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LETTER TO THE EDITOR

Spectral Domain Optical Coherence Tomography Findings of Subacute Sclerosing Panencephalitis Presenting with Macular Necrotizing Retinitis: A Case Report

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ABSTRACT

Purpose: To report the fundus photographs and spectral domain optical coherence tomography (SD-OCT) findings of a patient with subacute sclerosing panencephalitis (SSPE) presenting merely with ocular symptoms.

Case report: A 20-year-old patient presented with sudden loss of vision in the left eye (LE). Fundus photograph showed a yellow lesion in the macula and SD-OCT showed increased reflectivity of the inner retinal layers. Disorganization of the necrotizing retinal layers in the LE gradually progressed to the atrophic retina. Then, visual complaints began in the right eye (RE) accompanied by neurological symptoms. SD-OCT revealed the inner and outer plexiform layers edema and interruption of the ellipsoid zone in RE. Fundus photographs showed macular atrophy for both eyes on the day patient died.

Conclusion: This case report demonstrates the SD-OCT findings of SSPE retinitis with close follow-up from the acute retinitis to the total atrophic macula. These unique findings may be considered as characteristical for the diagnosis.

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Macular necrotizing retinitis; measles virus; moth-eaten appearance of retina; optical coherence tomography; subacute sclerosing panencephalitis

Subacute sclerosing panencephalitis (SSPE) is a neurodegenerative disease characterized by persistent and progressive infection of the measles virus in the central nervous system (CNS) which is frequently seen in children and young adults.[1] The latent period between the onset of SSPE and measles infection is often 7–10 years, but this period can vary from 1 month to 27 years.[2]

The ocular disease occurs in almost 50% of patients and results in severe vision loss.[3] The most characteristic ophthalmologic lesion is macular necrotizing retinitis that spreads centrifugally to involve the posterior pole.[4] Ocular findings may occur during the course of the disease or may precede neurological symptoms by weeks or months.[5]

We reported a case of SSPE, who presented with ocular symptoms, to demonstrate the fulminant progression of macular retinitis with sequential fundus photographs and spectral domain optical coherence tomography (SD-OCT) imaging from presentation to pass away and to emphasize the critical role of ophthalmologists in the early diagnosis of SSPE.

Case report

A 20-year-old male patient applied to our clinic with the complaint of the sudden loss of vision in the left eye (LE) that had begun 2 days ago. Systemic history was unremarkable except for bilateral neurosensorial hearing loss caused by a febrile illness in his childhood. His best-corrected visual acuity (BCVA) was 20/20 in the right eye (RE) and 20/32 in the LE. Anterior segment examination of the LE was normal. Fundus examination of the LE revealed an intraretinal yellow lesion in the macula extending like an arcuate pattern from the fovea to the optic disc (OD) and a hypopigmented lesion in the superonasal peripapillary area (Figure 1a; upper). There was no inflammation in the vitreous. SD-OCT imaging of the LE showed deterioration of the inner retinal layers, increased reflectivity, and hyporeflective cystoid cavities (Figure 1a; bottom). Although the findings of the fundus fluorescein angiography (FA) were normal in the early stage (Figure 1b; upper), a leakage was observed at the lesion area in the late stage (Figure 1b; bottom). Detailed ophthalmologic examination, color fundus photograph (Figure 1c; upper), and SD-OCT imaging of the RE were normal (Figure 1c; bottom). Complete blood count (CBC) and biochemical tests in addition to serological tests such as *Toxoplasma gondii*, human immunodeficiency virus, cytomegalovirus, herpes simplex virus type 1 and 2, varicella-zoster virus, syphilis, *Borrelia burgdorferi*, and brucella serum agglutination test were investigated. The patient was consulted with rheumatology and pulmonary medicine for the differential diagnosis of retinitis. Three days after the onset of the symptoms, the yellow lesion in the macula expanded, and schitic cavities were formed (Figure 2a; upper). The macular SD-OCT showed a deterioration of all retinal layers, and enlarged necrotizing cavities (Figure 2a; bottom). CBC and biochemical tests were normal, and serologies for all species were negative. Pulmonary medicine and rheumatology department consultations reported no pathology related to tuberculosis, sarcoidosis, or Behçet's disease. After serologic workup completed with normal results, oral methylprednisolone (1 mg/kg/day) was given due to the progressive decrease of BCVA. The lesion regressed, but the retinal deterioration on SD-OCT progressed and BCVA decreased to 20/200. Therefore, the patient was hospitalized, and pulse methylprednisolone therapy for 3 days

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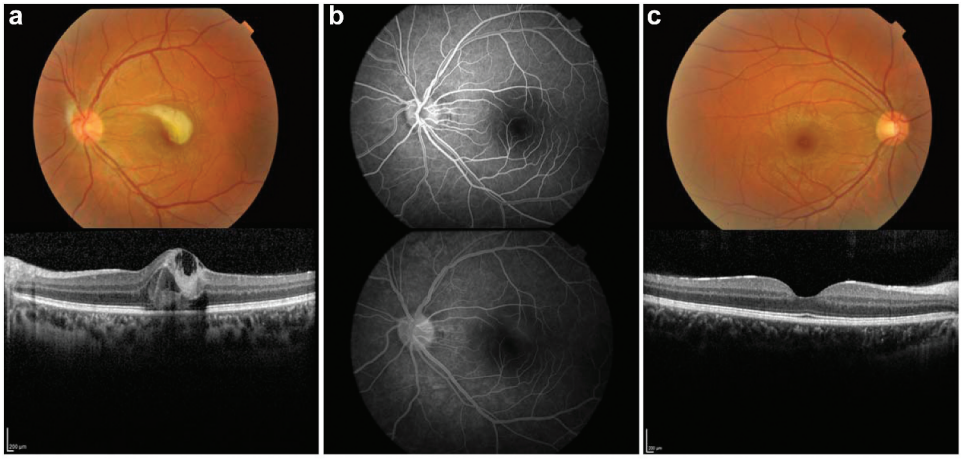

Figure 1. At presentation. Color fundus photograph of the left eye (LE) showed a yellow lesion extending from fovea to optic disc, and a hypopigmented lesion in the superonasal peripapillary area (a, upper) and spectral domain optical coherence tomography (SD-OCT) of the LE showed increased reflectivity of the inner retinal layers and hyporeflective cystic spaces (a, bottom). Fundus fluorescein angiography of the LE showed normal appearance at the early stage (b, upper) and mild hyperfluorescence leakage at the late stage (b, bottom). Color fundus photograph (c, upper) and SD-OCT of the right eye were normal (c, bottom).

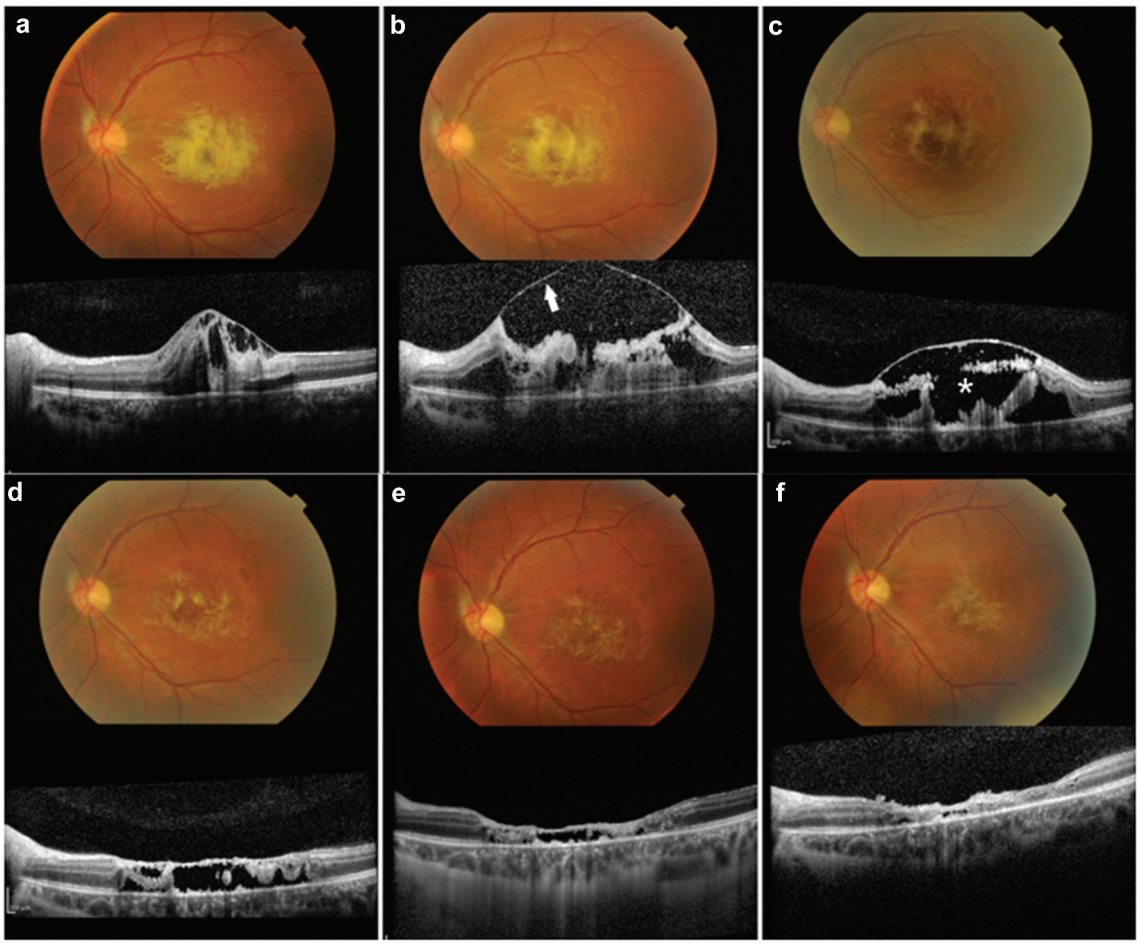

Figure 2. Sequential color fundus photograph, and spectral domain optical coherence tomography (SD-OCT) of the left eye (LE). Three days after the onset of the symptoms, the whole retinal structure had deteriorated (a, upper and bottom). One week after the onset of the symptoms, the lesion had enlarged, and ILM detachment (arrow) was observed (b, upper and bottom). Ten days after the presentation, there was a severe loss of retinal structure and moth-eaten appearance of the retina (asterisk) (c, upper and bottom). Color fundus photographs showed patchy retinal scarring (d, e, and f, upper), and SD-OCT showed macular necrotizing atrophy and hyperreflective dots in the retina and choroid at two weeks (d, bottom), three weeks (e, bottom), and one month (f, bottom) after the onset of the symptoms.

(1gr/day) was started. One week after presentation, fundus examination revealed the patchy atrophic macula and temporal optic disc pallor (Figure 2b,c; upper), and SD-OCT showed the internal limiting membrane (ILM) detachment, severe loss of retinal layers, and moth-eaten appearance of the macula (Figure 2b,c; bottom). SSPE was considered as a preliminary diagnosis because fundus examination revealed healing necrotizing retinitis patches despite methylprednisolone therapy and

SD-OCT showed the moth-eaten appearance of the macula. The vaccination certificate of the patient was requested from the parents. The patient was not vaccinated against measles. Serum measles antibodies were investigated and the serum level of measles ELISA (enzyme-linked immunosorbent assay)-IgG antibody was positive (179.57 IU/ml, range: 0.0–7.9), in contrast to IgM antibody levels. We planned to perform an anterior chamber tap or vitreous tap, and the patient and his relatives were informed. However, we decided to refer the patient to the infectious diseases and the neurology departments for lumbar puncture (LP) and electroencephalography (EEG) after retinal and SD-OCT findings became significantly consistent with SSPE-associated retinitis. The patient's neurological examination was normal, and no pathology was found on EEG and cranial magnetic resonance imaging (MRI). Although LP was tried three times, it could not be successfully performed in the clinic due to the patient's scoliosis. LP was recommended to be performed in the operating room, however, LP could not be done because the patient refused it. During this period, retinal thickness gradually decreased (Figure 2d–f; bottom). Three weeks after the onset of the lesion in LE, his visual complaints started in RE. On the same day, SD-OCT imaging of the RE showed increased thickness and reflectivity in the papillomacular region, especially in the inner and outer plexiform layers, and interruption in the ellipsoid zone under the fovea (Figure 3a,b; bottom). The lesion in the RE progressed rapidly, and the whole retinal architecture was deteriorated within 3 days (Figure 3c,d). Finally, the BCVA of the RE decreased to 20/200. Along with the RE symptoms, the patient developed delirium symptoms such as insomnia, disorientation, uncooperative behavior, and agitation. Repeated EEG revealed diffuse slow waves, intermittent epileptiform discharge, and disorganization consistent with generalized encephalopathy. He was transferred to the neurology clinic after a cranial MRI revealed diffuse dura mater thickening and thrombus extending from the right transverse sinus to the sigmoid-jugular vein. LP was performed in the operating room with the consent of the patient's relatives. Measles IgG antibodies was 29068.80 IU/ml (Negative: <25.0) in cerebrospinal fluid (CSF) sample and CSF-serum measles IgG index was 18.61 (Negative: <1.3, Equivocal: 1.3–1.5, Specific antibody production in CSF: >1.5), indicating intrathecal antibody synthesis. The patient was diagnosed with SSPE. The patient's clinical condition deteriorated rapidly, and he was transferred to the intensive care unit (ICU). His Glasgow Coma Scale (GCS) score dropped to 6. He was treated with inosine pranobex (100 mg/kg/day), levetiracetam (1000 mg/day), and sedative drugs in ICU; however, he died 50 days after the onset of visual complaints in LE. Fundus photograph taken in ICU showed patchy macular scarring and temporal optic disc pallor for both eyes on the day patient died (Figure 4a,b).

Discussion

We report a case of SSPE presenting with ocular findings from early stage to death of the patient with fundus photographs and SD-OCT imaging. The patient was followed up daily from the first presentation until transfer to the ICU. Therefore, in this case report, the SSPE-associated retinitis was recorded from the initiation to the total atrophic macula stage with fundus photographs and SD-OCT imaging.

The association between retinal and neurological involvement in SSPE is not yet fully understood. Because the measles virus acquires virulent neurotropism in the retina before invading the central nervous system, retinal findings may occur before neurological symptoms.[5] In vitro studies have indicated that the virus spreads between neurons by axonal connections; nevertheless, it has been postulated that the measles virus attaches to another cell receptor, which is concentrated at synapses, to enter neurons.[6] Synaptic connections in the retina are concentrated in the inner plexiform and outer plexiform layers.[7] In the presenting case, primary involvement of the plexiform layers on SD-OCT may indicate that measles viruses are concentrated at synapses in the retina. During the spread of the virus, necrotizing macular retinitis also progressed, in this way SD-OCT scans showed that inner retinal layers had increased reflectivity, hyporeflective cystoid cavities, and necrosis of retinal nerve fiber layer, ganglion cell layer, inner nuclear layer, and accompanying with ILM detachment in both eyes. The lesion progressed over the time; then, outer retinal layers necrosis, hyperreflective dots in the retina and choroid, the moth-eaten appearance, and consequently necrotizing atrophic retina were observed on SD-OCT in both eyes. Besides, although the fundus examination was normal in RE, SD-OCT frames revealed internal, and external plexiform layers edema, increased reflectivity of the inner retinal layers, and interruption of the ellipsoid zone at the earliest stage.

In this rare and fatal disease, it is very hard to diagnose with solely retinal findings in the absence of neurological involvement. Oray et al.[8] reported a case of SSPE presenting with retinitis that could be diagnosed with retinochoroidal biopsy. Baillif et al.[9] reported using SD-OCT for the first time that predominantly the nuclear layers were affected with a retinitis spreading from inner layers to outer layers and resulting in a moth-eaten appearance of the retina. Subsequently, a few case reports have been published demonstrating several SD-OCT findings seen in SSPE patients.[10,11] In addition to these specific aspects, the absence of vitreous inflammation and negative serological tests, may aid differentiation of SSPE from the other retinitis entities, such as Behçet's disease, hereditary degenerative retinal diseases, infectious retinitis, and toxoplasma retinochoroiditis, white dot syndromes, etc.[12] In this report, we aimed to reveal the prognosis of necrotizing macular retinitis of SSPE with daily fundus photographs and SD-OCT images. In our opinion, these findings are quite demonstrative for SSPE and the early diagnosis can be made easily with these specific fundus and SD-OCT findings without the need for biopsy or unnecessary steroid/immunosuppressive treatment in challenging cases principally presenting without neurological symptoms.

SSPE prevalence has decreased to 1 in 100,000 measles cases due to vaccination programs in developed countries.[13] Nonetheless, post-vaccine SSPE has also been rarely reported.[14] SSPE has a mortality rate of up to 95%, and the average life expectancy of a patient with SSPE is 3.8 years (45 days-12 years).[15] There is currently no proven treatment

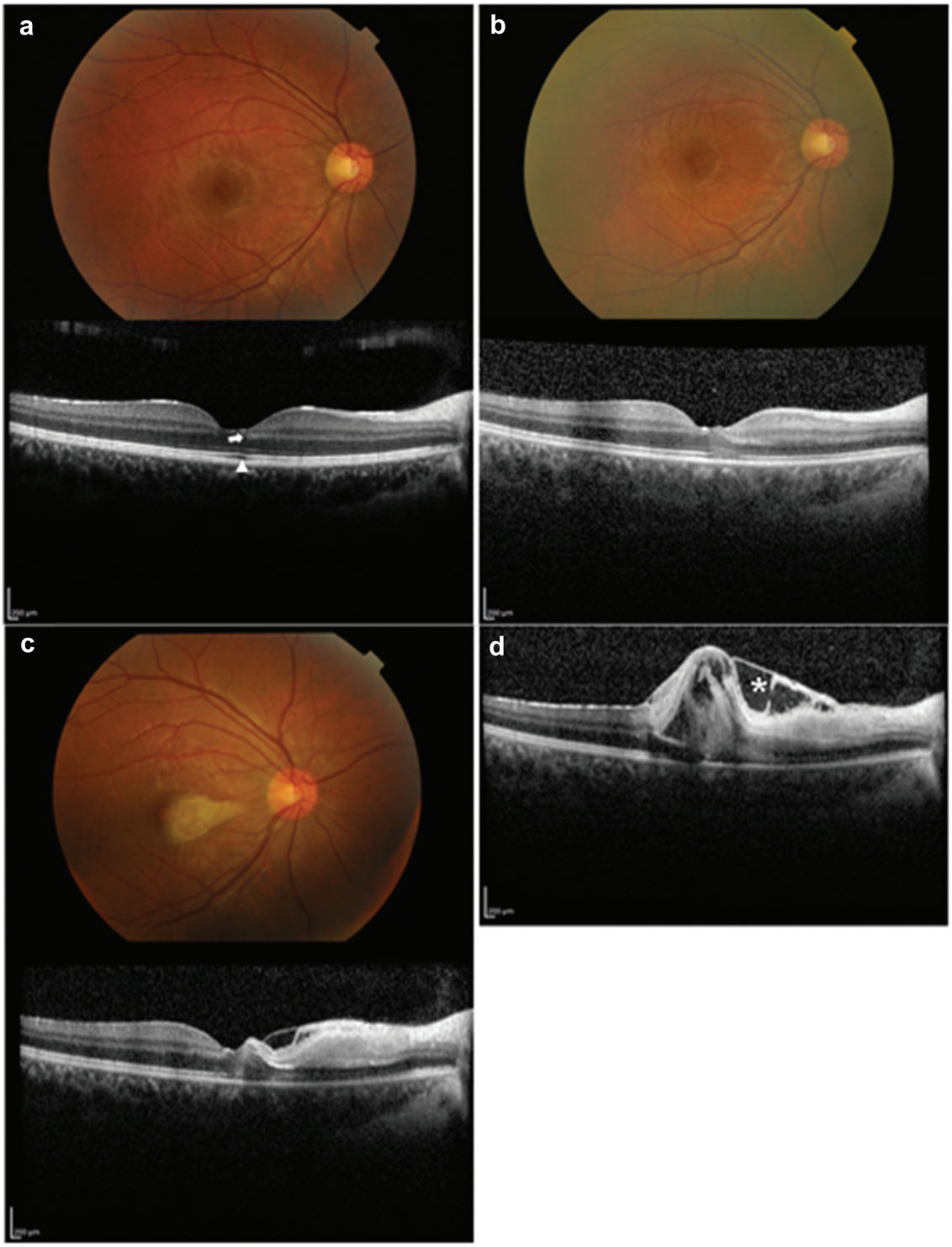

Figure 3. Sequential color fundus photograph, and spectral domain optical coherence tomography (SD-OCT) of the right eye (RE). Twelve hours before the onset of the symptoms in the RE, the color fundus photograph was normal (a, upper), and SD-OCT showed mildly increased reflectivity in the parafoveal inner and outer plexiform layers (arrow) and deviation in the ellipsoid zone (arrowhead) (a, bottom). A couple of hours after the onset of the symptoms, the color fundus photograph was normal (b, upper), and SD-OCT showed inner and outer plexiform layers edema, thickening and increased reflectivity in the inner retinal layers, and interruption of the ellipsoid zone were observed (b, bottom). Two days after the onset of the symptoms, the color fundus photograph revealed retinitis extending from fovea to optic disc (c, upper), and SD-OCT showed inner nasal retina lost its layered organization, and the retinal nerve fiber layer and ganglion cell layer necrosis (c, bottom). Three days after the onset of the symptoms, the whole retinal structure deteriorated and hyporeflective cystic spaces and ILM detachment (asterisk) were observed (No fundus photograph was taken today due to the patient's agitated behavior) (d).

for SSPE. Inosine pranobex, interferon-alpha and beta, ribavirin, amantadine, and lamivudine are tried for treatment. Timely initiation of current treatment regimes has been reported to prevent the progression of the disease and prolong the life of these patients, but with minimal clinical improvement.[16] Although there are no published randomized controlled trials, starting treatment before neurological symptoms appear may be an important factor in the treatment

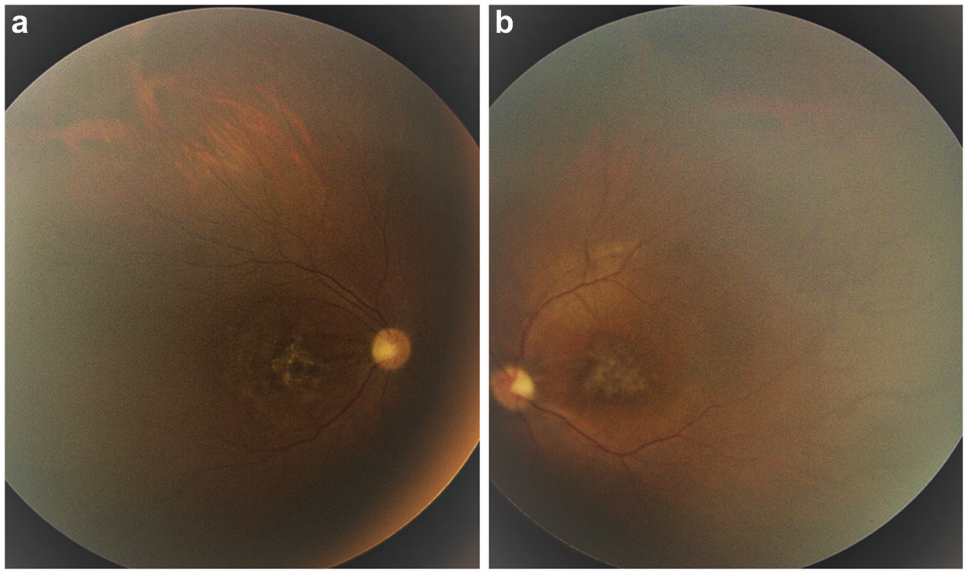

Figure 4. Color fundus photograph of the right eye (a) and left eye (b) showed patchy macular scarring and temporal optic disc pallor on the day patient died.

success.[3] In this case, treatment could not be started in the early period due to the logistical difficulties in the obtain of the drug from abroad. We hope that the findings of this case will facilitate early diagnosis for physicians working in countries where there may be a struggle with the supply of these special drugs.

Conclusion

In this case report, we aimed to demonstrate the retina and SD-OCT findings of SSPE-associated macular necrotizing retinitis at the whole stages of the disease. In our view, these featured and distinctive findings may be considered as characteristical in the diagnosis and follow-up of this fatal disorder. We hope that the sharing of this tragic case could help to immediately start the treatment before the appearance of neurological symptoms and may be life-saving for SSPE patients presenting with ocular symptoms, principally for the countries which have specific drug supply problems.

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