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Review Article

Systemic lupus erythematosus and its impact on eye

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Abstract

Systemic lupus erythematosus (SLE) is an autoimmune condition that affects the body's own tissues by identifying as foreign pathogens. It is characterized by multisystem involvement and can affect every organ, including the eyes. Limited data is available on the prevalence of SLE due to its similarity to other various autoimmune disorders and only a few genetic factors are known to be associated with the development of the disease. SLE can present as fatigue, malaise, loss of appetite, weight loss and fever followed by development of joint pain which affects the same joints on both the sides of the body. The characteristic butterfly rash - a flat red rash on the cheeks and bridge of the nose is significant for SLE. Around 40% of patients with SLE present with ocular complaints ranging from mild irritation to optic neuropathy or SLE retinopathy to severe sight threatening complications. Ocular findings can be the early presenting feature of SLE and it can reflect the underlying systemic involvement. Prompt diagnosis by the Ophthalmologist is crucial to avoid permanent visual loss. This article emphazises the significance of collaborative approach between the Ophthalmologists, General Physicians and Rheumatologist for proper identification and treatment of the disease.

Keywords: Systemic lupus erythematosus, Malar rash, Retinopathy, Intra vitreal injection, Vitreous haemorrhage.

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1. Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that occurs when the body's own tissues are identified as foreign pathogens and affected by the immune system.[1] It has a relapsing and remitting course. Women are commonly affected.[2] SLE presents with a wide variety of manifestations by affecting any organs of the body like skin, lungs, kidneys or the blood vessels and eye is not an exception.[3]

2. Research Gap

1. There is a gap in identifying the disease triggers and its tolerance loss to self-antigens
2. The exact mechanism is not well understood
3. There is lack in sensitivity of biomarkers at all stages of the disease.
4. Ocular manifestations are underreported.
5. There is limited data on the long term outcome of the disease.

3. Prevalence and Incidence

A conservative estimate suggests the prevalence of systemic lupus erythematosus to vary from 161,000 to 322,000 adults.[4] CDC Lupus registries estimated the annual prevalence of SLE to be higher in blacks than compared to whites.[5] But the exact prevalence could not be studied due to the similarity of the disorder to other autoimmune disorders. The prevalence

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of SLE was found to be higher in women than men and the risk develops in younger women peaking in child bearing age group.[6] The prevalence of SLE is very low in Asian and African countries in comparison to western countries. It is believed that increased tobacco usage and ethnic mixing in western countries may contribute to these factors.

While little data for prevalence is available, we lack in data for incidence of SLE due to difficulty in obtaining the data with SLE having an expensive diagnostic method. Affordable diagnostic tool kit for the diagnosis of SLE should be introduced which will in turn give us a wider knowledge about the incidence of the disease.

4. Etiology and Causes

The exact cause of the disorder is not studied but few genetic factors are known to be associated with the development of the disease. It is known to run in families but not all the people with gene variation develops this condition. Till date, over 80 loci variations are identified which suggests a complex balance between the susceptible and the protective genes.[7] The genes found to be linked with SLE are involved in immune system function. Other factors like stress, diet, exposure to chemicals and sunlight can trigger the disorder.

A rare form of SLE which follows Autosomal recessive pattern has been identified. The affected individual does not show any symptoms nor signs of this disease.

5. Presentation

SLE can present as fatigue, malaise, loss of appetite, weight loss and fever followed by development of joint pain which affects the same joints on both the sides of the body.[8] The characteristic butterfly rash - a flat red rash on the cheeks and bridge of the nose is significant of SLE which is more pronounced on exposure to sunlight. Other dermatological symptoms include calcinosis - a condition where calcium deposits under the skin, petechial spots, alopecia due to scarring of the scalp and vasculitis. Oral ulcers are not uncommon.[9]

SLE can lead to leucopenia which in turn can cause life threatening infections or easy bruising due to low platelet count. Other dangerous complication includes Deep vein thrombosis, pulmonary embolus or stroke. This is associated with the release of antiphospholipid antibodies which are abnormal proteins increasing the tendency of blood to clot.[10]

SLE can affect the kidneys leading to nephritis,[11] heart leading to pericarditis.[12] Other features include anxiety, depression and cognitive impairment.[13] SLE gradually worsens and can be life threatening when there is multi organ involvement.

6. SLE and Eye

Around 40% of patients with SLE presents with ocular complaints ranging from mild irritation to optic neuropathy or SLE retinopathy.[14]

Orbit is not commonly affected in SLE. The manifestation ranges from chemosis, proptosis to restricted extra ocular movements. Both unilateral and bilateral involvement of the orbit has been reported.[15] Due to lack in serological workup and follow up further diagnosis is hindered. Non-perfusion of the globe results due to orbital vasculitis which can lead to permanent vision loss owing to the damage to optic nerve.[16] Myositis often misdiagnosed as orbital cellulitis demands CT and ultrasound along with other markers like creatinine kinase and myoglobin.[8] The incidence of periorbital edema in SLE patients is around 4.8%.[17]

SLE manifests rarely in the eyelid as raised, scaly and atrophic discoid lesions mimicking erythema or blepharitis. These lesions most commonly occur on the sun exposed areas which starts as purple scaly macule or papule expanding into discoid plaques. [17] Scaling with hyperpigmentation is seen in the periphery with atrophic center. When these lesions affect the eyelid, it can lead to scarring, madarosis, entropion or ectropion.[18] HPE shows hyperkeratotic epithelium with liquefactive degeneration of basal cell layer with dense perivascular lymphocytic infiltration.[19] Treatment starts from sun protection as these are photosensitive followed by topical steroid creams, topical calcineurin inhibitors and topical retinoids.[20]

Keratoconjunctivitis Sicca is the most common manifestation of SLE which presents as dry eye due to decreased production of the aqueous layer of the tear film.[21] Most of the patients develop secondary Sjogrens syndrome. Patients present with burning sensation, photophobia with worsening of symptoms at the end of the day. According to Manoussakis et al., 9.2% developed Sjogrens syndrome out of 283 SLE patients.[22] HPE shows goblet cell loss, monocellular infiltration with granuloma formation in the substansia proper layer. Immunopathological studies reveal deposition of immune complex deposition in the epithelial basement membrane with increased CD4 + and CD8+ T cells with B cells and Macrophages. The patients are to be subjected to tear film evaluation, tear film break up time, Schirmer's test to evaluate the tear production. Treatment modalities include artificial tear substitutes, autologous serum drops and punctal plugs for advanced cases.[16]

The incidence of episcleritis in SLE patients is 2.4% and is usually self-limiting and does not require treatment.[24] The symptoms are usually mild like conjunctival congestion. In severe cases, topical steroids are responsive. Scleritis may be presenting feature of SLE and the incidence being 1%.[25] The patients usually present with diffuse scleritis or anterior nodular scleritis which more painful and vision threatening complication if not treated promptly.[26] Necrotising scleritis is

rare but can lead to scleral thinning. Posterior Scleritis can also occur rarely in patients with SLE.[27]

SLE can manifest as recurrent corneal erosion, ulcerative keratitis, interstitial keratitis and endothelitis which can serve as a marker of active systemic vasculitis.[28] This can be demonstrated by specular microscopy as corneal endothelial dysfunctioning. Immunological studies demonstrate Immune complex deposits in the basement membrane of the endothelial cells of the limbal blood vessels. This may release cytokines leading to corneal infiltration.[23] Treatment includes topical steroids. In severe cases, SLE may be associated with Keratoconus which is anterior thinning or coning of the central cornea.[29]

Retinopathy is one of the most common vision threatening complication in SLE patients and can occur in about 10% of the patients.[30] SLE retinopathy manifests as cotton wool spots, hard exudates, retinal hemorrhages, tortuous vessels, vasculitis and central retinal artery and/ or vein occlusion (**Figure 1**).[26] Purtscher-like retinopathy is attributed to the formation of micro emboli resulting in retinal vascular occlusion and microvascular infarcts.[31] The most common pattern is microangiopathy which mimics diabetic and hypertensive retinopathy.[7] Deposition of immune complexes along the vessel wall and micro emboli attributes to the pathogenesis of retinopathy. HPE shows deposits of immunoglobulin and complement factors with fibrinoid necrosis.[32] The findings can be confirmed by Fundus Fluorescein Angiography (FFA). FFA also serves as an early diagnostic marker when the fundus examination is normal. Treatment options include Laser Photocoagulation, Steroids, intravitreal anti-VEGF and Anticoagulants (**Figure 2**). Immunosuppressive therapy is effective in treating retinopathy.[33]

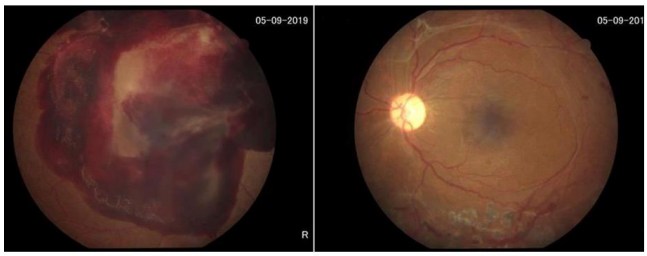

Figure 1: Right eye showing extensive vitreous hemorrhage. Left eye showing tractional bands and retinal haemorrhage

Exudative retinal detachment is a rare but serious vision threatening complication in SLE patients with active vasculitis. Baglio et al. described the subtle changes in the choroidal circulation using Indocyanine green angiography.[34] ICG shows focal and transient early hypo fluorescence phase followed by focal clusters of choroidal hyper fluorescence in the intermediate phase and late diffuse hyper fluorescence phase, choroidal vessels distortion.[35]

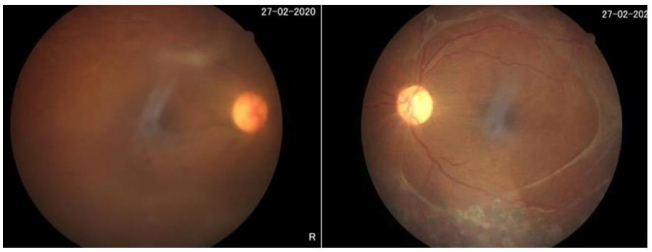

Figure 2: Right eye showing resolution of hemorrhage after intravitreal anti VEGf

Optic neuritis, papilledema and Ischemic optic neuropathy are rare manifestation of SLE which occurs in 1% of patients.[36] Optic neuritis in SLE is an ischemic process that leads to demylineation and axonal necrosis. Early Intravenous steroid therapy is the mainstay of treatment for optic neuropathy.[37] Ocular motility disorders occur in about 29% of patients. Other manifestations include internuclear ophthalmoplegia, nystagmus, post chiasmial vaculitits.[38]

7. Discussion

A myriad of manifestations has been described in SLE patients. Identifying these features at an earlier stage can be helpful in earlier treatment and better prognosis. Ocular manifestations can be the only presenting sign in few patients which should be carefully assessed by the Ophthalmologist. Patients with SLE retinopathy or choroidopathy has poor prognosis for both ocular and systemic morbidity. It can lead to permanent blindness. The most common finding in SLE was keratoconjunctivitis sicca. More severe form of ocular manifestations was retinal vasculitis and choroidopathy. The treatment of SLE is based mainly on systemic therapy while PRP is the mainstay of treatment for SLE retinopathy. More data is required to identify the heterogeneity of SLE which can reduce the toxic treatment regiments for SLE. Even in classification criteria for SLE in 2012, there is no ophthalmic involvement. Ocular symptoms can be early manifestations of SLE. Hence all the patients with SLE/ suspected to have SLE should be subjected for ophthalmic evaluation.

8. Conclusion

SLE is an immunologic condition affecting multiple organs. Ocular findings can be the early presenting feature of SLE and every Ophthalmologist must identify the findings at the earliest for early treatment to avoid complications. Every clinician must carefully evaluate SLE patients for systemic involvement and to promptly refer the patient to Ophthalmologist. Affordable diagnostic tool kit for the diagnosis of SLE should be introduced which will aid in wider knowledge about the incidence of the disease.

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None.

10. Conflict of Interest

None.

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