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Case report

Late re-activation of Coats disease

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ABSTRACT

Purpose: To report case of Coats disease with the longest known interval of disease quiescence prior to first reactivation (17 years).

Observation: A 25-year-old male was regularly followed for Coats disease since age 4. After initial treatment with cryoablation, disease quiescence was achieved at age 8. The disease activity was well controlled for 17 years after which he developed decreased vision in the right eye at age 25. Late reactivation of Coats disease was diagnosed and multiple treatments ensued. Despite aggressive therapy, the patient experienced progressive exudation warranting surgical management and eventually developed neovascular glaucoma.

Conclusion: Once diagnosed with Coats disease, lifelong monitoring is essential to early detection and treatment of potential disease reactivation. The interval between disease quiescence and reactivation is variable, with this case representing the longest known interval of disease quiescence prior to first reactivation (17 years).

1. Introduction

Coats disease is a nonhereditary retinal vascular disorder first described by George Coats in 1908[1] and further reported by Theodor Leber in 1912. It is characterized by telangiectatic retinal vessels with prominent aneurysmal changes and often progressive retinal exudation. Almost always occurring in young males (mean age of diagnosis of 5 years) with 95% unilateral presentation, patients typically present after failing vision screening at school due to decreased visual acuity, strabismus, or leukocoria.[2] Once a diagnosis is made, patients require lifelong follow-up to monitor for disease reactivation which may occur even after prolonged periods of quiescence. To our knowledge, we report herein the longest known interval (17 years) between Coats disease quiescence and reactivation.

2. Case report

A 25-year-old male with an established diagnosis of Coats disease was regularly followed in our pediatric retinal service every 6 months since age 4. At the time of diagnosis, best-corrected visual acuity (BCVA) was 20/60 in the right eye with a superior exudative retinal detachment and 20/40 in the left eye with an unremarkable fundus. He was initially treated with cryoablation in the right eye at ages 4, 7 and 8 respectively with an excellent response resulting in BCVA of 20/20 in both eyes. During follow-up, a thorough dilated fundus examination was performed at each visit, and given no changes in symptoms or clinical examination, serial fundus photography and angiography were not performed at each visit. The last fundus photograph before the reactivation episode taken at age 23 displayed stable chorioretinal scarring from prior cryotherapy in the right eye (Fig. 1A) with an unremarkable left eye (Fig. 1B). Fluorescein angiography (FA) at the same visit revealed disease quiescence corresponding to fundus photography (Fig. 1C–D). The most recent optical coherence tomography (OCT) prior to disease reactivation was performed at age 24, and showed a normal foveal contour without evidence of fluid or exudation (Fig. 1E). He remained asymptomatic with 20/20 vision in both eyes from age 8 to age 25 when he represented with decreased vision in the right eye to 20/25.

At re-presentation, the right eye displayed peripheral retinal telangiectasias with sclerotic retinal vessels superiorly and temporally, peripheral chorioretinal scars from prior cryotherapy, and increased retinal exudation in the inferior and temporal far periphery without central edema or subretinal fluid (Fig. 2A). The left eye was unchanged compared to prior (Fig. 1B). Wide-field fluorescein angiography of the right eye revealed early hypofluoresence consistent with blockage from retinal exudation and chorioretinal scarring as well as progressive late

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Fig. 1. Fundus, both eyes, at disease quiescence.
1A. Wide-field fundus photography, right eye, taken 2 years before reactivation, showing sclerotic vessels with chorioretinal scarring from prior cryotherapy superiorly and temporally. No exudation was noted. **1B.** Wide-field fundus photography, left eye, taken 2 years before reactivation, showing an unremarkable retina, **1C.** Wide-field fluorescein angiogram in the early phase, taken 1 year before reactivation, showing hypofluorescence in the area corresponding to the chorioretinal scar, **1D.** Wide-field fluorescein angiogram in the late phase from 1C, **1E.** Macular optical coherence tomography (OCT) of the right eye taken 1 year before reactivation, showing normal foveal contour without subretinal exudation or fibrosis.

hyperfluoresence consistent with leakage from telangiectatic vessels with microaneurysmal changes in the inferior and temporal retina (Fig. 2B–D). The OCT at this time displayed changes including subretinal exudation and fibrosis when compared to prior (Fig. 2E).

The diagnosis of Coats disease reactivation after a 17-year period of quiescence was made. The right eye was initially treated with intravitreal ranibizumab (0.5 mg/0.05 ml) followed by peripheral retinal ablation. During follow-up, the retinal exudation progressively encroached into the macula which was managed by further intravitreal ranibizumab and sub-tenons triamcinolone acetonide (40 mg/1 ml). Six months after reactivation, the vision was decreased to 20/200 with increased vitreous haze and retinal exudation. This progressive exudation was relatively refractory to ongoing treatment with sub-tenons triamcinolone injections every three months with the decline in BCVA to 20/400 due to posterior subcapsular cataract formation. B-scan ultrasonography revealed subretinal fluid and vitreoretinal traction with the area of greatest retinal elevation at the superior-nasal far periphery. The IOP rose to 31 mmHg, which eventually was controlled with two topical anti-glaucoma medications.

The decision was ultimately made for surgical intervention with 23-gauge pars plana vitrectomy, lensectomy, membrane peeling, endolaser, intraocular lens insertion, and sub-tenon triamcinolone. One month following surgery, BCVA continued to decline to hand motion with the subsequent development of neovascular glaucoma. Intravitreal ranibizumab (0.5 mg/0.05 ml) injection was administered with a plan for glaucoma specialist consultation.

3. Discussion

The classification of Coats disease consists of five stages.[3] Stage 1 is characterized by the presence of retinal telangiectasias without additional features. When exudate develops, the classification advances to stage 2A with extrafoveal exudation and stage 2B with foveal exudation. With progression to exudative retinal detachment, the disease is classified as stage 3A with subtotal detachment and stage 3B if total detachment is present. Stage 4 indicates a total retinal detachment with glaucoma while stage 5 indicates advanced end-stage disease with phthisis.

The patient described herein was initially diagnosed with Stage 2B Coats disease at age 4. His baseline demographic information corresponds with the prototypical Coats disease patient outlined in the literature as a young male with unilateral disease presenting with decreased visual acuity.[2,4] At reactivation 17 years after quiescence, his disease had progressed to stage 3B at the time vitreoretinal surgery was performed.

Once diagnosed with Coats disease, patients require long-term monitoring to evaluate the possibility of disease reactivation as described herein. Shields et al.[5] reported that patients have a 7% chance

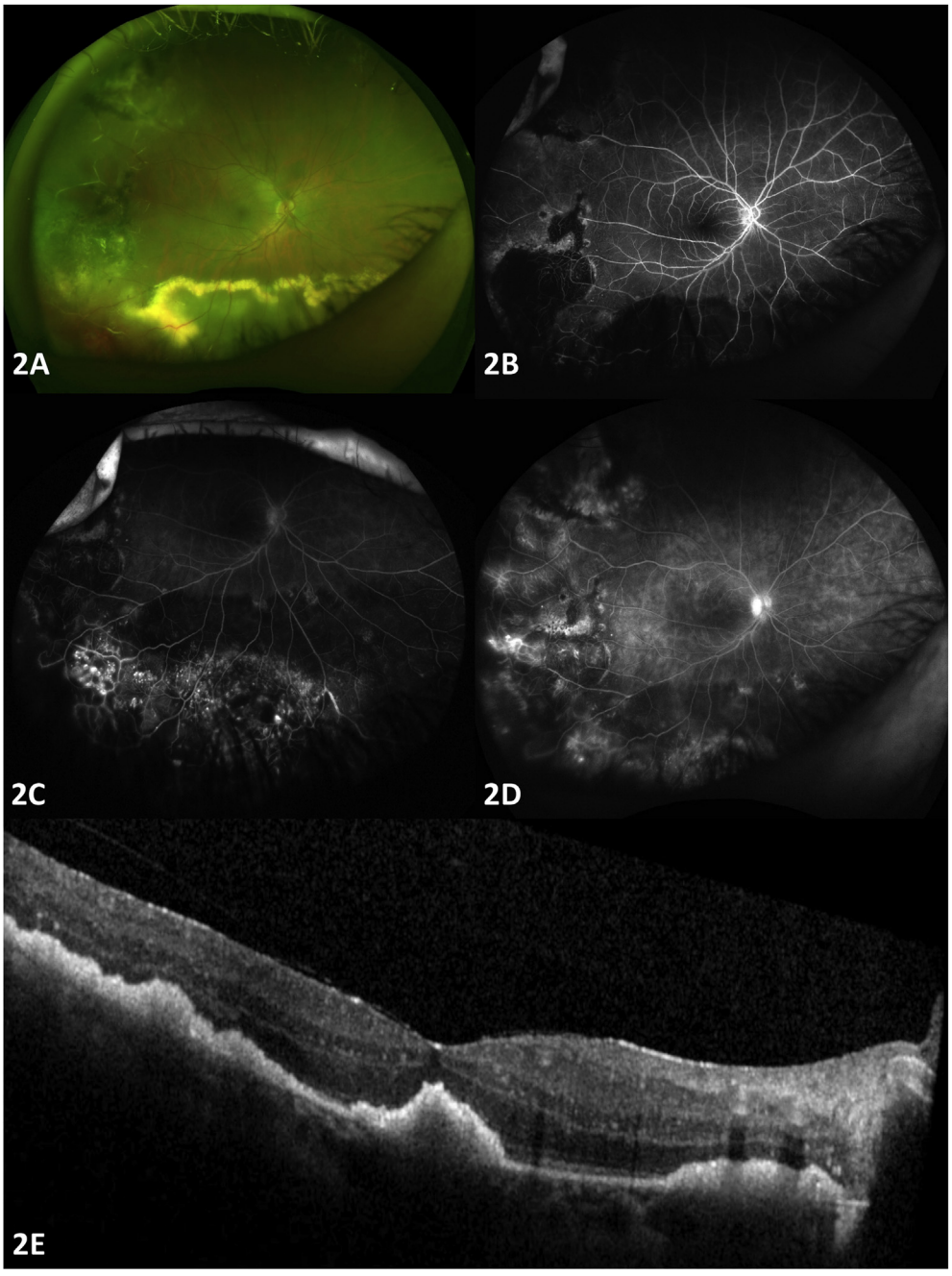

Fig. 2. Multi-modal retinal imaging at disease reactivation.
2A. Wide-field fundus photography, right eye, showing peripheral retinal telangiectasias with sclerotic vessels superiorly and temporally. Hard exudation was more prominent in the inferior retina. Chorioretinal scarring within the superotemporal retina was present from prior cryotherapy. **2B.** Wide-field fluorescein angiogram in the early phase. Hypofluorescence is present in the superotemporal retina corresponding to chronic chorioretinal scarring, and in the inferior retina corresponding to increased retinal exudation.**2C.** Mid phase widefield fluorescein angiogram exhibiting retina telangiectasias and microaneurysms.**2D.** Late phase widefield fluorescein angiogram showing increased hyperfluorescence consistent with leakage from peripheral telangiectasias. **2E.** Macular optical coherence tomography (OCT) of the right eye taken at the time of reactivation, showing subretinal hyperreflectivity corresponding to subretinal exudation and fibrosis.

of disease recurrence over a mean span of 10 years (range 4–14 years) even with appropriate treatment of retinal telangiectasias and exudation. Shienbaum et al.[6] reported that the average interval between successful treatment and first recurrence was 4.3 years (range from 3.3 to 5.4 years). When the first episode of recurrence occurs, typically multiple recurrences follow thereafter with a variable interval between them. While one case experienced 23 years and 7 months of stability between the second and third recurrence,[6] our patient described herein demonstrates the longest known period of disease quiescence between diagnosis and first recurrence with a 17-year interval between the ages of 8 and 25.

To date, the exact pathogenesis of Coats disease remains unclear. Reese et al.[7] studied two enucleated Coats Disease eyes and noted pathologic changes within inner retinal vascular beds of varying size and aneurysmal dilatations along with perivascular lymphocyte infiltration. Tarkkanen et al.[8] propose that the original pathologic insult may result in a chronically dysfunctional blood-retinal barrier. Black et al.[9] demonstrated a missense mutation within the NDP gene on chromosome Xp11.2 from a female with unilateral advanced Coats disease and her son who was diagnosed with Norrie disease; further analysis of nine eyes enucleated from males with Coats disease revealed an NDP gene mutation isolated from retinal tissue in one of the eyes. These findings may suggest that the NDP gene, which is essential in the process of retinal vasculogenesis, may also be involved in the pathogenesis of Coats disease.

Of note, the patient described in this case report had been coping with notable socio-psychological stressors from his personal life during the time of disease recurrence. We propose the novel idea that stress hormones, along with male sex hormones, may play a role in disease reactivation. To the best of our knowledge, there does not exist any data or recent literature to verify this hypothesis.

Management of Coats disease has been studied for nearly 100 years

with many reports investigating treatment according to the natural history of the disease.[4,8,10,11] Left untreated, Coats disease can progress to blindness secondary to total retinal detachment, macular exudation/fibrosis, secondary glaucoma, and/or phthisis.[2,4,10] Cryotherapy or laser photocoagulation of peripheral retinal non-perfusion, telangiectatic vessels, and aneurysms remains the initial mode of treatment to prevent further vascular leakage and retinal exudation.[3] We prefer to perform laser photocoagulation aiming directly at retinal blood vessels and "painting" them using a long duration until a whitening effect is observed, with more traditional scatter laser performed for nonperfused areas of the attached retina. It is possible to perform simultaneous cryotherapy for areas of the retina that are exudative detached, but the possibility of increased exudation must be entertained.

Several studies have shown some benefit of anti-vascular endothelial growth factor (VEGF) and steroid treatment for adjuvant therapy in Coats disease, as VEGF levels have been reported to be elevated in Coats disease.[12–16] However, exacerbated vitreoretinal traction and tractional retinal detachment after intravitreal anti-VEGF therapy have been observed.[17] Our patient received intravitreal ranibizumab upon initial disease recurrence, and his disease course remained stable for 4 months thereafter. Anti-VEGF therapy may also play a role in preventing the progression of foveal-adjacent exudation, although this has not been formally evaluated. The use of steroids is the well-established role in Coats disease as well as other retinal vascular conditions characterized by disruption of the blood-retinal barrier including diabetic macular edema, retinal vein occlusion, and cystoid macular edema. However, while intravitreal steroids have shown benefit in maintaining retinal vascular permeability in these aforementioned retinal vascular conditions, a similar effect in Coats disease is yet to be observed.[4] Our patient had been treated with sub-tenon triamcinolone acetonide injections early in his disease recurrence which showed some initial improvement, however, both anti-VEGF therapy and steroid treatment administered in a combined fashion were not sufficient to maintain vascular homeostasis of the entire retina. Surgical intervention ultimately became required in this case with vitrectomy and lensectomy when a visually significant cataract and prominent vitreoretinal traction became evident.

4. Conclusion

Coats disease is a slowly progressive idiopathic retinal vascular disease characterized by retinal telangiectasias, aneurysms, and retinal exudation. Lifelong follow-up remains essential for early detection of disease reactivation and intervention which may occur even 17 years after achieving initial disease quiescence.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Conflicts of interest

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajoc.2019.100458.

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