, reducing the likelihood of cracking and further irritation.

C. Systemic Treatment - Systemic Steroid: The dose of oral steroids is recommended 0.5 to 1.0 mg/kg/d for the acute stage for 5 to 7 days, then tapering the dose by 50% for the resolving phase upto 7 to 10 days or as required according to the presentation of the case to case.

D. Mixed Approach - Secondary Infected: Systemic and Topical antibiotics. If the cutaneous lesions are secondary infected the first infection should be treated with systemic or topical antibiotics according to the severity presentation followed by underlying condition.

Discussion

Table 3 compiles information from various research papers that focus on eyelid dermatitis, exploring its clinical aspects, diagnostic methods, and practical implications for management (Crouse et al., 2018; Warshaw et al., 2021) these papers investigate trends, clinical presentations, and the prevalence of eyelid dermatitis, emphasizing the importance of patch testing in diagnosis. Notably, studies by (Borghi et al., 2019; Moreira et al., 2017) delve into specific causes, including allergic reactions to acrylates in artificial nails and common culprits such as eye drops and cosmetics. Work challenges preconceptions about nickel allergy as the primary risk, highlighting the potential triggering role of pigmented eye makeup (Borghi et al., 2019). (Huang et al., 2021a) identify key allergen groups and propose management strategies, while (R et al., 1992; Vandersall & Katta, 2015) explore systemic connections and diagnostic approaches. (Parkinson, 1996) contribution underscores the importance of recognizing characteristics and employing patch tests for accurate diagnosis and effective treatment. This literature provides a concept of

eyelid dermatitis, offering valued in the field. understandings for clinicians and researchers

Name of Author	Insights	Practical plications
(Crouse et al., 2018)	The paper discusses trends in eyelid dermatitis, including the clinical description, diagnosis, and prevalence of various types of dermatitis.	Eyelid dermatitis can have multifactorial causes. Patch testing can help diagnose the specific allergens.
(Warshaw et al., 2021)	The paper provides a retrospective study of patients having eyelid dermatitis. It characterizes the patients and highlights the importance of patch testing in evaluating them.	To evaluate the causative factor for eyelid dermatitis patch testing can be performed. The eyelid dermatitis is more commonly affect the female, white, and older than 40 years, and have a history of hay fever and atopic dermatitis.
(G. M et al., 2018)	Eyelid dermatitis can occur due to allergic contact to acrylates in artificial nails, as reported in the paper.	The eyelid dermatitis occurred mostly due to contact with the allergens. To precisely diagnose it detailed exposure history is essential.
(Chisholm et al., 2017)	Eyelid dermatitis is commonly occurred due to eye drops, creams/lotions, and cosmetics. To identify and exclusion of the responsible allergens is required. In addition to this the use of topical corticosteroids recommended.	Allergic Eyelid dermatitis is mostly caused by eye drops, cosmetics, and skin care products. Identification and prevention of contact with the causative agents is key for management.
(Borghi et al., 2019)	The paper discusses the relation between nickel allergy, the utilization of pigmented makeup products, and self-reported eyelid dermatitis. It suggests that the utilization of pigmented eye makeup may be a triggering factor for eyelid dermatitis.	Nickel allergy is not the main risk factor for Eyelid dermatitis. Utilization of pigmented eye make-up may trigger Eyelid dermatitis.
(Huang et al., 2021b)	The paper discusses common allergens causing eyelid dermatitis and provides strategies for	Identification of most common seven allergen groups causing eyelid dermatitis. Empiric counselling and allergen avoidance

	managing its recurrence.	programs for management
(Vandersall & Katta, 2015)	Eyelid dermatitis can be a manifestation of systemic contact dermatitis, and in some cases, it may be caused by the ingestion of cinnamon.	Fragrance-free and formaldehyde-free products may help improve Eyelid dermatitis. Avoiding cinnamon ingestion can lead to clearance of dermatitis.
(R et al., 1992)	Eyelid dermatitis was evaluated in 150 patients, with 65.3% diagnosed as allergic contact dermatitis, 16.6% as irritant contact dermatitis, 14% as atopic dermatitis, and 4% as seborrhoeic dermatitis.	Patch test reactions can help diagnose Eyelid dermatitis. Nickel sulphate, Kathon CG, and Fragrance-mix are common triggers.
(Parkinson, 1996)	The paper discusses the diagnosis and treatment of eyelid dermatitis, including the importance of recognizing its characteristics, obtaining a good history, and performing a skin examination. It also mentions the use of patch tests and prescribing medications.	Recognition and diagnosis of different causes of Eyelid dermatitis. Proper treatment and prevention strategies for patients.

Above literature analysis depicts that aetiology of eyelid dermatitis is multifactorial and confirmation test for the causative allergen is patch testing and management includes combination of steroids, calcineurin inhibitors, emollient and antihistamines. While to prevent recurrence counselling is uppermost important.

Newer Drugs in management of eyelid dermatitis

Biologics and JAK (Janus Kinase Inhibitors) (Davis et al., 2024) - These novel drugs have been found effective for inflammatory skin conditions and including eyelid dermatitis.

Topical drugs (American Academy of Dermatology Issues Updated Guidelines for the Management of Atopic Dermatitis in Adults with Topical Therapies, n.d.) - Phosphodiesterase-4 inhibitor – Topical crisaborole ointment and Janus kinase inhibitor - ruxolitinib cream can be considered.

Conclusion

Above literature analysis depicts that aetiology of eyelid dermatitis is multifactorial and confirmation test for the causative allergen is patch testing and management includes combination of steroids, calcineurin inhibitors, emollient and antihistamines. While to prevent recurrence counselling is uppermost important. Eyelid dermatitis causes considerable distress to the patient due to its chronicity. The correlation of a proper detailed history, meticulous cutaneous examination, and timely identification of the causative allergen through necessary investigations can provide relief to the patient and improve the quality of life.

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