Morning glory syndrome: a histopathological study

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Abstract
The clinical and histopathological findings in a case of morning glory syndrome are described. Axial optic nerve retrodisplacement into a peripapillary scleral ectasia (staphyloma), absence of fibrous lamina cribrosa, and optic nerve atrophy were associated with various other, non-inherent ocular developmental anomalies. The uninterrupted lining of the inner wall of the staphyloma by one-layered, normal retinal pigment epithelium proves that the syndrome is not due to a neuroectodermal closure defect.

The term 'morning glory syndrome' (MGS) was introduced by Kindler, because the papillary region in the affected eye is reminiscent of a (withering) flower of 'morning glory'. Clinical reports3-4 and four histopathological studies5-13 gave rise to a definition of MGS as an 'unilateral malformation involving the optic disc ... associated with a peripapillary scleral defect, absence of a lamina cribrosa and a recess formed by an axial retrodisplacement of the optic nerve'.13 These authors postulated that MGS should be considered as a mesodermal disorder. The central posterior scleral malformation may be associated with other intraocular anomalies, of which non-rhegmatogenous retinal detachment is the most frequent.

The rarity of histopathological reports and the rarity of anterior segment pathology, which was not described in previous microscopically studied cases, warrant a report on the clinicopathological data from a further case, which substantiates the postulate13 that MGS is a mesodermal congenital lesion and not a coloboma of the optic nerve or disc.

Case report
A male infant aged 7 weeks showed unilateral microphthalmos, central corneal opacity, loss of the anterior chamber, and a mature cataract. Ultrasonography did not reveal an intraocular tumour. The ocular tension was 13 mmHg. Six weeks later, it was 30 mmHg, and 11 weeks later it was 36 mmHg. A CT scan then revealed a retrobulbar cyst connected with the sclera. Enucleation was performed, because retinoblastoma could not be excluded.

Pathology
Macroscopic examination. The globe measured 19×18×17 mm, the cornea 11 mm. A limbal circular constriction had caused an almost spherical cornea, with a prominence of 4 mm. The optic nerve was noticeably thickened: its diameter was 6 mm, its length 5-5 mm. When its posterior limit was cut for processing through paraffin for identification of possible spread of a tumour, clear fluid escaped from a hole in the new plane of section.

Microscopic examination. The cross section of the optic nerve limit showed no evidence of tumour cells. Its central part contained agglomerations of fragments of axons with varicose swellings, and there was reactive proliferation of collagenous connective tissue.

Nitrocellulose embedded serial sections of the globe revealed an abnormal number of keratocytes with deep stromal oedema and absence of Descemet's membrane, and endothelium in the central cornea (Peters' anomaly of cornea). There was total loss of the anterior chamber; the chamber angle, trabecular lamellae and Schlemm's canal could not be observed (Figs 1 and 2A). The dislocated lens showed a hypermature cataract and a partly calcified, anterior and equatorial subcapsular cataract. A rupture in the posterior capsule was filled by connective tissue, originating from a fibrovascular retrolental membrane, which was characteristic of hyperplastic persistent primary vitreous. The membrane contained lens tissue (Fig 2B) and was attached to elongated ciliary processes. Its contraction had caused the circular limbal constriction.

A tent-like totally detached retina contained a falciform fold, which ran from the posterior stalk of the retina to the central part of the retrolental membrane. The fold showed numerous pseudorosettes and defects in the nuclear layers. The macular area contained a reduced but noteworthy number of ganglion cells. The nerve fibre layer was markedly reduced.

The posterior pole was characterised by a

Figure 1: Horizontal section showing scleral peripapillary staphyloma (S) with retrodisplaced optic nerve, total retinal detachment with axial stalk, and posterior part of falciform fold (F). (Nitrocellulose section, H and E, ×4.)
of the central vessels had occurred at its normal site adjacent to the neuroectodermal lamina cribrosa, in which no fibrous tissue was found. Anomalous blood vessels were not observed within the retinal stalk.

**Histopathological diagnoses.** Peters’s anomaly of cornea, aplasia of the chamber angle, congenital cataract, hyperplasia of persistent primary vitreous, total detachment of atrophic, dysplastic non-rhegmatogenous retina, falciform retinal fold, axial optic nerve retrodisplacement into peripapillary scleral staphyloma, absence of fibrous lamina cribrosa, and optic nerve atrophy.

**Discussion**

The first description of MGS is attributed to Handmann, who reported six cases of identical (?) hereditary anomalies of the optic disc. Heredity and bilaterality of peripapillary staphylomas have been described exception-ally. The normal visual acuity in some of these cases justifies some doubt whether they were of MGS.

The main clinical features of MGS are (1) an apparently enlarged, sometimes excavated optic disc with a central mass of whitish-grey tissue; (2) a disc surrounded by a peripapillary scleral staphyloma, which in its turn may be surrounded by an elevated peripapillary ring of white, often pigmented tissue; (3) attenuated, branching arterial and venous retinal vessels, radiating from below the epipapillary mass of whitish tissue. These radiating vessels often appeared to be more numerous than the retinal vessels in the fellow eye and showed fewer bifurcations. Visual acuity is poor. Systemic defects rarely accompany the ophthalmoscopic findings.

The main histopathological features of MGS are axial retrodisplacement of the optic nerve and a peripapillary, funnel shaped scleral staphyloma. The scleral ectasia is thought to be due to a developmental central posterior scleral anomaly. The optic nerve sheaths may be affected and may be partly replaced by fibroadipose and smooth muscle tissue. The fundamental observation in the present case of uninterrupted retinal pigment epithelium covering the entire inner wall of the staphyloma confirms that MGS is not due to a neuroectodermal closure defect. An identical continuous inner layer of pigment epithelium has been described by Cogan. Rack and Wright and Dempster et al reported respectively a 'broad collar of collagenous tissue in which pigmented cells are numerous' and 'nodules of metaplasic pigment epithelium which formed a ring around the neck of the recess', but not a continuous layer of pigment epithelium overlying the inner wall of the recess.

A non-rhegmatogenous retinal detachment has been reported in five cases. The present sixth case with its total detachment and axial stalk within the staphyloma seems to substantiate the postulate that these non-rhegmatogenous detachments in MGS most probably are due to continuous traction exerted by the gradually increasing axial retrodisplacement of the optic nerve. A primary non-attachment of the retina.

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**Figure 2:** A: Total anterior synechia (A), ectopic cataractous lens, hyperplastic persistent primary vitreous (V), elongated ciliary processes, anterior part of falciform fold (F). (H and E, ×6.) B: Posterior lens capsule with rupture (arrows), lens substance (L) in hyperplastic persistent primary vitreous (V). (H and E, ×50.) C: Nasal wall of peripapillary staphyloma lined by retinal pigment epithelium. Note inner and outer scleral layer. Black arrow: peripheral part of base of staphyloma. Open arrow: pigment epithelium represented in Figure 2D. (H and E, ×40.) D: Detail of Figure 2C indicated by open arrow (×260).

4 mm deep peripapillary, funnel shaped scleral ectasia (staphyloma); its diameter was 5 mm. The inner wall of the ectasia and the periphery of its base were uninterruptedly covered by one layer of normal retinal pigment epithelium (Figs 2C, 2D). Remnants of the choroid could not be recognised below the layer of pigment epithelium. The extended inner and outer scleral layer were separated by a narrow fissure. The outer layer merged into the optic nerve dura; the inner layer surrounded the retrodisplaced optic nerve head in the base of the recess. Small numbers of smooth muscle cells could be recognised within the outer scleral layer, while clusters of fat cells could be observed within the narrow fissure. The stalk of the detached, non-rhegmatogenous retina arose from the nerve head and ran completely free from the inner wall of the recess axially through the scleral aperture into the lumen of the eye. The central retinal vessels and their first branches could be recognised within the stalk. The first branching
appears unlikely. Rack and Wright¹ and Cogan² depicted macroscopic and microscopic features of the radiating folds round and in the entrance of the peripapillary staphyloma.

The frequently described unduly numerous attenuated branches of the central vessels, which radiate peripherally in a sometimes striking straight course from below the central white tissue, are most probably the normally more peripherally situated branches after their second ramification. In MGS they are more centrally located by the retrodisplacement of the optic nerve head, which was 4 mm (1) in the case of Rack and Wright¹ and in the present case.

The disc appears generally enlarged. It should, however, be realised, that in most cases the nerve head cannot be observed owing to its axial retrodisplacement and the whitish tissue which overlies and sometimes surrounds the nerve head.¹¹ This whitish tissue consisted in all histopathologically studied cases, including the present case, of folded retina with glial, fibrous, and pigment epithelial proliferation.

The depressed or elevated peripapillary, whitish often hyperpigmented ring represents the entrance of the peripapillary staphyloma. Either the retina is attached to the wall of the aperture, or retinal folds or a retinal stalk pass freely through the aperture. An elevated peripapillary ring consists of pseudofibrotic metaphysical retinal pigment epithelium, covered by a degenerated retina. It hides the aperture to the ectatic lumen.

A persistent hyaloïd artery has been reported twice.⁹¹ The present case showed a thick layer of retrolental fibrovascular tissue, originating from hyperplastic persistent anterior primary vitreous. It was connected with stretched ciliary processes, and it had ruptured the posterior lens capsule.

Ipsilateral Peters’s anomaly of cornea has so far not been described in MGS. In avian embryos the ‘mesectoderm’ of the head derived from the neural crest is the source of most ocular tissues. The corneal endothelium and keratocytes are entirely so, the sclera is almost entirely of neural crest origin, while the vitreous has an unqualified derivation from the neural crest.¹⁴ Comparative studies indicate that normal crest development is fundamentally similar in all vertebrate embryos.¹⁵ Experimental evidence necessary to define clearly the origin of ocular tissues in mammals is not yet available, but recently experimental work has provided direct evidence that the neural crest contributes to cranial-facial development in mammals.¹⁶ The association of Peters’s anomaly of the cornea and hyperplasia of persistent primary vitreous with the posterior scleral malformation in MGS may be purely coincidental, but it might also be a manifestation of a neural-crest-derived ‘mesoectodermal’ disturbance: a ‘neurocrisopathy’¹⁶ Some contractile peripapillary staphylomas have been reported.¹⁶,¹⁷ Their movements can be explained by the presence of heterotopic smooth muscle tissue in the posterior sclera or choroid.¹³ This smooth muscle tissue is often accompanied by heterotopic adipose tissue in the choroid and/or in the enlarged distal region of the optic nerve and its sheaths. It occurred unilaterally in 24 of 26 cases.¹³ Smooth muscle cells and fat cells were also observed in the ectatic scleral tissue of the peripapillary staphyloma in the present case.

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