Intercalary membrane as the inner wall overlying optic and chorio-retinal colobomas. Deep penetration Swept Source-OCT study

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Five eyes of four patients were studied to analyze the structure of the inner wall of optic and chorioretinal colobomas using swept-source optical coherence tomography (SS-OCT). The colobomatous cavities and their relationship with adjacent structures were examined. SS-OCT permitted the study of the colobomatous cavities in all cases. In four of those cases, a Y-shaped intercalary membrane (ICM) was identified, with an origin in the retinal nerve fiber layer (RNFL), which covered the coloboma and in one case the coloboma was in contact with the vitreous cavity. Vitreous adhesion to the internal wall of the coloboma was found in three cases. No clinical or tomographic maculopathy was observed in any patient. High-resolution deep penetration SS-OCT allows *in vivo* study of optic and chorioretinal colobomas, identifying the RNFL as the main component of the ICM overlying the colobomatous cavities.

Key words: Chorioretinal coloboma, optic coloboma, subarachnoid space, swept-source optical coherence tomography

Congenital disc pit, chorioretinal coloboma and morning glory anomaly belong to the same group of congenital optic nerve anomalies.[1-4] Colobomas are optic disc anomalies originated by a closure defect of the embryonic fissure and/or alterations in the peripapillary sclera.[5] Even though, some authors state that there is a cause-effect relation between closure defects and congenital disc pits, this has not been clearly defined in the case of colobomas and morning glory anomaly.[6] That is why they are included in the group of atypical colobomas as isolated congenital cavitary anomalies.[6]

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Macular involvement may be present in 32%–50% of the patients suffering from these two diseases.[1,7] It appears to be secondary to schisis-like vitreous detachment, while peripapillary traction may favor fluid leak toward the intraretinal space.[2,8,9] Patient's visual acuity can be further affected by the appearance of retinal detachments (RDs), which have been described in up to 40% of eyes affected by this condition.[3,10]

They can be classified into three groups depending on their macular involvement as follows: without macular affection; optical coherence tomography (OCT) signs of maculopathy that cannot be detected with biomicroscopy; and eyes with clinical and tomographic maculopathy.[1]

We analyzed the characteristics of the inner wall and findings of optic and retinochoroid-sclera colobomas with swept-source OCT (SS-OCT).

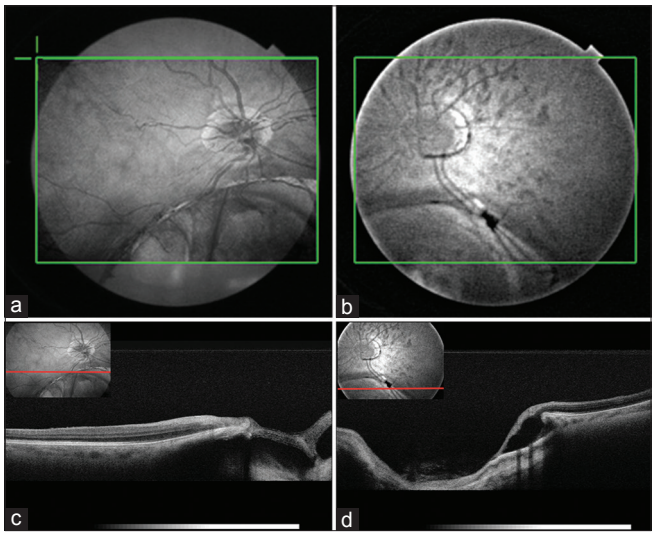

Figure 1: (a) Fundus photography of the first case (the right eye). (b) Fundus photography of the first case (the left eye). (c) Case 1 right eye. B-scan swept-source optical coherence tomography shows a "Y-shaped" retina in the colobomatous area. All the retinal layers are fused. The transition zone between the normal retina and the coloboma shows a hyper-reflective layer in continuation with chorioretinal layers but lacking the typical layering of normal retina, with marked choroidal cavitation. (d) Case 1 left eye. The left eye showed an ecstatic sclera in the area of the coloboma with an abrupt transition from the normal retina to intercalary membrane. Note the total lack of layering in the intercalary membrane. The subintercalary membrane space indicates an elevated intercalary membrane and subintercalary membrane fluid. Note the intact zone of least resistance and hence no spread of the sub-intercalary membrane fluid into subretinal space

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Case Report

Case 1 (both eyes)

A 51-year-old male patient with retinachoroid-sclera inferior coloboma in both eyes with normal retina between the optic disc and the coloboma [Fig. 1a and b]. SS-OCT showed a "Y-shaped" retina in the right eye (RE) with a fusion of retinal layers, not being able to identify any retinal layers at this level, toward the edge of the coloboma [Fig. 1c]. The abrupt transition zone between the normal retina into the intercalary membrane (ICM) at the level of the coloboma showed a hyper-reflective area in continuation with chorioretinal layers but lacking the typical layering of normal retina [Fig. 1c].

The left eye (LE) showed an ecstatic sclera in the area of the coloboma with an abrupt transition from the normal retina to ICM. Note the total lack of layering in the ICM. The subICM space indicates an elevated ICM and subICM fluid. Note the intact zone of least resistance and hence no spread of the subICM fluid into the subretinal space [Fig. 1d]. This case shows the same abrupt transition between the normal retina and the ICM in continuation with the retinal nerve fiber layer (RNFL). The retinal pigment epithelium (RPE) and the choroid end abruptly, whereas the retina, choroid, and sclera appear as a single layer in the nasal aspect, forming the nasal wall of the coloboma. Macula was normal in both eyes.

Case 2

A 23-year-old female patient with RD of RE secondary to optic coloboma, presented optic nerve and retinachoroid-sclera inferior coloboma in her LE [Fig. 2a]. SS-OCT showed a "Y-shaped" image inside the coloboma [Fig. 2b]. The retina was reduced to a single hyper-reflective layer, in apparent continuity with the inner layers of the retina, especially the RNFL, even though this is not as clear as in the previous case (arrow). Remnants of external retinal layers could be observed in the temporal edge of the coloboma (arrow head).

The subretinal space seems connected with the subarachnoid space (SAS) in its nasal aspect (arrow), with no cystic changes of the retina [Fig. 2b]. Superior sectors showed no visible connection with the SAS [Fig. 2c] and minimal cystic changes (arrow) could be seen in the temporal one [Fig. 2d]. Normal macula and healthy retina surrounding the coloboma could be observed transitioning progressively toward a disappearance of the external retinal layers [Fig. 2e].

Case 3

A 55-year-old female patient with LE phthisis bulbi secondary to RD, presented a retinachoroid-sclera coloboma in the RE [Fig. 3a]. A "Y-shaped" image formed by the ICM was observed [Fig. 3b], together with vitreoretinal adhesions and small cystic cavities affecting the external temporal retina. The transition between the normal retina and the ICM shows

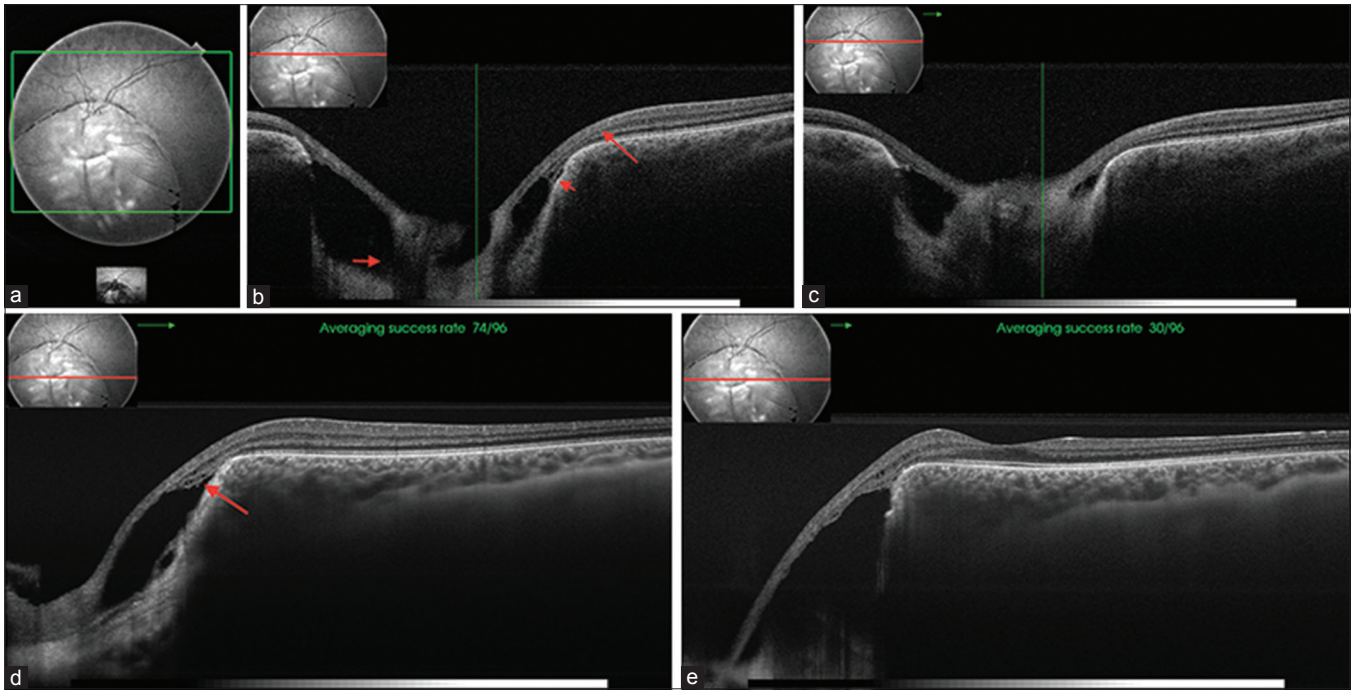

Figure 2: (a) Fundus photography of case two. (b) Case 2 left eye. B-scan swept-source optical coherence tomography shows a similar centrally excavated "Y-shaped" image. The retina is reduced to a single intercalary membrane. Remnants of the retinal layers can be observed in the temporal aspect. The existing cavities seem connected with the subarachnoid space in both sides. This fluid does not induce any alteration in the retina. (c) Case 2 left eye. B-scan swept-source optical coherence tomography at the bottom of the coloboma shows the same structures with smaller cavities, bigger central structures. Connection with the subarachnoid space is not visible. (d) Case 2 left eye. B-scan swept-source optical coherence tomography at temporal sector of the colobomatous cavity in greater detail, shows an intramural cystic space in the wall of the coloboma and the cavity formed by the intercalary membrane. Small round-shaped cystic spaces are clearly visible in the inner nuclear layer and the outer plexiform layer. The fluid of the cavity does not affect the retina. (e) Case 2 left eye. B-scan swept-source optical coherence tomography scan centered on the macula, shows normal, healthy retina. In the edge of the coloboma a transition area can be seen with fusion of retinal layers. Small cystic spaces are visible in the inner nuclear layer

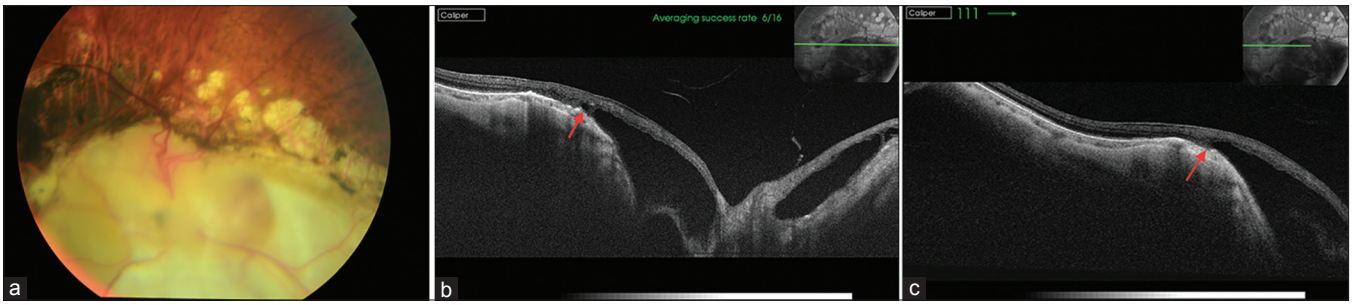

Figure 3: (a) Fundus photography of third case. (b) Case 3 right eye. B-scan swept-source optical coherence tomography shows a "Y-shaped" image formed by the intercalary membrane reaching the bottom of the coloboma. There is a vitreoretinal attachment in the nasal aspect and a small cystic cavity affecting the external retina in the temporal sector. The transition between the normal retina and the OCM shows a progressive disappearance of the outer retinal layers (arrow) when it reaches the colobomatous cavity. This case shows a higher reflectivity in the nasal side, making its continuation with the retinal nerve fiber layer more likely. (c) Case 3 right eye. B-scan swept-source optical coherence tomography at the retinal transition in greater detail in the temporal sector

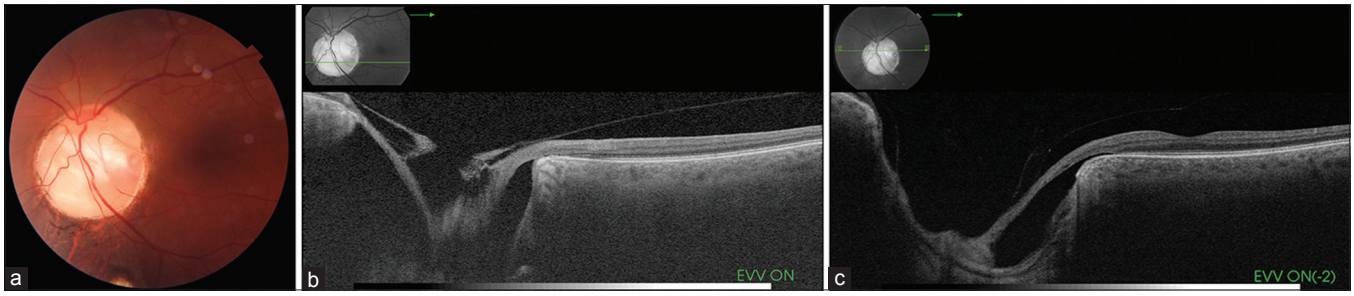

Figure 4: (a) Case 4. Fundus photography of the optic nerve coloboma in the left eye. (b) Case 4. B-scan swept-source optical coherence tomography showed a "Y-shaped" image inside the coloboma with important vitreoretinal adhesion to the inner wall of the coloboma. (c) Case 4. B-scan swept-source optical coherence tomography. The retina was reduced as in the previous cases to a single intercalary membrane. The fovea was normal

a progressive disappearance of the outer retinal layers (arrow) when it reaches the colobomatous cavity. This case shows a higher reflectivity in the nasal side, making its RNFL origin more likely.

Vertical scans showed a flattened, poorly differentiated retina overlying the coloboma. The temporal scan showed the same transition in greater detail [Fig. 3c], showing the disappearance of external layers of the retina come the cavity (arrow).

Case 4

A 42-year-old woman with RD of RE secondary to optic coloboma, presented optic nerve coloboma in her LE [Fig. 4a]. SS-OCT showed a "Y-shaped" image inside the coloboma with important vitreoretinal adhesion to the inner wall of the coloboma [Fig. 4b]. The retina was reduced as in the previous cases to a single hyper-reflective RNFL [Fig. 4c] with progressive disappearance of the external layers of the retina once they reach the cavity (arrow).

Discussion

Pathological studies in eyes with optic disc colobomas have described a widened scleral canal with optic nerve atrophy and posterior displacement of the lamina cribrosa.[11,12] Ohno-Matsui found the SAS posterior to the colobomatous excavation (SS-OCT), with a thin hyper-reflective tissue between the subretinal space and the SAS, considered as pia mater.[2] A communication between the colobomatous cavity and the SAS has not been previously published, but silicone oil migration into the cerebral structures has been reported in a patient with disc pit and surgeries with elevated intraocular pressure.[13] Fig. 2b shows this connection between the SAS and the colobomatous cavity in our case series.

The neural retina continues as ICM in the area of the coloboma.[3] This transition may be abrupt or, more often, gradual.[6] Histopathologic studies have shown that there is a gradual thinning of the retina into the ICM,[3] and have revealed that the ICM consisting of rudimentary retinal tissue including aberrant nerve fibers and pigmented tissue resembling RPE.[14] The outer layers of the retina disappear while inner layers turn into the ICM.[3,6] Our cases show that the ICM is mainly made from RNFL in our SS-OCT images.

The concave shape that appears inside the colobomatous cavities [Figs. 1d, 2b-e, 3b-c, and 4b-c] would indicate they are full of fluid. This subICM fluid may be originated in the SAS in cases in which the optic disc is included in the coloboma but not when it is located outside of it. Gopal *et al*.[15] states that the origin of the subICM fluid is the vitreous cavity through small breaks in the area of least resistance, named "Locus minoris resistentiae", and located on the edge of the coloboma at the level of the ICM.[16]

Doyle identified a membrane-spanning across the optic disc in patients with optic disc coloboma that might prevent them from suffering maculopathy.[1] Following a detailed study of our images, we can identify this membrane as originated mainly from RNFL [Figs. 1d, 2b-d, 3b-c, and 4c].

The limitations of our study are the number of eyes studied, the difficulties to obtain the images with enough quality of the entire colobomatous cavities and the impossibility to obtain good images from the deepest area of the colobomas.

Conclusion

We describe this pathology "*in vivo*" using SS-OCT, with a Y-shaped ICM forming several cavities in the colobomatous pit, originated mainly from RNFL. The ovoid morphology of the cavities suggests that they are full of fluid. SS-OCT helped identify the RNFL as the main component of the ICM overlying the colobomatous cavities.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient had given his consent for his images and other clinical information to be reported in the journal. The patients understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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