Progress in Retinal and Eye Research 36 (2013) 247–259

Contents lists available at ScienceDirect

Progress in Retinal and Eye Research

journal homepage: www.elsevier.com/locate/prer

Regional morphology and pathophysiology of retinal vascular disease

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ARTICLE INFO

Article history:
Available online 26 July 2013

Keywords:
Retina
Morphology
Regional
Vascular

ABSTRACT

Disturbances in the retinal vascular supply are involved in the pathophysiology of the most frequent diseases causing visual impairment and blindness in the Western World. These diseases are diagnosed by noting how morphological lesions in the retina vary in shape, size, location and dynamics, and subsequently concluding the presence of a specific disease entity. This diagnostic approach can be used to identify the site of a retinal vascular occlusion, to assess whether retinal diseases are primarily due to changes in the larger retinal vessels or the microcirculation, and to differentiate the relative involvement of the choroidal and the retinal vascular systems. However, a number of morphological manifestations of retinal vascular disease cannot presently be related to the underlying pathophysiology.

The review concludes that there is a need for developing new methods for assessing vascular structure and function in the ciliary vascular system supplying the choroid and the optic nerve head. Presently, the study of these structures relies on imaging techniques with limited penetration and resolution into the tissue. Secondly, there is a need for studying oscillations in retinal vascular function occurring within days to weeks, and for studying regional manifestations of retinal vascular disease. This may constitute the basis for future research in retinal vascular pathophysiology and for the development of new treatment modalities to reduce blindness secondary to retinal vascular disease.

Contents

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[1] Percentage of work contributed by each author in the production of the manuscript is as follows: Toke Bek: 100%.

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http://dx.doi.org/10.1016/j.preteyeres.2013.07.002

1. Introduction

Diseases involving the retinal vascular system constitute the most frequent causes of visual impairment and blindness in the Western World (Prokofyeva and Zrenner, 2012). These diseases present a number of retinal lesions, such as haemorrhages, exudates, retinal atrophy and neovascularisations. Clinical diagnoses are made by noting how these lesions vary in shape, size, localisation and dynamics, and subsequently integrating this information into an overall picture that is concluded to represent a specific disease entity. However, the regional variation of retinal vascular diseases also reflects the pathophysiology of these conditions, and in cases where a causal relation can be established between pathophysiology and the distribution of retinal vascular lesions, this information may help predicting the course of and in devising new therapeutic interventions for the disease.

A precondition for studying regional variations in retinal vascular disease is to have access to methods that allow the resolution of these regional variations in retinal vascular structure and function. Morphological changes are traditionally recorded by imaging the retina through the optics of the eye by fundus photography and fluorescein angiography. Recently, other examination techniques have become available to document the consequences of retinal vascular disease, such as optical coherence tomography (OCT) scanning and adaptive optics imaging, but these techniques have not yet contributed significantly to understanding regional variations in retinal vascular disease. The purpose of the present review is to comprehend knowledge of how regional variations in retinal morphology reflects the pathophysiology of retinal vascular disease. This may give an insight-based approach to diagnosing retinal disease, and in cases where the relation between pathophysiology and clinical presentation is not obvious, this lack of knowledge may point to relevant areas for initiating research activities aimed at understanding retinal vascular disease.

2. The fundus background

Imaging of the retina through the optics of the eye gives an excellent view of the inner retinal vascular supply, whereas the outer retinal vessels in the choroid are seen more indirectly by the diffuse reddish background colour originating from the blood in these vessels (Hayreh, 1974). However, the visibility of the choroidal vascular system also depends on the density of melanin, photoreceptor pigment or xantophyl in the retina and the choroid. Reduced melanin pigmentation is often observed in the triangular area located between the lower temporal and nasal vascular arcades (Fig. 1). This may be due to an incomplete development of this area where the lips of the optic cup on each side of the choroid fissure fuse in foetal life to encircle the future intraocular vascular system. Therefore, the hypopigmented inferior retinal area, although representing and area with normal visual function, can be considered to be developmentally related to colobomas (Rutnin, 1967). However, reduced pigmentation may also be due to diseases in the retina and the choroid. Dystrophic conditions in the retina involve atrophy of the photoreceptors and the underlying pigment epithelium (Zobor and Zrenner, 2012). When the primary photoreceptor degeneration includes the central cones, either in congenital cone dystrophy (Zervas and Smith, 1987) or in acquired conditions such as toxic retinopathy (Hanna et al., 2008), the retina may display a pericentral ring-shaped atrophic area contrasting with the normal fovea, much resembling a shooting target. This ring-shaped area coincides with the area where the retinal ganglion cell layer is thickest, but it is unknown whether this is related to the pathogenesis of the toxic reaction. Central retinal dystrophies may also present a number of other characteristic morphological appearances that may inspire the initiation of future investigations of the pathophysiological background of these diseases (Francis et al., 2005).

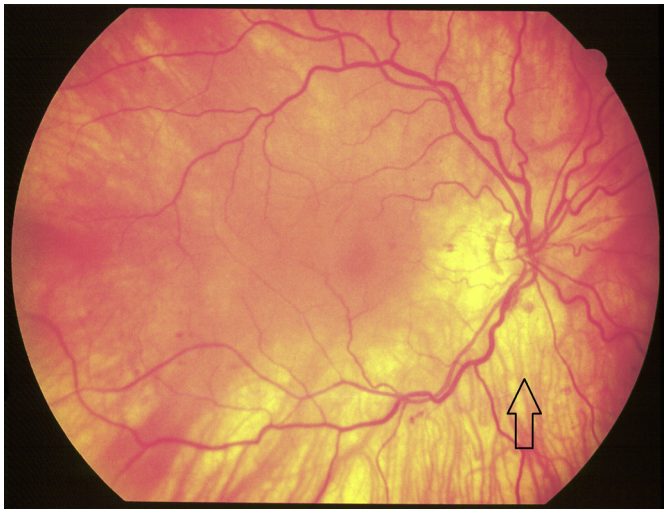

Fig. 1. Fundus photograph showing hypopigmentation in the triangle between the lower temporal and nasal vascular arcades (arrow).

3. Retinal vascular supply

Both the inner and the outer retinal vascular supply display regional differences in structure and function that are reflected in the disease patterns developing in these vascular regions.

3.1. The outer retinal vascular supply

3.1.1. Physiology

The vertebrate retina is inverted with the photoreceptors oriented outwards to be in close contact with the choroidal vascular supply. The choroidal blood flow is much higher than what would be expected if it should only meet the metabolic demand of the outer retina (Bill, 1975), but also acts to divert the heat generated when light passes the photoreceptors and is absorbed in the pigmented layers of the retina and the choroid (Nicla and Wallman, 2010). This results in a low extraction of metabolites and has the consequence that the metabolic environment of the choroidal veins and the outer retina is almost similar to that of the arterial blood (Yu and Cringle, 2001).

3.1.2. Lobular structure

The larger choroidal vessels can be observed by ophthalmoscopy when the ocular pigmentation is sparse, either because of a constitutional lack of melanin as seen in albinism (Summers, 2009), or because of retinal atrophy secondary to chorioretinal disease. The colour of the choroidal vessels is normally red, but may change to white if choroidal disease causes the vessels to become sclerotic (Hwang et al., 2010). The choroidal capillary system is generally organised as lobules arranged in a honey comb-like pattern supplied by a central end arteriole and drained through venules leaving from the periphery of the lobules (Torczynski and Tso, 1976; Zhang, 1994). The ciliary vascular system has been studied by casting with plastic polymers in which small impressions can be seen to represent protrusions of the endothelial cell nuclei into the vascular lumen. In arterioles from other tissues these impressions are oriented in parallel with the blood flow, and thereby with the length