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Congenital simple hamartoma of the retinal pigment epithelium: What is the probable cause?

A B S T R A C T

Congenital simple hamartoma of the retinal pigment epithelium is localized to the retinal tissue only with variable amount of surface extension. With consistent morphological and OCT features of the lesion around fovea, it appears that some of the embryologically undifferentiated ectopic progenitor cells destined for RPE within the retinal tissue may not undergo any further differentiation due to lack of necessary homeostatic factors leading to only hyperplasia and accumulation of the cells within the retina leading to simple hamartoma.

Introduction

Congenital simple hamartoma of the retinal pigment epithelial (CSHRPE) is a rare entity characterized by round solid pigmented lesion within the macula [1–3]. With the available evidence in the literature, the lesion appears to be congenital but its pathogenesis remains an enigma [1–10]. Here in this report we elaborate the probable mechanism involved in the development of this lesion with the critical assessment of the reported cases and their correlation with embryology of the retinal pigment epithelium and neurosensory retina.

What the literature says

Laqua first described the clinical characteristics of these lesions in two young patients. One of these lesions involved the fovea thus affecting the visual acuity [1]. In 1989 Gass described three such cases and termed this pathology as CSHRPE [2]. Gass hypothesised three patterns of growth of these lesions. The type 1 lesion involved only the surface of the retina and type 2 involved the full thickness of the retina with surface extension and the type 3 also involved the full thickness of the retina extensively with surface vascularization and retinal surface extension [2].

The OCT features of CSHRPE have been noted in various case reports [5–9,11]. The OCT features described are almost similar in all cases, i.e. the tumour is seen as a variably elevated convex shaped hyper-reflective superficial pigment epithelial layer facing the vitreous cavity [5,6,8,9]. In one case there was a concavity along the vitreous cavity due to vitreo-macular traction [7] and associated macular edema was seen in another case [11]. All reports suggest sharp margins with well demarcation of the lesion from the surrounding retina with prominent posterior shadowing. The structures beneath the hyper-reflective superficial layer are completely shadowed thus masking the visualization of deeper retinal layers, RPE, Bruch's membrane, choroid and the sclera.

The fluorescence angiography in some cases revealed completely blocked fluorescence throughout the lesion [3]. In a case reported by us, OCTA showed only a mild change/distortion of the foveal avascular zone along the superficial retinal plexus [8].

Barnes et al, published a histopathological analysis of the CSHRPE lesions which endangered vision due to associated vitreo-macular traction secondary to the lesion. Histopathology following vitrectomy revealed a central foci of hyperplastic RPE cells surrounded by fibrosis. However, following surgery, the underlying retina showed focal photoreceptor and RPE atrophy. There was no discontinuity in the underlying RPE and the tumour also did not involve the entire thickness of the retina. The authors propose that the tumour might have formed due to migration of few RPE cells to the retinal surface during embryogenesis [7]. Holz reported a biphasic composition of these tumors consisting of hyperplastic RPE cells and vascular proliferation [4]. Embryologically the progenitor cells within the optic vesicle possess trans differentiation potential. The inner layer of the optic cup differentiates into neural retina following signalling from the surface ectoderm. The outer layer differentiates into a monolayer of RPE. The progenitor cells in both the layers are same. Thus, depending on appropriate signalling from the adjacent tissue they differentiate either into the RPE or neural retina [12–15]. After critically analysing these findings we propose the following mechanism for development of CSHRPE as a focal lesion within the neural retina.

Probable mechanism

It is possible that some inner layer progenitor cells differentiate into RPE like cells rather than neural retina. However, these ectopic RPE progenitor cells lying in the retinal tissue may not undergo any further differentiation into mature RPE because of lack of necessary local homeostatic factors. Thus these ectopic cells may just undergo hyperplasia and fibrosis and rest within the retinal tissue. Depending upon the amount of cell rest, the hyperplasia may be limited to the superficial retina, full thickness or it may go beyond the retinal surface. As these cells lack a connection with the actual retinal pigment epithelium it was possible by Barnes et al to surgically remove it without creating a full thickness retinal defect and without disturbing the underlying RPE. Thus it is likely that congenital simple hamartoma of the retinal pigment epithelial is due to ectopic differentiation of progenitor cells into RPE cells within the neural retina with subsequent arrest of further development leading to localized hyperplasia and fibrosis forming an intra-retinal mass lesion depending upon the cell density.

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Conflict of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mehy.2018.12.019.

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