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Type 4 macular neovascularization: expanding the OCT classification in AMD

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This article describes a novel phenotype of macular neovascularization (MNV) in age-related macular degeneration (AMD). The authors propose a distinct entity, termed Type 4 MNV, characterized by aggressive intraretinal and preretinal proliferation. This subtype combines features of Type 1 and Type 2 neovascularization, with marked vascular extension into the inner retinal and preretinal compartments identified by optical coherence tomography (OCT) and OCT angiography (OCTA).

This retrospective multicenter case series included 11 patients with neovascular AMD. Multimodal imaging enabled consistent characterization across centers. The analysis demonstrated a reproducible pattern of advanced retinal disorganization associated with neovascular complexes extending from the choroid to the inner retinal surface. Key findings included the hyperreflective oblique band (HOB) sign in all cases and central posterior hyaloid fibrosis in 81.8% of eyes. Epiretinal membranes were also frequently observed (81.8%), often accompanied by radial tractional changes, suggesting a mechanical contribution to disease architecture. OCTA confirmed that these structures corresponded to active neovascular flow, forming an anastomotic network connecting the choroidal, intraretinal, and preretinal compartments.

These findings suggest that Type 4 MNV represents an advanced stage of neovascular remodeling, potentially evolving from Type 2 lesions with an underlying Type 1 component. This progression appears to be associated with widespread retinal architectural disruption involving multiple retinal layers. The study supports a model of disorganized angiogenesis combined with early fibrosis and mechanical factors, including vitreoretinal traction. The consistent presence of the HOB sign may represent an early indicator of this transition; however, this hypothesis requires validation in longitudinal studies.

Clinically, the most relevant aspect of this phenotype is its poor visual prognosis. Most patients presented with severe visual impairment at diagnosis (≤20/630), and no meaningful functional improvement was observed following anti-VEGF therapy, even among previously treated eyes. These findings suggest that Type 4 MNV may represent a treatment-refractory phenotype driven by early subretinal fibrosis, complex vascular architecture, and tractional forces associated with intraretinal proliferation and epiretinal membrane formation, ultimately leading to irreversible retinal damage.

Despite its novelty, the study has several important limitations. The retrospective design and small sample size limit its statistical power and generalizability. Furthermore, the absence of a control group prevents estimation of the prevalence of this phenotype within the broader AMD population. The lack of longitudinal follow-up also limits understanding of disease evolution and the potential transition from other MNV subtypes. In addition, the absence of histopathological correlation restricts validation of the proposed mechanisms, particularly those related to central posterior hyaloid fibrosis.

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Another important consideration is the clinical applicability of this classification. Although Type 4 MNV represents a meaningful anatomical refinement, its immediate impact on therapeutic decision-making remains uncertain, as current management of neovascular AMD continues to rely primarily on anti-VEGF therapy. Therefore, its principal value may lie in prognostic stratification and in identifying eyes with advanced structural damage and limited potential for visual recovery.

In conclusion, this study refines the classification of macular neovascularization in AMD by defining a phenotype associated with aggressive behavior, extensive retinal disorganization, and poor visual outcomes. Early recognition of Type 4 MNV may facilitate more realistic patient counseling and help avoid unnecessary treatment escalation in eyes with established fibrosis and apparent treatment resistance. Nevertheless, validation of Type 4 MNV as a distinct clinical entity will require larger prospective studies, longitudinal imaging analyses, and histopathological confirmation. Future investigations should also determine whether early identification of this phenotype can influence therapeutic strategies and alter disease progression.