Systemic Lupus Erythematosus

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Introduction

Systemic lupus erythematosus (SLE), a systemic, connective tissue disease that can affect multiple organ systems, affects women, especially Asian and African women more commonly (Silpa-archa et al. 2016). Up to one-third of SLE patients experience some kind of ocular manifestation (Palejwala et al. 2012), keratoconjunctivitis sicca being the most common form, and retinal and choroidal involvement being most associated with visual impairment (Sivaraj et al. 2007; Palejwala et al. 2012). Although, the prevalence of SLE as a cause of uveitis was estimated to be 0.47% in a recent review of the literature (Gallagher et al. 2015), ocular involvement in SLE is important as it may correlate with systemic disease activity and precede other systemic symptoms.

Pathogenesis

The pathogenesis of SLE is multifactorial. Inflammation is thought to be caused by the formation of autoantibodies and immune complexes, and following the activation of the complement system, causing multi-organ damage manifesting as nephritis, vasculitis, and arthritis.

Clinical Features

Anterior Segment Involvement

Anterior segment involvement reported in SLE include episcleritis, scleritis, and iridocyclitis. Heron et al. reported a 2% prevalence of SLE-associated scleritis (Heron et al. 2014). There are a few reports of iritis or iridocyclitis; hypopyon or fibrinous anterior uveitis has been reported (Stavrou et al. 2002; Zink et al. 2005), and one adult presenting with bilateral keratitis and iridocyclitis which responded well to chloroquine has also been reported (Halmay and Ludwig 1964).

Posterior Segment Involvement

Lupus Retinopathy

Posterior segment involvement includes lupus retinopathy (microangiopathy, vasculitis, vascular occlusion) and choroidopathy. The prevalence of retinopathy varies, considerably lower in patients with well-controlled disease (3–29%) (Davies and Rao 2008). Retinal or choroidal involvement is thought to correlate with systemic disease activity, especially cerebral disease (Jabs et al. 1986; Stafford-Brady et al. 1988). Microangiopathy is thought to be an immune complex-mediated vasculopathy (Levine and Ward 1970; Aronson et al. 1979) and includes cotton wool spots, microaneurysms, hard exudates, and dot hemorrhages, with usually a good visual prognosis (Fig. 13.1). Vasculitis, which is thought to be a result of immune complex deposition, complements activation with microvascular thrombosis and fibrinoid degeneration of the vascular wall, presents with vascular sheathing in arterioles and/or venules, and may result in vascular occlusion (Talat et al. 2014; Yen et al. 2013) (Fig. 13.2). In most cases, vasculitis is associated with antiphospholipid antibodies (Palejwala et al. 2012). Vascular occlusion is the more severe form, manifesting with widespread retinal capillary nonperfusion, multiple branch retinal artery occlusions, ocular neovascularization resulting in vitreous hemorrhage, tractional retinal detachment, neovascular glaucoma, and visual loss (Read et al. 2000; Au and O'Day 2004; Kim et al. 2013) (Fig. 13.3).

Lupus Choroidopathy

Lupus choroidopathy can occur either independently or with lupus retinopathy, including single or multiple areas of

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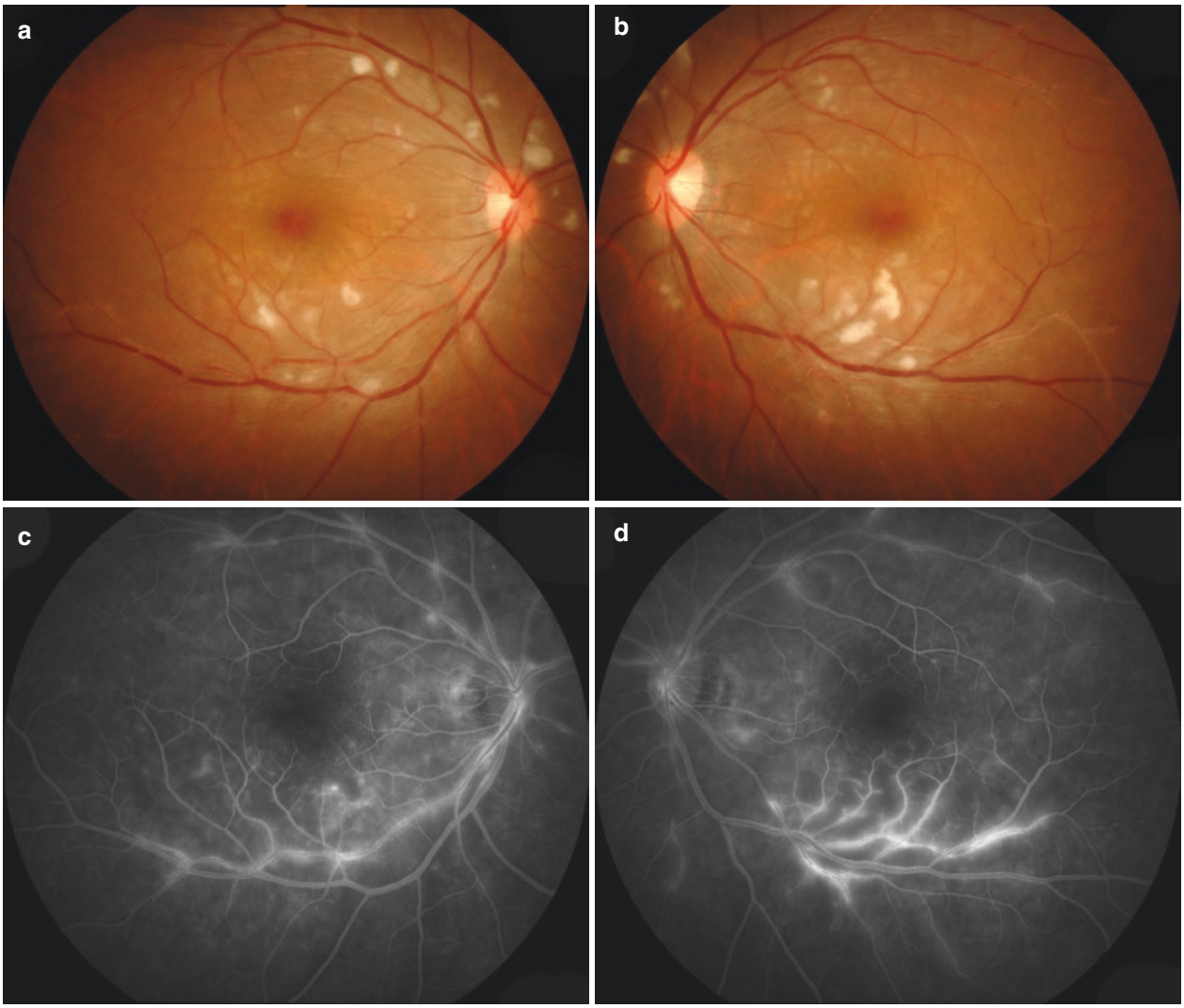

Fig. 13.1 32-year-old female with systemic lupus erythematosus. Bilateral multiple cotton wool spots and retinal hemorrhage with vascular sheathing is noted (**a**, **b**), with vessel wall staining on fluorescein angiography (**c**, **d**)

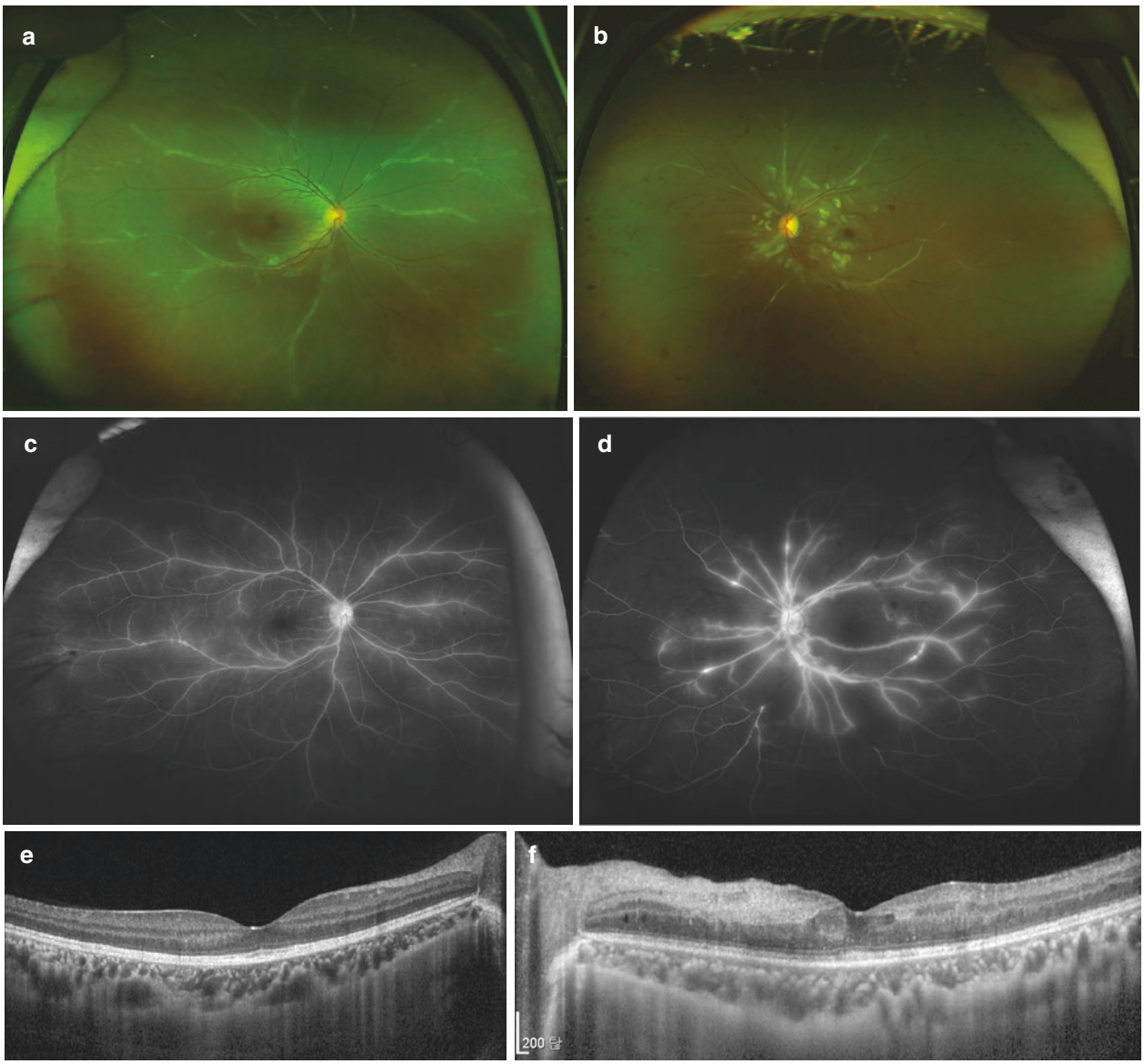

Fig. 13.2 19-year-old female with systemic lupus erythematosus with severe vasculitis and vaso-occlusive retinopathy. (**a**, **b**) Fundus findings revealed multiple cotton wool patches, retinal hemorrhage and diffuse retinal vascular sheathing. (**c**, **d**) Fluorescein angiography showed diffuse vessel wall staining in both eyes and severe capillary non perfusion in left eye. (**e**, **f**) Spectral-domain optical coherence tomographic findings showed severe inner retinal ischemic change in left eye

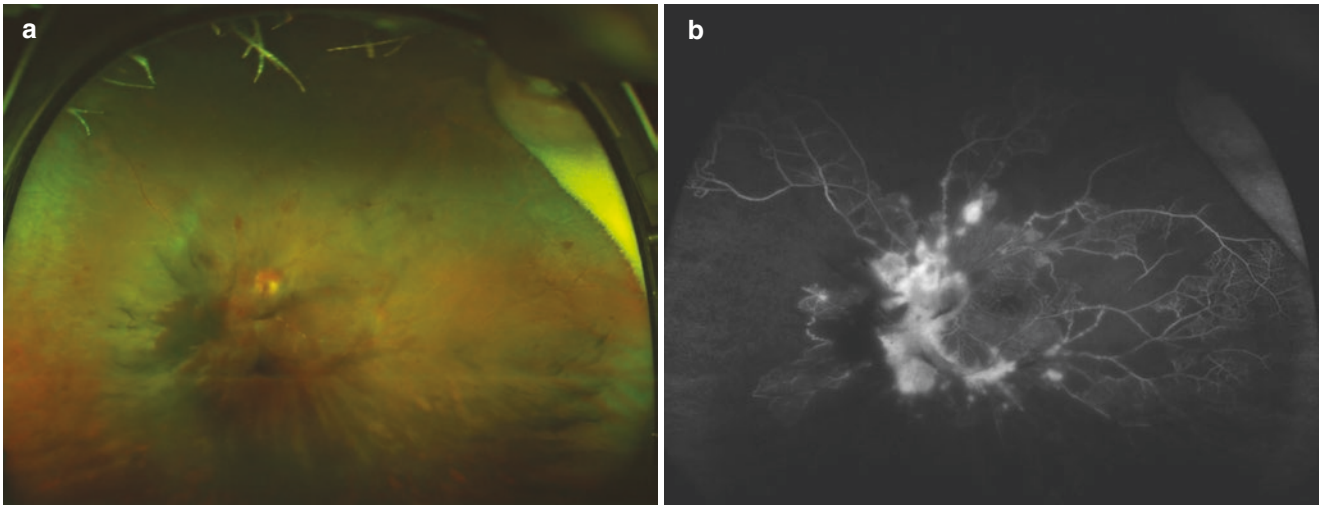

Fig. 13.3 The patient in Fig. 13.2 developed neovascularization (shown in fundus photograph (**a**), and fluorescein angiography (**b**)), causing vitreous hemorrhage in her left eye 6 months after presentation, requiring vitrectomy

serous or exudative retinal detachment, retinal pigment epithelium detachment or retinal pigment epitheliopathy (Nguyen et al. 2000). Subretinal hypopigmented patches on angiography which are areas of choroidal ischemia may also be present (Silpa-archa et al. 2016). Secondary angle closure glaucoma has also been reported from choroidal effusion leading to anterior shifting of the lens-iris diaphragm (Ahn and Choi 2016). Lupus choroidopathy resolves with appropriate immunosuppressive treatment and vision usually recovers (Nguyen et al. 2000).

Management

Systemic Management

Systemic treatment often requires a collaborative team approach. Nonsteroidal anti-inflammatory drugs, antimalarials (hydroxychloroquine), systemic corticosteroids, immunosuppressive therapy, and biologics may be effective. Systemic corticosteroids are used in the acute stage, and nonsteroidal anti-inflammatory drugs and hydroxychloroquine are used in mild patients. A variety of immunosuppressive agents have demonstrated efficacy in ocular SLE including methotrexate, mycophenolate mofetil, azathioprine, and cyclophosphamide (Palejwala et al. 2012; Silpa-archa et al. 2016). Biologics targeting cytokines, B and T lymphocytes, and B-cell-activating factors are also considered in patients refractory to other treatment. Belimumab is the first biologic agent approved by the Federal Drug Administration in 2011 for SLE, which inactivates B-cell-activating factor (Dooley et al. 2013; Navarra et al. 2011; Touma et al. 2013). Others include rituximab, epratuzumab, sifalimumab, and ocrelizumab.

Local Therapy

Local treatment according to the specific pathology along with systemic treatment may play a role in the treatment. For vascular occlusion and ischemia, laser photocoagulation can be used (Fig. 13.4). Vitrectomy may be performed for complicated neovascularization such as vitreous hemorrhage and tractional retinal detachment. Intravitreal anti-VEGF injection has also been reported as an effective therapy for vaso-occlusion and vasculitis in SLE (Kurup et al. 2009; Lee et al. 2013).

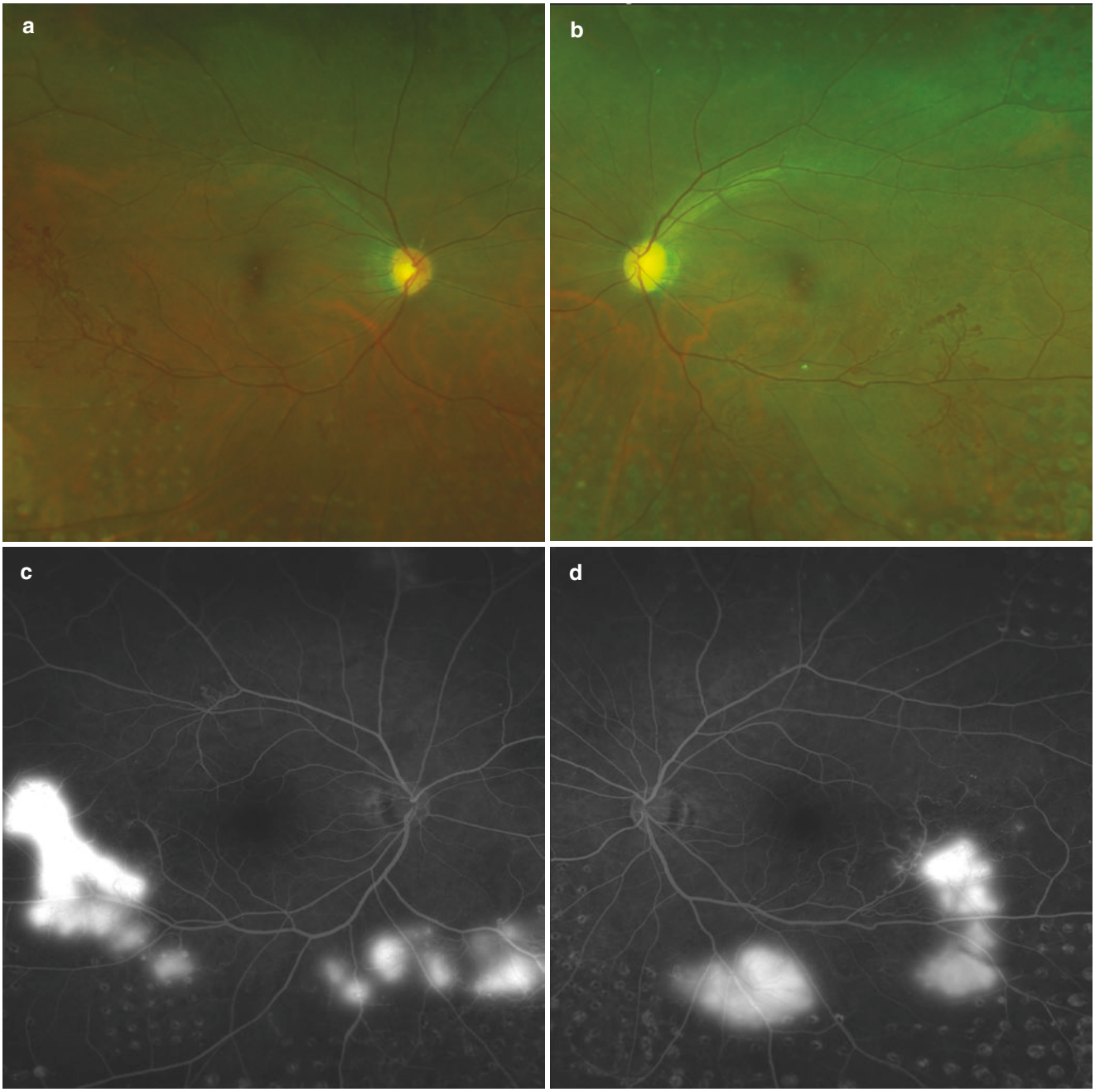

Fig. 13.4 The patient in Fig. 13.1 developed neovascularization in both eyes 4 years after presentation despite systemic therapy. She received laser photocoagulation in both eyes (shown in fundus photograph (**a**, **b**), and fluorescein angiography (**c**, **d**))

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