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The Central Vascular Pattern of the Eyeground in Children with Drusen of the Optic Disk*

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Summary. In a series of 50 children with optic disk drusen the anomaly was found to be associated with unusual properties. A cilioretinal artery was more frequent in the series with drusen than in a control series of the same age. The emergence and course of the central retinal vessels were studied in the right-sided fundi of 46 of the children and in two control series (the fundi of the "better" eyes of 46 strabismic children and the fundi of one of the eyes of 10 children or young adults with papilledema). Analysis of the measurements indicated that early branching of the central vessels and vascular tortuosity are so frequently associated with optic disk drusen that they can be considered features of the anomaly. On the other hand, the fundal vascular features in papilledema seem to be distinguishable by the method used from those associated with optic disk drusen. When the peripapillary choroidal vascular pattern was studied by fluorescein angiography, choriocapillaris filling was delayed in about the half of the angiograms. The aberrant vascular features found on and around optic disks with drusen can be explained by an embryonic affection of the developing vascular system at the optic nerve head. In this respect the anomaly seems to resemble congenital disorders of mesodermal origin.

Zusammenfassung. Der Augenhintergrund von 50 Kindern mit Drusenpapille wies bei der Mehrzahl ein abweichendes Gefäßmuster auf. Eine zilioretinale Arterie kam in der Gruppe mit Drusenpapille häufiger vor als in der Kontrollgruppe mit entsprechender Altersverteilung. Die zentralen Netzhautgefäße wurden nach Austritt und Verlauf untersucht und mit denen zweier Kontrollegruppen verglichen. Als Kontrolle diente in der ersten der Augenhintergrund von 46 „gesunden" Augen von Kindern mit Strabismus, in der zweiten der Augenhintergrund des rechten oder linken Auges von 10 Kindern oder jungen Erwachsenen mit Papillenödem. Hieraus ergab sich, daß die frühe Verzweigung und die Schlängelung der Gefäße zum Wesen der Anomalie gehören. Anderseits unterschied sich auch das Gefäßmuster bei Papillenödem von dem der Drusenpapille mit der angewandten Methode. In dem peripapillaren, chorioidalen Gefäßsystem, das mittels der Fluoreszein-Angiographie untersucht wurde, lag eine verlangsamte Füllung der Choriokapillaris bei etwa der Hälfte der Untersuchten vor.

Das spezielle Gefäßmuster der Drusenpapille läßt sich mit früher Einwirkung der hereditären Anomalie auf die Entwicklung des vaskularen Systems erklären. In dieser Beziehung scheint die Drusenpapille kongenitalen Zuständen mesodermalen Ursprungs ähnlich.

Introduction

The congenital ocular anomaly known as drusen of the optic disk has an irregularly dominant mode of inheritance. But, although the hereditary nature of the anomaly is well documented (Lorentzen, 1966), there is no consensus as to the origin and genesis of the drusen of the optic nerve head. Reese (1951) believed that these excresences are produced by degeneration of immature glial tissue within

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the optic nerve head. According to Seitz and Kersting (1962), the drusen are derived from the degeneration of the axoplasm. Cibis (1940), in his histological specimens of optic disk drusen, found alterations in the vessel walls of the disk. The vasculature in the area of the optic nerve heads with drusen has attracted great interest, because it shows characteristics of congenital aberrations (Lorentzen, 1966; Collier, 1959). The vascular findings often eclipse the ophthalmoscopic observations of optic disk drusen, giving rise to such terms as "pseudoneuritis with drusen".

Because physiological and acquired changes in vasculature become more common with advancing age, observations made in children probably give a truer picture of the basic vascular conditions associated with an anomaly. In the series of children with optic disk drusen studied by Erkkilä (1975) the peripapillary vascular pattern showed a high frequency of unusual features. These observations prompted a detailed study of the vascular conditions associated with optic disk drusen in the same series of children.

Material and Methods

The series of 50 subjects under 15 years old with optic disk drusen presented by Erkkilä (1975) was documented in colour fundus photographs (transparencies). The series covers nearly all the cases of optic disk drusen diagnosed in children in 1971–1974 at Helsinki University Eye Clinic. According to the criteria presented by Hoyt and Pont (1962), 92 fundi—46 right-sided and 46 left-sided—of the series were considered to have optic disk drusen. The fundi were photographed with a Zeiss fundus camera on Agfachrome 1000 S colour reversal film.

For the vascular findings a control series was used which comprised 46 consecutive subjects aged 4–15 years treated in the strabismus outpatient clinic of Helsinki University Eye Hospital. In the control series the optic disk area of the "better" eye was photographed by the same procedure as in the series studied. Children with a fundal disease or ametropia of 5 diopters or more were not included in the control series.

Another control series comprising right or left optic disk of ten children or young adults with true papilledema was used additionally in the analysis of some of the vascular features studied (symbols N and T). The colour transparencies were used for qualitative and quantitative analysis of the fundal vessels of the optic disk area. The qualitative analysis concerned the source and configuration of the aberrant vessels. The quantitative analysis dealt with measurements of three variables; N, L and T, on magnified projections of the transparencies.

These measurements were made with an arrangement similar to that presented by Forsius *et al.* (1964). The colour transparencies were projected on the glass screen of a mirror projector Porst Visomat TL 12. Concentric counting circles with radii of 10, 20 and 40 mm were drawn on transparent paper (Fig. 1). Before each measurement, the entire fundus picture was magnified to a diameter of 118 mm, which corresponds to the projection of optimal sharpness. The counting circles were centred with the optic disk on the underlying projection picture. The lengths of the vessels were measured with a HCHB map measurer in millimeters on the projected picture.

N is the number of vessels crossing a peripapillary counting circle (⌀ 40 mm); vessels so faint that they could not be seen to cross the outermost counting circle (⌀ 80 mm) were not counted. A similar counting method was used by Kagan *et al.* (1967). L is the length of the superior and inferior branches of the central retinal vein and artery measured with a map measurer between the respective second branching points. T is a measure of the tortuosity expressed as a ratio: the sum of the measured lengths of the eight largest vessels between the two counting circles (⌀ 20 and 80 mm) divided by the sum of the corresponding radial lengths (= 240 mm). This method is a modification of the estimation of tortuosity presented by Irinoda (1970).

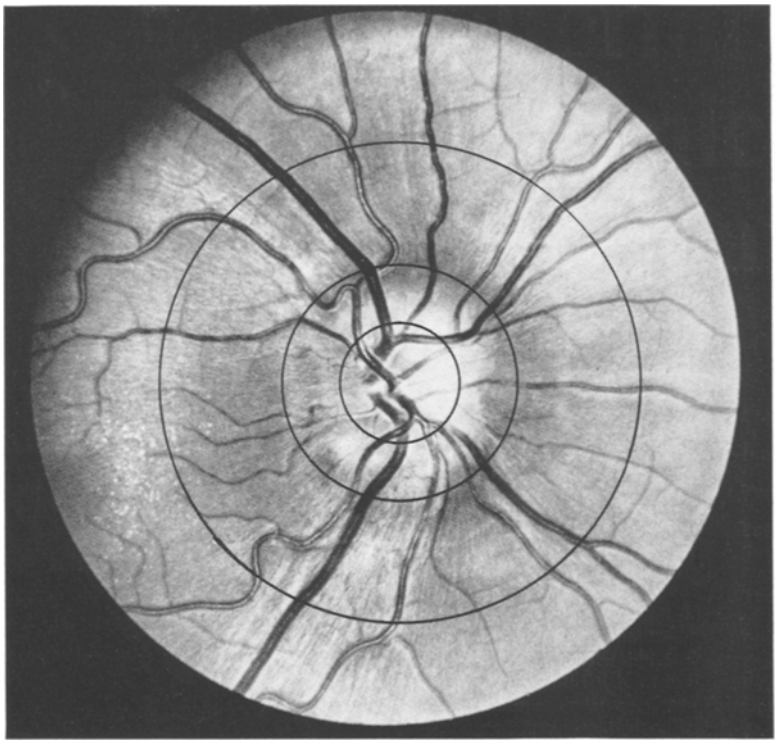

Fig. 1. Counting circles drawn on a fundus photograph with the same relative lengths of radius as on transparent paper placed over optic disk of the projected picture

The origins of some vessels and the choroidal vascular pattern around the optic disks with drusen were analyzed by fluorescein angiography in 32 eyes of 28 subjects.

Fluorescein angiography was performed with 5 c^3 10% sodium fluorescein injected intravenously into an antecubital vein. Angiography was started 6 s after injection with a modified Zeiss Robot fundus camera. A Baird Atomic B 4 interference filter was employed as the excitation filter and the barrier filter was a Kodak Wratten 15. The film used was Kodak Tri-X Pan. In the early phase of angiography pictures were taken at 1–2s intervals; late pictures were exposed at 5 and 10 min. Some of the angiographies were performed in general anesthesia by the method used in Helsinki University Eye Clinic (Raitta and Karhunen, 1975).

Results

In the right-sided fundi with optic disk drusen of 46 of the 50 children of the series a cilioretinal artery was present in 20. In one of them a double cilioretinal artery was seen emerging from the temporal margin of the disk (Fig. 2). In the others the cilioretinal artery started as a single vessel. In 17 subjects a single cilioretinal artery was seen on the temporal circumference of the disk. In 15 of them the vessel emerged at the macular approach to the disk, in one subject at the upper third of the temporal margin and in another one at the lower third of the temporal margin of the disk. In two subjects the cilioretinal artery was a nasal vessel. Most of the cilioretinal arteries were small, but in two fundi the nutritional sector was larger than a fifth of the entire peripapillary circumference.

a b

Fig. 2 a and b. Unusual vessel configurations associated with optic disk drusen. A double cilioretinal artery emerging from the temporal margin of the right optic disk of a boy aged 14 (a). A trichotomous branching of the inferior retinal artery in the right fundus of a girl aged 14 (b)

In the control group a single cilioretinal artery was seen in 11 of the 46 fundi, in all of them on the temporal circumference of the disk. In seven fundi the vessel emerged at the macular approach to the disk, in two at the upper third of the temporal margin and in the other two at the lower third of the temporal margin of the disk. All the cilioretinal arteries of the control group had a nutritional sector less than a fifth of the entire peripapillary circumference.

Small tortuous aberrant vessels were seen on the optic disks of 4 of the 92 eyes with drusen. All cases were unilateral and the four subjects were submitted to fluorescein angiography. The aberrant vessels were seen to be small veins draining outside the main venous trunk (Fig. 3). No similar small vessels suggesting retinociliary or opticociliary veins were seen in the control series.

Among the 92 eyes with drusen a remnant of the hyaloid artery was found in one left eye. In all fundi with optic disk drusen the mode of branching of the central vessels was dichotomous except in one eye in which the inferior retinal artery branched trichotomously (Fig. 2). Only dichotomous branching was seen in the control series. In no subject of the control series did the inferior or superior temporal branch of the central retinal artery cross the horizontal radius. This unusual feature was noted in two fundi of 92 of the series studied.

A quantitative analysis of the central retinal vessels in the optic disk area is presented in Table 1.

In the fundus photographs of the 46 right eyes with optic disk drusen the number of vessels crossing the counting circle, N, varied between 15 and 24 vessels, with an average of about 19 vessels. In the control group consisting of the "better" eyes of 46 strabismic children the range was 12–21 vessels, averaging about 16 vessels (Fig. 4). The other control group comprising one of the eyes of ten children or young adults with true papilledema shows a range of 13–18 vessels on the counting circle, with an average of about 16 vessels.

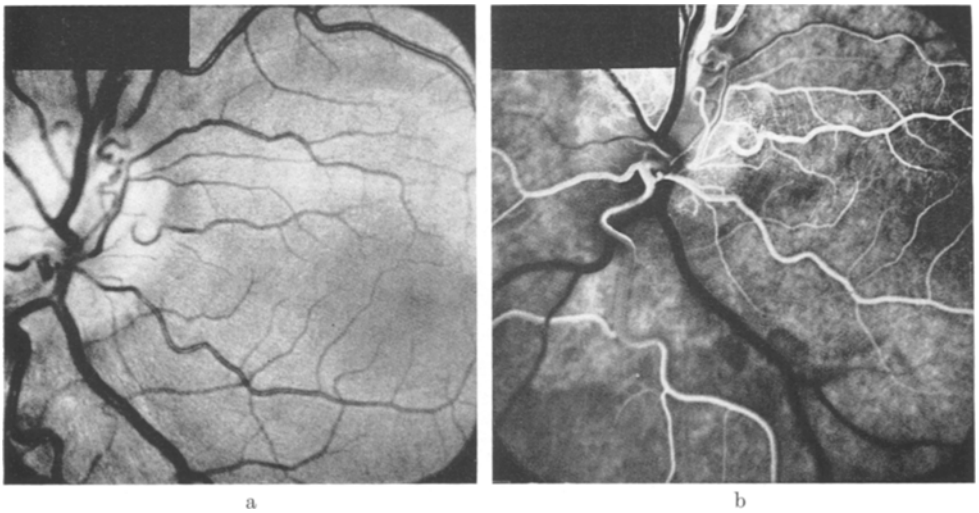

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Fig. 3 a and b. Abnormal tortuous vessels on the optic disk with drusen. In the fluorescein angiogram the vessels are seen to fill centrifugally at the early venous phase

Table 1. Summary of values of the variables N, L, and T

Variable N	Group studied	Control I	Control II	Variable L	Group studied	Control I	Variable T	Group studied	Control I	Control II
	number of cases			number of cases			number of cases			
12	0	2	0	0	8	2	250/240	5	7	2
13	0	4	1	5	5	7	255/240	6	8	0
14	0	4	2	10	14	10	260/240	4	17	4
15	4	5	1	15	8	9	265/240	4	6	1
16	3	16	2	20	7	8	270/240	7	3	1
17	7	5	3	25	1	5	275/240	4	3	2
18	6	4	1	30	2	3	280/240	6	2	0
19	8	3	0	35	0	0	285/240	3	0	0
20	10	1	0	40	1	2	290/240	1	0	0
21	3	1	0				295/240	2	0	0
22	2	1	0				300/240	3	0	0
23	2	0	0				305/240	0	0	0
24	1	0	0				310/240	0	0	0
							315/240	1	0	0
Total	46	46	10		46	46		46	46	10
Range	15–24	12–21	13–18		0–40	0–40		1.04 1.31	1.04 1.17	1.04 1.15
Mean	18.78	16.09	15.70		12.0	15.8		1.13	1.09	1.09
Standard deviation	2.21	2.18	1.64		8.6	9.4		0.07	0.03	0.04
Difference of means		2.69	3.08			3.8			0.05	0.04
Level of significance (t-test)		$P<0.01$	$P<0.01$			$P<0.05$			$P<0.01$	$P<0.05$

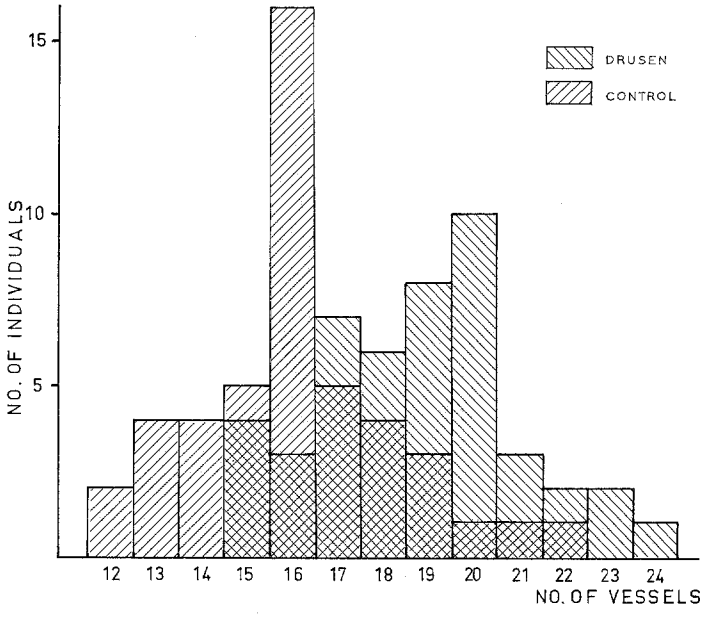

Fig. 4. Distribution of tested and control groups according to number of retinal vessels crossing the middle counting circle and extending beyond the outer counting circle

The values of L, indicating the summed length of the two main branches of the central retinal artery and vein proximally to the second branching points, varied in the drusen series between 40 and 0 units, as measured in millimeters on the projector screen when the diameter of the entire picture was 118 mm. In a high proportion of the fundi the length of the primary branches was considered to be 0 because the artery emerged as four vessels of second degree, and there was no visible union between the veins of second degree that form the superior and inferior papillary veins.

The average summed length of the central retinal vessels of first degree was about 12 units. In the control series the summed length of the first branches varied between 40 and 0 units, averaging 16 units.

The course of the peripapillary vessels is characterized by the variable T, a ratio calculated from the vessel lengths in an endeavour to express the tortuosity. In the series of optic disk drusen the T values varied between 1.04 and 1.31, with an average of 1.13. In the control group with strabismus the range was 1.04–1.17, the average 1.09. The other control group with true papilledema had T values between 1.04–1.15, with an average of 1.09.

The peripapillary choroidal vascular pattern was studied by means of fluorescein angiography. The findings were classified with respect to the filling sequence of the choriocapillaris in the peripapillary area. Four of the 32 angiograms taken in the eyes with optic disk drusen were too difficult to evaluate. Six angiograms show even filling of the peripapillary choriocapillaris. In three of them filling was completed before the retinal arterial phase, in one during the arterial phase, and in the other two only after the beginning of the venous phase. In 22 angio-

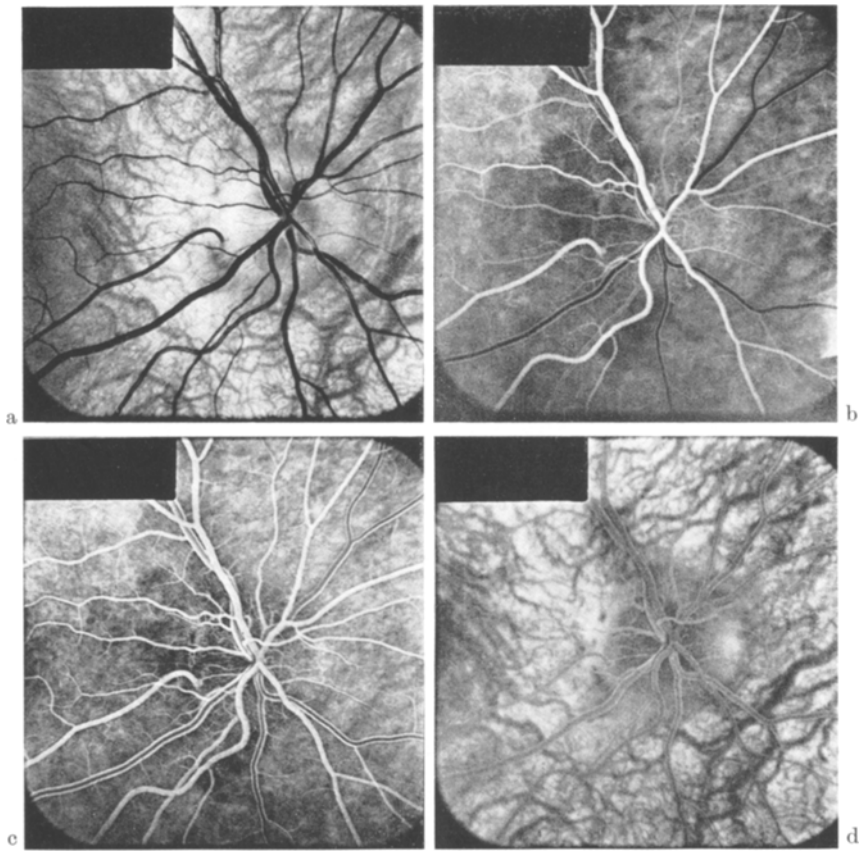

Fig. 5 a—d. Optic disk drusen seen in fluorescein angiography of the right fundus of a boy aged 13. Uneven filling of choriocapillaris in the peripapillary area at the early (b) and middle (c) venous phase. Accumulation of dye in the buried drusen in the late phase of angiography (d)

grams filling of the choriocapillaris was uneven (Fig. 5). In twelve of them the area of delay disappeared before the retinal venous phase of angiography. In the remaining ten angiograms the area of delayed choriocapillary filling could still be seen after the retinal venous phase had begun. In 15 angiograms, the area of delayed dye filling of the peripapillary choriocapillaris was sectoral, and in seven of them could still be seen at the retinal venous phase of angiography. In a further seven angiograms a circumpapillary mode of delay was seen, in three of them still visible at the retinal venous phase.

The distribution of the sectoral areas of underfilling shows an accumulation of the delay in the lower parts of the peripapillary choroid. In thirteen angiograms the delay occurred in the area between the temporal and nasal branches of the main inferior retinal vessels. In two angiograms the sectoral delay was seen in the areas adjacent to the superior margins of the optic disk. In one it was seen in the nasal peripapillary choroid. In three angiograms the delay occurred temporally to the optic disk.

Discussion

The frequency of the cilioretinal arteries found in this series of fundi with optic disk drusen was significantly higher than in the control series used ($\chi^2 = 9.68$). In his series of healthy subjects Lorentzen (1970) found this vessel with a frequency of 15 percent of eyes. The frequency found in the present control series used is of a somewhat greater order. In the fundi of the control series the cilioretinal arteries were quite small, the nutritional sector being less than a fifth of the entire peripapillary circumference. In some of the subjects with optic disk drusen, however, the cilioretinal vessels made a considerable contribution to the retinal arterial circulation. According to Dejean *et al.* (1958) an abundant cilioretinal vascular supply in the fundi can be considered a consequence of a local disturbance that acted upon the embryonic development of the central retinal vessels. The extent of the cilioretinal vasculature could be an expression of the need to replace that part of the retinal vasculature which because of the disturbing factor, could not be supplied by the developing vessels emerging from the proximal cone of the hyaloid artery.

According to Hayreh (1974) retinociliary veins arising from optic disks with drusen are the result of a local circulatory disturbance produced by the pressure of the drusen. The small tortuous aberrant vessels seen on 4 of the 92 optic disks with drusen in the present series were identified by fluorescein angiography as veins draining outside the main retinal venous trunk. This can be explained by a tendency in the subjects with optic disk drusen to form shunting opticociliary venous communications even in childhood. The venous communications between the central retinal and choroidal circulation found in children with optic disk drusen may be expected to become more marked with advancing age as reported by Karel *et al.* (1972).

The method used in the analysis of the central retinal vessels can be criticized with regard to accuracy, because the length of the eyes was not shown to be constant throughout the series studied and the control groups. However, the age and refraction distributions in drusen and control groups were very similar. Therefore it is assumed that in the three series compared the variation of the eye length did not appreciably diminish the comparability of the photogrammetrically measured variables.

The number of peripapillary vessels crossing the counting circle and extending beyond the outer concentric circle was found to be significantly ($P < 0.01$) higher in the fundi with optic disk drusen than in the control group of the same size. The summed lengths of the two main branches of the central retinal artery and vein were greater in the control series than in the series studied ($P < 0.05$). These differences appear to result from the early bifurcation of the vessels on and around optic disks with drusen (Fig. 1 and 2).

The variable used to express the tortuosity of the peripapillary vessels was on a significantly ($P < 0.01$) higher level in the series of drusen than in the controls with strabismus. This finding would be expected if vascular tortuosity is a feature associated with optic disk drusen.

True papilledema is known to be accompanied by supernumerary vessels—because of congestive widening of some otherwise invisible small vessels and neo-

vascularization—and by tortuous veins. An abundance of peripapillary vessels and tortuosity of the vessels in association with an elevated ill-demarcated optic disk might therefore be taken to indicate a malignant or inflammatory process behind a optic disk with an unusual appearance. The findings in this series, however, indicate that such a vascular picture, when combined with an elevated optic nerve head, may merely suggest optic disk drusen. To check whether the two conditions are associated with supernumerary vessels and tortuosity to an indistinguishable extent, I examined a control group of children or young adults with true papilledema. In this comparison a similar significant difference was noted in the number of vessels as when the first control series was used, but the difference in tortuosity, as expressed by the variable used, was less significant ($P<0.05$). The reason is that the supernumerary vessels associated with true papilledema are too small to be counted by the method used. The displacement of the dilated veins in true papilledema seems not to result in as much general tortuosity of the central retinal vessels as does the association with optic disk drusen.

Hereditary disorders with tortuosity of the retinal vessels are suggested to be manifestations of a mesodermal dysplasia (Ehlers and Jensen 1973). An increased number of peripapillary retinal vessels is characteristic of the fundi in Down's syndrome (Williams *et al.*, 1973). When the two features are found in the same hereditary ocular anomaly, i.e. drusen of the optic disk, an embryonic affection due to a single local factor appears very likely.

The fluorescein angiographic findings of the series with optic disk drusen can be considered divergent in regard to the filling of the choriocapillaris compared with the fluorescein studies of the normal choroidal circulation made by Archer *et al.* (1970). The recurrent finding of delayed filling in peripapillary areas of the choriocapillaris also supports the suggestion that the congenital affection of the optic nerve known as optic disk drusen alters the embryonic development of both the central retinal and posterior ciliary vascular systems. The histological studies made by Cibis (1940) showed deposits of hyaline material identical with that of small drusen inside and outside the cells of the tiny capillaries in optic disks with drusen, which indicate mesodermal changes.

The findings in the series studied tend to show that the anomaly known as optic disk drusen is so frequently associated with vascular aberrations that they should be considered a feature of the anomaly rather than coincidental. When the diagnosis of optic disk drusen is made there is no need for terms like "pseudoneuritis with drusen", because the features suggestive of an inflammatory process are probably true characteristics of the anomaly.

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