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Coats Plus Syndrome Presenting in an Adult

Fae B. Kayarian, BS[1], Steven M. Cohen, MD, FACS[2,3], Mark L. Cohen, MD[4], and Daniel E. Sammartino, MD[5]

Abstract

Purpose: To present a case of retinal vascular disease characterized primarily by capillary nonperfusion in an adult with Coats plus syndrome (CPS). **Methods**: A case and its findings were analyzed. **Results**: A 38-year-old woman with a history of poliosis, thrombocytopenia, seizures, and white-matter brain lesions was referred for evaluation of bilateral blurred central vision. Fluorescein angiography showed extensive bilateral retinal capillary nonperfusion with retinal arteriolitis in the right eye. Genetic testing found 2 pathological mutations in the conserved telomere maintenance component 1 (*CTC1*) gene, diagnostic of CPS. **Conclusions**: Genetic testing may be diagnostic in patients who present with retinal vascular disease and systemic disease suggestive of CPS.

Keywords

Coats plus syndrome, cerebroretinal microangiopathy with calcifications and cysts, *CTC1*, retina, retinal telangiectasia exudates, leukodystrophy, retinal vascular disease, capillary nonperfusion

Introduction

Coats plus syndrome (CPS), also known as cerebroretinal microangiopathy with calcifications and cysts, is a multisystem disorder that can include retinal capillary nonperfusion and exudation. CPS is autosomal recessive, manifesting in people with mutations in both copies of the conserved telomere maintenance component 1 (*CTC1*) gene.[1] Because the spectrum of findings seen in patients with CPS is variable and the disease is rare, it can present a diagnostic challenge.[2] Patients with CPS usually become symptomatic in childhood.

Of the 30 cases of CPS in the literature,[2–23] only 3 presented in patients older than 18 years; those patients were 19 years old, 21 years old, and 23 years old.[21–23] We report a 38-year-old woman with a complex medical history and fluorescein angiographic evidence of severe bilateral retinal capillary nonperfusion with retinal arteriolitis who had genetic testing that confirmed the diagnosis of CPS.

Case Report

A 38-year-old woman presented to our retina clinic with moderately blurred central vision. Her visual acuity was 20/25 OD and 20/60 OS. She was born with neonatal abstinence syndrome because of exposure to opioid drugs in utero and did not know whether she was born prematurely. At age 14 years, she developed a white patch in the middle of her hair. A few years ago, all her hair turned white, including the hair on her arms. She has a distant history of endometriosis and osteomyelitis of the jaw with a poor dental history. Her husband was an ophthalmic technician who noted that she had a 20-year history of optic nerve pallor.

At age 35 years, the patient presented with seizures; a magnetic resonance imaging scan of her head showed an irregularly marginated enhancing 4.7 cm × 5.2 cm × 3.1 cm lesion in the medial right frontal lobe with calcifications, extensive vasogenic edema, and midline shift (Figure 1). The patient was started on intravenous (IV) dexamethasone, and a right frontal craniotomy was performed. Pathology noted extensive necrosis, astrogliosis, and collections of calcospherites, but no malignancy. Flow cytometry was not diagnostic.

The patient's hospital course was complicated by recurrent unexplained fevers and macrocytic anemia with thrombocytopenia. The thrombocytopenia was treated with dexamethasone and IV immunoglobulin with a transient improvement, and she eventually responded to eltrombopag. A bone marrow biopsy showed 10% to 20% trilineage hematopoiesis and erythroid hyperplasia with no significant increase in blasts and no granulomas. Flow cytometry showed no abnormal B-cell or

[1] Rush Medical College of Rush University Medical Center, Chicago, IL, USA
[2] University of South Florida, Tampa, FL, USA
[3] Retina Vitreous Associates of Florida, Clearwater, FL, USA
[4] National Prion Disease Pathology Surveillance Center, Case Western Reserve University, University Hospitals Cleveland Medical Center, Cleveland, OH, USA
[5] Oncology & Hematology of White Plains, White Plains, NY, USA

Corresponding Author:
Steven M. Cohen, MD, FACS, Retina Vitreous Associates of Florida, 579 S Duncan Ave, Clearwater, FL 33756, USA.
Email: scohen@rvaf.com

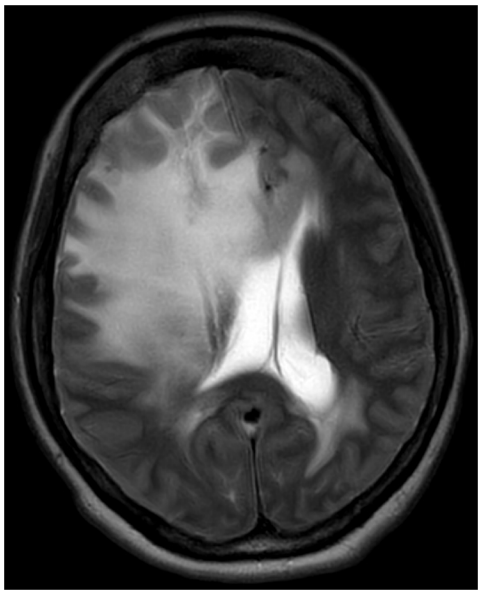

Figure 1. Magnetic resonance imaging of the brain with T2 image shows extensive vasogenic edema extending into portions of the basal ganglia, internal capsule, and subsinsular regions with evidence of a midline shift and local mass effect.

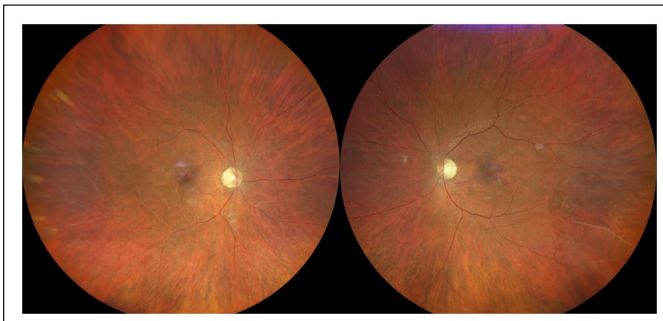

Figure 2. Color fundus photograph of both eyes shows optic nerve pallor, ghost vessels, and rare, faded cotton-wool spots.

T-cell populations, and a myelodysplastic syndrome fluorescence in situ hybridization (MDS-FISH) panel was negative. Positron emission tomography/computed tomography for lymphoma was negative but showed bilateral interstitial lung disease.

At our clinic, retinal imaging showed a pale optic nerve, ghost vessels, and faded cotton-wool spots in both eyes (Figure 2). Widefield fluorescein angiography showed extensive capillary nonperfusion and peripheral drusenoid pigment epithelial detachments in both eyes and patches of retinal arteriolitis in the right eye (Figure 3).[2]

Genetic testing showed 2 pathologic mutations in the *CTC1* gene, confirming the diagnosis of CPS. Both pathological variants, c.2954_2956del, result from the deletion of 1 amino acid of the CTC1 protein (p.Cys985del). The patient had panretinal photocoagulation (PRP) in the right eye to the area of capillary nonperfusion.

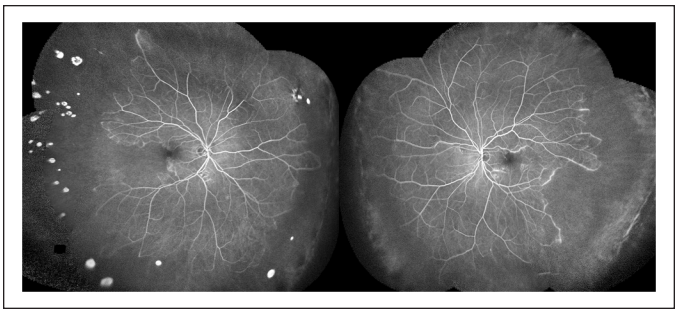

Figure 3. Wide-angle montage fluorescein angiogram shows capillary nonperfusion and peripheral hyperfluorescent spots in both eyes. The left eye shows fluorescein staining of the wall of the retinal arterioles in the macula.

Conclusions

CPS is a rare, autosomal recessive disorder caused by loss-of-function mutations in both copies of the *CTC1* gene that results in characteristic brain lesions, such as intracranial calcification and cysts; retinal capillary nonperfusion, telangiectasia, and exudates; and leukodystrophy. Patients also develop non-neurologic disease including malformations of the gastrointestinal tract, poliosis, and osteopenia.[1,3] Usually, the systemic workup for CPS occurs between infancy and adolescence. Typical initial presentations include gastrointestinal bleeding, seizures, developmental delay, and bone fractures.[4–6]

Because CPS is rare, the best treatment for CPS retinopathy is unknown. In a recent article published in this journal, Sears et al[24] reviewed treatments of infants with CPS including laser photocoagulation; cryotherapy; intravitreal anti-vascular endothelial growth factor injections; intraocular, periocular, and systemic steroids; and surgery. Even though our patient did not have posterior pole or anterior segment neovascularization, we chose to apply PRP to the area of nonperfused retina in the more affected eye. The decision to treat the more affected eye was driven by case reports describing treatment of other patients with CPS and the patient's poor follow-up in our office for care. When she was first seen, she had a history of no eye care for the preceding 8 years. After her first visit, she missed half of her appointments and has since been lost to follow-up.

In conclusion, our 35-year-old patient was diagnosed with CPS after presenting with extensive, peripheral, retinal capillary nonperfusion in both eyes. Retina specialists should consider this rare diagnosis in their patients who present with retinal vascular disease and systemic disease suggestive of CPS.

Ethical Approval

This case report was conducted in accordance with the Declaration of Helsinki. The collection and evaluation of all protected patient health

information was performed in a US Health Insurance Portability and Accountability Act–compliant manner.

Statement of Informed Consent

Written informed consent was obtained from the patient for the publication of this case report.

Declaration of Conflicting Interests

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ORCID iD

Fae B. Kayarian https://orcid.org/0000-0003-0434-6060

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