Dermatology Practical & Conceptual

Dermatological Indicators of Systemic Autoimmune Disease: Clinical Links to Ocular Involvement

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ABSTRACT

Introduction: Systemic autoimmune diseases frequently involve both the skin and eyes, with early cutaneous manifestations often serving as visible indicators of deeper, multisystem pathology. Conditions such as systemic lupus erythematosus, dermatomyositis, sarcoidosis, and Sjögren's syndrome display characteristic skin findings, including malar rash, heliotrope eruption, lupus pernio, or xerosis, which may precede or parallel serious ocular complications, including uveitis, retinal vasculitis, conjunctival granulomas, and keratoconjunctivitis sicca. Despite this overlap, diagnostic and therapeutic strategies remain fragmented across specialties.

Objectives: By highlighting the clinical intersections between dermatological and ocular manifestations in systemic autoimmune diseases, we aim to promote earlier recognition, integrated treatment, and improved outcomes for patients affected by these multisystem disorders.

Methods: This review synthesizes the literature from the last fifteen years, between 2010 and 2025, on four major autoimmune conditions: systemic lupus erythematosus, dermatomyositis, sarcoidosis, and Sjögren's syndrome.

Results: We examine disease-specific immunopathology, diagnostic modalities, and therapeutic strategies, while also discussing the need for interdisciplinary management models, including those that bridge dermatology and ophthalmology.

Conclusion: By highlighting these clinical intersections, we aim to promote earlier recognition, integrated treatment, and improved outcomes for patients affected by these multisystem disorders.

Introduction

Immunological Crossroads of Skin and Eye

Many dermatological conditions are complicated by ocular involvement, with eye symptoms sometimes preceding skin manifestations, as seen in sarcoidosis. The skin and eye share and ectodermal origin and genetic regulators of melanin [1,2]. As a result, both tissues share epithelial vulnerabilities to ultraviolet radiation, allergens, infections, and trauma.

Immunologically, the skin and eye engage similar defense mechanisms. The conjunctiva is part of the mucosal immune system, with dendritic cells that closely resemble Langerhans cells in the skin. When activated, these dendritic cells migrate to regional lymph nodes, including the cervical lymph nodes [3]. Mast cells in the eye function similarly to those in the skin, contributing to allergic responses and recruiting neutrophils. Both tissues share inflammatory cytokine pathways, which play a role in autoimmune diseases. For example, lymphocytic infiltration of the lacrimal gland leads to keratoconjunctivitis sicca, while lymphocyte accumulation at the dermal-epidermal junction results in cutaneous lupus. [4,5]

From 2011 to 2022, an estimated 4.6% of the U.S. population was diagnosed with an autoimmune disease [6]. Many autoimmune disorders are rare and heterogeneous, contributing to underdiagnosis. Thus, collaboration between dermatologists and ophthalmologists is essential to recognizing signs and symptoms, leading to earlier diagnosis and improved patient outcomes. The overlap between ocular and dermatologic manifestations in systemic diseases underscores the need for integrated care to reduce morbidity. Given that many of these conditions share therapeutic targets, treating one aspect may help slow the progression of others. In this review, we highlight systemic diseases with both skin and eye involvement, such as systemic lupus erythematosus, dermatomyositis, systemic sclerosis, Behçet's disease, relapsing polychondritis, and other rare disorders. We also discuss diagnostic tools used in both specialties and explore future directions for collaborative care.

Objectives

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Methods

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Results

Systemic Lupus Erythematosus: Cutaneous and Ocular Overlap

Systemic lupus erythematosus (SLE) is a multisystemic disease of obscure etiology in which genetic, hormonal, and environmental determinants interact. Familial aggregation and twin studies indicate heritable predisposition, especially in major histocompatibility complex and complement genes [7]. Hormonal effects are key: estrogen and prolactin increase immune activation and help explain SLE's female predominance. Exogenous estrogen and progesterone enhance disease activity, which increases flare risk 1.34 fold [7]. Additionally, low dehydroepiandrosterone (DHEA) disrupts androgen-mediated immunosuppression, worsening disease [8]. Moreover, environmental triggers, ultraviolet light, silica exposure, and viral infections further aggravate the pathogenesis of disease activity, acting through cell injury and molecular mimicry mechanisms. Together, these factors indicate the multifactorial etiology of systemic lupus erythematosus and give the context of the disease's complex clinical manifestations.

Cutaneous manifestations are among the most frequent clinical features of SLE, second in frequency only to musculoskeletal disease, and are generally characterized by a continuum that mirrors systemic activity. The division of cutaneous lupus erythematosus (CLE) into acute (ACLE), subacute (SCLE), and chronic (CCLE) by Gillian and Sontheimer is still clinically applicable, but due to the lack of specific criteria, the diagnosis still mainly depends on histopathological examination and in-depth clinical history [9]. Within this context, malar rash, characteristic of ACLE, is

notable due to its photosensitivity and close associations with active systemic disease, especially in females of reproductive age. Its nonscarring, temporary characteristic distinguishes it from the other mimics like sunburn, rosacea, or seborrheic dermatitis, and perivascular lymphocytic infiltration and basal vacuolization under microscopic examination can aid in the differentiation of diagnosis [10]. On the other hand, chronic lesions like those found in discoid lupus erythematosus (DLE) indicate more persistent illness and appear as scaly, well-defined plaques that are easily confused with chronic blepharitis. About 25% develop discoid lesions, and 10–20% progress to systemic disease, highlighting the cutaneous–systemic continuum [10]. This underscores the importance of lesion classification for diagnosis and prognosis. Therapeutically, malar and discoid lesions are known to respond well to systemic anti-inflammatory medication, with hydroxychloroquine being a staple, further supporting the conceptual integration of cutaneous and systemic treatment [11]. Ultimately, the continuum of cutaneous manifestations of lupus serves both as a diagnostic tool and as a prognostic factor and thus the significance of skin lesions in the understanding and management of SLE.

Systemic lupus erythematosus involves inflammatory mechanisms that spread beyond the systemic realm to involve ocular structures, manifesting clinically as scleritis, retinal vasculitis, and dry eye syndrome, with a different disease activity pattern. Scleritis is relatively common, usually presenting with diffuse or nodular anterior inflammation which can evolve to necrotizing types that can compromise scleral integrity and, eventually, sight; its temporal correlation with systemic flares makes it an important indicator of disease activity [11]. Retinal vasculitis, which is less frequently seen as an initial presentation, is an indication of a more vigorous course of the disease because the deposition of immune complexes and activation of complement leads to vascular damage, retinopathy, and irreversible blindness unless treated early [12]. Both scleritis and retinal vasculitis emphasize the relevance of ocular involvement as a clinical indicator of increased systemic immune activity that usually requires systemic immunosuppression. In turn, dry eye syndrome is more prone to occur both earlier and more frequently, indicative of the immune-mediated dysregulation of the lacrimal and Meibomian glands and cytokine-mediated inflammation of the ocular surface. Chronically dry eyes may cause morbidity through altered tear feedback [12]. Its involvement in diminished corneal sensitivity also describes how the pathology of the eye can alter signals into the lacrimal reflex. In addition, its predilection towards mucocutaneous presentation of SLE shows that immune dysregulation is interrelated and can manifest in other tissues [12]. Together, these conditions show that ocular manifestations of SLE represent a continuum of the spectrum of severity that includes self-limited surface inflammation to sight-threatening vasculitis and thus the value of ocular presence in SLE as a diagnostic tool and systemic disease activity indicator.

Dermatomyositis and its Link to Ocular Involvement

Dermatomyositis (DM) is a rare inflammatory myopathy that, like SLE, presents with cutaneous findings, but is distinguished by disease-specific hallmarks. Early cutaneous presentations of DM include Gottron's papules, characterized by overlaying erythematous or violaceous papules over dorsal knuckle and finger joints, and heliotrope rashes, characterized by erythematous or violaceous rashes on the upper eyelids [13]. These characteristic findings often precede muscle weakness and respiratory symptoms, making comprehensive dermatological assessment critical to early DM detection and prevention of systemic complications. Moreover, DM is frequently misclassified as cutaneous lupus erythematosus due to malar rash being an overlapping clinical manifestation; however, Gottron's papules are specific to DM and may help differentiate between the two [14]. Further, periorbital edema, or swelling around the eyes, frequently co-occurs with the heliotrope rash but was mistaken for allergies in a patient of West African descent, highlighting diagnostic delays in underrepresented skin tones [15].

Although ocular involvement is central to lupus diagnostics, it is far less common in dermatomyositis. Rare cases of DM-associated retinopathy and retinal vasculitis, characterized by cotton-wool spots and vascular sheathing, have been treated with high-dose steroids and monitored with optical coherence tomography [16]. Thus, systemic microangiopathy in DM may be reversible with early immunosuppressive management and reveal themselves through existing imaging modalities for office monitoring. Retinopathy in dermatomyositis is rare, and vision loss generally recovers over time, though a few cases of permanent damage have reported pigment clumping and optic disk pallor that resulted in permanent vision loss [17]. Other rare but reported retinal vasculopathies include retinal vein and occlusions, hemorrhages, and edema [18]. As such, awareness of these rare but serious outcomes is important for counseling patients when ocular symptoms do persist. Juvenile dermatomyositis (JMD) also demonstrates ocular overlap, with lid manifestations and corticosteroid-induced cataracts more frequently documented than vasculitis, demonstrating the need to evaluate the role of steroid-sparing agents against JMD [19]. While DM ocular disease mirrors lupus in microangiopathy mechanisms, its rarity and reversible course set it apart from ocular involvement in SLE. Together, these cutaneous and ocular manifestations showcase the importance of diversifying medical research and performing early diagnostic assessments to prevent systemic complications.

Despite the characteristic skin and eye signs, DM is often misclassified or diagnosed late. Amyopathic dermatomyositis (ADM) is commonly misdiagnosed as eczema due to the overlap in erythematous appearance and itching symptoms, though skin biopsies can prevent these misdiagnoses [20]. Increasing the availability of diagnostic infrastructure rather than relying solely on cutaneous symptoms will improve future DM identification. Moreover, this study highlights the importance of interdisciplinary collaborations between rheumatology, dermatology, and pathology to differentiate between disorders with similar presentations.

Future studies should expand representation in diverse skin tones to reduce bias and diagnostic delays [21].

Taken together, the clinical features of dermatomyositis highlight the central role of cutaneous manifestations in early recognition, while its occasional ocular involvement mirrors, but rarely matches, that of lupus. The diagnostic overlap with SLE reinforces the importance of interdisciplinary collaboration between dermatology, rheumatology, ophthalmology, and pathology to ensure timely, accurate identification of systemic autoimmune diseases.

Sarcoidosis and Sjogren's Syndrome: Multisystem Involvement of Skin and Eye

Sarcoidosis and Sjögren's syndrome, though distinct in pathology, share the clinical reality of multisystem involvement and the demand for nuanced, multidisciplinary care. Different forms of immune dysregulation lead to the convergence of both sarcoidosis and Sjögren's syndrome on skin and eyes. Sarcoidosis usually presents with skin symptoms. Lupus pernio on the nose and cheeks indicates chronic refractory disease with systemic involvement, but papules and subcutaneous nodules suggest milder disease courses [22,23]. The immunopathology rests on granuloma formation, driven by macrophage and CD4+ T-cell activation with cytokines such as TNF-α and IFN-γ orchestrating inflammation.

Ocular disease is equally pivotal: granulomatous uveitis occurs in up to half of patients and ranges from self-limited anterior inflammation to vision-threatening panuveitis requiring long-term immunosuppression [24]. Lacrimal gland infiltration further blurs boundaries between local and systemic pathology, manifesting with dry eye and orbital swelling [25]. Diagnosis is complex, relying on a constellation of imaging, laboratory findings, and histopathology, often guided by the International Workshop on Ocular Sarcoidosis criteria [26]. Outcomes vary: acute anterior uveitis tends to remit with corticosteroids, whereas chronic panuveitis, particularly in middle-aged females, is vision-threatening and demands long-term immunosuppression [27]. Managing sarcoidosis is multidisciplinary, as 40% with cutaneous disease also have silent systemic involvement [28]. Collaboration improves diagnosis, but algorithms remain inconsistent and prognosis varies [29,30].

Similarly, the skin and ocular surface of patients with Sjögren's syndrome display symptoms of the disease. Xerosis is the most common cutaneous finding, while vasculitic purpura signals systemic activity and heightened complication risk. Annular erythema occurs infrequently, yet its appearance strongly correlates with SSA/SSB autoantibody presence [31]. The ocular manifestation of keratoconjunctivitis sicca results from lacrimal gland lymphocytic destruction, which occasionally causes corneal melt and perforation when inflammation is not controlled [32]. The diagnosis depends on serological tests, although a significant number of patients lack detectable antibodies; therefore, healthcare providers must integrate salivary gland biopsy results with clinical assessment [33].

Sarcoidosis involves Th1/Th17 pathways, while Sjögren's is B-cell driven, with occasional overlap [34,35]. The risk and severity of these diseases vary according to ethnic background and sex; African-American females experience the highest sarcoidosis mortality, and Sjögren's shows predominantly female patients [36].

The treatment options for both diseases fall behind the current standard of biological therapy for autoimmune disorders. The standard treatment for sarcoidosis includes corticosteroids and conventional immunosuppressive drugs, with anti-TNF agents being used for patients who do not respond to other therapies [37]. B cell and cytokine-targeting biologics trials for Sjögren's have been conducted, but no medication has received FDA approval [38]. The development of precision medicine approaches for these diseases focuses on immune phenotyping and genetic risk assessment to improve future treatment options.

Other Autoimmune Disorders with Oculodermal Findings

Beyond lupus, dermatomyositis, sarcoidosis, and Sjögren's, several other systemic autoimmune diseases display important skin–eye intersections. Although less common, these disorders highlight recurring themes of vasculitis, fibrosis, and chronic inflammation that threaten both cutaneous and ocular tissue. Oculodermal findings have been reported in patients with other autoimmune disorders such as systemic sclerosis (SSc). SSc is a chronic connective tissue disease that is characterized by vasculopathy, immune dysregulation, and progressive fibrosis. Sclerodactyly and telangiectasia, affecting the facial skin and eyelids predominantly, are common dermatological manifestations of the disease [39]. Ophthalmic involvement is common, with manifestations occurring in both the posterior and anterior segments of the eye and adnexa [39]. SSc retinal changes range from pigment epithelial atrophy to choroidal scarring [39]. Lacrimal glands,

responsible for aqueous fluid production, are likely to undergo fibrosis, leading to dry eye symptoms. Among SSc patients, 37–79% are likely to experience dry eye disease [40]. Behçet's disease (BD), by contrast, is a multisystem vasculitis characterized by attacks of acute inflammation, affecting almost every vascularized area of the body [41]. Classic manifestations of BD include recurrent oral aphthous ulcers and genital ulcers which often scar, while cutaneous signs include papulopustular and erythema nodosum [41]. Ocular involvement is common, as bilateral uveitis and retinal vasculitis are seen in 30–70% of BD patients, succeeding oral and genital ulcers by 2–3 years [41]. Recurrent, nongranulomatous bilateral uveitis typically affects anterior, posterior, or both segments of the eye. Other findings include retinal vein occlusion, optic neuritis, and vitreous hemorrhage [41]. Another immune-mediated condition associated with BD is relapsing polychondritis (RPC). Auricular chondritis is a common manifestation in 60–90% of RPC patients, with ocular involvement occurring in 20–61% patients as the initial presenting symptom [42]. RPC frequently presents as bilateral recurrent scleritis that may be diffuse, nodular, or necrotizing, and it threatens vision more significantly than do other systemic diseases. Other possible ocular manifestations include uveitis, keratitis, conjunctivitis, retinopathy, and optic neuropathy [42]. Other rare but vision-threatening systemic conditions include Cogan's syndrome and granulomatosis with polyangiitis (GPA). Cogan's syndrome is an autoimmune vasculitis with interstitial keratitis and audiovestibular involvement which can cause permanent vision and hearing loss if left untreated [43]. GPA is a vasculitis of the small and medium blood vessels, with over half of patients experiencing ocular symptoms and potential long-term blindness [43]. Identification of these oculodermal presentations in various autoimmune diseases is necessary, as prompt, multidisciplinary management can avoid permanent visual loss and improve long-term patient outcomes.

Diagnostic Tools and Biomarkers: Skin-to-Eye Clues

Early diagnosis of autoimmune disease depends on both cutaneous and ocular findings. In the world of dermatology, skin biopsy continues to be the gold standard for establishing inflammatory and immune-mediated processes. For instance, with biopsy, lupus erythematosus can be realized with histopathologic recognition of interface dermatitis or granulomatous inflammation in sarcoidosis [44,45]. Direct immunofluorescence (DIF) can add a layer of diagnostic specificity by revealing characteristic immune deposits, like IgG and C3 found along the dermoepidermal junction in lupus [9]. Dermoscopy, a less invasive yet informative technique, offers real-time inspection of vascular patterns and pigmentary changes that may indicate more destructive lesions, therefore serving as a bridge between clinical and histopathologic examination [46].

Ophthalmic examination is also key in systemic disease diagnosis. For instance, slit-lamp examination enables recognition of keratoconjunctivitis sicca in Sjögren's syndrome or scleritis in lupus and relapsing polychondritis [47,48]. Schirmer's test is the gold standard measure of tear production and is used in clinical and research practice in suspected exocrinopathie. [49] .High-resolution imaging of the retina and choroid can be obtained using optical coherence tomography to allow early identification of autoimmune uveitis, retinal vasculitis, and choroidal thickening in sarcoidosis [50]. Laboratory biomarkers augment tissue and imaging diagnostics. Antinuclear antibodies (ANA) and nuclear antigen subsets like anti-SSA/Ro and anti-SSB/La are important in the diagnosis of Sjögren's syndrome and systemic lupus erythematosus [51,52]. Angiotensin-converting enzyme (ACE) levels are helpful in monitoring the progression of sarcoidosis, although specificity is poor [53]. HLA typing also adds diagnostic and prognostic information in conditions like Behçet's disease (HLA-B51) and ankylosing spondylitis with ocular involvement (HLA-B27) [54,55].

Combining serology and imaging strengthens systemic autoimmune diagnosis. These kinds of multidisciplinary diagnoses promote earlier identification of systemic autoimmune disease, prior to the development of irreversible damage.

Conclusion

Cutaneous and ocular manifestations of systemic autoimmune diseases often mirror each other during presentation due to shared immunopathology, highlighting the need for collaboration across specialties. Many conditions, such as SLE, sarcoidosis, and Behçet's disease, demonstrate how dermatological findings can foreshadow or coincide with sight-threatening ocular complications. For example, a patient with SLE may have discoid lesions correlating with higher rates of retinal vasculitis, while lupus pernio in sarcoidosis is strongly associated with chronic uveitis. Timely differentiation, diagnosis, and management of these ocular conditions is critical in preventing irreversible vision loss. Better prognosis can be achieved by recognizing these overlaps as signs of early detection in systemic activity. Skin findings and examinations are often less invasive and more accessible predictors of ocular disease involvement. Dermatologists discovering external markers of systemic inflammation through lesions such as malar rashes, erythema nodosum, or vasculitis purpura can refer patients for ophthalmological evaluation and rheumatological workup. Once such patterns are recognized upon examination, a cross-specialty team-based approach is

necessary for long-term management. Integrated dermatology-ophthalmology-rheumatology care improves accuracy and quality of life. Shared clinics reduce fragmented care and patient burden in complex multisystem disease. Future directions should align research initiatives with clinical innovation that can be translated into effective and coordinated interdisciplinary care. Advancements in biomarker discovery, such as autoantibodies and cytokines, are continuously expanding and demonstrating the potential to predict autoimmune flares across various organ systems. Combining specialty clinics and offering virtual care may reduce access disparities. Underserved populations are disproportionately affected by systemic autoimmune diseases such as SLE, shown through increased disease severity and poorer outcomes. Bridging dermatology, ophthalmology, and rheumatology offers a unique opportunity to integrate skin and eye findings into systemic autoimmune disease management. Coordinated care increases the likelihood of detecting systemic autoimmune disease early on, which can prevent vision loss, address equitable access to care, and reduce long-term morbidity across several organ systems.

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