ISSN: 2476 - 2415

Research Article

International Journal of Clinical & Experimental Dermatology

The Prototypal Utricle-Erythema Multiforme

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Submitted: 02 May 2022; **Accepted:** 09 May 2022; **Published:** 20 May 2022

Citation: *Dr. Anubha Bajaj.(2022). The Prototypal Utricle-Erythema Multiforme, Int J Clin Expl Dermatol,7(1), 23 -26.*

Preface

Erythema multiforme arises as a spectrum of reactive muco-cutaneous disorders exhibiting maculopapular or vesiculo-bullous eruptions. The condition may be designated as erythema multiforme (major or minor), toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS). Aforesaid disorders exhibit significant involvement oforal mucosa along with epidermal necrosis. Erythema multiforme is an acute, self limiting, immune mediated disorder which emerges as a hypersensitivity reactionto pertinent antigenic stimuli. The condition may arise due to diverse carcinomas, collagen vascular diseases, drugs or bacterial and viral infections and is associated with a favourable prognosis [1,2].

Oral erythema multiforme is a variant singularly exemplifying oral lesions in the absence of cutaneous lesions.Characteristically, the acute condition exhibits papules, bullous or necrotic lesions within cutaneous or mucosal surfaces.Mucosal lesions heal gradually wherein muco-cutaneous lesions heal in the absence of scarring although dyschromia is frequent [1,2].Lesion reoccurrence is due to secondary infection with herpes simplex virus (HSV) and appears in below < 5% instances [1,2].Apart from an exhaustive clinical history, cogent histological features or serological investigations, immunofluorescence and ultrastructural examination may be adopted for precise disease discernment [1,2].

Disease Characteristics

Majority of lesions appear within three days of antigen exposure and heal within three weeks. Lesions are localized and commonly discerned within the extremities.Mucous membranes are incriminated in around 2% to 10% individuals.Although erythema multiforme is clinically a mild condition, severe instances can be life threatening [1, 2].Diverse viral, fungal and bacterial agents are implicated in disease emergence.Antibiotic agents such as penicillin, cephalosporin, macrolides, sulfonamides, anti-tubercular drugs, antipyretics, drugs as sertraline, alendronate sodium, infliximab, barbiturates or non-steroidal anti-inflammatory drugs (NSAIDs) may engender the condition [1,2].Besides, heavy metals, topical or herbal agents or poison ivy may trigger the disease [1, 2].A racial or ethnic predilection is absent. Young adults between 20 years to 30 years or within third decade to fourth decade are commonly implicated although no age of disease emergence is exempt [3,4).Nevertheless, children and adolescents can be incriminated and roughly 20% instances occur in children [3,4].A gender predilection is absent or a male predominance may be observed with a male to female proportion of 5:1.Disease prevalence is usually beneath <1% [3,4].Of multifactorial aetiology, contributing factors are infection with herpes simplex virus type 1 and 2 (HSV1 and 2), Epstein Barr virus, mycoplasma pneumoniae or histoplasmosis. Lesions arising due to herpes virus may reappear. Drugs, vaccines or diverse therapeutic agents are commonly associated with emergence of erythema multiforme [3,4].Infection with herpes simplex virus 1(HSV1) frequently contributes to disease emergence wherein the infection may be asymptomatic, reoccurring or precede the emergence of erythema multiforme. Mycoplasma pneumoniae may engender erythema multiformein around ~10% incriminated children which especially display mucosal lesions. Additionally, viral agents such as adenovirus, influenza virus, Epstein Barr virus, hepatitis virus, Herpes labialis, Coxsackie, parvovirus B19, human immunodeficiency virus(HIV) or bacterial agents as Mycobacterium tuberculosis, Mycoplasma pneumoniae or streptococci may generate erythema multiforme.Fungal agents or vaccination within paediatric subjects may initiate the emergence of erythema multiforme.Also, immunosuppressed subjects on corticosteroids, human immune deficiency virus (HIV) infection, bone marrow transplantation or autoimmune conditions as lupus demonstrate a predilection for erythema multiforme [3,4].Human leukocyte antigen DQ3 (HLA-DQ3) is associated with erythema multiforme arising due to herpes simplex virus(HSV). Diverse human leukocyte antigen(HLA) groups may emerge as indicators of reoccurring erythema multiforme. Degeneration of epithelial cells occurs on account of cellmediated immunity [3,4].Preliminary disease stage exhibits an influx of macrophages and cytotoxic T lymphocytes (CD8) which secrete various cytokines mediating cellular inflammation and demise. Hypersensitivity reaction to various drugs is accompanied by necrosis of keratinocytes within the initial stage [3,4].

Clinical Elucidation

Initial phase of erythema multiforme exhibitspyrexia and uneasiness which may precede or accompany the cutaneous eruption. Arthralgia or joint swelling may concur occasionally.Erythema multiforme exemplifies a characteristic clinicallesion, designated as "target lesion" which is regular, spherical and exhibits three concentric circles of variable colour, a welldemarcated perimeterand is usuallyaround ~ 3 centimetres in greatest magnitude. The erythematous peripheral ring may occasionally depict micro-vesicleswith a clear, oedematous, palpable medial zone and an erythematous centric region with a superimposed blister. Thus, aforesaid target lesion configures various stages ofan evolutionary lesion [4,5].Atypical target lesion of erythema multiforme manifests as a raised lesion with a dual zone of altered colouration. Configuration of a centric bulla within typical or atypical target lesion is indicative of epidermal involvement [4,5].Target lesion is predominantly acral wherein symmetrical lesions are observed within the palms, dorsal surface of hand, foot and extensor surface of limbs. Lesions upon face or ears may be discerned although the trunk may be spared. Pruritus is absent although a sensation of burning can be enunciated [4,5].Oral mucosal lesions are common although genital or ocular mucous membranes may be incriminated. Preliminary lesions are bullous followed by painful erosions. Labial lesions are superimposed with a dense, haemorrhagic crust whereas mucosal erosions within cheek, palate or genitalia exhibit a whitish, fibrinous coating. Aforesaid mucosal lesions concur with cutaneous lesions although may precede or appear subsequent to mucosal eruption. Mucosal lesions are frequently painful, in contrast to non painful cutaneous lesions [4,5].Pulmonary symptoms as cough or dyspnoeamay emerge commonly due to mycoplasma pneumoniae induced erythema multiforme. Dehydration, anorexia or weight loss may ensue with extensive cutaneous lesions [4,5]. Erythema multiforme may be categorized as•erythema multiforme minor (EMm) which exhibits typical, symmetrical,acral lesions essentially adherent to cutaneous surfaces. Mucosa is infrequently incriminated wherein mucosal lesions are mild and confined to a singular mucosal region, generally the oral cavity. Lesions may be spontaneously alleviated within 3 weeks [6,7].•erythema multiforme major (EMM) with extensive cutaneous lesions confined to below< 10% of body surface area. Characteristic target lesions are observed within the oral mucosa. Mucosa is severely incriminated with the involvement of minimally two diverse mucosal sites.Lesions may spontaneously recover within 6 weeks [6,7].Prognostic outcomes are contingent to area of body surface detachment [6,7].

Histological Elucidation

Cogent tissue sampling with a punch biopsy may be utilized as a confirmatory measure for determining erythema multiforme [6,7].Classically, vacuolar interface dermatitis is accompanied by significant infiltration of lymphocytes along the dermo-epidermal junction. Upon examination, epithelial intercellular oedema with necrosis of keratinocytes engenders an intra-epidermal or sub-epidermal blister with a superimposed necrotic epidermal layer.Superficial dermis exemplifies a perivascular lymphocytic and histiocytic infiltrate. Necrotic vascular lesions are absent [6,7]. However, aforesaid lesions may be undiscernible upon direct immunofluorescence.The condition exhibits accumulation of necrotic keratinocytes, spongiosis of epidermal layer and liquefaction of basal layer. The dermis exemplifies oedema whereas lymphocytes appear aggregated within the perivascular zone or the dermal-epidermal interface [6,7].Upon microscopy, epidermal alterations such as hyperkeratosis,papillary edema, epidermal necrosis, acanthosis, configuration of a scab, hemorrhage and ulceration may be observed.Dermal manifestations appear as perivascular inflammation, granulation tissue, collagen mucinous degeneration and fibrin thrombi [6,7].Oral mucosaexhibits ulceration with the occurrence of erythematous, plaque-like lesions. Lesions with active epithelial necrosis may progress to superficial mucosal ulceration with irregular, erosive edges [6,7].A predominance of cytotoxic T lymphocytes(CD8) and macrophages is observed. Hydropic alterations and dyskeratosis of basal keratinocytes may occur. Advanced lesions display epidermal necrosis, sub-epidermal blisters and vesicular modifications [6,7].

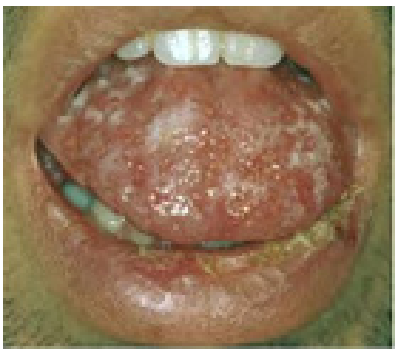

Figure 1: Erythema multiforme enunciating bullous lesions within the oral mucosa with a characteristic erythematous centric zone and micro-vesicles[10].

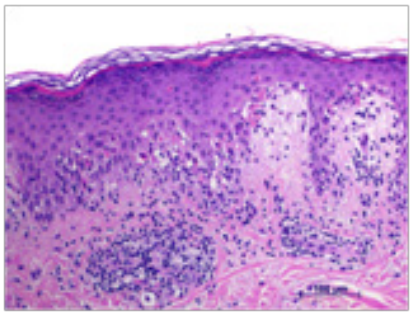

Figure 2: Erythema multiforme exhibiting superimposed stratified squamous epithelial layer with acanthosis, hyperkeratosis, parakeratosis and a moderate, chronic, dermal inflammatory infiltrate[11].

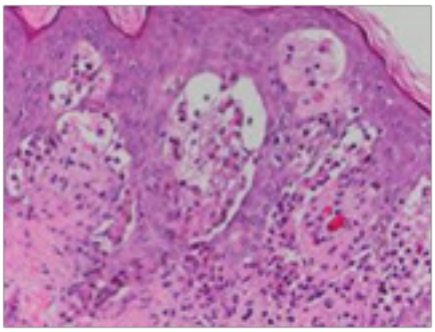

Figure 3: Erythema multiforme exemplifying necrotic keratinocytes admixed with red cells and a chronic inflammatory exudate of lymphocytes enmeshed within a hyperkeratotic stratified squamous epithelial layer[12].

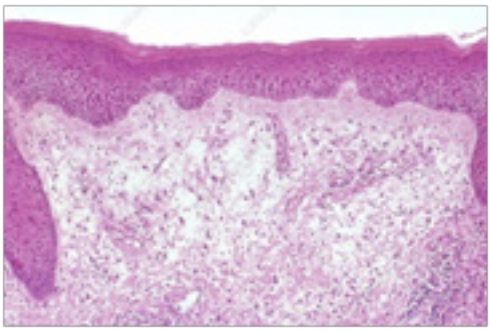

Figure 4: Erythema multiforme delineating a moderate dermal inflammatory infiltrate of lymphocytes with a superimposed stratified squamous epithelial layer with hyperkeratosis, acanthosis and parakeratosis[13].

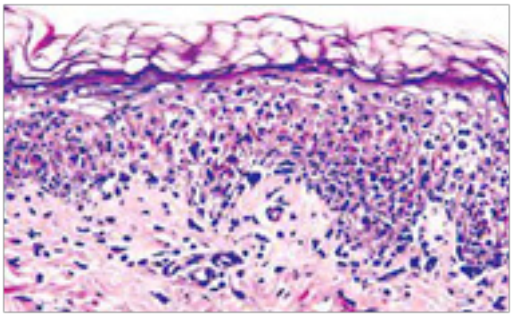

Figure 5: Erythema multiforme demonstrating an intense upper dermal chronic inflammatory exudate of mature lymphocytes and macrophages superimposed with stratified squamous epidermal layer with spongiosis[14].

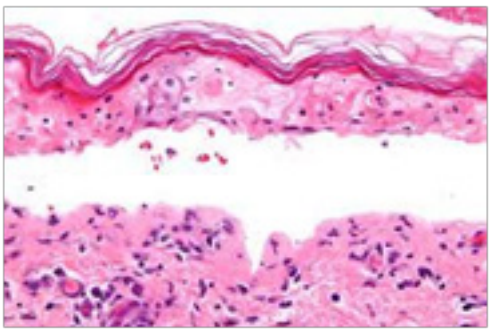

Figure 6: Erythema multiforme displaying a bullous lesion with necrotic keratinocytes, moderate chronic inflammatory exudate and a superimposed hyperkeratotic squamous epithelial layer[15].

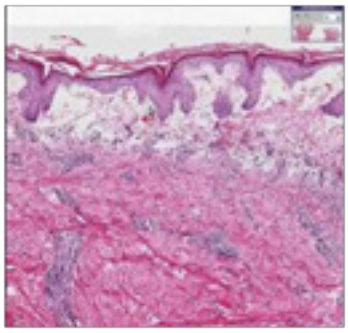

Figure 7 : Erythema multiformedepicting micro-vesicles with necrotic keratinocytes, dermal chronic inflammatory cells and a superimposed stratified squamous epithelial layer with parakeratosis[16].

Differential Diagnosis

Erythema multiforme requires a segregation from conditions such as•Stevens-Johnson syndrome (SJS) which is a drug induced condition and incriminates an estimated 10% of body surface area. Although mucosal lesions are identical to erythema multiforme, cutaneous lesions are predominantly axial and an absence of typical target lesions is observed. However, asymmetrical target-like lesions are configured of dual concentric zones and may evolve into purpuric lesions. Severe instances may progress into Lyell syndrome [7,8].Additionally, distinction is required from conditions such as pemphigus vulgaris, paraneoplastic pemphigus, mucosal bullous pemphigoid, linear IgA dermatosis, primary herpetic infection, viral infection as hand-foot-mouth disease, erosive lichen planus, fixed drug eruption, lupus erythematosus, urticaria, cutaneous vasculitis and specific neutrophilic dermatoses [1,2].

Investigative Assay

Although preponderantly a clinical diagnosis, erythema multiformecan be discerned with cogent tissue sampling from centre of the lesion followed by immunofluorescence.Plain radiographs may exhibit aninterstitial inflammatory infiltrate due to mycoplasma pneumoniae induced erythema multiforme. Although described, renal, hepatic or haematological lesions may be overlooked in

mild disease forms [7,8].Haematological investigations may reveal mild leucocytosis, neutropenia or mild anaemia. Electrolyte values may be altered in dehydrated subjects or in individuals with renal failure [7,8].

Therapeutic Options

Acute phase of erythema multiforme can be treated with topical antiseptic mouthwashes and anaesthetic agents. Moisturizing of lips and application of vitamin A ointment upon eye lesions is beneficial [7,8].Symptomatic therapy is mandated in individuals manifesting difficulty in feeding. Also, alleviation of pain and adequate hydration is necessitated. Systemic corticosteroids and intravenous immunoglobulins may be inefficacious. Extensive lesions require regular monitoring [7,8].Aetiological agents such as mycoplasma pneumoniae or herpes simplex (HSV) infection may be treated with antibiotics or antiviral agents [8,9].Recurrent lesions due to herpetic infection may be circumvented with antiviral therapy. Besides, drugs such as hydroxychloroquine, dapsone or preliminary therapy with cyclical systemic corticosteroids may be adopted [8,9].

Disease Outcome

Oral or genital mucosal lesions of extended duration may develop synechiae.Ocular lesions may terminate in blindness. Instances with severe mucosal involvement and bacterial superinfection mandate extensive monitoring [8,9].Contributory factors as renal dysfunction, preceding bone marrow transplant, implication of diverse viscera and advancing age are associated with an inferior outcome [8,9].Recalcitrant or perpetual lesions of erythema multiforme may ensue in subjects infected with herpes simplex virus (HSV), reactivation of Epstein- Barr viral (EBV) infection, inflammatory bowel disease or occult renal cell cancer [8,9].Although mucosal lesions undergo comprehensive alleviation, cutaneous lesions heal with scarring. Strictures of urethra, oesophagus, vagina or anal region may ensue. Subsequently, urinary retention, phimosis and haematocolpos may occur due to strictures [8,9].Ocular complications such as uveitis, conjunctivitis, corneal scarring, dry eye syndrome, panophthalmitis or permanent blindness may arise. Constriction of nasolacrimal duct generates epiphora [8,9].

References

1. Tahir, D., Souliman, M., De La Rosa, A. M., Al-Jobory, O., & Naguib, T. (2021). Erythema Multiforme-Like Presentation in an Asymptomatic COVID-19 Patient. Cureus, 13(12).
2. Fitzpatrick, S. G., Cohen, D. M., & Clark, A. N. (2019). Ulcerated lesions of the oral mucosa: clinical and histologic review. Head and neck pathology, 13(1), 91-102.
3. Magri, F., Chello, C., Pranteda, G., & Pranteda, G. (2019). Erythema multiforme: Differences between HSV-1 and HSV-2 and management of the disease—A case report and mini review. Dermatologic therapy, 32(3), e12847.
4. de Risi-Pugliese, T., Sbidian, E., Ingen-Housz-Oro, S., & Le Cleach, L. (2019). Interventions for erythema multiforme: a systematic review. Journal of the European Academy of Dermatology and Venereology, 33(5), 842-849.
5. Paulino, L., Hamblin, D. J., Osondu, N., & Amini, R. (2018). Variants of erythema multiforme: a case report and literature review. Cureus, 10(10).
6. Hashemi, D. A., Carlos, C., & Rosenbach, M. (2019). Herpes-associated erythema multiforme. JAMA dermatology, 155(1), 108-108.
7. La Placa, M., & Chessa, M. A. (2018). Erythema multiforme major with swollen lips and crusted erosions. The Lancet, 392(10147), 592.
8. Lerch, M., Mainetti, C., Terziroli Beretta-Piccoli, B., & Harr, T. (2018). Current perspectives on erythema multiforme. Clinical reviews in allergy & immunology, 54(1), 177-184.
9. Khan, P., Mudassar, M., Waqas, M., & Khan, A. (2020). Spectrum of morphological changes in erythema multiforme. Journal of Medical Sciences, 28(3), 218-222.