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Choroidopathy in systemic lupus erythematosus: Report of two cases with literature review

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Abstract

The ophthalmic manifestations of Systemic Lupus Erythematosus (SLE) are protean, however, choroidopathy is rare. We present two SLE cases with choroidal involvement as the first manifestation, and relevant literatures are reviewed. Both ophthalmists and rheumatologists should be aware of choroidopathy as a rare manifestation of active SLE. Early recognition and proper treatment are important for good prognosis.

Keywords: Choroidopathy; Systemic lupus erythematosus; Lupus; Visual acuity.

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Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune disease with multiple organ involvement [1,2]. The ophthalmic manifestations of SLE are protean. Almost all ocular structures can be involved in SLE with diverse presentations. Sometimes eye problems can be sight-threatening if not promptly and properly treated [3]. However, the choroidopathy in SLE patients is rare. We present two SLEcases with choroidal involvement as the first manifestation.

Cases presentations

Case 1: A 39-year-old woman was admitted to our hospital on Oct 30, 2018 because of edema and blurred vision for two weeks. She presented with blurred vision accompanied by edema on face, eyelids and hands, then gradually developed arthralgia. Urine protein 3+, blood +-. Blood tests showed the platelet count 72X109/L, albumin 25.8 g/L, ANA1: 10000, anti-nRNP antibody +++, negative anti-dsDNA antibodies, and dramatically decreased complement with C3 0.302 g/L (0.6-1.5), C4 0.017 g/L (0.12-0.36). Imaging examinations revealed bilateral pleural effusion, pericardial effusion, peritoneal and pelvic effusion. She gained 13 kg of her body weight with hypertension. On ophthalmological examination at admission, the uncorrected distant visual acuity was 20/1000 in both eyes, and the uncorrected near visual acuity was normal. Intraocular Pressure (IOP) was 30 mmHg in the right eye and 26 mmHg in the left eye. Slit-lamp biomicroscopy revealed bilateral shallowed anterior chambers. Fundus copy revealed elevations of peripheral retina and choroid, especially in the inferior part (Figure 1). Ultrasonography showed ciliary choroidal detachment (Figure 2a). Retinal effusion (Figure 3a), subretinal fluid and focal Pigment Epithelium Detachment (PED) was observed Onoptical Coherence Tomography (OCT).

She was diagnosed as SLE, lupus choroidopathy, lupus nephritis, thrombocytopenia. Intravenous methylprednisolone 80 mg/d was immediately initiated, in addition to eye drops (tobikamide, tobramycin and dexamethasone, cartilol hydrochloride) with intermittent albumin infusion and diuretics. Seven days later, the edema and multiple serous effusion were significantly improved with normal platelet count and urinary protein

1+, however no improvement in herblurred vision. Repeated ophthalmic examinations showed normal intraocular pressure, but the visual acuity and choroidal detachment was not significantly improved (Figure 2b), with more retinal effusion (Figure 3b). Fluoxyprednisolone 40 mg was paraocularly injected to each eye. One week later, the uncorrected distant visual acuity was elevated to 20/40, and the IOP was reduced to 14 mmHg in both eyes. Ultrasonography showed ciliary choroidal was reattached (Figure 2c), and anterior chamber wasobviously deepened. OCT showed intraretinal and subretinal fluid was relieved (Figure 3c). Except Cartilolhydrochloride, all other eye drops were maintained as before. Prednisolone 60 mg/d was followed after methylprednisolone 80 mg/d for two weeks, in combination with azathioprine 100 mg/d. Mean while, polyserous effusion as well as eyelids and face edema gradually disappeared. Her body weight returned to normal. One month after admission repeated lab tests showed normal complete blood count andurine routine, serum albumin 36.4 g/L, C3 0.398 g/L, C4 0.091g/L, and negative anti-ds-DNA. The patient was followed up regularly in our outpatient department, her lupus condition was stable, and the vision recovered completely. Glucocorticoid has been reduced to prednisolone 5 mg / d.

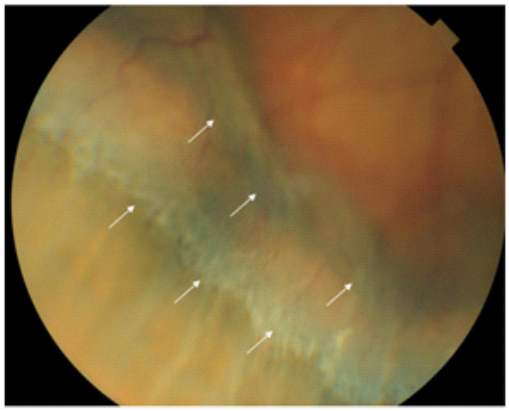

Figure 1: Funduscopy. Peripheral retinal and choroidal detachment in the inferior part (arrow).

Case 2: A 35-year old Chinese woman complained of decreased bilateral visual acuity and eyelid swelling for a month. Laboratory examinations showed roughly normalcomplete blood count, urine protein 2+, 24-hour urinary protein 1.66 g, serum albumin 23.6 g/L, ANA1: 640, anti-ds-DNA negative, anti-nRNP and anti-Sm antibodiespositive, C3 0.306 g/L (0.6-1.5), C4 0.056 g/L (0.12-0.36). Imaging revealed polyserous effusions. Renal biopsy confirmed type II lupus nephritis. She was diagnosed as SLE with lupus nephritis. Intravenousmethyl prednisolone 40 mg/d and hydroxychloroquine 200 mg twice daily were initiated. Five days later, the patient complained of aggravated blurred vision with chest distress and dyspnea. Ophthalmological examination found uncorrected visual acuity 20/600, intraocular pressure 23 mmHg for both eyes. Focal subretinal fluid was found in the macular of both eyes was found on OCT. Considering the possibility of glucocorticoid related ocular diseases, methylprednisolone and hydroxychloroquine were replaced by cyclosporine 75 mg bid in combination with mycophenolate 500 mg bid, and YAG laser peripheral iridectomy. Unfortunately, no improvement in her vision was observed, but diarrhea 6-7 times a day occurred, with normalstool examination. She was then referred to our medical center.Her blood pressure was 130/101 mmHg at first visit. Fundusfluoresce in Angiography (FFA) showed scattered pinpoint leaks at early phase (Figure 4A), and multifocal subretinal leaks and pooling of dye at late phase (Figure 4B) in both eyes. Several abnormalities on OCT were found, includingfocalretinal detachment in the macular of both eyes; choroidthickening, (Figure 4C). Lupus choroidopathy was considered. $^{99}Tc^{m}$-labeled human albumin scintigraphy provided evidences of protein loss in the ileum.

The patient was finally diagnosed as SLE, lupus choroidopathy, lupus nephritis, protein loss enteropathy and polyserous effusion, with SLE disease activity index of 18 points. Intravenous methylprednisolone 80 mg/d, combined with hydroxychloroquine 200 mg twice daily, and intravenous cyclophosphamide 0.5 g every other week was initiated, with intermittent supplement with albumin and plasma. Gradually her uncorrected visual acuity was improved to 20/60 in the right eye and 20/40 in the left eye. The glucocorticoid was tapered. Two month later,

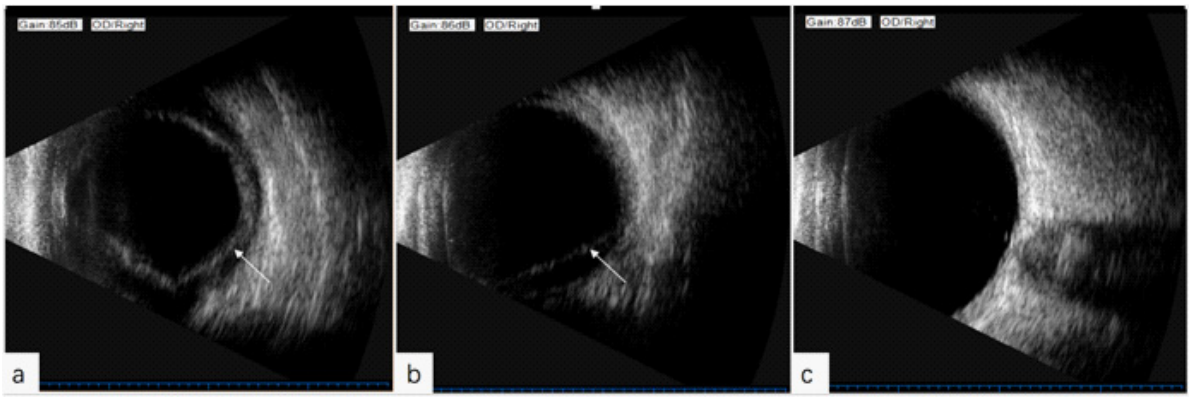

Figure 2: Choroidal detachment (arrow) on B-mode ultrasonography. At onset (a); No significant improvement after methylprednisolone 80 mg/d for 7 days (b); Completely recovered after additional par ocular injection of fluoxyprednisolone 40 mg for each eye (c).

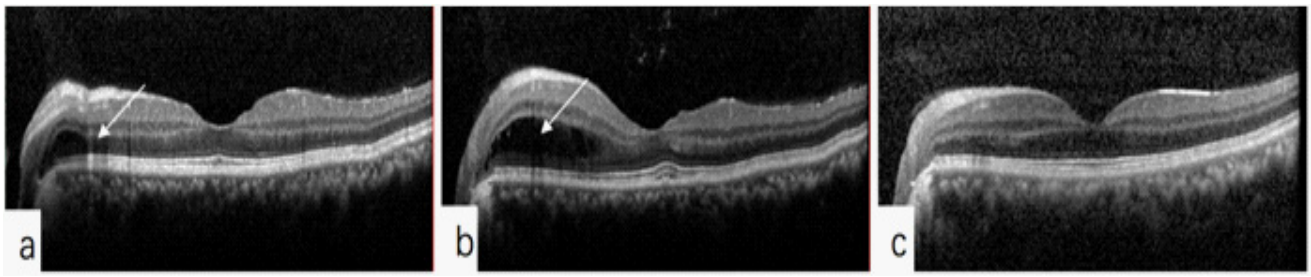

Figure 3: Intraretinal accumulating of fluid (arrow) on optical coherence tomography. At onset on Oct 30, 2018 (a); Aggravated on Nov 6, 2018 (b); Improved on Nov 13, 2018 (c).

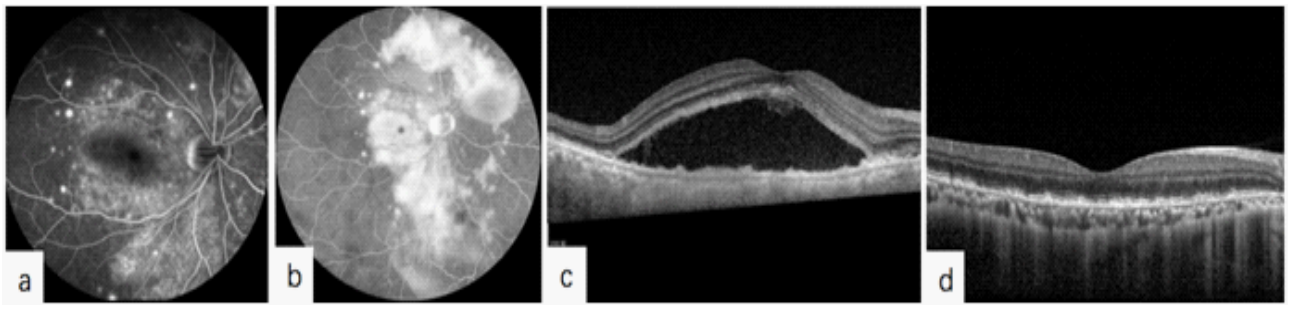

Figure 4: Fluorescein angiography showedpinpoint leaks at the early phase (a), and at the late phase (b). OCT showed focalretinal detachment in the macular, and (c); the lesions were significantly improved after treatment (d).

repeated examinations demonstrated normal urine routine, serum albumin 40 g/L, C_3 0.440 g/L, C_4 0.027 g/L, negative anti-ds-DNA, and disappearance of pleural effusion on chest X-ray. OCT showed retinal detachment was also significantly improved (Figure 4D). The combination strategy of glucocorticoid with hydroxychloroquine and cyclophosphamide was continued. The patient was followed up regularly in our outpatient department, and her lupusand vision condition were stable. Glucocorticoid has been reduced to methylprednisolone 4 mg every other day; azathioprine was use for maintenance therapy after the cumulative dose of cyclophosphamide reached 10.3 g.

Discussion

Ophthalmic manifestations occurring in approximately one-third of SLE patients, may be presented as early symptoms or appear during the evolution. Although SLE can affect any part of the visual system [3], choroidal lesions are relatively rare. 46 cases with lupus choroidopathy have been reported in English literature since 1968. The clinical features of 46 cases plus two of our new cases were summarized in Supplementary Table 1. The typical manifestations of SLE choroidopathy are multifocal exudative retinal pigment epithelium and neuroepithelial detachment. Involvement of macula may lead to decreased visual acuity. Most of the reported patients were female (89.6%) with active lupus andnephritis,and sometimes central nervous system involvement and hypertension.Both of our patients had active SLE with nephritis and hypertension at the time of choroidopathy development, and importantly, the choroidopathy was the initial manifestation of the SLE. Improvement or complete resolution of serous detachment and choroidopathy was reported in 37 patients (80.4%)by systemic application of glucocorticoid and immunosuppressants, even methylprednisolone-pulse therapy in some cases. Therefore, prompt control of lupus disease activity with systemic immunosuppressant therapy is the key step. In case of insufficient resolution of choroidopathy, glucocorticoid paraocular injection, focal laser and/or photodynamic therapy, Pars Plana Vitrectomy may be considered in the early course of disease [4,5].

Although the pathogenesis of choroidopathy remains unclear, several possibilities have been proposed. First, deposition of immune complex at the choroid and choriocapillaris, as well as the presence of autoantibodies against RPE [6] may lead to hypoperfusion and secondary breakdown of the blood–retinal barrier. Second, thrombosis may contribute to choroidopathy by causing microangiopathy [6]. Third, uncontrolled hypertension associated with SLE nephrotic injury may constrict choroidal blood flow, with resultant ischemia and breakdown of the outer blood–retinal barrier at the RPE [7]. Besides, hypoalbuminemia is also a possible risk factor. A combination of above aggravates hypoperfusion of choriocapillaris, resulting in RPE damage and leakage of liquid into the subretinal space.

Central Serous Chorioretinopathy (CSC) is also characterized by choroid thickening, accumulation of subretinal fluid. But the detrimental effects of steroid on CSC, makes the differential diagnosis between CSC and SLE choroidopathy extremely important. Imaging modalities including fund us fluoresce in angiography, and OCT were helpful for the differential diagnosis [8]. Other differential diagnosis includes Vogt–Koyanagi–Harada syndrome and hypertensive choroidopathy.

Conclusion

We here report two cases with choroidopathy as the initial presentation and prominent manifestation of SLE. Both ophthalmists and rheumatologists should be aware of choroidopathy as a rare manifestation of active SLE. Early recognition and proper treatments are important for good prognosis.

Table 1: Choroidopathy in systemic lupus erythematosus.

Source	Patient no./ age/ sex/eye	Ocular disease	Systemic disease	Treatment	Outcome of choroidopathy
Gass [9], 1968	1/14/F/OU	Bilateral macular serous detachments; early patchy fluoresece in leakage	Hypertension		Resolution
Coppeto J *et al* [10], 1977	2/32/F/OD	Retinal vasculitis; intraretinal hemorrage; disc edema; focal detachment of RPE	Pancytopenia; nephritis; CNS lupus		No resolution
Diddie *et al* [11], 1977	3/19/F/OU	Discrete serous retinal detachments; multiple grayish yellow spots in outer retina	Nephritis; hypertension		Resolution
Kinyoun JL *et al* [12], 1986	4/28/F/OD	Macular serous detachment	Nephritis; hypertension		Resolution
	5/25/F/OS	Macular serous detachment; diffusely yellow-white RPE; widespread non-perfusion of choriocapillaris; late fluorescein leakage into subretinal space	DIC; TTP; CNS lupus		Resolution of detachment, but eventual death from cerebral hemorrhage
Klinkhoff *et al* [13], 1986	6/38/F/OD	Serous retinal detachment	Vasculitis		Resolution
Matsuo *et al* [14], 1987	7/50/F/OU	Serous retinal detachments; multifocal pigment epithelial damages with secondary fluorescein leakage in subretinal space	Leukopenia; anemia; polyarthritis		Resolution
	8/18/F/OU	Serous retinal detachment; multifocal pigment epithelial damages with secondary fluorescein leakage in subretinal space	Raynaud's phenomenon; DIC		No resolution, eventual death from DIC
Jabs *et al* [15], 1988	9/48/F/OD	Multiple focal serous detachments of the sensory pigment epithelial damages with secondary fluorescein leakage in subretinal space	Nephritis; hypertension Raynaud's phenomenon		Progression of exudative RD; died of cardio pulmonary failure
	10/46/M/OU	Multiple focal serous RPE detachment, with overlying detachment of the sensory retina	Vasculitis		Resolution
	11/26/F/OS	Focal serous detachments of the sensory retina	Vasculitis; Raynaud's phenomenon		Resolution
	12/26/F/OU	Focal serous detachments of the sensory retina	Vasculitis; Raynaud's phenomenon		Resolution
	13/31/F/OU	Pigment epithelial scarring	Nephritis; hypertension		Resolution
	14/29/F/OU	Cotton-wool spots; multiple focal serous elevations; exudative retinal detachment; delayed choroidal perfusion with late fluorescein leakage	Nephritis; hypertension; CNS lupus		Resolution
Snyers B *et al* [16], 1990	15/37/F/OU	Multifocal derangement in the retinal pigment epithelium, resulting from severe bilateral occlusive choroidopathy which produced localized retinal detachments that spontaneously reattached	Nephropathy; pericarditis; hypertension		Resolution
Eckstein M *et al* [17], 1993	16/44/F/OS	Central serous retinal detachment; fluorescein angiography showed delayed choroidal filling	CNS lupus; nephropathy; hypertension		Resolution
	17/44/F/OD	Central serous retinal detachment, pigment epithelial lesion	CNS lupus		Resolution
Nasser *et al* [18], 1993	18/32/F/OU	Choroidal infarction and macular edema confirmed by fluorescein angiography	CNS lupus; nephrotic syndrome; Raynaud's phenomenon; hypertension		Progression to blindness and death from cerebral hemorrage
Carpenter *et al* [19], 1994	19/68/F/OU	Mutifocal, serous elevations of retinal pigment epithelium; fluorescein angiography showed focal RPE detachments	Pericarditis; nephritis; CNS lupus		Resolution
Benitez del Castillo *et al* [7], 1994	20/47/F/OU	Multiple focal serous elevations of the sensory retina and serous detachments of the retinal pigment epithelium, confirmed by FFA	Discoid lupus; anemia; hypertension; nephrotic syndrome		Partial resolution
Hannouche *et al* [20], 1995	21/30/F/OU	Central serous retinal detachment; delayed fluorescein angiography showed choroidal filling	CNS lupus; arthropathy choroidopathy		Resolution

El-Asrar *et al* [21], 1995	22/23/F/OU	Multiple yellow lesions at level of retinal pigment epithelium with multifocal serous elevations of neurosensory retina; FFA disclosed delayed choroidal filling	Nephrotic syndrome; arthritis; CNS lupus		Resolution
Cunningham *et al* [22], 1996	23/45/F/OU	Neurosensory detachments, RPE clumping; FFA showed hyperfluorescence corresponding to RPE alterations and leaks; CSC	Nephritis; hypertension		Resolution
	24/43/F/OU	Neurosensory and RPE detachments, subretinal fibrin; FFA showed areas of hyperfluorescence corresponding to RPE leaks; CSC	Nephritis; hypertension; coronary artery disease		Progression to subretinal fibrosis and scar
	25/53/F/OU	RPE detachments, RPE atrophy; areas of hyperfluorescence corresponding to RPE leaks; CSC	Hypertension		Resolution
Nguyen, *et al* [6], 2000	26/30/M/OU	Hemorrhage in retinal and subretinal layers; fluorescein showed subretinal and choroidal leakage	Hypertension; nephritis; CNS lupus	Systemic prednisone +CYC	Resolution
	27/40/F/OU	Multiple areas of serous elevations of sensory retina; FFA revealed choroidal non-perfusion or late choroidal filling	Nephritis	prednisone 70 mg/day+ AZA 75 mg/day	Resolution
	28/16/F/OD	Detachment of the RPE; retinal fold and elevation	Anemia, nephritis; pancytopenia	Intravenous methylprednisolone 60 mg twice daily prednisone 60 mg/day+CYC (1 g/m^2)	Resolution
Khng,C.G. *et al* [23], 2000	29/24/F/OD	Central serous retinal detachment FFA showed a progressive leak into the subretinal space of inkblot configuration	Hypertension, nephritis,	Prednisolone 45 mg/ day+ AZA	Resolution
	30/54/F/OU	central serous detachment	pleural effusion, nephritis	Prednisolone 50 mg/ day+ AZA	Resolution
	31/46/F/OU	serous detachment FFA showed a small window defect	nephritis (end-stage renal failure and haemodialysis)	NA	No resoultion
	32/37/F/OU	central serous detachment	lupus ephritis haemolytic anaemia; hypertension	NA	Resolution
Gharbiya *et al* [24], 2002.	33/32/F/OU	multiple spots of pigment epithelial atrophy, FFA disclosed focal areas of hyperfluorescence. ICGA showed fuzziness of large choroidal vessels, from the early-to-intermediate phases, with late diffuse zonal choroidal hyperfluorescence; large, poorly-defined areas of choroidal hypofluorescence from the intermediate-to-late phases, scattered in the midperiphery; focal clusters of pinpoint spots of indocyanine green choroidal hyperfluorescence from the intermediate-to-late phases	Discoid lupus, nephritis, thrombophlebitis	NA	NA
	34/39/F/OU	RPE detachment, FFA disclosed multiple pinpoint hypofluorescent and hyperfluorescent spots, ICGA showed focal, transient hypofluorescent areas in the very early phase; fuzziness of large choroidal vessels with late diffuse zonal choroidal hyperfluorescence; poorly-defined areas of choroidal hypofluorescence visible up to the late phase; and focal cluster of pinpoint spots of choroidal hyperfluorescence visible from the intermediate to late phase	arthritis, serositis, and lupus nephritis	NA	NA
Hirabayashi Y, *et al* [25], 2003	35/43/F/OS	serous retinal detachment, FFA showed fluorescein leakage. ICGA showed an area of choroidal vascular hyperfluorescence	Mononeuritis multiplex, protein-losing gastroenteropathy	Prednisolone 40 mg/day CYC50 mg/day	Resolution
Kouprianoff S. *et al* [26], 2010	36/16/F/OU	multiple serous retinal detachments; ICGA showed irregular filling with hyperfluorescent areas, hypofluorescent focal, and poorly defined areas of choroidal hypofluorescence in the very early phase, and focal cluster pinpoints of choroidal hyperfluorescence, OCT showed a hyporeflective space between the neurosensory retina and the RPE at the late phase	Fever, lymphopenia, and pericarditis	systemic corticosteroid (500 mg/day for 3 days intravenously, then 1 mg/ kg orally for 4 weeks followed by a progressive decrease) and azathioprine 135 mg/day.	Resolution

Edouard S. *et al* [27], 2011	37/35/F/OU	serous retinal detachment. FFA found multiple leakage point	articular and cutaneous signs, Raynaud phenomenon, pleuropericarditis	Steroids were given at 250 mg per day for 3 days followed by 1 mg/kg/day	Resolution
Ozturk B. *et al* [28], 2011	38/36/F/OU	disc edema, edematous and pale retina with widespread cotton wool spots, intraretinal hemorrhages and serous retinal detachment, FFA demonstrated focal hypofluorescence of choriocapillaris in the early phase, leakage in the subretinal space in middle and late phases and disc staining, fast macular scan protocol of the OCT-3 and revealed intraretinal and subretinal fluid accumulation creating cystic cavities	lupus nephritis	intravenous methylprednisolone 1000 mg/day for 3 days followed by oral prednisolone, oral acetylsalicylic acid (300 mg/day), cyclosporine (300 mg/day).	Vision improvement but died due to cardiac arrest
NicholsonL. *et al* [5], 2013	39/39/M/OU	FFA demonstrated multiple leakage points; OCT showed a considerable amount of highly reflective material under the macula consistent with fibrin	NA	prednisone 60 mg/day, mycophenolate 750 mg twice daily, and leflunomide 40 mg/day, focal laser Photocoagulation-pars Plana Vitrectomy (PPV)	visual acuity improvement
Nishiguchi K.M. *et al* [29] 2013	40/33/F/OU	Bilateral retinal vasculitis, bilateral central retinal artery occlusion and vein occlusion severe choroidopathy	discoid rashes, oral ulcers, Antiphospholipid Syndrome (APS) and nephritis, CNS vasculitis	Intravenous heparin and methylprednisolone	The patient never regained light perception.
Cho H.Y. *et al* [4], 2014	41/44/M/OU	multifocal serous retinal detachments	lupus nephritis	prednisone 40 mg/day and mycophenolate mofetil 750 mg twice daily, then switched to infliximab; focal laser treatment	visual acuity improved
	42/55/M/OU	multiple leakage points, diffuse subretinal fluid and cystic edema in both eyes	nephritis and arthritis	CYC, rituximab and a tapering course of oral prednisone. Focal laser photocoagulation and photodynamic therapy	Vision remained poor
	43/43/F/OU	one point of leakage and associated subretinal fluid superotemporal to the fovea OD.	carditis, nephritis, enteritis and pancreatitis	mycophenolate mofetil 500 mg twice daily and a tapering course of methylprednisolone which was at 32 mg daily at first; focal laser treatment	Resolution
Han Y.S. *et al* [30], 2015.	44/31/F/OU	serous retinal detachment choroidal thickening with effusion secondary angle closure glaucoma, multiple leakage points were found in FAG findings	malar rash, serositis, renal disorder, neurologic disorders	Intravenous methylprednisolone 250 mg per day, then 60 mg prednisolone	Resolution
Hafidi Z, *et al* [31], 2015	45/32/F/OU	FFA showed early hyperfluorescence of the described lesions with minim late dye leakage, Funduscopy showing disseminated small yellowish lesions	rash and arthritis, impaired renal function	oral corticosteroids (1 mg/kg)	improvement of visual acuity
Lee KR, *et al* [32], 2018	46/34/F/OD	Few intraretinal hemorrhages with multiple spots of retinal pigment epithelial atrophy at the superior arcade, the early- to mid-phase ICGA revealed patchy ill-defined areas of choroidal hypofluorescence within the macula region that represents delayed choroidal perfusion. The mid- to late-phase ICGA showed extensive fuzzy large choroidal vessels with diffuse choroidal hyperfluorescence and leakage, indicating choroidal vasculitis	NA	intravenous methylprednisolone 1g daily, concurrent with intravenous immunoglobulin 400 mg/kg body weight daily, for 5 days. followed by a tapering dose of oral prednisolone at 1 mg/kg body weight daily over 8 weeks	despite the anatomical improvement, the functional outcome was status quo and the right eye vision remained at counting fingers.
Present study	47/39/F/OU	Elevated IOP, ciliary body detachment choroidal detachment, intraretinal and subretinal fluid, focal retinal pigment epitheliumdetachment	Hypertension lupus nephritis, thrombocytopeni-apolyserositis	methylprednisolone 80 mg per day fluoxyprednisolone 40 mg paraocularl injection and AZA 100 mg/d	resolution
Present study	48/35/F/OU	FFA showed pinpoint leaks at the early phase, and multifocal subretinal leaks and pooling of dye at the late phase. OCT showed bilateral subretinal fluid in the macula	lupus nephritis, protein loss enteropathy and polyserous effusion	Intravenous methylprednisolone 80 mg/d, combined with intravenous CYC 0.5 g every other week; YAG laser peripheral iridectomy	improved

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