ASRS American Society of Retina Specialists

Journal of VitreoRetinal Diseases
2025, Vol. 9(5) 727–730

DOI: 10.1177/24741264251351661
journals.sagepub.com/home/jvrd
Sage

A Novel Case of Optic Disc Edema Associated With VEXAS Syndrome

Mary A. Gao, DO[1], Tianyu Liu, MD[2], and Sandeep Randhawa, MD[2]

Abstract

Purpose: To describe a novel case of optic disc edema in the setting of VEXAS syndrome. **Methods:** A single case is evaluated. **Results:** A 77-year-old man presented with optic disc edema and hemorrhage and was initially diagnosed with relapsing chondritis. Subsequently, he was diagnosed with VEXAS syndrome, which resolved with an increase in immunosuppressive treatment. **Conclusions:** Patients with VEXAS syndrome may present with a spectrum of ocular manifestations, including optic disc edema.

Keywords

retina, autoimmune, inflammation

Introduction

First described by Beck et al,[1] VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is an autoinflammatory disease that typically affects men older than 50 years of age. It results from a somatic mutation of the X-linked *UBA1* gene at p.Met41, causing overexpression of innate immune pathways. The multisystemic involvement characteristically causes various hematologic disorders and autoinflammatory findings, including fever, chondritis, dermatologic findings, and arthritis. VEXAS syndrome commonly presents concurrently with rheumatologic conditions such as relapsing polychondritis, polyarteritis nodosa, and Still disease. As a result, it can be challenging to differentiate the syndrome from other autoinflammatory conditions.[1,2]

Relapsing polychondritis is a disease entity with a presentation similar to VEXAS syndrome. Ocular manifestations have been reported in 20% to 61% of patients.[3] However, in recent years, some studies have shown that patients with VEXAS syndrome may have a higher prevalence of ocular involvement than patients with relapsing polychondritis.[3,4]

Case Report

A 77-year-old man presented with an acute onset of a visual disturbance 1 to 2 weeks previously, which he described as a purple blob temporal to fixation in his right eye. His ocular history included treatment for a retinal tear. Included in the patient's review of symptoms were 3 months of cyclical night sweats, intermittent rhinorrhea, and an acute episode of dry cough a few months previously that resolved after treatment with methylprednisolone. He denied any eye pain, new fevers, joint pain, rashes, weight loss, headache, numbness, or weakness. His medical history included an original diagnosis of relapsing polychondritis in 2017 followed by a diagnosis of VEXAS syndrome in 2021, as well as hypertension, hyperlipidemia, recurrent pneumonia, pancytopenia, myelodysplastic syndrome, chronic dyspnea at baseline, and prostate cancer treated with radiation therapy. Maintenance therapy for VEXAS-associated inflammation consisted of methotrexate 15 mg weekly and prednisone 5 mg daily.

On examination, the patient's best-corrected visual acuity (BCVA) was $20/50^{+2}$ OD (previous BCVA, 20/40) and $20/50^{-2}$ OS. Intraocular pressure was 14 mm Hg OD and 16 mm Hg OS. Color vision in the left eye was normal and in the right eye was mildly decreased (7/8 Ishihara plates), with no afferent pupillary defect. He had mild tenderness of his trochleas bilaterally. Fundus examination was significant for mild 360-degree optic disc edema with nasal disc hemorrhage in the right eye and normal optic disc appearance in the left eye (Figure 1, A and B). Fluorescein angiography showed leakage from the right optic disc (Figure 1, C and D). Optical coherence tomography (OCT) of the retinal nerve fiber layer confirmed mild thickening of the right optic nerve fiber layer (Figure 1E). Humphrey visual fields were performed but were unreliable with repeated testing due to fixation losses.

[1] Department of Ophthalmology, Corewell Health Taylor Hospital, Taylor, MI, USA
[2] Associated Retinal Consultants, Royal Oak, MI, USA

Corresponding Author:
Mary A. Gao, DO, Department of Ophthalmology, Corewell Health Taylor Hospital, 10000 Telegraph Rd, Taylor, MI 48180, USA.
Email: maryalicegao@gmail.com

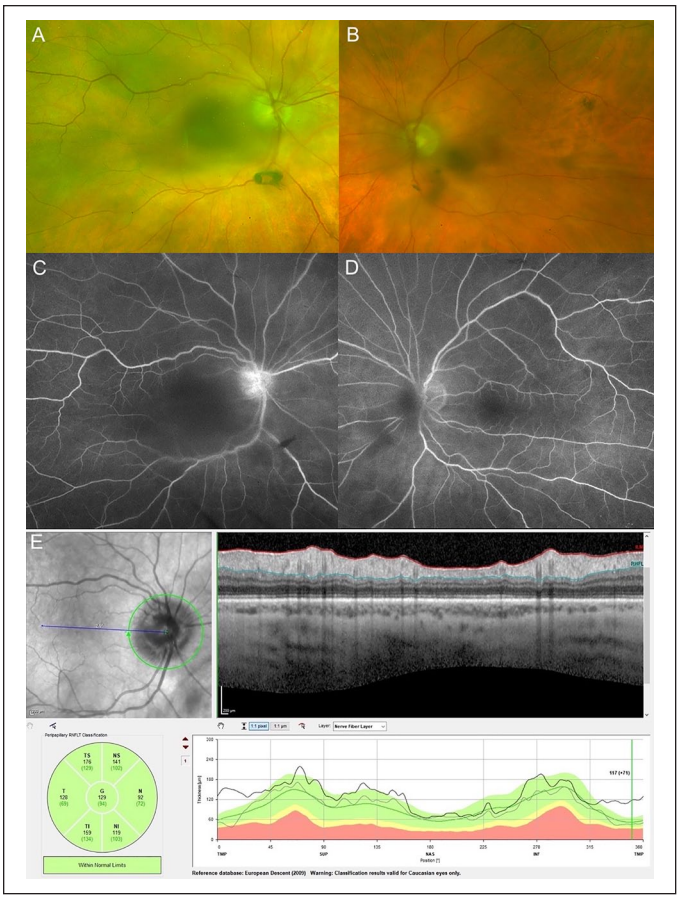

Figure 1. Fundus photography shows optic disc edema and hemorrhage of the (A) right eye and normal optic disc in the (B) left eye. Fluorescein angiography shows optic disc leakage of the (C) right eye with no leakage in the (D) left eye. (E) Optical coherence tomography of the right eye shows mildly increased thickness of the retinal nerve fiber layer, especially temporally.

Laboratory evaluation showed known overall stable pancytopenia with macrocytosis, elevated erythrocyte sedimentation rate (61 mm/hr, baseline 27-38 mm/hr), elevated plasma lysozyme with normal angiotensin-converting enzyme, indeterminate QuantiFERON-Tb Gold, and negative antibodies for syphilis, Lyme disease, *Bartonella*, and toxoplasmosis. Given the patient's systemic symptoms, neutropenia, and indeterminate QuantiFERON-Tb Gold, his rheumatologist advised that he stop his prednisone until completion of an infectious workup. At the patient's 1-month follow-up (while off prednisone), the BCVA decreased to 20/80 OD with persistent optic disc edema. Subsequently, a repeat QuantiFERON-Tb Gold was negative, chest x-ray showed no infiltrates or signs of infection, and magnetic resonance imaging of the brain and orbits was unremarkable with no enhancement of the optic pathways. The patient's medications were increased to methotrexate 25 mg weekly and prednisone 60 mg daily with a weekly taper. Two weeks after increasing his medication dosage (6 weeks after initial presentation), the patient reported subjective improvement in scotoma, although the BCVA remained at 20/80. Examination showed improving disc edema and resolution of the disc hemorrhage in the right eye. At the patient's last follow-up, the BCVA had improved to 20/60 OD, with resolution of disc edema (Figure 2, A and B).

Conclusions

VEXAS syndrome is a multisystemic autoinflammatory disease caused by a mutation in the *UBA1* gene. *UBA1* is an enzyme that plays an important role in protein ubiquitylation, marking proteins for proteasomal degradation. In VEXAS syndrome, the depletion of *UBA1* results in a proinflammatory phenotype, including upregulation of the innate immune system, release of inflammatory cytokines, and abnormal differentiation of B cells. This leads to progressive and recurrent inflammation that can involve multiple organ systems, including the eye and orbit.[5]

The overstimulation of the immune system in VEXAS syndrome creates symptoms that overlap with rheumatologic and hematologic disorders, particularly relapsing polychondritis. Beck et al[1] reported that 60% of the initial 25 patients with *UBA1* mutations studied met the diagnostic criteria for the disorder. In a subsequent study, 7.6% of patients with relapsing polychondritis had *UBA1* mutations (VEXAS-relapsing polychondritis).[4] One characteristic potentially differentiating the syndromes is a higher reported prevalence of ocular involvement in patients with VEXAS syndrome and VEXAS-relapsing polychondritis overlap syndrome compared with patients with idiopathic relapsing polychondritis.[4] Ocular involvement in VEXAS syndrome is estimated to be seen in 28% to 40% of cases.[6] Periorbital edema is the most commonly reported ophthalmic manifestation and was the presenting symptom in 1 case report.[7] Other ocular findings include episcleritis, scleritis, dacryoadenitis, uveitis, angle closure, chemosis, ocular pain, and orbital inflammation.[1,6–9] While there has been 1 reported case of optic perineuritis in VEXAS syndrome,[10] to our knowledge, the current study is the first case to report optic disc edema.

Our patient was diagnosed with VEXAS syndrome in 2021 based on genetic testing performed at the National Institutes of Health. He was started on methotrexate as a steroid-sparing agent in 2022 and remained stable until the months leading up to his presentation. The patient initially reported increased night sweats, rhinorrhea, and dry cough during the few months prior, and his erythrocyte sedimentation rate and C-reactive protein during this time was elevated above his usual baseline. These systemic manifestations correlated temporally with the onset of his visual symptoms. Furthermore, we noted mild tenderness of his trochleas bilaterally, which could have represented trochleitis consistent with previously reported orbital findings in VEXAS syndrome. After increasing his methotrexate and prednisone dosages, the erythrocyte sedimentation rate and C-reactive protein both normalized. The patient's improvement in systemic symptoms coincided with the improvement of his optic disc edema, further suggesting that the ocular findings were related to a flare of VEXAS syndrome.

Our patient presented with optic disc edema and a disc hemorrhage, findings that can also be seen with nonarteritic anterior ischemic optic neuropathy. However, the absence of a disc-at-risk

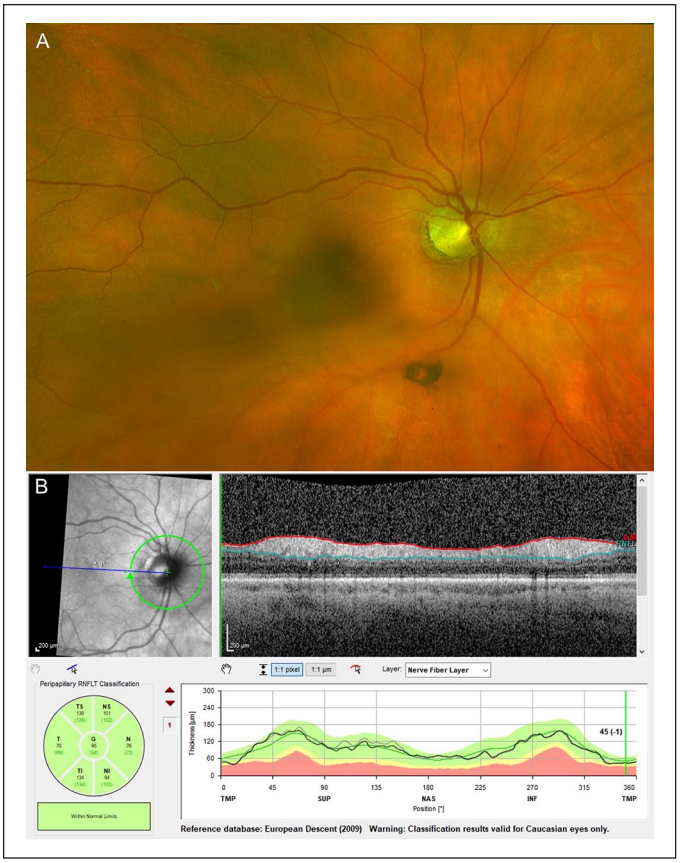

Figure 2. (A) Five months after presentation, fundus photography and (B) optical coherence tomography of the right eye shows resolution of the optic disc edema.

in the contralateral eye, and the timing of improvement in our patient's signs and symptoms after increasing his immunosuppression, raises the possibility that the optic disc edema represented an inflammatory papillitis. Many previously reported ocular manifestations of VEXAS syndrome involve inflammation of the ocular tissues, and a similar mechanism may be at play in our patient's presentation.

Optic disc edema can also be seen in infectious and inflammatory optic neuropathies, including associated with sarcoidosis. Our patient had an elevated lysozyme level, which can be seen in sarcoidosis but is also reported in the setting of myelodysplastic syndrome, with which our patient had been diagnosed. Furthermore, our patient had a normal serum angiotensin-converting enzyme level and no hilar lymphadenopathy on recent computed tomography of the chest, making sarcoidosis less likely. To our knowledge, an association between VEXAS syndrome and elevated serum lysozyme levels has not been previously reported. Our patient also initially had an indeterminate QuantiFERON-Tb Gold result that was negative on repeat testing. Indeterminate results have been reported with immunocompromise, lymphopenia, renal insufficiency,[11] and steroid use,[12] all of which our patient exhibited.

Both relapsing polychondritis and VEXAS syndrome share the feature of innate immune system overactivation and thus have similar management regimens. Systemic corticosteroids are the mainstay of treatment, with adjuvant systemic disease-modifying agents or biologic agents considered for use. In patients with orbital involvement, oral prednisone 20 mg to 40 mg was effective.[8] Similarly, our patient's optic disc edema resolved after increasing his dosages of methotrexate and prednisone.

In conclusion, we present a novel case of optic disc edema in a patient with VEXAS syndrome that resolved with increased systemic immunosuppression. The exact mechanism by which immune dysregulation in VEXAS syndrome affects ocular tissues remains unknown.

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 Health Insurance Portability and Accountability Act (HIPAA)-compliant manner.

Statement of Informed Consent

Written informed consent for publication of patient information and images was not required, as no personal identifiable information is included.

Declaration of Conflicting Interests

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Mary A. Gao https://orcid.org/0000-0001-8246-4973
Tianyu Liu https://orcid.org/0000-0002-2590-6082

References

1. Beck DB, Ferrada MA, Sikora KA, et al. Somatic mutations in UBA1 and severe adult-onset autoinflammatory disease. *N Engl J Med*. 2020;383(27):2628-2638. doi:10.1056/NEJMoa2026834
2. Koster MJ, Warrington KJ. VEXAS within the spectrum of rheumatologic disease. *Semin Hematol*. 2021;58(4):218-225. doi:10.1053/j.seminhematol.2021.10.002
3. Fukuda K, Mizobuchi T, Nakajima I, Kishimoto T, Miura Y, Taniguchi Y. Ocular involvement in relapsing polychondritis. *J Clin Med*. 2021;10(21):4970. doi:10.3390/jcm10214970
4. Ferrada MA, Sikora KA, Luo Y, et al. Somatic mutations in UBA1 define a distinct subset of relapsing polychondritis patients with VEXAS. *Arthritis Rheumatol*. 2021;73(10):1886-1895. doi:10.1002/art.41743
5. Cardoneanu A, Rezus II, Burlui AM, et al. Autoimmunity and autoinflammation: relapsing polychondritis and VEXAS syndrome challenge. *Int J Mol Sci*. 2024;25(4):2261. doi:10.3390/ijms25042261
6. Fanlo P, Román ML de S, Fonollosa A, Ilarramendi J, Heras H, Grayson P. Episcleritis and periorbital edema secondary to VEXAS syndrome. *Arch Soc Esp Oftalmol (Engl Ed)*. 2023;98(10):607-610. doi:10.1016/j.oftale.2023.07.004

7. Lokhande A, Jarmale S, Vaishnav YJ, Schaefer J. An orbital manifestation of VEXAS syndrome. *Ophthalmic Plast Reconstr Surg*. 2023;39(6):e194-e197. doi:10.1097/IOP.0000000000002450
8. Abumanhal M, Leibovitch I, Zisapel M, Eviatar T, Edel Y, Ben Cnaan R. Ocular and orbital manifestations in VEXAS syndrome. *Eye*. 2024;38(9):1748-1754. doi:10.1038/s41433-024-03014-3
9. Georgin-Lavialle S, Terrier B, Guedon AF, et al. Further characterization of clinical and laboratory features in VEXAS syndrome: large-scale analysis of a multicentre case series of 116 French patients. *Br J Dermatol*. 2022;186(3):564-574. doi:10.1111/bjd.20805
10. Takahashi N, Takeichi T, Nishida T, et al. Extensive multiple organ involvement in VEXAS syndrome. *Arthritis Rheumatol*. 2021;73(10):1896-1897. doi:10.1002/art.41775
11. Bellagha R, Dhaouadi T, Riahi A, et al. A regression predictive model for QuantiFERON-TB Gold Plus® indeterminate results in immunosuppressed patients. *SAGE Open Med*. 2024;12:20503121241279116. doi:10.1177/20503121241279116
12. Helwig U, Müller M, Hedderich J, Schreiber S. Corticosteroids and immunosuppressive therapy influence the result of QuantiFERON TB Gold testing in inflammatory bowel disease patients. *J Crohns Colitis*. 2012;6(4):419-424. doi:10.1016/j.crohns.2011.09.011