OCULAR COMPLICATIONS IN CUTANEOUS LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW

Yovita*

*Faculty of Medicine, Maranatha Christian University, Indonesia

*Corresponding Author:
viviyo.vita93@yahoo.com

Abstract
Introduction: Dry eye disease (DED) is a multifactorial disorder of the ocular surface characterized by disruption of tear film homeostasis, instability of the tear film, and inflammation of the ocular surface. Although the precise mechanism of action is still inadequately understood, numerous studies have demonstrated that IPL has the potential to alleviate both the signs and symptoms of dry eye.

The aim: This article showed ocular complications in cutaneous lupus erythematosus.

Methods: By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

Result: In the PubMed database, the results of our search brought up 115 articles, whereas the results of our search on SagePub brought up 97 articles. The results of the search conducted for the last year of 2013 yielded a total 32 articles for PubMed and 26 articles for SagePub. In the end, we compiled a total of 27 papers, 14 of which came from PubMed and 13 of which came from SagePub. We included nine research that met the criteria.

Conclusion: SLE ocular symptoms can indicate active SLE. In daily ophthalmology, SLE should be considered a differential diagnosis, especially for symptoms. Systemic treatment is based on ophthalmology. SLE management requires division and medical field collaboration. Systemic treatment includes antimalartials, corticosteroids, immunomodulators, and biologics.

Keyword: Eye; Cutaneous lupus erythematosus; Ocular complications
INTRODUCTION

It is estimated that the incidence of cutaneous lupus erythematosus (CLE) is two to three times more common than that of systemic lupus erythematosus (SLE). CLE comprises a wide spectrum of dermatologic symptoms. Acute cutaneous lupus exanthem (ACLE), subacute cutaneous lupus exanthem (SCLE), and chronic cutaneous lupus exanthem (CCLE) are the three subtypes of cutaneous lupus. CCLE is comprised of the following subtypes of lupus: discoid lupus erythematosus (DLE), lupus profundus (LEP), chilblain lupus erythematosus (CHLE), and lupus tumidus (LET). The most prevalent type of CCLE, known as discoid lesions, can be found in.

The fourth and fifth decades of a woman’s life are the most common times she will experience DLE. 60–80 percent of discoid lesions are seen in parts of the body that are directly exposed to sunlight, such as the head, neck, scalp, ears, and cheeks. On occasion, DLE can manifest itself on the mucosal surfaces of the mouth, nose, and genital organs. This includes the lips as well as the oral, nasal, and genital mucosa. A cutaneous lesion may begin as erythematous maculae or papules with a scaly surface. These will gradually expand peripherally into bigger adherent discoid plaques, and when they heal, they will leave an atrophic scar as well as pigmentary alterations.

Histological analysis of a DLE lesion that has been active for a significant amount of time reveals hyperkeratosis, dilated compact keratin-filled follicles, vacuolar degeneration of the basal keratinocytes, and a strongly inflammatory dermal infiltration. All of these characteristics are associated with DLE. In terms of serology, patients with DLE show a reduced incidence of antibodies such as ANA, dsDNA, Sm, U1RNP, and Ro/SSA compared to individuals with other CLE subtypes. The lupus band test is positive in 90% of DLE lesions, and C3 and IgM are the most common immune deposits that are seen in these lesions.

LEP is a variant that is not as frequent as CLE. Panniculitis is characterized by the presence of subcutaneous nodules in the lower dermis and in the subcutaneous adipose tissue. The upper arms and legs, face, and breasts are the areas that are affected most frequently by this condition. Histology reveals lobular panniculitis alongside a substantial lymphocytic infiltration in the affected tissue. LEP typically follows a chronic path and can leave behind atrophic scarring. The present investigation demonstrated ocular complications in cutaneous lupus erythematosus.

METHODS

In accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 standards, the researcher of this study undertook measures to assure strict adherence to these criteria. The adoption of this method is meant to ensure the correctness of the investigation’s outcomes. The primary goal of this review was to demonstrate the efficacy of strong pulsed light treatment on the signs and symptoms of dry eye illness. The fundamental goal of this work is to highlight the significance of the aforementioned issues discussed in the text.

To be eligible for participation in the study, researchers had to meet the following criteria: the article's composition should be in English, and its focus should be on the ocular complications in cutaneous lupus erythematosus. Both of these criteria must be met by the paper in order for it to be published. A number of the articles under consideration were published between 2013 and the predetermined timeframe deemed relevant for this systematic review. Editorials, submissions without a Digital Object Identifier (DOI), previously published review articles, and entries that are effectively duplicates of previously published journal pieces are all disallowed.

We used “ocular complications” and “cutaneous lupus erythematosus” as keywords. The search for studies to be included in the systematic review was carried out from August, 19th 2023 using the PubMed and SagePub databases by inputting the words: (("ocular"[All Fields] OR "oculars"[All Fields]) AND ("complications"[All Fields] OR "complicate"[All Fields] OR "complicated"[All Fields] OR "complicates"[All Fields] OR "complicating"[All Fields] OR "complication"[All Fields] OR "complication s"[All Fields] OR "complications"[MeSH Subheading] OR "complications"[All Fields]) AND ("lupus erythematosus, cutaneous"[MeSH Terms] OR ("lupus"[All Fields] AND "erythematosus"[All Fields] AND "cutaneous"[All Fields]) OR "cutaneous lupus erythematosus"[All Fields] OR ("cutaneous"[All Fields] AND "lupus"[All Fields] AND "erythematosus"[All Fields])) AND ((y_10[Filter]) AND (clinicaltrial[Filter])) used in searching the literature.
The authors evaluated each study's abstract and title to determine if it met the inclusion criteria. The authors then determined which prior studies would serve as the article's sources and selected those studies. Numerous studies that appeared to indicate the same trend were analyzed in order to reach this conclusion. All submissions must be written in English and unpublished before submission. Only publications satisfying all inclusion criteria were considered for the systematic review. This reduces the number of search results to only those that are relevant to your query. We disregard any study's results that do not meet our criteria. The research findings will then be thoroughly analyzed.

This study's investigation revealed the following: names, authors, publication dates, location, study activities, and parameters. Before deciding which publications to investigate further, each author performed independent research on the research included in the publication's title and abstract. The subsequent step is to evaluate all of the articles that satisfy the inclusion criteria for the review. Then, we will choose which articles to include in the review based on the findings. This criterion is used to select documents for additional examination. To facilitate as much as possible the selection of papers for evaluation. This section discusses the prior studies conducted and the aspects of those studies that justified their inclusion in the review.

RESULT

In the PubMed database, the results of our search brought up 115 articles, whereas the results of our search on SagePub brought up 97 articles. The results of the search conducted for the last year of 2013 yielded a total 32 articles for PubMed and 26 articles for SagePub. In the end, we compiled a total of 27 papers, 14 of which came from PubMed and 13 of which came from SagePub. We included nine research that met the criteria.

Vijayasankar, et al (2022) showed discoid lupus erythematosus (DLE) is the prevailing manifestation of chronic cutaneous lupus erythematosus, frequently observed in areas of the skin that are exposed to sunlight. The occurrence of eyelid involvement in DLE is relatively infrequent. In this study, we present three instances of DLE characterized by the involvement of the eyelids. The resemblance to other clinical illnesses is significant, resulting in a delay in diagnosis. If left untreated, this condition might give rise to several consequences. The objective of this case series is to underscore the importance of ophthalmologists and dermatologists being knowledgeable about the diverse manifestations of DLE in the eyelids, in order to mitigate the risk of misdiagnosis.
<table>
<thead>
<tr>
<th>Author</th>
<th>Origin</th>
<th>Method</th>
<th>Sample Size</th>
<th>Complication</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vijayasankar, 2022</td>
<td>India</td>
<td>Case series</td>
<td>Three patients</td>
<td>Eyelid involvement</td>
<td>The objective of this case series is to underscore the importance of ophthalmologists and dermatologists being knowledgeable about the diverse manifestations of DLE in the eyelids, in order to mitigate the risk of misdiagnosis.</td>
</tr>
<tr>
<td>Theisen, 2022</td>
<td>United State of America</td>
<td>Retrospective cohort study</td>
<td>9 patients with DLE</td>
<td>Eyelid and periorbital lupus</td>
<td>Rarely associated with systemic disease, periorbital DLE is an uncommon manifestation of chronic cutaneous lupus. Frequently, delayed diagnosis results in chronic recurrent lesions that can cause scarring and pigmentation changes. Providers should be aware of this uncommon condition in order to ensure prompt treatment that limits scarring and possible visual complications.</td>
</tr>
<tr>
<td>Chan, 2020</td>
<td>Canada</td>
<td>Case report</td>
<td>One patient</td>
<td>Orbital myositis</td>
<td>Even in the absence of systemic disease activity, it is essential to maintain a high index of suspicion for orbital myositis in patients with SLE so that early treatment can be initiated. In addition, it is essential to rule out other potential mimics, such as orbital cellulitis and thyroid eye disease.</td>
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<tr>
<td>Lo, 2020</td>
<td>China</td>
<td>Case report</td>
<td>One patient</td>
<td>Periorbital heliotrope edema</td>
<td>They report a case with heliotrope edema as an initial manifestation of juvenile-onset SLE. This report highlights the importance of taking SLE into consideration when dealing with periorbital heliotrope edema.</td>
</tr>
<tr>
<td>Rico, 2016</td>
<td>Spain</td>
<td>Case report</td>
<td>One patient</td>
<td>Orbital inflammatory pseudotumor</td>
<td>A rare complication of systemic lupus erythematosus is orbital inflammatory pseudotumor. It may be difficult to make a differential diagnosis, particularly in the context of treatment with hydroxychloroquine, although dosage and duration of treatment may provide guidance.</td>
</tr>
<tr>
<td>Cakici, 2016</td>
<td>Turkey</td>
<td>Case report</td>
<td>One patient</td>
<td>Periorbital DLE</td>
<td>The presence of periorbital discoid lupus erythematosus is a rare occurrence and warrants consideration while evaluating erythematosus lesions in the periorbital region.</td>
</tr>
<tr>
<td>Arrico, 2014</td>
<td>Italy</td>
<td>Case report</td>
<td>One patient</td>
<td>Proptosis and orbital myositis</td>
<td>This case report describes a unique instance of orbital myositis in a patient diagnosed with discoid lupus erythematosus, who presented with sudden protrusion of the eye, double vision, and isolated involvement of a single extraocular muscle.</td>
</tr>
<tr>
<td>Kono, 2014</td>
<td>Japan</td>
<td>Case report</td>
<td>One patient</td>
<td>Orbital myositis</td>
<td>This is the first case report of discoid lupus erythematosus and orbital myositis. Diagnostic signs included painful diplopia and extraocular muscle abnormalities on orbital magnetic resonance imaging (MRI). Early corticosteroid treatment confirmed the diagnosis and reduced the danger of irreparable cicatricial injury from ocular muscle changes.</td>
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<tr>
<td>Kopsachilis, 2013</td>
<td>Greece</td>
<td>Case report</td>
<td>One patient</td>
<td>Blepharitis</td>
<td>Cicatricial ectropion developed as a consequence of significant scarring of the marginal eyelids that persisted even after the inflammation of the eyelids had subsided.</td>
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Theisen, et al (2022)\textsuperscript{12} showed people with DLE often have other skin diseases at the same time as eyelid involvement, which happens in 5% to 6% of cases.\textsuperscript{2} Rarely does the disease only affect the skin around the eye. Unfortunately, periorbital DLE is often not found for years, which is something that our group noticed. Untreated periorbital DLE can cause skin scarring and hypopigmentation, as well as conjunctival scarring, symblepharon formation, trichiasis, and ectropion.\textsuperscript{4} This is why it is important to get a quick evaluation. They saw limited systemic involvement in our group, which is in line with the fact that people with limited DLE lesions have a low chance of getting systemic lupus erythematosus.

Chan, et al (2020)\textsuperscript{13} reported a case with a 45-year-old woman presented with right eye pain, chemosis, proptosis, and restricted abduction. Her orbital computed tomography revealed a hypertrophy of her right lateral rectus muscle. There
were no additional systemic symptoms. There was no increase in inflammation or disease activity biomarkers. She was administered a high dose of corticosteroids, and her symptoms resolved quickly. Even in the absence of systemic disease activity, it is essential to maintain a high index of suspicion for orbital myositis in patients with SLE so that early treatment can be initiated. In addition, it is essential to rule out other potential mimics, such as orbital cellulitis and thyroid eye disease.

Lo, et al (2020)\textsuperscript{14} showed juvenile-onset SLE patients have more severe disease activity compared with those with adult onset disorder. Early detection and treatment are important. Systemic corticosteroid is the mainstay treatment. Immunosuppressive agents such as hydroxychloroquine, azathioprine, and mycophenolate mofetil should be considered as steroid-sparing agents. In conclusion, they report a case with heliotrope edema as an initial manifestation of juvenile-onset SLE. This report highlights the importance of taking SLE into consideration when dealing with periorbital heliotrope edema.

Rico, et al (2016)\textsuperscript{15} report a case with 49-year-old female with suspected right optic neuritis was referred to the Neurology Division. At the time of presentation, she was taking azathioprine 50 mg three times daily, prednisone 5 mg daily, and belimumab 640 milligrams intravenously every four weeks for systemic lupus erythematosus (SLE). A rare complication of systemic lupus erythematosus is orbital inflammatory pseudotumor. It may be difficult to make a differential diagnosis, particularly in the context of treatment with hydroxychloroquine, although dosage and duration of treatment may provide guidance.

Arrico, et al (2014)\textsuperscript{17} showed exophthalmos, periorbital pain, and blurred vision in her right eye were the presenting symptoms for a 37-year-old Caucasian lady who had a history of discoid lupus erythematosus over the previous 5 years. A laboratory examination as well as an orbital computed tomography were carried out. An expansion of the right medial rectus muscle was seen on the imaging performed using computed tomography. It was determined that the patient did not have thyroid eye illness or orbital cellulitis. The symptoms were completely eliminated by the use of corticosteroids in treatment.

Kono, et al (2014)\textsuperscript{18} conducted a case report. Their report is the first time that discoid lupus erythematosus has been reported in conjunction with orbital myositis. Diagnostic hints included the presence of painful diplopia as well as anomalies of the extraocular muscles on the orbital MRI. Early therapy with a corticosteroid was beneficial for both confirming the diagnosis and avoiding permanent cicatricial ocular muscle alterations from occurring.

Kopsachilis, et al (2013)\textsuperscript{19} provide the clinical profile of a 45-year-old female of Caucasian ethnicity who has been experiencing symptoms of eyelid redness and irritation for a duration of 21 years. The patient had a treatment regimen consisting of antibiotics, steroids, and eyelid hygiene, which yielded temporary alleviation of symptoms. Over the course of the past year, the patient's symptoms have appeared to worsen, despite the implementation of a localized therapeutic intervention. After performing a biopsy, the medical professionals verified a diagnosis of discoid lupus erythematosus. Subsequently, patient was prescribed hydroxychloroquine.

**DISCUSSION**

The occurrence of ocular involvement in people diagnosed with cutaneous lupus erythematosus (CLE) is rather infrequent. When examining different subtypes of cutaneous lupus erythematosus (CLE), there is a predominant focus on instances involving discoid lupus erythematosus (DLE) and its associated ocular problems, often in comparison to patients impacted by lupus erythematosus profundus (LEP). The initial documentation of chronic blepharitis in individuals with discoid lupus erythematosus (DLE) was published by Aubaret in 1930.\textsuperscript{5}

Subsequently, Duke-Elder and Donzi documented further instances of this condition after a span of three decades. The literature has documented a total of seventy-one recorded cases of ocular problems associated with Discoid Lupus Erythematosus (DLE) since the early 1980s. In contrast, there have been only six reported cases of individuals with Lupus Erythematosus Profundus (LEP) experiencing ocular difficulties. There is no documentation of any ocular problems associated with the remaining subtypes of cutaneous lupus erythematosus (CLE), namely acute CLE (ACLE), subacute CLE (SCLE), chronic CLE (CHLE), and lupus erythematosus tumidus (LET).\textsuperscript{5}

Bilateral blepharitis is the prevailing manifestation observed in the majority of patients. In certain instances, the manifestation exhibits asymmetry, whereas in a limited number of cases, it is unilateral. The majority of lesions tend to manifest on the lower part of the eyelid and are characterized as reddish, erythematosus, mildly infiltrated plaques, which may or may not exhibit scales, atrophy, or scarring. It is reported that conjunctivitis, meibomitis, madarosis, and chronic ocular erythema lid plaque lesions are associated with anomalous pigmentation. Rosacea blepharconjunctivitis, seborrheic blepharitis, chronic staphylococcal blepharitis, contact dermatitis, eczema, psoriasis, sebaceous cell carcinoma, lid-involving sarcoidosis, lichen planus, lichenoid drug eruption, and tinea faciei are included in the differential diagnosis of DLE eyelid involvement.\textsuperscript{20}

Ophthalmic manifestations may correlate with the systemic activity of the underlying disease and depend on the susceptibility of the patient. Ophthalmic changes may manifest at the onset of the disease or during its progression. Ocular
involvement is categorized as low to moderately common in the course of SLE; however, cases have been reported indicating that it may pose a significant risk to vision. Disease manifestations may include abnormalities of the eye's protective apparatus, primarily the eyelids, the area of the orbit, the eye's appendages, the eye's structures, and the optic nerve.¹

During SLE, keratoconjunctivitis sicca (dry eye disease), iritis, ciliary body inflammation, and retinal vascular alterations are the most frequently diagnosed conditions, whereas optic neuritis and occlusive vasculitis are the most detrimental to vision and cause blindness. Active inflammation in the retina and choroid can resemble systemic vasculitis that can affect other organs. Pathological alterations in the posterior segment of the eye (optic nerve, retina, uvea) frequently precede other systemic manifestations of the disease and can aid in the diagnosis and implementation of appropriate therapy for SLE.³

CONCLUSION
SLE ocular symptoms can indicate active SLE. In daily ophthalmology, SLE should be considered a differential diagnosis, especially for symptoms. Systemic treatment is based on ophthalmology. SLE management requires division and medical field collaboration. Systemic treatment includes antimalarials, corticosteroids, immunomodulators, and biologics.

REFERENCES