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Macular telangiectasia type 2

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ABSTRACT

Macular telangiectasia type 2 is a bilateral disease of unknown cause with characteristic alterations of the macular capillary network and neurosensory atrophy. Its prevalence may be underestimated and has recently been shown to be as high as 0.1% in persons 40 years and older. Biomicroscopy may show reduced retinal transparency, crystalline deposits, mildly ectatic capillaries, blunted venules, retinal pigment plaques, foveal atrophy, and neovascular complexes. Fluorescein angiography shows telangiectatic capillaries predominantly temporal to the foveola in the early phase and a diffuse hyperfluorescence in the late phase. High-resolution optical coherence tomography (OCT) may reveal disruption of the photoreceptor inner segment–outer segment border, hyporeflective cavities at the level of the inner or outer retina, and atrophy of the retina in later stages. Macular telangiectasia type 2 shows a unique depletion of the macular pigment in the central retina and recent therapeutic trials showed that such depleted areas cannot re-accumulate lutein and zeaxanthin after oral supplementation. There have been various therapeutic approaches with limited or no efficacy. Recent clinical trials with compounds that block vascular endothelial growth factor (VEGF) have established the role of VEGF in the pathophysiology of the disease, but have not shown significant efficacy, at least for the non-neovascular disease stages. Recent progress in structure–function correlation may help to develop surrogate outcome measures for future clinical trials.

In this review article, we summarize the current knowledge on macular telangiectasia type 2, including the epidemiology, the genetics, the clinical findings, the staging and the differential diagnosis of the disease. Findings using retinal imaging are discussed, including fluorescein angiography, OCT, adaptive optics imaging, confocal scanning laser ophthalmoscopy, and fundus autofluorescence, as are the findings using visual function testing including visual acuity and fundus-controlled microperimetry. We provide an overview of the therapeutic approaches for both non-neovascular and neovascular disease stages and provide a perspective of future directions including animal models and potential therapeutic approaches.

Contents

Abbreviations: AF, autofluorescence; MacTel, macular telangiectasia; OCT, optical coherence tomography; PDT, photodynamic therapy; VEGF, vascular endothelial growth factor.

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1. Introduction

Macular telangiectasia (MacTel) type 2 is a bilateral disease of unknown cause with characteristic alterations of the macular capillary network and neurosensory atrophy. The disease manifests initially temporal to the foveal center, but may later encompass an oval area with a radius of about 6° horizontally and 5° vertically centered on the foveola. Symptoms typically start in the fifth or sixth decade of life. Some patients have a positive family history. Possibly due to low disease awareness, both amongst clinicians and patients, the diagnosis of MacTel is often delayed. It may also be misdiagnosed as age-related macular degeneration in the presence of neovascularization.

Beginning in 2005, the *Macular Telangiectasia Project* (*"MacTel Project"*; http://www.mactelresearch.org) has initiated major research activity on MacTel type 2. In an effort involving a number of clinical centers and basic science laboratories, this privately funded project aims to develop a better understanding of the clinical features and natural history of the disease, to elucidate a genetic association, to identify animal models which may improve the understanding of intrinsic pathogenetic mechanisms, and ultimately, to identify and test potential treatments.

This increased research interest in MacTel type 2 has helped to gain new insights in the disease in several ways. Characteristic phenotypic findings have been identified using various imaging techniques that now allow an improved clinical differentiation of this entity from other retinal diseases. Moreover, the description of affected but asymptomatic family members of patients together with the higher than expected prevalence in population based studies should clearly increase the awareness of the disease.

In this review, updated phenotypic characterization of MacTel type 2 including morphologic data (derived from retinal imaging and histopathology), data on retinal dysfunction, epidemiology, genetics, together with a review of likely pathogenic mechanisms and attempted treatments are provided.

2. Terminology

A variety of terms have been used for MacTel type 2. The first description of the disease was likely a short report of Donald Gass on *"bilateral paracentral capillary telangiectasia of unknown cause"* (Gass, 1977) followed by a case series on *"focal parafoveal retinal telangiectasis"* (Hutton et al., 1978) which further characterized the disease as a distinct clinical entity with familial occurrence. The term "retinal telangiectasis" was introduced earlier by Reese to describe various retinopathies characterized by dilated and incompetent vessels (Reese, 1956). However, his case series, as well as a later fluorescein angiographic study on retinal telangiectasis (Gass, 1968), did not include MacTel type 2.

In a revised version of an earlier publication (Gass and Oyakawa, 1982), Gass and Blodi classified various disease entities with ectatic