MACULAR DEGENERATION

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Title: MACULAR RETINAL DYSTROPHY, DEAFNESS AND DIABETES MELLITUS , ASSOCIATED WITH A MUTATION OF MITOCHONDRIAL DNA (tRNA $^{leu(3243)}$)

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Purpose:To report the association of macular dystrophy with maternally inherited diabetes mellitus, deafness and "pigmentary retinopathy", due to a mutation of mitochondrial DNA (tRNA (leu (3243)) .

Methods:We examined 8 diabetic probands with this mutation to precise the characteristics of the retinopathy associated with this mutation.

Results: These probands belonged to 6 different families; six of them had deafness. The 8 patients had a bilateral macular dystrophy, called "pattern dystrophy", characterized by radiate pattern of pigmented lesions surrounding the macula, and atrophic changes in the posterior pole. The periphery of the fundus was unaffected. The extent of pigmented lesions and atrophic changes differed with cases, but the 3 probands of the same family had the same aspect of the fundus. Visual acuity was normal in 7 patients, and slightly decreased in one. Electroretinogram was normal, that definitively eliminates the diagnosis of retinitis pigmentosa.

Conclusion: the retinal lesion associated with maternally inherited diabetes mellitus due to a mutation of mitochondrial DNA (tRNA $^{(leu\ (3243))}$ is a macular pattern dystrophy, whose visual prognosis is relatively good . This aspect could be a good marker of the mutation.

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Zermatt Macular Dystrophy: a new autosomal dominant phenotype and exclusion of known macular genes.

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Purpose: Age related macular degeneration remains the leading cause of blindness in the Western countries in adults over 65 years of age. For a subgroup of familial macular dystrophies such as Best disease, North Carolina macular dystrophy, pattern dystrophies and Sorsby's fundus dystrophy the genetic defect has been mapped or identified. The purpose of this paper is to describe a yet unrecognized autosomal dominant progressive macular dystrophy, named "Zermatt Macular Dystrophy" after the origin of the affected family, and to procede with a mutational analysis of the known macular genes.

Methods: The family was ascertained through the macular clinic at Jules Gonin Eye Hospital in Lausanne. After informed consent, a comprehensive eye examination, including fluorescein angiogram was performed on every family member at risk of carrying the disease gene. Blood was drawn for DNA extraction and mutational analysis of known macular genes was performed.

Results: The four generation Swiss family originated from Zermatt (Valais region). Of a total of 51 individuals at risk, 23 were affected. The early phenotypic changes consisted of central pigmentary alterations during adolescence followed by multiple drusenoid deposits in the course of the second and third decade. Early symptoms include dyschromatopsia and progressive perifoveal scotomas, ultimately leading to the loss of central vision in the fourth decade due to extensive geographical atrophy. The transmission of the disease is autosomal dominant and penetrance appeared to be complete.
No mutation was identified in the known macular genes.

Conclusions: Zermatt macular dystrophy appears to be a new macular phenotype for which the genetic defect remains unidentified. A linkage analysis of this family will be the next approach.

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TITLE: "KINETIC B-SCAN ULTRASONOGRAPHY OF THE POSTERIOR VITREORETINAL INTERFACE IN EYES WITH AGE RELATED MACULAR HOLES"

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PURPOSE: The etiopathology of age related macular holes remains uncertain. There's general agreement that macular vitreoretinal interface plays a determinant role in the pathogenesis. In this paper we will investigate which is this role by the ultrasonography point of view.

METHODS: By using kinetic B-scan ultrasonography we evaluate the posterior vitreoretinal interface of 30 eyes having macular holes, without retinal detachment, which were previously diagnosed by biomicroscopy.

RESULTS: A complete posterior vitreous detachment was confirmed in 5 patients, an operculae or pseudo-operculae could be visualiced in 10 patients. Incomplete posterior vitreous separation with vitreous still attached to the macular area was demonstrated in 25 patients. Macular thickness was evident in 22 patients, while foveal "depression" could be confirmed in 18 eyes.

CONCLUSIONS: Some hypothesis are based on the active contraction of the posterior vitreous cortex over the macula. Vitreous induced retraction can produce foveal detachment as the first step in the development of a macular hole, cases which show incomplete vitreous separation may have vitreous cortex still adherent to the macula what provokes continuos or intermittent traction on the macula. Ecographically detectable opercula or pseudo-opercula, may contribute to better distinguish the evolutive stage of the macular hole.

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IDENTIFICATION OF GLYCOSAMINOGLYCANS IN AGE-RELATED MACULAR DEPOSITS

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Purpose. To investigate the presence and localisation of glycosaminoglycans (GAGs) in human maculae with age-related maculopathy (ARM).

Methods. ARM was defined as presence of basal laminar deposit (BLD) and/or drusen in the macula on histology. The presence and localisation of GAGs in 25 paraffin-embedded human maculae were examined immunohistochemically with monoclonal antibodies specific for chondroitin-4-sulfate, heparan sulfate proteoglycan, and keratan sulfate. Furthermore, macular homogenates were separately analysed with two-dimensional electrophoresis on cellulose acetate membranes. Quantitative analysis of GAGs was done spectrophotometrically.

Results. Immunohistochemically, all BLD stained positive for chondroitin-4-sulfate, and focally positive for heparan sulfate proteoglycan. Drusen did not stain with any of the monoclonal antibodies. With two-dimensional electrophoresis it was demonstrated that all macular extracts contained chondroitin sulfate. Heparan sulfate was only expressed in maculae with ARM. The total amount of GAGs in macular extracts with BLD was significantly higher than in maculae without BLD ($p=0.001$). There was no relation between the amount of GAGs and drusen.

Conclusions. Significant differences in amount and composition of GAGs, between maculae with ARM and controls, were demonstrated with these techniques. Furthermore, chondroitin-4-sulfate and heparan sulfate proteoglycan were detected immunohistochemically in BLD, but not in drusen.