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Exudative Vitreoretinopathy With a Coats-Like Response in Poretti-Boltshauser Syndrome

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Abstract

Purpose: To report a unique case of retinal exudation consistent with a Coats-like response and associated with mutations in *LAMA1*, confirming the diagnosis of Poretti-Boltshauser syndrome. **Methods:** A case and its findings were analyzed. **Results:** A 24-year-old woman presented with mild peripheral avascularity, circumferential membranes at the edge of the vascularized retina, exudation, numerous vessels with aneurysmal changes, and inferior retinal elevation in both eyes. Molecular Vision Laboratory panel testing (Molecular Vision Laboratory Corp) found 2 variants in the *LAMA1* gene, confirming a diagnosis of Poretti-Boltshauser syndrome. Treatment with bevacizumab and sub-Tenon triamcinolone provided no improvement. Eventually, scleral buckling with pars plana vitrectomy was performed, which reattached the retina but did not improve visual acuity. **Conclusions:** This report shows the importance of investigating for an underlying genetic disorder in young patients with atypical exudation and abnormal vasculature and the persistent progression and challenging treatment course of patients presenting with Poretti-Boltshauser syndrome.

Keywords

Poretti-Boltshauser syndrome, Coats-like response, *LAMA1* gene

Introduction

Poretti et al[1] described a condition in which children have cerebellar dysplasia and cysts in addition to oculomotor apraxia, intellectual disability, and language impairment. Today, Poretti-Boltshauser syndrome is recognized as an autosomal recessive inherited progressive cerebellar syndrome that presents with a clinical spectrum of neurologic and ophthalmic manifestations, including but not limited to symptoms of cerebellar ataxia, oculomotor apraxia, language impairment, and intellectual disability.[2–4] Poretti-Boltshauser syndrome is associated with mutations in the *LAMA1* gene, which codes for extracellular matrix proteins.[2,3] Ocular symptoms, such as apraxia, and ocular pathology in the form of myopia, juvenile cataracts, microphthalmia, and retinal dysplasia are also characteristic of the disorder.[1,3]

A variety of vitreoretinopathies exist, including but not limited to familial exudative vitreoretinopathy (FEVR), Coats disease, persistent fetal vasculature, incontinentia pigmenti, and retinopathy of prematurity. The degree of exudation with which these vitreoretinopathies present and how they affect vision also vary.[5]

This report describes a unique presentation and management of exudative vitreoretinopathy with a Coats-like response in the setting of Poretti-Boltshauser syndrome.

Case Report

A 24-year-old woman, born full-term via cesarean delivery with no complications and with a history of congenital cataracts and myopia, presented to the ophthalmic emergency department reporting decreased visual acuity (VA) in the right eye over the past month. The patient had no systemic medical history or surgical history. Consanguinity in the form of multiple first cousin marriages within her family was reported, but there was no family history of systemic or ocular diseases.

The VA was 20/300 OD and 20/30 OS. The refraction was $-10.00 + 0.50 \times 127$ and $-10.75 + 0.75 \times 92$, respectively. The intraocular pressure was normal in both eyes. A slitlamp examination showed a trace nuclear sclerotic cataract in both eyes. A fundus examination showed mild peripheral avascularity, circumferential

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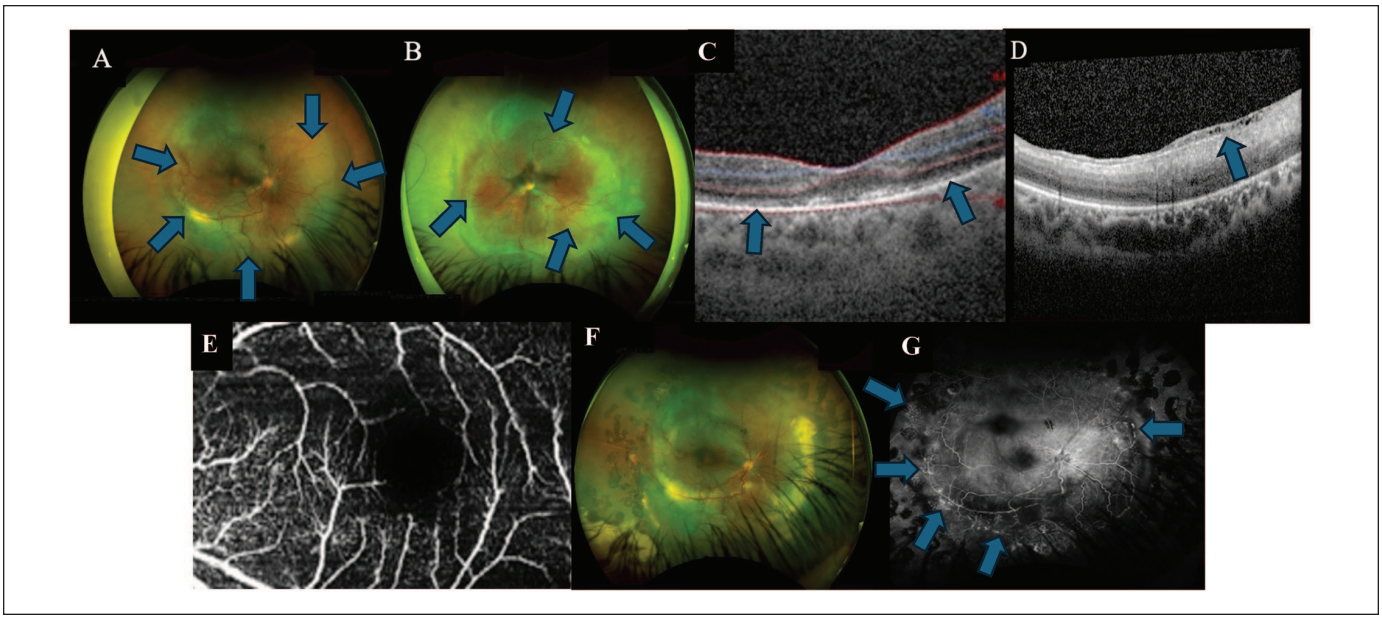

Figure 1. Fundus photography shows peripheral avascularity, circumferential membranes at the edge of the vascularized retina, exudation, and vessels with aneurysmal changes and inferior elevation in both eyes, but worse in the right eye (A) than in the left eye (B). (C) Optical coherence tomography (OCT) shows diffuse loss of photoreceptors everywhere except in the macula and (D) mild peripheral retinal nerve fiber layer schisis in the right eye. (E) OCT angiography shows an enlarged avascular foveal zone in the left eye. (F) Fundus photography shows increased fibrosis and exudation in the right eye despite treatment. (G) Fluorescein angiography shows persistent leakage and aneurysmal dilations in the right eye.

membranes at the edge of the vascularized retina, severe exudation, numerous vessels with aneurysmal changes, and elevation of the retina inferiorly in both eyes. The right eye (Figure 1A) was worse than the left eye (Figure 1B). The circumferential membranes exerted traction in the right eye; however, neither eye showed neovascularization. The membranes were not clearly associated with retinal detachment (RD) in either eye, which appeared exudative in nature.

Fluorescein angiography (FA) showed mildly incomplete peripheral retinal vascularization in both eyes and many telangiectatic vessels at the edge of the vascularized retina. Optical coherence tomography (OCT) showed a diffuse loss of photoreceptors everywhere in the right eye except in the macula (Figure 1C) in addition to mild peripheral retinal nerve fiber layer schisis (Figure 1D). OCT angiography showed an enlarged avascular foveal zone in the left eye (Figure 1E). At this time, FA-guided peripheral photocoagulation was administered to the avascular retina with an 810 nm diode laser, and injections of intravitreal (IVT) bevacizumab and sub-Tenon triamcinolone were given in the operating room. The specific laser size was preferred by the treating physician because of its larger spot size and ability to titrate burns on continuous mode.

Given the patient's unusual fundus presentation, an Invitae Inherited Retinal Disease panel (Invitae Corp) was ordered, which found no pathogenic variants. Molecular Vision Laboratory (MVL) panel testing (Molecular Vision Laboratory Corp) was then ordered to test a larger panel of genes. Two variants were found in the *LAMA1* gene, 1 of unknown significance (NM_005559.4(LAMA1):c.206G>T (p.Cys69Phe) and 1 pathologic mutation (NM_00559.3 exon 1-3 deletion). These variants were validated by next-generation Sanger sequencing and were found to cause autosomal recessively inherited Poretti-Boltshauser syndrome. Because Poretti-Boltshauser syndrome is a cerebellar syndrome, the patient was referred to a neurologist and had magnetic resonance imaging (MRI) of the brain, which showed a hypoplastic inferior vermis and enlarged fourth ventricle with communication between the fourth ventricle and the posterior fossa cerebral spinal serous fluid space. An abnormally shaped fourth ventricle has specifically been reported in cases of genetically confirmed Poretti-Boltshauser syndrome.[3] The combination of a pathologic *LAMA1* mutation and the MRI findings confirmed an abnormality within the cerebellum and the diagnosis of Poretti-Boltshauser syndrome.

Over the next year, the patient's VA fluctuated between 20/300 and 20/200 OD and remained 20/30 OS. The right eye developed increased fibrosis and exudation (Figure 1F), an epiretinal membrane, persistent leakage, and aneurysmal dilations on FA (Figure 1G) and a persistent inferior exudative RD despite laser photocoagulation and 2 injections of bevacizumab. Scleral buckling with pars plana vitrectomy, endolaser photocoagulation, and 1000 cs silicone oil (SO) tamponade were performed 2.5 years after the patient's initial presentation. During the vitrectomy, the vitreous was noted to have an abnormal, gummy consistency with a tightly adherent hyaloid. A cutter, forceps, and flex loop were used to remove as much of the hyaloid as possible. The peripheral vitreous was shaved to the vitreous base

with scleral depression, and after fluid–air exchange, the retina was noted to be attached under air. An endolaser was then used to perform photocoagulation in the few remaining areas of avascularity and in areas in which the vascularity was abnormal. Eight months postoperatively, the retina remained attached.

Over the next year, the patient developed more exudation inferiorly in the right eye despite IVT bevacizumab injections every 4 to 6 weeks. Seven months after the initial surgery, the cataract in the right eye had worsened and the patient had SO exchange and cataract extraction with intraocular lens placement. At the patient's last follow-up, the macula remained attached, although the VA was light perception OD and 20/30 OS. The left eye remained stable off treatment and will continue to be observed.

Conclusions

This case suggests that the *LAMA1* gene may play a role in retinal vascular disease, and further studies are warranted to explore this possibility. An exudative vitreoretinopathy coexisting with a Coats-like response in a patient with Poretti-Boltshauser syndrome has not been previously reported and therefore deserves discussion among retina specialists.

FEVR is characterized by incomplete vascularization of the peripheral retina, poor vascular differentiation, and variable expressivity.[5] Associations have been reported between Poretti-Boltshauser syndrome and retinal dystrophy, atrophic and pigmentary changes, lattice degeneration, severe peripheral retinal avascularity, and neovascularization, leading to its presentation being compared with that of FEVR.[3,6,7]

Coats disease is an ocular disorder that usually presents unilaterally[8] and is characterized by retinal exudation, telangiectasia, and aneurysms.[9,10] The retinal exudation can be extensive and associated with RD.[11] A Coats-like response has a similar clinical appearance to Coats disease but occurs in the setting of another ocular or systemic disease.[12–15] Coats-like vasculopathy has been associated with a number of diseases, including but not limited to facioscapulohumeral dystrophy,[16] Parry-Romberg syndrome,[17] and Senior-Loken syndrome.[18] Specifically, Varela et al[13] reported a prevalence of Coats-like vasculopathy in a cohort of patients with inherited RD, 54% of whom had isolated retinitis pigmentosa (RP). The loss of photoreceptors found on OCT in our patient's right eye could have been mistakenly associated with Coats-like vasculopathy in the setting of RP if genetic testing had not determined the correct underlying pathology of Poretti-Boltshauser syndrome.

Our patient's presentation is consistent with an exudative vitreoretinopathy with a Coats-like response. Although peripheral avascularity was found, it was mild in our patient compared with a report by Marlow et al,[7] based on a comparison between the description, fundus photographs, and FA images provided for their cases and ours. Furthermore, Varela et al[13] reported that the most common features of patients in their cohort with Coats-like vasculopathy included telangiectasia, exudates, and exudative RD affecting the inferior and temporal retina. Our patient possessed all these features, specifically severe exudation from retinal vessels with aneurysmal and telangiectatic abnormalities that resulted in an inferior RD. Therefore, our patient's ocular presentation of Poretti-Boltshauser syndrome is most consistent with an exudative vitreoretinopathy with a Coats-like response.

Basic science research and animal model literature, specifically in mice, suggest a role for *LAMA1* gene mutations in retinal vasculopathy.[19,20] The *LAMA1* gene encodes laminins, which are critical players in ocular development.[2] Laminins are glycoproteins that make up the basement membrane and extracellular matrix and are expressed early in embryonic development,[21] specifically affecting lens development, retinal organization, and retinal angiogenesis.[2] Disruptions in this process can lead to retinal vascular abnormalities[2] as well as astrocyte and vessel migration that transverses the inner limiting membrane into the vitreous.[20] Once in the vitreous, these vessels can anastomose with portions of the hyaloid vasculature closest to the developing retina.[20] These vessels then reenter the retina, where they eventually form the inner and outer retinal capillary networks. However, the previously migrated astrocytes can continue to proliferate in the vitreous.[20] This causes the vitreous to form a dense mesh,[20] which was likely responsible for the abnormal gummy consistency of the patient's vitreous noticed during vitrectomy and the membrane-like hyaloid with abnormally tight adherence.

Regarding treatment of exudative RD associated with a Coats-like response, the literature reports improved visual outcomes in eyes treated with laser photocoagulation, cryotherapy, and antivascular endothelial growth factor injections, with or without sub-Tenon triamcinolone.[22–24] This may halt or at least delay the progression of retinal exudation and is considered a first-line treatment. In this patient's case, exudative vitreoretinopathy with a Coats-like response in the setting of Poretti-Boltshauser syndrome and mutation of the *LAMA1* gene may have made the patient less responsive to these treatment modalities, and a surgical approach was ultimately required. Because of the abnormal gummy consistency of the vitreous and severe exudation, surgical management in these patients can be challenging and carries a high risk for retinal tears, proliferative vitreoretinopathy, and other complications.[25] Therefore, surgical management of exudative vitreoretinopathy with a Coats-like response in the setting of Poretti-Boltshauser syndrome should be reserved for cases that are recalcitrant to medical therapy.

Limitations to our case report exist. Although the MVL panel found 2 variants in the *LAMA1* gene, only 1 of them (NM_00559.3 exon 1-3 deletion) was pathologic. More studies are warranted to substantiate and explore the pathogenicity of the variant of unknown significance (NM_005559.4(LAMA1):c.206G>T (p.Cys69Phe), especially on a separate allele.

Clinicians should consider Poretti-Boltshauser syndrome in the differential diagnosis of young patients with exudative vitreoretinopathy with a Coats-like response. Genetic testing to determine the specific pathology is essential to guide management and understand the long-term ocular and systemic complications.

Ethical Approval

The University of Miami Institutional Review Board waived ethical approval of this case report because the patient data are de-identified. This case report adhered to the tenets of the Declaration of Helsinki.

Statement of Informed Consent

Written consent was not sought for the present study because the patient data are de-identified.

Declaration of Conflicting Interests

Dr. Berrocal is a consultant to Alcon, Allergan, Zeiss, Dutch Ophthalmic Research Center, Novartis, ProQR, and Oculus. None of the other authors declared potential conflicts of interest with respect to the research, authorship, and/or publication of the article.

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References

1. Poretti A, Häusler M, von Moers A, et al. Ataxia, intellectual disability, and ocular apraxia with cerebellar cysts: a new disease? *Cerebellum*. 2014;13(1):79-88. doi:10.1007/s12311-013-0521-8
2. Cai CX, Go M, Kelly MP, Holgado S, Toth CA. Ocular manifestations of Poretti-Boltshauser syndrome: findings from multimodal imaging and electrophysiology. *Retin Cases Brief Rep*. 2022;16(3):270-274. doi:10.1097/ICB.0000000000000991
3. Micalizzi A, Poretti A, Romani M, et al. Clinical, neuroradiological and molecular characterization of cerebellar dysplasia with cysts (Poretti-Boltshauser syndrome). *Eur J Hum Genet*. 2016;24(9):1262-1267. doi:10.1038/ejhg.2016.19
4. Geerts C, Sznajer Y, D'haenens E, Dumitriu D, Nassogne MC. Phenotypic spectrum of patients with Poretti-Boltshauser syndrome: patient report of antenatal ventriculomegaly and esophageal atresia. *Eur J Med Genet*. 2023;66(2):104692. doi:10.1016/j.ejmg.2022.104692
5. Gilmour DF. Familial exudative vitreoretinopathy and related retinopathies. *Eye (Lond)*. 2015;29(1):1-14. doi:10.1038/eye.2014.70
6. Aldinger KA, Mosca SJ, Tétreault M, et al. Mutations in *LAMA1* cause cerebellar dysplasia and cysts with and without retinal dystrophy. *Am J Hum Genet*. 2014;95(2):227-34. doi:10.1016/j.ajhg.2014.07.007. Erratum in: *Am J Hum Genet*. 2014;95(4):472. doi:10.1016/j.ajhg.2014.08.012
7. Marlow E, Chan RVP, Oltra E, Rusu I, Gupta MP. Retinal avascularity and neovascularization associated with *LAMA1* (laminin1) mutation in Poretti-Boltshauser syndrome. *JAMA Ophthalmol*. 2018;136(1):96-97. doi:10.1001/jamaophthalmol.2017.5060
8. Shields JA, Shields CL, Honavar SG, Demirci H. Clinical variations and complications of Coats disease in 150 cases: the 2000 Sanford Gifford Memorial Lecture. *Am J Ophthalmol*. 2001;131(5):561-571. doi:10.1016/s0002-9394(00)00883-7
9. Shields JA, Shields CL, Honavar SG, Demirci H, Cater J. Classification and management of Coats disease: the 2000 Proctor Lecture. *Am J Ophthalmol*. 2001;131(5):572-583. doi:10.1016/s0002-9394(01)00896-0
10. Dalvin LA, Udyaver S, Lim LAS, et al. Coats disease: clinical features and outcomes by age category in 351 cases. *J Pediatr Ophthalmol Strabismus*. 2019;56(5):288-296. doi:10.3928/01913913-20190716-01
11. Luckie AP, Hamilton AMP. Adult Coats' disease in branch retinal vein occlusion. *Aust N Z J Ophthalmol*. 1994;22(3):203-206. doi:10.1111/j.1442-9071.1994.tb01717.x
12. Bass SJ, Sherman J, Giovinazzo V. Bilateral Coats' response in a female patient leads to diagnosis of facioscapulohumeral muscular dystrophy. *Optometry*. 2011;82(2):72-76. doi:10.1016/j.optm.2010.07.028
13. Varela MD, Conti GM, Malka S, et al. Coats-like vasculopathy in inherited retinal disease: prevalence, characteristics, genetics and management. *Ophthalmology*. 2023;130(12):1327-1335. doi:10.1016/j.ophtha.2023.07.027
14. Fan KC, McAllister MA, Yannuzzi NA, et al. X-linked retinoschisis and a Coats-like response in the setting of retinopathy of prematurity. *J Vitreoretin Dis*. 2020;4(6):525-529. doi:10.1177/2474126420939734
15. Silva RA, Dubovy SR, Fernandes CE, Hess DJ, Murray TG. Retinoblastoma with Coats' response. *Ophthalmic Surg Lasers Imaging*. 2011;42(6):139-143. doi:10.3928/15428877-20111208-04
16. Goselink RJM, Schreur V, van Kernebeek CR, et al. Ophthalmological findings in facioscapulohumeral dystrophy. *Brain Commun*. 2019;1(1):1-9. doi:10.1093/braincomms/fcz023
17. Agarwal A, Pilania RK, Anjani G, Choudhary H, Gupta A, Gupta V. Retinal vasculitis with Coats-like response in a young girl with Parry-Romberg syndrome. *J Clin Rheumatol*. 2021;27(8S):S543-S545. doi:10.1097/RHU.0000000000001052
18. Sato T, Mimura M, Sugiyama T, et al. Senior–Loken syndrome complicated with severe Coats disease–like exudative retinopathy. *Retin Cases Brief Rep*. 2007;1(3):172-174. doi:10.1097/01.ICB.0000279653.16358.ce
19. Gnanaguru G, Bachay G, Biswas S, Pinzón-Duarte G, Hunter DD, Brunken WJ. Laminins containing the β2 and γ3 chains regulate astrocyte migration and angiogenesis in the retina. *Development*. 2013;140(9):2050-2061. doi:10.1242/dev.087817
20. Edwards MM, McLeod DS, Grebe R, Heng C, Lefebvre O, Lutty GA. *Lama1* mutations lead to vitreoretinal blood vessel formation, persistence of fetal vasculature, and epiretinal membrane formation in mice. *BMC Dev Biol*. 2011;11:60. doi:10.1186/1471-213X-11-60
21. Vilboux T, Malicdan MC, Chang YM, et al. Cystic cerebellar dysplasia and biallelic *LAMA1* mutations: a lamininopathy associated with tics, obsessive compulsive traits and myopia due to cell adhesion and migration defects. *J Med Genet*. 2016;53(5):318-329. doi:10.1136/jmedgenet-2015-103416
22. Sein J, Tzu JH, Murray TG, Berrocal AM. Treatment of Coats' disease with combination therapy of intravitreal bevacizumab, laser photocoagulation, and sub-Tenon corticosteroids. *Ophthalmic Surg Lasers Imaging Retina*. 2016;47(5):443-449. doi:10.3928/23258160-20160419-07
23. Villegas VM, Gold AS, Berrocal AM, Murray TG. Advanced Coats' disease treated with intravitreal bevacizumab combined with laser vascular ablation. *Clin Ophthalmol*. 2014;8:973-976. doi:10.2147/OPTH.S62816
24. Shields C, Udyaver S, Dalvin L, Atalay H, Khoo CL, Mazloumi M. Coats disease in 351 eyes: analysis of features and outcomes over 45 years (by decade) at a single center. *Indian J Ophthalmol*. 2019;67(6):772-783. doi:10.4103/ijo.IJO_449_19
25. Kusaka S. Surgical management of Coats disease. *Asia Pac J Ophthalmol (Phila)*. 2018;7(3):156-159. doi:10.22608/APO.201867