

## Pattern of blood vessels in eyes with coloboma

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**Background:** Choroidal coloboma, especially with optic disc involvement affects the blood vessel (BV) pattern in the fundus. **Aim:** The aim of this study was to report the observations on the pattern of retinal BVs in eyes with fundus coloboma. **Design:** Retrospective observational study. **Materials and Methods:** Twenty four eyes of 19 patients with fundus coloboma and the disc involvement in the coloboma was classified according to a previous publication. **Results:** Four varieties of BVs were identified in the area of coloboma – BVs that were continuous with those arising from the optic disc; vessels emanating from the floor of coloboma whose continuity with central retinal artery or its branches could be indirectly established; and those emanating from the floor of coloboma whose continuity with central retinal artery could not be established. In addition, extraocular BVs were visible through the thinned sclera. The retinal BVs often traversed the coloboma to reach the normal retina. The disc itself was found to be small and had no physiological cup (if not colobomatous). **Conclusions:** One should be aware of the major BVs transgressing the coloboma while performing relaxing cuts in the intercalary membrane, during the surgery for retinal detachments in eyes with coloboma. Physiological cup is usually absent (when the disc is not colobomatous). Hence, any cupping in such eyes should be viewed with suspicion.

**Key words:** Coloboma of the choroid, coloboma optic disc, indo cyanine green angiography, vascular pattern

Coloboma of choroid is caused by the defective closure of the embryonal fissure.<sup>[1]</sup> Typically, the area affected by the coloboma lacks choroid and retinal pigment epithelium (RPE). The retina is ill developed and consists of the inner layers of the retina continuing as intercalary membrane. Proportional to the severity of the defect, the size and anteroposterior extent can vary. In addition, the optic disc can be involved in the process to a variable extent. Six types of disc involvement have been described in eyes with coloboma of the choroid.<sup>[2]</sup> Types 1, 2 and 3 have the optic disc located outside the coloboma of the choroid with Type 1 having normal looking disc, Type 2 having abnormal and sometimes dysplastic disc and Type 3 having independent coloboma of the disc. In Type 3, the coloboma of the disc was described both as a concentric or eccentric lesion. Types 4, 5 and 6 have the disc included within the coloboma of the choroid with Type 4 having a nearly normal looking disc, Type 5 with coloboma of the disc as well and Type 6 having no recognizable disc substance inside a large coloboma of the choroid. The pattern of both retinal and choroidal blood vessels (BVs) is affected in the area of the coloboma. Casper (as quoted by Duke Elder) described three patterns of emergence of BVs from the optic disc in these cases.<sup>[3]</sup> (1) The most common arrangement was found to be the emergence of BVs from the lower part of the colobomatous disc. The BVs meant for the inferior fundus made a sharp bend, kinking over the edge before proceeding inferiorly while the BVs meant for superior

fundus progress directly across the excavated portion of the colobomatous disc. (2) A normal looking arrangement of BVs emanating from approximately the center of the colobomatous disc. (3) Bvs emanate from the edge of the colobomatous disc resembling cilio-retinal vessels. While Casper's observations are in principle true, a lot more variation was noted in our study.

### Materials and Methods

This is a study of 24 eyes of 19 patients (5 were bilateral) with coloboma of the choroid. The study was conducted after approval from the Institutional Ethics Committee. In 19 eyes, color pictures (14 montage) were analyzed while in 5 eyes, indo cyanine green (ICG) angiography was carried out in addition to color photography. The color pictures were from the already existing records while five patients were prospectively enrolled for ICG angiography. These were from among patients with fundus coloboma that were seen in the out-patient department and who were willing to go through ICG angiography. We categorized the cases with reference to the type of optic disc involvement in the choroidal coloboma.<sup>[2]</sup>

There were eight eyes with Type 1 disc involvement (normal looking disc outside the fundus coloboma); two eyes with Type 2 disc involvement (disc outside of the fundus coloboma and dysplastic), two eyes with Type 3 disc involvement (disc outside of the fundus coloboma and independently colobomatous), one eye with Type 4 disc involvement (disc normal looking but inside the fundus coloboma); 10 eyes with Type 5 disc involvement (disc involved within the fundus coloboma and also colobomatous) and one with Type 6 involvement (disc substance not made out clinically).

The color pictures and the angiograms were studied to evaluate the pattern of BVs emerging from the optic disc and the affect that the choroidal coloboma had on the distribution of the BVs in the inferior fundus. ICG angiography was carried out in five eyes to specifically study the choroidal vasculature.

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Incidentally, it also permitted the tracing of BVs to decide the true origin of the same.

## Results

Since the optic disc involvement in the coloboma seems to be the most important factor that dictated the pattern of BVs observed, we chose to present our results in terms of variation in the emergence of the BVs from the optic disc, their subsequent course and the variety of BVs noted in relation to the coloboma of choroid. The salient features observed in each of the 24 eyes are listed in Tables 1 and 2.

### Emergence of BVs from disc

#### Type 1

There were eight eyes with Type 1 involvement of disc in the coloboma [Figs. 1-3]. In Type 1, the disc is located outside the coloboma and is essentially normal. However, a flattening of the inferior border was noted in all the cases and this feature was more prominent when the disc was relatively close to the upper border of the coloboma of the choroid. The BVs emanated from the disc normally, but those for the upper part of the fundus had their course modified depending on the size of the choroidal coloboma. There is no uniformity in this alteration.

1. In some, the BVs were pushed to the margin of the coloboma
2. In others, the BVs coursed smoothly across the coloboma to reach the normal retina (unaltered course)
3. In two cases, the inferotemporal vessels had a relatively vertical course down into the coloboma (as if they have been pulled down), from where they looped up across the coloboma into the normal temporal retina while the infero nasal BVs had unaltered course across the coloboma. The choroidal coloboma in both these eyes reached up to the macula.

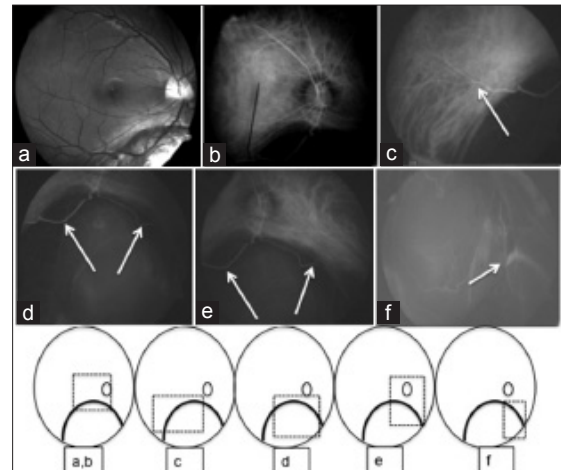
The physiological cup was found to be absent in all cases of Type 1 in this series.

#### Type 2

There were two eyes in this category [Fig. 4]. The optic discs were dysplastic, but located outside the coloboma of the choroid. The pattern of emergence of BVs from the optic disc and the modification in the course of the inferior BVs was similar to Type 1. No physiological cup was noted in the optic disc.

#### Type 3

Two eyes in this series belonged to Type 3 where in the



**Figure 1:** Black and white photo (a) and indo cyanine green angiogram (b-f) of the right eye with coloboma (Type 1); (b) demonstrates a total lack of choroidal vasculature in the area of coloboma; (c) inferotemporal blood vessel is seen going across the coloboma into the normal temporal retina (white arrow); (d and e) inferotemporal and infero nasal blood vessels from the optic disc going across the coloboma (white arrows); (f) the extraocular vortex vein made out inferonasally (white arrow) (line drawings were added to give better orientation of the photographs in relation to the coloboma)

**Table 1: Pattern of blood vessels in types 1, 2 and 3 (disc outside the choroidal coloboma)\***

Patient no.	Type	Optic disc cup	Emergence of BV from disc	BV transiting coloboma to reach normal retina	BV emerging from the floor of coloboma	Extraocular BV visible
1						
OD	1	Absent	Normal	√	√	×
OS	1	Absent	Normal	√	√	×
2 <sup>†</sup>	1	Absent	Normal	√	√	√
3 <sup>†</sup>	1	Absent	Normal	√	×	√
4 <sup>†</sup>	1	Absent	Normal	√	√	√
5 <sup>†</sup>	1	Absent	Normal	√	√	√
6						
OD	1	Absent	Normal	√	√	×
OS	1	Absent	Normal	√	√	×
7 <sup>†</sup>	2	Absent	Normal	√	√	√
8	2	Absent	Normal	×	×	×
9 <sup>††</sup>	3	Eccentric disc coloboma	Inferotemporal BV pushed towards 6 o' clock by disc coloboma	NA	NA	NA
10 <sup>††</sup>	3	Concentric disc coloboma	Mimics glaucomatous cupping	NA	NA	NA

\*Classification according to Gopal *et al.* ophthalmology, 1996. <sup>†</sup>Five eyes had indo cyanine green angiography, <sup>††</sup>The fundus pictures in these two cases did not cover the choroidal coloboma area well and hence we could comment only on the vessel emergence from the optic disc and not on the subsequent passage.

√: Present; ×: Absent, NA: Information not available, OD: Right eye, OS: Left eye, BV: Blood vessel

**Table 2: Pattern of blood vessels in types 4, 5 and 6 (disc inside the choroidal coloboma)\***

Patient no.	Type	Optic disc	Emergence of superior vessels	Emergence of inferior vessels	BV transiting coloboma to reach normal retina	BV emerging from the floor of coloboma	Extra ocular BV visible
11	Type 4	No cup seen	Normal	Normal	√	×	×
12							
OD	Type 5	Disc coloboma inside choroidal coloboma	Arise from the inferior border of identifiable disc and loop upwards across the disc	None seen directly from disc	√	√	√
OS	Type 5	Disc coloboma inside choroidal coloboma	Arise from inferior border of identifiable disc and loop upwards across disc	None seen directly from disc	√	√	√
13							
OD	Type 5	Disc coloboma inside choroidal coloboma	Arise from inferior border of identifiable disc and loop laterally across disc	Inferonasal BV emerges from disc	√	√	×
OS	Type 5	Disc coloboma inside choroidal coloboma	Arise from inferior border of identifiable disc. Superior-temporal BV goes across disc, while superonasal BV goes across coloboma	None seen directly from disc	√	√	×
14	Type 5	Disc coloboma inside choroidal coloboma	Arise from inferior border of identifiable disc and loop upwards across disc	None seen directly from disc	√	√	×
15	Type 5	Disc coloboma inside choroidal coloboma	Arise from inferior border of identifiable disc and loop upwards across disc	None seen directly from disc	√	√	√
16	Type 5	Disc coloboma inside choroidal coloboma	Arise from inferior border of identifiable disc and loop upwards across disc	None seen directly from disc	√	√	√
17							
OD	Type 5	Disc coloboma inside choroidal coloboma	Arise from inferior border of identifiable disc and loop upwards across disc	None seen directly from disc	√	√	×
OS	Type 5	Disc coloboma inside choroidal coloboma	Arise from inferior border of identifiable disc and loop upwards across disc	None seen directly from disc	√	√	×
18	Type 5	Disc coloboma inside choroidal coloboma	Arise from inferior border of identifiable disc and loop upwards across disc	None seen directly from disc	√	√	×
19	Type 6	Disc substance not identified clinically	BV seen emerging at margin of coloboma	BV seen emerging at margin of coloboma	NA	NA	NA

\*Classification according to Gopal *et al.* ophthalmology, 1996. √: Present, ×: Absent, NA: Information not available, OD: Right eye, OS: Left eye, BV: Blood vessel

optic disc is independently colobomatous and separated from the choroidal coloboma. In the eye with eccentrically located disc coloboma, the superior vessels emanated normally while the inferotemporal vessels were displaced nasally. In the eye with central coloboma, the vessels emanate normally – the upper vessels coming out superiorly and lower ones inferiorly – almost mimicking glaucomatous cupping.

#### Type 4

There was one case with Type 4 abnormality. The disc was of normal shape and located inside the coloboma of the choroid. The inferior vessels emerged normally from the center of the disc and spread downward across the coloboma. The superior trunk was partly hidden by the coloboma margin. No physiological cup was observed.

#### Type 5

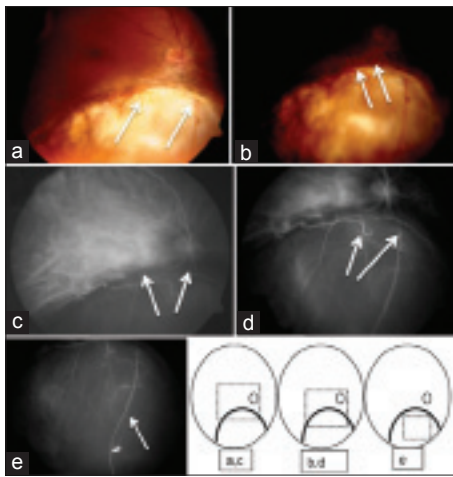
There were 10 eyes with Type 5 abnormality, where in the optic disc coloboma is continuous with choroidal coloboma [Fig. 5].

#### Emergence of superior BVs

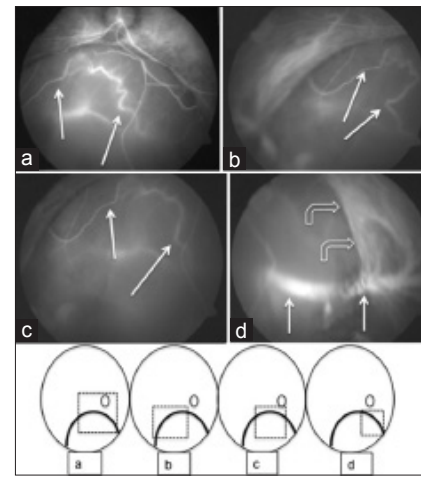
The vessels for superior fundus emanated from the inferior border of the identifiable part of the optic disc. In eight eyes, they were seen to loop upward across the optic disc to reach the upper fundus. In one eye, they looped laterally and in another the BVs coursed across the coloboma to reach the upper fundus.

#### Emergence of inferior BVs

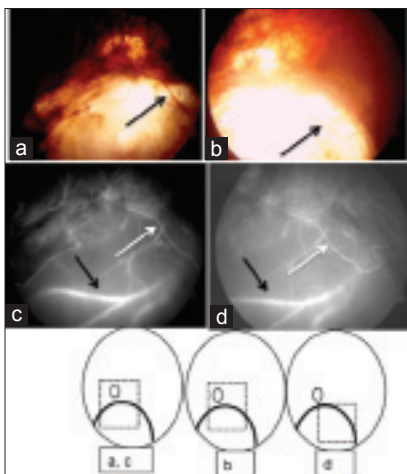
The vessels meant for the inferior fundus did not have a fixed point of emergence. In most cases, a deeply excavated area was seen immediately below the identifiable optic disc-perhaps



**Figure 2:** Right eye with coloboma (Type 1). (a) Color photograph depicting the inferotemporal and inferonasal veins emerging from the floor of coloboma (white arrows); (b and c) color photograph and indo cyanine green (ICG) angiogram showing the retro illuminant patch of hypopigmentation between coloboma and disc margin and the lack of choroidal vasculature in this area (white arrows); (d) the continuity between the emergence of inferotemporal and inferonasal blood vessels at the disc and their reemergence from the floor of coloboma (the segment in between being intra scleral) can be inferred from this ICG angiogram; (e) Course of inferonasal vessel in the coloboma seen on ICG angiogram. Note the near absence of any branches (line drawings were added to give better orientation of the photographs in relation to the coloboma)

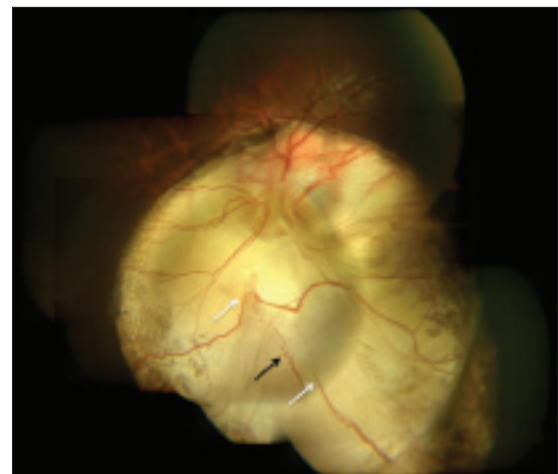


**Figure 3:** Right eye with coloboma (Type 1). (a-c) Indo cyanine green (ICG) angiogram showing varying shape of the same vessel seen in different frames (observe the segment between the two white arrows); (d) ICG angiogram showing the vortex ampulla and extraocular part of vortex vein (straight white arrows). The bent arrows identify the coloboma margin where the choroidal vasculature stops short (line drawings were added to give better orientation of the photographs in relation to the coloboma)



**Figure 4:** Left eye with coloboma (Type 2). (a and b) Color photographs showing the inferotemporal vessel from the optic disc continuing across coloboma in to normal temporal retina; (c and d) the same vessel is better identified in its entire length on indo cyanine green angiogram (white arrow). Note the extraocular vessel seen inferiorly (black arrow). Fine retinal blood vessels are also seen in a random fashion within the coloboma (line drawings were added to give better orientation of the photographs in relation to the coloboma)

representative of the optic disc part of the coloboma. The inferior vessels were seen to emanate along the side of this ridge-usually as multiple BVs rather than as a single trunk. There were also other point sources of BVs within the floor of coloboma with no continuity seen with the optic disc BVs. Some of these had corkscrew shape.



**Figure 5:** Color photograph of Type 5 disc involvement in coloboma of choroid-left eye. Note superior vessels emanating from the lower border of identifiable disc substance and proceeding upward. Vessels for lower fundus emanate at multiple points in the floor of the coloboma (white arrows)-these vessels perhaps are not continuous with the central retinal artery and could represent cilio-retinal arteries. Some of them could be traced into the normal retina. Note also the corkscrew shaped blood vessel in the floor of coloboma (black arrow)

#### Type 6

No photographs could be taken, due to severe nystagmus. Disc substance was difficult to identify clinically. BVs emanated from the margin of the coloboma of disc/choroid as well as from the bed of the coloboma. The vessels were mostly identified as cilio-retinal vessels.

#### Further course of the retinal BVs

Retinal BVs that supplied the normal extra-colobomatous retina was seen to either transit outside the coloboma or across the

coloboma. Within the coloboma, the BVs transited either within the intercalary membrane or within the ectatic sclera. While in the intercalary membrane, not many branches were given off and part of the vessel was sometimes hidden under the ledge of the coloboma. Once the vessel reached the normal retina, the normal pattern of branching was restored. Segments of the BVs were sometimes hidden in the ectatic sclera [Fig. 2]. On occasions, angiography was able to demonstrate the full extent of the vessel [Fig. 4].

### Choroidal vasculature

On ICG, choroidal vasculature was found to be completely absent in the area of coloboma. Choroidal vasculature was also absent in the areas just beyond the coloboma where there were pigmented or non-pigmented atrophic areas seen clinically. In one case where there is a narrow isthmus between the disc and the coloboma margin, this area was also found to be devoid of choroidal vasculature [Fig. 2].

### BVs seen in the colobomatous area

Four varieties of BVs were noted within the colobomatous area.

1. Retinal BVs that was continuous with the vessels emanating from the optic disc [Figs. 1 and 4]
2. Retinal BVs emanating from bed of coloboma whose continuity with central retinal artery or its branches emanating from the disc could be indirectly established [Fig. 2]
3. Retinal BVs emanating from the base of coloboma that were possibly cilio-retinal arteries and whose continuity with central retinal artery was not established [Fig. 5]. Some of these were purposeless BVs that emanated and ended within the coloboma and did not supply functional retina
4. Broad, deep BVs seen through the thinned sclera - presumably extraocular vessels [Figs. 3 and 4].

Large caliber vessels noted in the area of coloboma (no. 4 noted above) on ICG angiography were inferred to be extraocular vessels based on the following points:

- a. Clinically they are hard to decipher
- b. The shape of the BV appears to change in the different frames of the angiogram [Fig. 3]
- c. The margins of these vessels are rather blurred
- d. No continuity can be established with any intra ocular vasculature.

## Discussion

Developmentally, the embryonal fissure (fetal fissure) is formed in the ventral part of the optic vesicle and permits the entry of vascular mesoderm into the eyeball.<sup>[4,5]</sup> The hyaloid vessels are thus formed from the mesoderm and the proximal portions of these vessels are destined to be the central retinal BVs. The fetal fissure closes gradually between 5<sup>th</sup> and 6<sup>th</sup> week of gestation leaving a permanent opening at the anterior end of the optic stalk to permit the entry and exit of the hyaloid vessels.<sup>[4]</sup> In eyes with defective closure of the fissure, the inner layer (destined to develop into the neurosensory retina) grows faster than the outer layer (destined to develop into RPE), leading to eversion which laterally displaces the pigment epithelium-sometimes leading to the development of double layer of photoreceptors facing each other.<sup>[4,6]</sup> In view of this eversion, RPE is absent at the site of the defective fissure closure (coloboma). Since choroidal development is influenced by pigment epithelium, the choroid is absent in the area of coloboma as well.

The emergence of BVs into the fundus in a colobomatous eye and their subsequent distribution is a matter of great interest. Barring the description by Casper quoted by Duke Elder, the literature has been largely silent on this subject.<sup>[3]</sup> In our previous publication on the optic disc in coloboma, we have described six varieties of presentation based on the location of the optic disc inside or outside the anatomical limits of the choroidal coloboma as well as the disc shape or involvement in the coloboma.<sup>[2]</sup>

In the present observational study, we studied the pattern of BVs both within and outside the coloboma by careful evaluation of color pictures and in some cases with additional ICG angiography.

In the development of retinal vasculature, the peripapillary vessels are formed by a process of vasculogenesis from the vascular precursor cells while the rest of the vascularization proceeds by angiogenesis and is vascular endothelial growth factor (VEGF) dependent. The physiological hypoxia induced by the maturation of the retina liberates the VEGF in a controlled fashion and this leads to progressive angiogenesis. Thus, physiological angiogenesis is understood as a sequential mechanism proceeding from disc – anteriorly.<sup>[7]</sup>

Hence in a coloboma where in the retina is not properly developed in the area of involvement, one would expect no retinal vasculature - since there is no VEGF driven impetus for the vascularization. Although to a great extent this is true, there are some anomalies that defy simple explanation. Major BVs supplying the inferior normal fundus (outside the coloboma) has been seen to course through the coloboma either in the intercalary membrane or the ectatic sclera itself. More commonly however, they are located just outside the margin of the coloboma – as if they are splayed apart by the coloboma. In addition, some vessels similar to retinal vessels were seen to emerge from variable points in the bed of the coloboma and traverse down without supplying any normal retina. This suggests that major retinal BVs can form without functional retina to spur their growth.

One striking feature seen is the ease with which broad episcleral vessels are seen through the thin sclera.<sup>[8]</sup> In a previous study, we confused these BVs with large choroidal vessels.<sup>[2]</sup> However, our observations on ICG clarify that these are indeed extraocular vessels.

Although purely descriptive in nature, this study may have clinical significance. We observed that BVs supplying the extra colobomatous retina can bridge the coloboma in the intercalary membrane. This fact is important during the vitreo retinal surgery for retinal detachment. On occasions, the intercalary membrane can be taut and be responsible for failure to reattach the retina. Incisions in the taut intercalary membrane (a la retinotomies) can be done to relax the same.<sup>[9,10]</sup> However, such incisions should be carefully planned and executed in order to avoid any damage to the transgressing retinal BVs.

It was observed that the disc, when not colobomatous (Types 1, 2 and 4), is small with no physiological cup. Theoretically speaking, a small disc with no cup could be due to the normal number of nerve fibers that are crowded in a narrow scleral aperture (crowded disc) or less number of nerve fibers that did not need a larger scleral aperture. Where the disc is not colobomatous (Types 1, 2 and 4), one would intuitively expect

the disc size to be inversely proportional to the size of the choroidal coloboma (larger colobomas should have smaller discs). This explains why in eyes with choroidal coloboma, the disc is either small or is large but colobomatous with nerve fibers displaced to the periphery.

While this series does not contain eyes with suspected glaucoma, the observation that there is no physiological cup in eyes with choroidal coloboma and no coloboma of the disc, could be important. This could be a potential area for future studies.

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