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A case of adult-onset Still's disease presenting with multifocal central serous chorioretinopathy

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Abstract. – Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder of unknown etiology with no specific histological features. In this study, we reported a 43-year-old woman who developed AOSD with multifocal central serous chorioretinopathy (CSC). Up to now, the patient is still on close follow-up. Besides, we reviewed the literature emphasized on the ophthalmological features of AOSD.

Key Words:
Adult-onset Still's disease, Multifocal central serous chorioretinopathy, Ophthalmological features.

Introduction

Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder of unknown etiology with no specific histological features, characterized by fever, rash, organomegaly and serositis. The reported prevalence ranges from 1 to 10 per million[1]. Diagnosis of AOSD is based on Yamaguchi's criteria[2] after exclusion of infectious diseases, malignancies or autoimmune disorders. It is common for AOSD patients to have symptoms involving multiple organs such as liver, kidney, bone marrow, lungs, etc. However, it was rarely reported for AOSD patients to have ocular signs. Here we report a case of AOSD with multifocal central serous chorioretinopathy (CSC) with a review of literature that emphasizes the ophthalmological features of AOSD.

Case Report

A 43 year-old woman complained of fever, muscular soreness and skin rash for 10 days after catching a cold 4 days before. Fever relapsed several times a day and the top most temperature reached 39°C. Aggravating muscular haphalgesia and skin rash existed in her whole body. She had nonproductive cough but no weight loss. Laboratory test revealed that the blood leukocyte count was 14.3×10^9/L with a differential count 87.2% of neutrophils. Her past medical history and family history was unremarkable. She denied either exposure to high risk of sexual activities or drug abuse and did not consume alcohol or cigarettes. She was admitted into the Department of Respiration of our Hospital as sepsis. On examination, the pulse rate was 85bpm and temperature was 38.1°C; blood pressure, 110/65 mmHg; respiratory frequency, 23 breaths per minute. The needle-tip red papule was predominant at chest and back. The rest of physical examination was unremarkable.

The results of laboratoty tests were notable and summarized in Table I. Renal function, urine analysis, HIV and HBV serology, autoantibody repertorie, TORCH (Toxoplasmosis, Rubella, Cytomegalovirus, and Herpes simplex virus) and tuberculin skin test were all negative. Three times of hemoculture and medulloculture were also negative as well. Abdominopelvic ultrasonography showed normal results. Erythrocyte sedimentation rate (ESR) was 64 mm/hr. Computed topography (CT) scan of chest showed bilateral pleural effusion and little pericardial effusion (Figures 1 and 2). ECG was normal but UCG (ultrasound cardiography) revealed few mitral valve backstreaming. The patient was first diagnosed as septicemia and intravenous mezlocillin sulbactam sodium (7.5 g/day) and sofoselis (2 g/day) were administered. Seven days later, the patient had no improvement in her symptoms and signs and presented left knee joint pain. After a consultation with rheumatologists, we confirmed the patient as AOSD[3] (Table II), and started on intravenous dexamethasone 10 mg per day. This resulted in a prompt resolution of her fever, muscular haphalgesia and skin rash within 24 hours. The patient was discharged after one week because

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Table I. Routine laboratory findings for the case.

	Pre-treatment	Post-treatment	Normal values
CRP (mg/L)	81.6	11.7	0-8
D-dimer (ug/L)	2030	245	0-232
Hemoglobin (g/L)	110	103	107-153
Leukocytes ($\times 10^9$/L)	14.3	9.3	3.5-9.7
Neutrophils (%)	87.2	79.5	50-70
Platelets ($\times 10^9$/L)	326	350	94-268
ALT (IU/L)	204.5	18.3	5-40
AST (IU/L)	78.4	35.8	5-40
LDH (IU/L)	328.3	106.7	109-245
Serum ferritin (ng/mL)	900.74	364.28	30-400

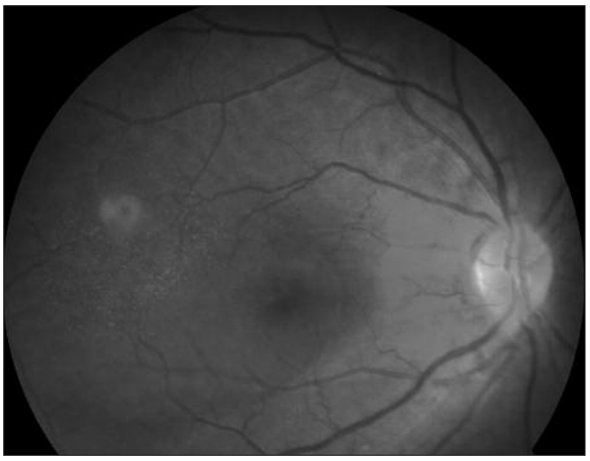

Figure 1. The fundus of the right eye.

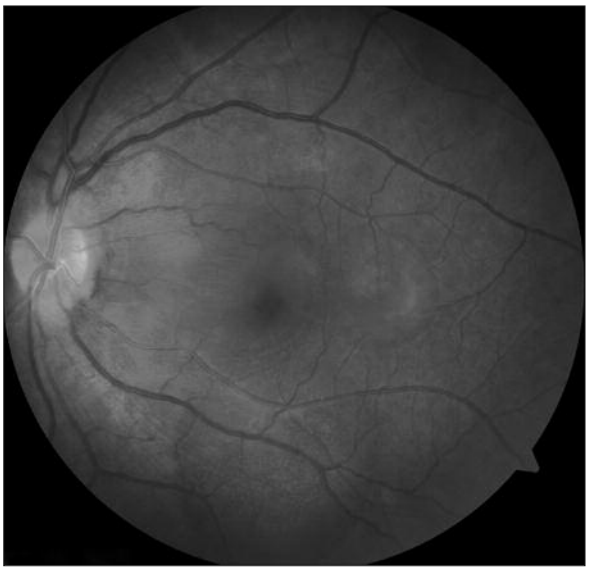

Figure 2. The fundus of the left eye.

her own demand. Oral administration of prednisone of 40 mg per day was used for the next two weeks after discharge. Unfortunately, the patient stopped the treatment unauthorizedly at the fourth week even being educated to decrease the dosage gradually. Three days later, she felt blurred in both eyes and went to the ophthalmologist. The serous detachment between retinal pigment epithelium (RPE) and neuro-epithelium aroud the macular area was noticed in both eyes (Zeiss, Visucam pro NM, Jena, Germany) (Figures 1 and 2). The fundus fluorescein angiography (FFA, Heidelberg, HRA2, Germany) showed multifocal vascular leaking on the arch ring and disc-shaped detachment of RPE (Figures 3 and 4), which was confirmed as fluid sonolucent area on the optical coherence tomog-

Table II. Criteria for AOSD by Yamaguchi et al[3].

Major criteria
Fever ≥ 39°C lasting one week or more
Arthralgia lasting two weeks or more
Typical skin rash: maculopapular, non-pruritic, salmon-pink rash with concomitant fever spikes
Leukocytosis ≥ 10×10^9/L with neutrophil, polymorphomuclear count ≥ 80%

Minor criteria
Pharyngitis sore throat
Lymphadenopathy and/or splenomegaly
Liver enzyme abnormalities (aminotransferases)
Negative for rheumatoid factor or antinuclear antibodies

Exclusion criteria
Absence of infection, especially sepsis and Epstein-Barr viral infection
Absence of malignant disease, especially lymphomas
Absence of inflammatory disease, especially polyarteritis nodosa

Classification of adult Still's disease requires 5 or more criteria including 2 or more major criteria.

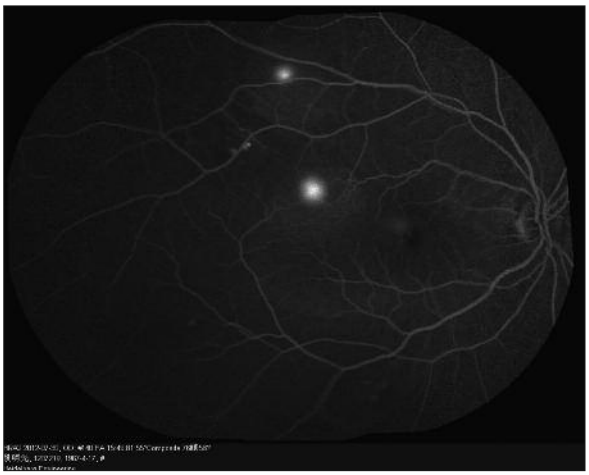

Figure 3. The late phase of the right eye in FFA.

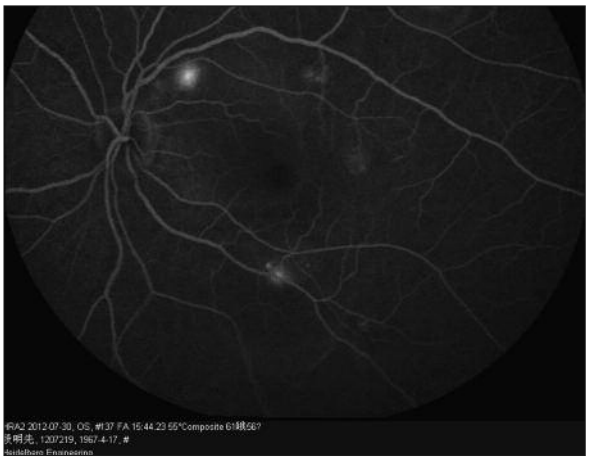

Figure 4. The late phase of the left eye in FFA.

raphy (OCT, Heidelberg, OCT Spectralis, Germany) (Figures 5 and 6). So the diagnosis of multifocal CSC was made then and photodynamic therapy (PDT) with verteporfin towards the leaking points was recommended. Up to now, the patient is still on close follow-up.

Discussion

Ocular complications were rarely reported in patients with AOSD. As far as we know, the case is the first one reported to have ocular problems. CSC was first reported by von Grade in 1866. The reason for CSC is generally thought as serous detachment of RPE (retinal pigment epithelioma) as a result of dysfunction of the RPE's barrier, which was discovered by Maumenee with the development of FFA (fluorescein fundus angiography) technology in 1965[4].

The A-type behavior characteristics are very common among the patients with CSC. Before the onset of disease, stress often occurs upon the patient with the high levels of catecholamine and glucocorticoid in the blood[5]. In animal experiments, repeated injections of norepinephrine epinephrine and glucocorticoids could induce the similar clinical performance of CSC. Maybe that our patient had fairly large glucocorticoids in blood and withdrew quietly fast is the main rea-

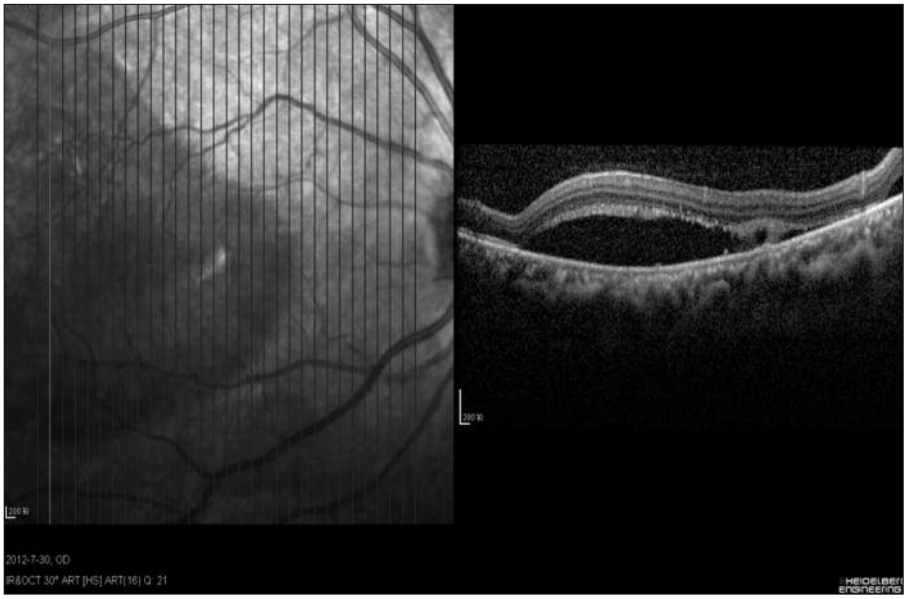

Figure 5. The OCT scanning of the right eye.

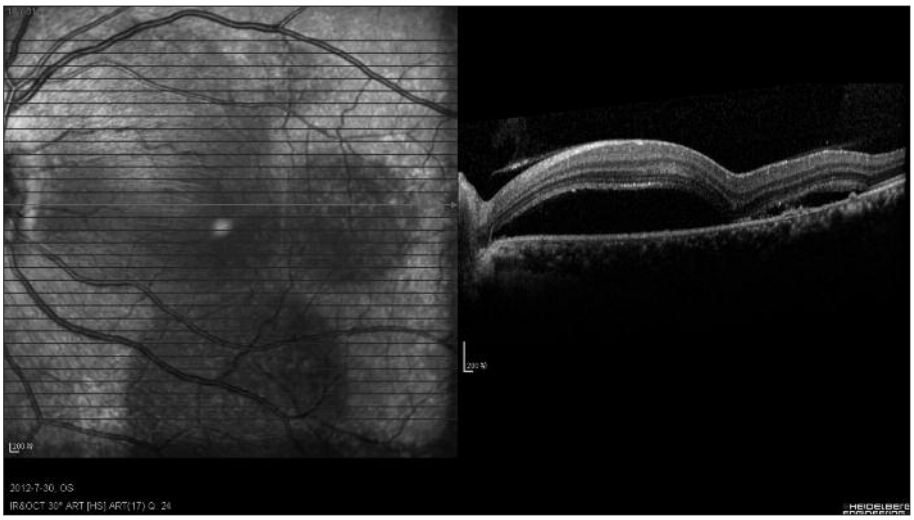

Figure 6. The OCT scanning of the left eye.

son for her CSC. Other risk factors of the disease include smoking, alcohol abusement, utilizing of antibiotics and antihistamines, autoimmune diseases, hypertension, and adrenal tumors. Most of the acute patients would get recovery after 4 to 6 months, returning to normal vision. Therefore, the CSC is usually considered to be a self-limiting disease. However, some abnormal visual function changes sustain, such as visual distortion, decreased contrast sensitivity, abnormality of color vision, etc. What's more, some patients gained prolonged course, which may last more than 6 months. The chronic CSC is defined by the lesion area of the diffused decompensation of RPE. Some cases of the patients are serious, which is often accompanied by permanent vision loss[6, 7]. The renascent choroidal neovascularization (CNV) on condition of prolonged healing can even lead to permanent vision loss. The relapse rate of patients who first developed CSC is about 30~50%[7] and 10% of patients may relapse more than 3 times[8].

Based upon the understanding of CSC as self-limiting disease, many ophthalmologists preferred conservative therapy for the treatment of CSC. The way is to take no treatment toward the disease; another way is to provide the patients with placebo treatment like vitamin C, B, P, inosine and so on. These treatments seem to be efficient because of the self-limiting feature of the disease. The majority of patients can get recovery after 4 to 6 months with the conservative therapy, but there are still 5% of patients with delayed healing or more serious situation, causing severe visual impairment.

In addition, the common method for treatment of CSC is laser photocoagulation. Previous understanding of the pathogenesis of CSC is mainly derived from the FFA examination results. On account of clear leaking point of the RPE through the method of FFA, we could make it clear that the primary lesion is located in the RPE layer. But the deep-seated factors caused dysfunction of the RPE barrier, serous detachment of RPE and neural retinal are still unknown. The theoretical basis of laser photocoagulation treatment for CSC is that the thermal effect of the laser will trigger solidification of the leaking point on the RPE. Though clinical evidence shows that laser photocoagulation therapy can block out the leaking point, speed up the absorption of serous RPE detachment and shorten the course of the disease, the long-term observation has no indications about improvement of the long-term efficacy in patients or decrease of the recurrence rate[9-13].

The clinical studies that applied the technology of ICGA (indocyanine green angiography) have confirmed that the permeability of choroid membrane of the CSC patients is quitely high, which would lead to excessive hydrostatic pressure in the choroid tissue, triggering the detachment of RPE and the mechanical damage of RPE barrier. Furthermore, the leakage into the retina would induce the detachment of neuroepithelial in retina. These have made for further understanding of the pathology of CSC. Nowadays, many people share the view that the expansion and leakage of capillary vessels in choroid membrane is the main reason that

caused CSC. And the dilatation and leakage cannot be meliorated by laser photocoagulation, which may be the key point of relapse. Laser treatment is not suitable for leak points that occurred in foveal. And laser may also cause paracentral scotoma or even CNV because of the damage of Bruch's membrane[13]. Recent years, the methods of PDT have gained great success on treatment of CSC, which may be the effect of embolism of the capillary vessels that PDT caused, preventing the leakage of choroid membrane. Despite the effective termination of the leakage of the PDT, there are still a lot of controversies upon the expensive price as well as the security of the treatment, for example, it may caused ischemia of choroid membrane or even the CNV. Zhao, et al[14] found that the safe effective lowest dose of verteporfin for injection of the PDT treatment is as 30% as the dose that used for the conventional treatment of CNV. This dose for treatment can either shorten the patient's course of disease, or reduce their economic burden. Other treatments including micro-pulse laser, transpupillary thermotherapy and intraocular injection of anti-vascular endothelial growth factor (VEGF) drugs are applicable now.

Conclusions

Patients with AOSD would have ocular complications and need to be followed up closely. The treatments that aiming at risk factors of CSC are important and the pathogenesis and treatment for CSC will be the hot point in the near future. With the improvement of the technology and analytical level for ocular fundus diagnosis, the examination of ICGA and OCT will provide us with more objective information that are crucial for understanding the pathological pathways of the disease, which contributes to deepening understanding of the pathogenesis of CSC and raising the level of clinical treatment.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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