Retinal vascular changes in untreated retinoblastoma

Resemblance to von Hippel-Lindau disease

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Retinoblastoma is a rare but well recognized tumour occurring typically in young children. The clinical features and pathology have been well described. Early diagnosis is important, not only to save life, but also because modern methods of treatment, using various forms of radiation (Reese and Ellsworth, 1963; Stallard, 1966; Bedford, 1968), light coagulation (Höpping and Meyer-Schwickerath, 1964), cryosurgery (Lincoff, McLearn and Long, 1967), or chemotherapy (Hyman, Ellsworth, Feind, and Tretter, 1968), may enable the clinician to deal effectively with the disease.

The differential diagnosis of lesions simulating retinoblastoma has been reviewed by Howard and Ellsworth (1965). Recently it has become apparent whilst documenting new cases that a retinoblastoma may develop large feeder vessels. Hitherto it was presumed that the presence of large tortuous feeding vessels associated with solitary peripheral retinal tumours, indicated a diagnosis of an angiomatous lesion (von Hippel-Lindau disease). It has not been stressed previously that large feeding vessels may be associated with retinoblastoma, not only at the periphery but also at any other site in the fundus. It is the purpose of this paper to draw attention to the significance of retinal vascular changes in the differential diagnosis of a retinal tumour and to emphasize that the presence of these large vessels does not exclude retinoblastoma, particularly in the age group 0 to 5 years.

Material

- (a) In two cases a clinical diagnosis of von Hippel-Lindau disease had been made. Each proved to be a retinoblastoma on subsequent pathological examination.
- (b) In four cases of retinoblastoma the vessel changes before and after treatment were studied in fundus photographs.

Case reports

Case 1, a baby girl aged 13 months. A white pupil was noticed, a diagnosis of haemangioblastoma was made elsewhere, and the patient was referred to Moorfields Eye Hospital. Examination under anaesthesia on October 22, 1962, showed a solid peripheral retinal lesion with large tortuous feeding vessels (Fig. 1). These were thought to confirm the diagnosis of haemangioblastoma and light-coagulation was applied to the lesion. Several months later a further examination showed the large tumour still present at the periphery of the retina and, in addition, there were seedlings in the retina and vitreous (Fig. 2). A diagnosis of retinoblastoma was then made and the eye was enucleated.

FIG. 1 Case 1. Fundus painting, showing solid peripheral tumour with large tortuous feeding vessels

FIG. 2 Case 1. Fundus painting 7 months after light-coagulation, showing change in appearance of tumour with seedlings in the retina and vitreous

Pathological examination

MACROSCOPICAL

There is a white mass in the inferonasal quadrant of the retina with numerous deposits elsewhere in the retina (Fig. 3).

MICROSCOPICAL

A poorly differentiated retinoblastoma is associated with a localized retinal detachment. Areas of necrosis and seedlings are seen on the retinal surface. There is no evidence of extension to the optic nerve. The rest of the eye is normal apart from some posterior synechiae (Fig. 4).

FIG. 3 Case 1. Painting of right eye opened, showing white mass occupying inferonasal quadrant, tumour deposits on the retina and in the vitreous, and prominent vessels leading to the tumour

FIG. 4 Case 1. Whole eye section, showing retinoblastoma with localized retinal detachment. Haematoxylin and eosin. $\times 3$

Further sections from the posterior edge of the growth (Fig. 5) showed prominent vessels which were traced to the optic disc.

FIG. 5 Case 1. Posterior edge of tumour, showing large vessels in cross-section. Haematoxylin and eosin. $\times 130$.

Case 2, a boy aged 3 years. A white pupil was noticed and the presence of a retinal tumour with large feeder vessels was thought to indicate haemangioma. The child was subsequently examined at the Tumour Unit of St. Bartholomew's Hospital, where a diagnosis of retinoblastoma was made. The eye was enucleated because the size and situation of the growth precluded conservative treatment.

Pathological examination

MACROSCOPICAL

The opened eye reveals a whitish friable mass in the posterior segment on the nasal side with enormously dilated feeder vessels in the same quadrant (Fig. 6).

FIG. 6 Case 2. Painting of right eye opened, showing white mass on nasal side with large feeder vessels.

FIG. 7 Case 2. Whole eye section, showing necrotic retinoblastoma. Tumour deposits lie on the surface of the lesion at the posterior pole. There is infiltration of the nerve fibres at the optic disc but no extension beyond the lamina cribrosa. Haematoxylin and eosin. $\times 3$.

MICROSCOPICAL

Section shows a largely necrotic retinoblastoma occupying the vitreous on the left side (Fig. 7). Tumour deposits lie on the surface of the retina and there is infiltration of the nerve fibres overlying the optic nerve head, but in the sections examined there is no obvious extension beyond the lamina cribrosa. Some attempt at rosette formation is seen, but on the whole where viable tumour tissue is present differentiation is poor. The retina is *in situ* and there is no infiltration of the choroid.

Case 3, a girl aged 3 years. She was first seen in October, 1967, with a 5-weeks' history of a white pupil reflex. Examination under anaesthesia showed a large white tumour in the right eye occupying much of the vitreous cavity. Inspection of the base showed the typical pinkish retinoblastoma surface with fine new vessels over it. The left eye was normal.

The tumour was considered too large for treatment with a cobalt plaque and therefore cobalt beam therapy was started. Further examination in December, 1967, showed marked regression of the mass to the typical inert tumour debris. A similar appearance was seen at further examinations until May, 1968, when a classical recurrence was noticed at the posterior edge of the tumour with slightly enlarged vessels leading to it (Fig. 8). A cobalt plaque was applied and the tumour regressed rapidly, the vessels returning to normal in 6 weeks.

FIG. 8 Fundus photograph, showing recurrence at posterior edge of previously treated retinoblastoma with slightly enlarged vessels

FIG. 9 Case 4. Photograph, showing peripheral tumour with dilated vessels

Case 4, a boy aged 2 years. He was first seen in November, 1964, when a white reflex was noted in the right eye. This child was a member of the third generation of a family known to be affected by retinoblastoma. Examination showed a large tumour occupying the temporal half of the right fundus with a smaller tumour in the left eye. The lesion in the left eye was treated by light-coagulation and cobalt beam therapy was commenced to the right eye.

Subsequent examination in January, 1965, showed that the tumour mass in the right eye was inert, but the left eye required further treatment with a cobalt plaque. In March, 1965, all tumour masses appeared inert. Further examinations over a period of 15 months showed no activity, but in December, 1966, a cobalt plaque was applied to the right eye as there was evidence of a new tumour with dilated vessels at the periphery (Fig. 9). One week later the tumour showed signs of regression and the vessels were smaller.

Case 5, a baby boy aged 1 year. He was first seen in July, 1967, when the right eye was noticed to be completely disorganized with a high tension, while the left showed two large retinal tumours inferiorly with engorged feeding vessels (Fig. 10). The right eye was enucleated and the histology showed retinoblastoma. Because of the size and shape of the tumours in the left eye cobalt beam therapy was instituted. Subsequent examination showed regression of the growth in the remaining eye with shrinkage of the previously enlarged feeding vessels (Fig. 11). In spite of this treatment further examination in subsequent months showed the presence of multiple tumours and this eye too was eventually enucleated.

FIG. 10 Case 5. Fundus photograph of left eye, showing engorged inferior retinal vessels

FIG. 11 Case 5. Shrinkage of retinal vessels shown in Fig. 10 after regression of tumour following cobalt beam therapy

Histological study There was "a poorly differentiated retinoblastoma which is affecting particularly the peripheral portion of the retina. Deposits of tumour are seen in the vitreous and sub-retinal space but there does not seem to be any evidence of invasion of the choroid or the optic nerve".

FIG. 12 Case 6. Fundus photograph, showing large retinoblastoma close to optic disc

Case 6, a baby boy aged 3 months. He was first seen in January, 1966, with a known family history of retinoblastoma. His brother had bilateral retinoblastoma, the diagnosis being proved histologically after the removal of one eye. This child was noticed to have a "cat's eye reflex" in the right eye and a large tumour was found involving the macular area up to the optic nerve. The left eye was normal.

Because of the size and shape of the tumour cobalt beam therapy was instituted and the tumour regressed satisfactorily. Further examination in May, 1966, showed a doubtful area immediately temporal to the disc with a large vessel coursing over it. Continued observation showed that this area was undoubtedly enlarging (Fig. 12) and a cobalt plaque was applied in October, 1966. Several months later the tumour had regressed considerably and the vessels had returned to a more normal calibre. Subsequent progress showed no activity of the tumour but a radiation cataract appeared and later vitreous haemorrhages occurred. In May, 1968, a broad iridectomy was done as the cataract had remained localized and this facilitated further examinations which have shown no further growth of the tumour.

Discussion

There would seem to be little doubt from these findings that retinoblastoma may induce vascular changes which, at times, may be so gross that an angiomatous tumour may be simulated and the correct treatment may be postponed. However, the true nature of the neoplasm is apparent if the surface of the tumour is examined very carefully, particularly in a patient under the age of 5 years. The retinoblastoma surface is pinkish-white and uneven with many fine vessels coursing over its surface. Occasionally the retinoblastoma may break into the vitreous, in which case the surface presents a uniform white fluffy appearance, but the classical appearance just described may still be seen around the base.

Summary

- (1) Case reports are presented to show that a retinoblastoma anywhere in the fundus may induce vascular changes simulating an angiomatous tumour.
- (2) When the tumour is at the periphery, the appearance may be confused with that of von Hippel-Lindau disease.
- (3) The enlarged retinal vessels rapidly regress after successful treatment.

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