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CASE REPORT

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VITREOUS HEMORRHAGE IN TYPE 3 GAUCHER DISEASE: AN ANGIOGRAPHIC AND PATHOLOGIC ANALYSIS

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Abstract

Purpose:

To describe the case of a 12-year-old woman with vitreoretinal manifestations of Type 3 Gaucher disease.

Methods:

A retrospective case report including multimodal imaging and histologic examination of the vitreous.

Results:

A 12-year-old woman with a history of Gaucher disease Type 3 was referred to the ophthalmology service for evaluation of vitreous deposits in both eyes. Funduscopic examination was notable for white vitreous opacities in both eyes. Ultra-widefield fluorescein angiography demonstrated areas of blockage associated with the deposits and focal areas of leakage. Optical coherence tomography angiography showed shadow artifact without intrinsic flow at these sites. Three years after presentation, she developed a right hemorrhagic posterior vitreous detachment requiring pars plana vitrectomy with scleral buckle. A vitreous sample was sent to pathology, which demonstrated Gaucher cells.

Conclusion:

Gaucher disease is a rare metabolic condition caused by an autosomal recessive deficiency of glucocerebrosidase. To the best of our knowledge, this is the first report of hemorrhagic posterior vitreous detachment in Type 3 Gaucher disease, including ultra-widefield imaging, optical coherence tomography angiography, and histopathology.

Gaucher disease is a rare, autosomal recessive metabolic condition caused by a deficiency of the glucocerebrosidase enzyme. The deficiency of this lysosomal hydrolase results in the accumulation of glucocerebroside in monocytes and macrophages in multiple organs including the liver, spleen, bone marrow, and lungs. Three variants of the disease have been identified. Type 1 is the most benign, with clinical signs of generalized weakness, mild fatigue, musculoskeletal complains, splenomegaly, and hematologic manifestations. Type 2, the rarest, is the severe acute neuropathic form resulting in death by age 2–3. Type 3 is the chronic neuropathic form of the disease which is characterized by slowly progressive neurological decline. Ocular involvement has been noted in all three types of Gaucher disease. Since 1991, the severity of disease has been ameliorated by the use of enzyme replacement therapies, such as algucerase and imiglucerase.

The ocular signs and symptoms of Gaucher disease range from horizontal supranuclear and nuclear gaze palsies, vestibulo-ocular system manifestations, corneal clouding, cataracts, preretinal and vitreous opacities, retinal vascular abnormalities, epiretinal membrane formation, and changes on electroretinography. The first reported retinal finding in the literature was preretinal white dots, described in 1980 by Cogan et al. Other reported retinal findings include choroidal neovascularization, vitreous opacities, tractional retinal detachment, and epiretinal membrane.

Shrier et al have reported the presence of Gaucher cells in vitreous aspirate specimens of patients with vitreous opacities as well as the presence of glucosylceramide on chromatography. Sheck et al have described these vitreous opacities at the interface of the nerve fiber layer of the retina and the posterior hyaloid face, associated with localized posterior vitreous detachment (PVD). Our case report adds to the existing literature since, to the best of our knowledge, it is the first report of hemorrhagic PVD in Gaucher disease, including ultra-widefield imaging and optical coherence tomography (OCT) angiography in the characterization of these vitreous opacities.

Case Report

A 12-year-old girl with a history of Gaucher disease Type 3 (glucocerebrosidase p.L444P homozygote) was referred for evaluation of possible pars planitis. She was originally diagnosed with Gaucher disease in infancy and started on enzyme replacement therapy with imiglucerase (44 U/kg/week). She has been managed by pulmonology for Gaucher-related interstitial lung disease as well as recurrent otitis media and hearing loss. In addition, she is enrolled in special education because of learning difficulties. She also has a family history of Gaucher disease, with a sister who developed bilateral epiretinal membranes requiring pars plana vitrectomy.

At presentation, the patient had no ocular symptoms. Her visual acuity was 20 of 80 in the right eye and 20 of 60 in the left. Intraocular pressures, pupillary examination, and anterior segment examinations were within normal limits. Her posterior examination in both eyes was notable for diffuse white vitreous opacities organized in a sheet-like configuration around the posterior pole (). The retina appeared otherwise normal. Ultra-widefield fluorescein angiography showed blockage from the vitreous opacities (). However, there were also linear fluorescent structures corresponding to the Gaucher material that did not appear to be consistent with retinal vessels, with some exhibiting late leakage (). There was no optic disc or retinal vascular leakage. Optical coherence tomography angiography revealed normal superficial and deep vascular plexuses in the macula. Peripheral OCT angiography through the areas of nonvascular late leakage demonstrated blockage without intrinsic flow signal (). Structural OCT of the right macula demonstrated a complete PVD with optically empty vitreous. The left macula had an attached hyaloid with a premacular bursa. Inferior cuts revealed the presence of vitreous opacities at the vitreoretinal interface (). The patient was observed, and 1 year later, her visual acuity improved to 20 of 30 in both eyes.

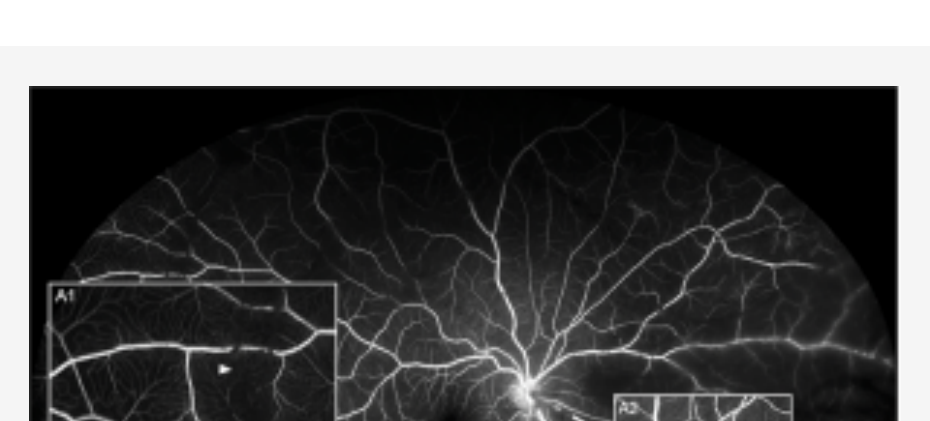

Fig. 1.
Optos pseudocolor images of Type 3 Gaucher patient at presentation. Ultra-widefield images of the right (**A**) and left (**B**) eyes demonstrate bilateral vitreous opacities in a sheet-like configuration.

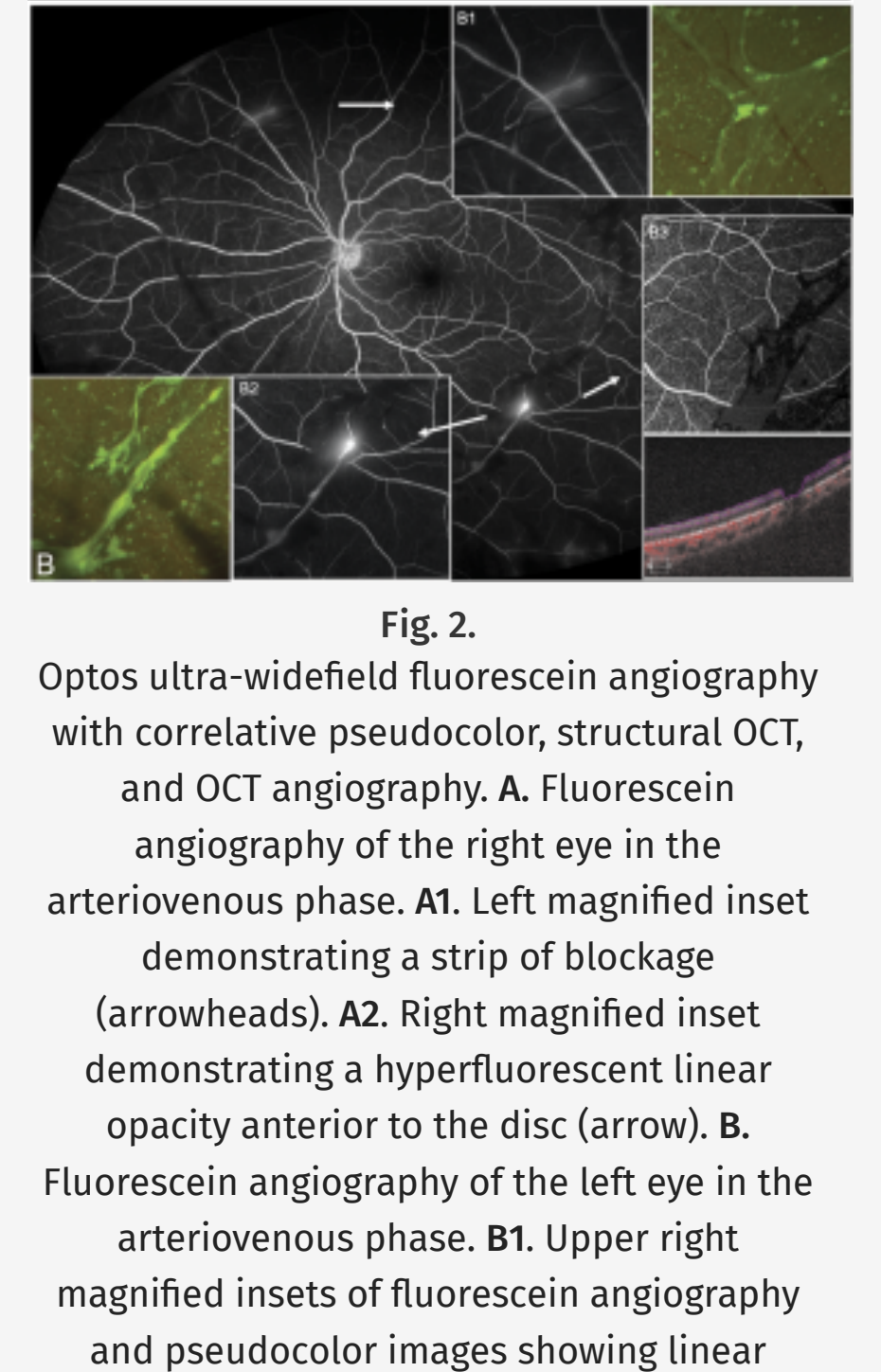

Fig. 2.
Optos ultra-widefield fluorescein angiography with correlative pseudocolor, structural OCT, and OCT angiography. **A.** Fluorescein angiography of the right eye in the arteriovenous phase. **A1.** Left magnified inset demonstrating a strip of blockage (arrowheads). **A2.** Right magnified inset demonstrating a hyperfluorescent linear opacity anterior to the disc (arrow). **B.** Fluorescein angiography of the left eye in the arteriovenous phase. **B1.** Upper right magnified insets of fluorescein angiography and pseudocolor images showing linear preretinal deposits orthogonal to retinal vessels. **B2.** Lower left magnified insets of fluorescein angiography and pseudocolor images, corresponding to the region indicated by the adjacent arrow showing linear preretinal deposits orthogonal to retinal vessels. **B3.** Optical coherence tomography angiography 6 mm × 6 mm image of the superficial vascular plexus corresponding to the region indicated by the adjacent arrow demonstrates blockage artifact without intrinsic flow signal. The corresponding structural B-scan with flow overlay shows segmentation artifact without evidence of flow.

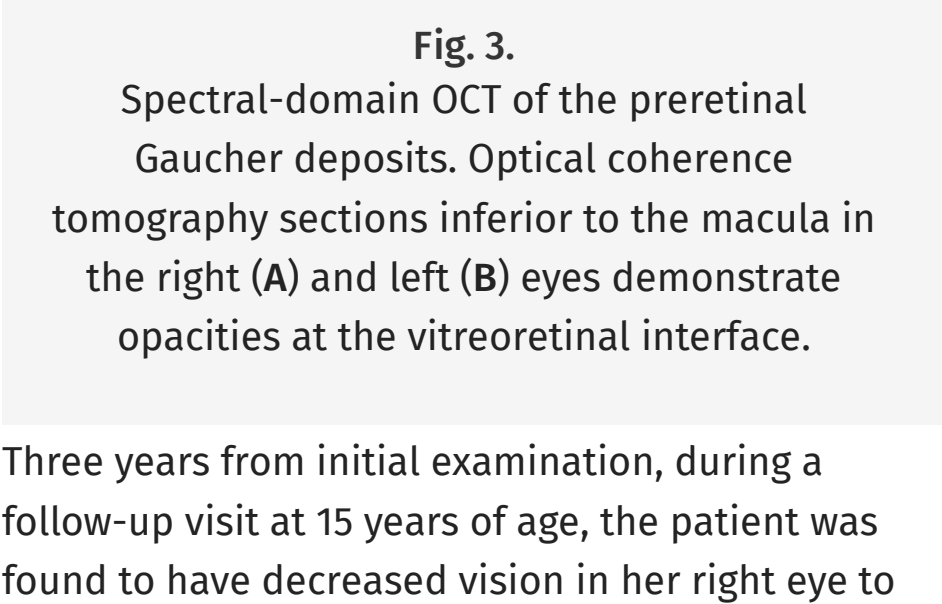

Fig. 3.
Spectral-domain OCT of the preretinal Gaucher deposits. Optical coherence tomography sections inferior to the macula in the right (**A**) and left (**B**) eyes demonstrate opacities at the vitreoretinal interface.

Three years from initial examination, during a follow-up visit at 15 years of age, the patient was found to have decreased vision in her right eye to hand motion. Dilated fundus examination revealed vitreous opacities with dense underlying vitreous hemorrhage (). On ultrasonography, the retina was attached with vitreous opacities and a thickened hyaloid face detached from the optic nerve (). Close monitoring for 8 weeks after presentation revealed no improvement. The decision was made to proceed with vitrectomy and scleral buckle placement to support any peripheral traction. Intraoperatively, she was found to have a subhyaloid hemorrhage with an epiretinal membrane, which was confirmed on intraoperative OCT. The epiretinal membrane and inner limiting membrane were peeled. A vitreous biopsy was sent to pathology.

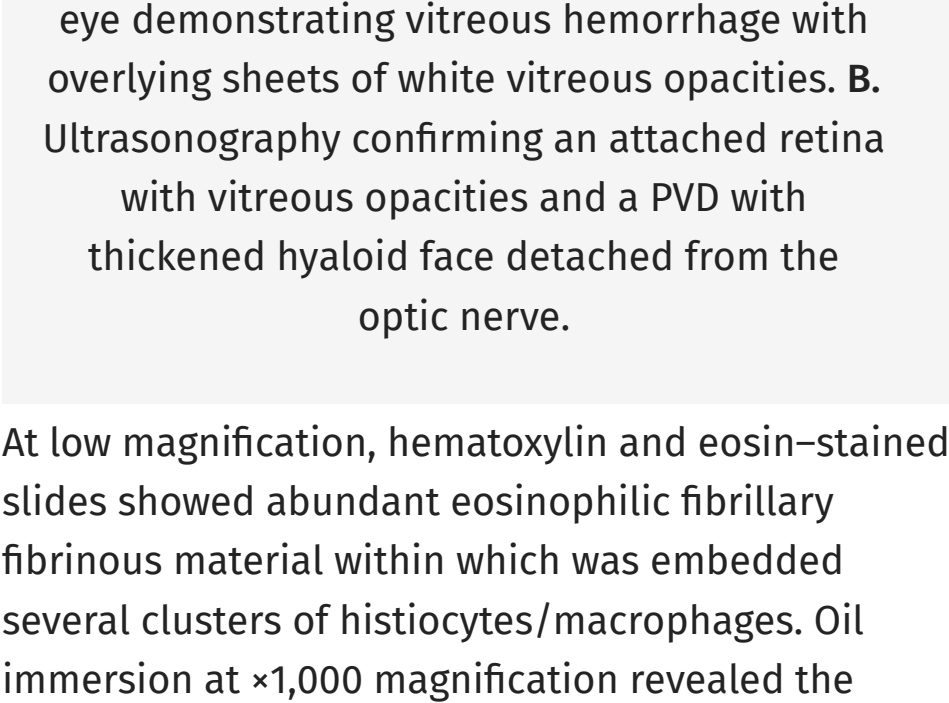

Fig. 4.
Hemorrhagic posterior vitreous separation in the right eye. **A.** Optos ultra-widefield pseudocolor fundus photograph of the right eye demonstrating vitreous hemorrhage with overlying sheets of white vitreous opacities. **B.** Ultrasonography confirming an attached retina with vitreous opacities and a PVD with thickened hyaloid face detached from the optic nerve.

At low magnification, hematoxylin and eosin–stained slides showed abundant eosinophilic fibrillary fibrinous material within which was embedded several clusters of histiocytes/macrophages. Oil immersion at ×1,000 magnification revealed the characteristic crinkled tissue paper cytoplasmic appearance (, red arrows) of these Gaucher cells as well as the nuclear folds (, black arrows), a telltale feature of histiocytes. The Gaucher cells were highlighted with the periodic acid-Schiff stain (PAS), revealing an intensely pink cytoplasmic staining pattern against the pale-pink fibrinous background (). By immunohistochemistry, the cells showed strong and diffuse cytoplasmic staining with CD68 () and CD163 () immunohistochemical stains, confirming the histiocytic nature of these cells. Overall, these histopathologic features are consistent with intraocular involvement of Gaucher disease. There are previous reports of Gaucher cells with wrinkled cytoplasm from vitreous biopsy in two other cases, but here, we include additional stains (CD68 and CD163) to confirm their histiocytic nature.

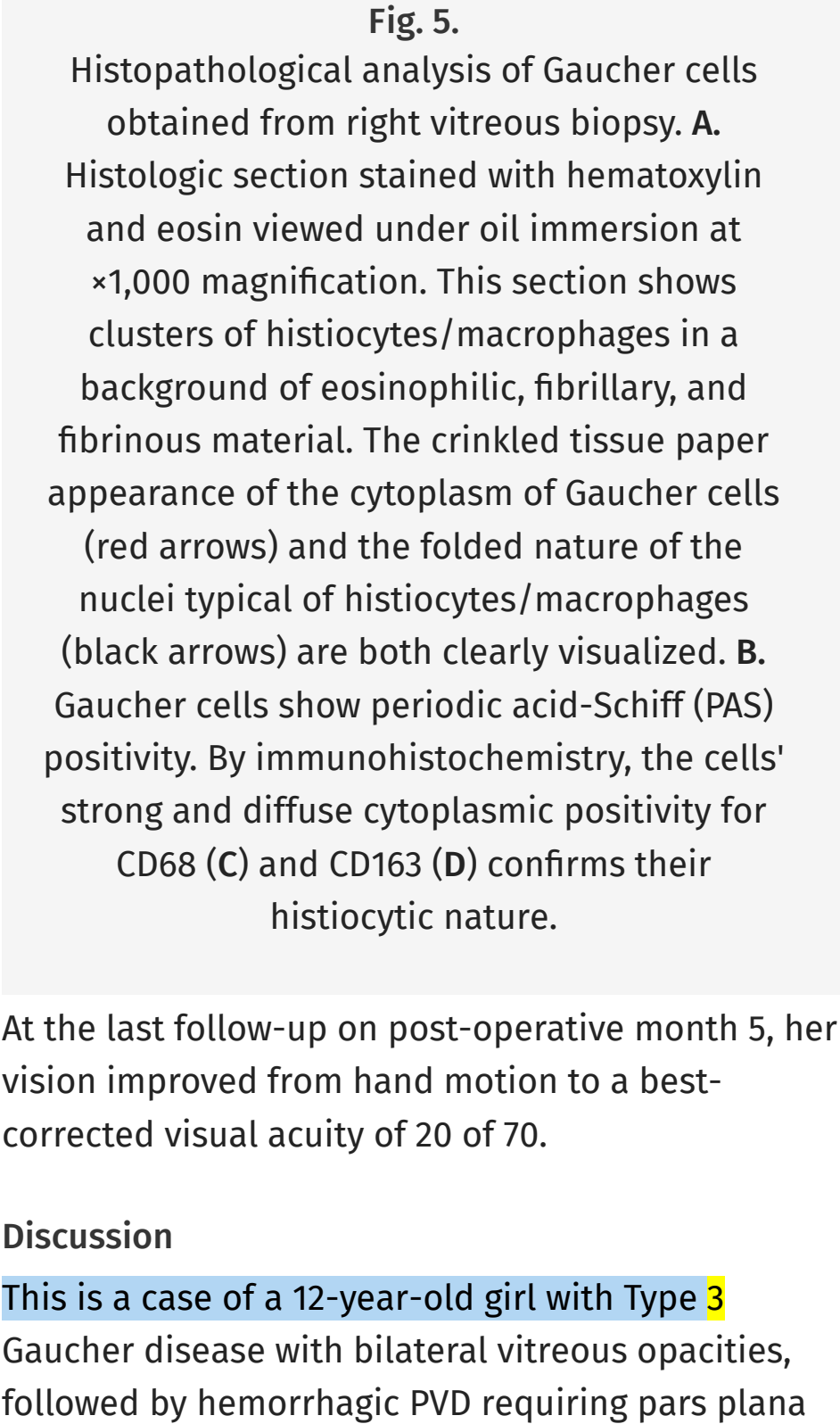

Fig. 5.
Histopathological analysis of Gaucher cells obtained from right vitreous biopsy. **A.** Histologic section stained with hematoxylin and eosin viewed under oil immersion at ×1,000 magnification. This section shows clusters of histiocytes/macrophages in a background of eosinophilic, fibrillary, and fibrinous material. The crinkled tissue paper appearance of the cytoplasm of Gaucher cells (red arrows) and the folded nature of the nuclei typical of histiocytes/macrophages (black arrows) are both clearly visualized. **B.** Gaucher cells show periodic acid-Schiff (PAS) positivity. By immunohistochemistry, the cells' strong and diffuse cytoplasmic positivity for CD68 (**C**) and CD163 (**D**) confirms their histiocytic nature.

At the last follow-up on post-operative month 5, her vision improved from hand motion to a best-corrected visual acuity of 20 of 70.

Discussion

This is a case of a 12-year-old girl with Type 3 Gaucher disease with bilateral vitreous opacities, followed by hemorrhagic PVD requiring pars plana vitrectomy. The differential diagnosis for bilateral vitreous opacities in our patient included ophthalmic involvement of Gaucher, pars planitis, and less likely malignancy. Notably, our patient had a quiet anterior segment examination without active vitreous cells or evidence of a choroidal or retinal mass. Later, pathology from the vitreous biopsy confirmed the presence of Gaucher cells without evidence of malignancy.

Gaucher disease is a rare, autosomal recessive disorder because of glucocerebrosidase enzyme deficiency, leading to the accumulation of glucosylceramide in various tissues and is associated with a number of ophthalmic manifestations. The extent of vitreous involvement can be mild, with vitreous opacities at the vitreoretinal interface, to severe, leading to epiretinal membrane formation and tractional retinal detachment. Our case is consistent with previous cases in that tractional complications developed from the abnormal vitreous, in this case hemorrhagic PVD. Ultra-widefield fluorescein angiography revealed staining and leakage from the linear Gaucher opacities—possibly a result of intrinsic fluorescence of the material or more likely from retinal traction (). The OCT angiography performed here () argues against any intrinsic vascular flow of these opacities. The opacities at the vitreoretinal interface on spectral domain OCT have been reported in three other cases. Other spectral domain OCT findings in Gaucher disease include epiretinal membrane and subretinal drusen-like deposits. To the best of our knowledge, these fluorescein and OCT angiography findings have not been reported previously in the literature.

A few years after initial presentation, this patient had a hemorrhagic PVD. Tractional retinal detachments as a result of intraocular involvement by Gaucher disease have been reported previously in the literature, but to the best of our knowledge, this is the first report of hemorrhagic PVD in Gaucher requiring pars plana vitrectomy. Previous case reports have noted vitreous syneresis during pars plana vitrectomy and have postulated an association between localized vitreous detachments and retinal traction. A similar mechanism may be responsible for our patient's hemorrhagic PVD and led to the decision to place a band to support the vitreous base.

Although patients with Gaucher commonly have thrombocytopenia and clotting factor abnormalities, our patient had a normal platelet count, prothrombin time, and partial thromboplastin time. Interestingly, there have been reports of thrombocytopathy in Gaucher causing bleeding abnormalities in spite of normal platelet count and coagulation studies. Previous vitrectomy specimens in patients with Gaucher disease have revealed the presence of Gaucher cells (macrophages laden with glycolipid products) and high concentrations of glucocerebroside seen on thin-layer chromatography. The pathology in this case revealed similar Gaucher cells ().

In summary, we present a case of a 12-year-old woman with Type 3 Gaucher disease and bilateral vitreous opacities characterized by ultra-widefield fluorescein and OCT angiography. Evaluation of the vitreous by histopathology confirmed the presence of Gaucher cells.

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