

微囊样黄斑水肿在神经眼科疾病中的研究进展

崔雪晴^{1,2}, 邹文军^{1,2}

引用:崔雪晴,邹文军. 微囊样黄斑水肿在神经眼科疾病中的研究进展. 国际眼科杂志, 2026,26(11):1932-1937.

基金项目:无锡市“太湖之光”科技攻关项目(No.Y20242204);
无锡市卫生健康“三名”战略项目

作者单位:¹(214000)中国江苏省无锡市,江南大学附属中心医院 无锡市第二人民医院;²(214122)中国江苏省无锡市,江南大学无锡医学院

作者简介:崔雪晴,女,在读硕士研究生,研究方向:眼底病、神经眼科。

通讯作者:邹文军,女,博士,主任医师,主任,硕士研究生导师,研究方向:眼底病、神经眼科. wenjunzou2022@163.com

收稿日期:2026-04-07 修回日期:2026-09-07

摘要

微囊样黄斑水肿(MME)是位于视网膜内核层(INL)的一种特征性影像学表现,该表现最早在多发性硬化(MS)相关视神经炎患者中被报道,后续研究发现,MME可见于多种神经眼科疾病,包括视神经脊髓炎谱系疾病(NMOSD)、非动脉炎性前部缺血性视神经病变(NAION)及遗传性视神经病变等,并与疾病严重程度及视功能损害密切相关。目前认为,MME在神经眼科疾病中的发生可能与逆行跨突触变性、玻璃体黄斑牵引等机制相关。深入探究MME的临床特征与病理生理机制,能够为各类神经眼科疾病的临床诊断、病情监测及预后评估提供全新视角与科学依据。

关键词:微囊样黄斑水肿;内核层;视神经脊髓炎谱系疾病;光学相干断层扫描

DOI:10.3980/j.issn.1672-5123.2026.11.11

Research progress of microcystic macular edema in neuro-ophthalmic diseases

Cui Xueqing^{1,2}, Zou Wenjun^{1,2}

Foundation items: Wuxi “Taihu Light” Science and Technology Key Project (No.Y20242204); “Three Famous” Strategic Project of Wuxi Health Commission

¹Jiangnan University Medical Center; Wuxi No.2 People’s Hospital, Wuxi 214000, Jiangsu Province, China; ²Wuxi School of Medicine, Jiangnan University, Wuxi 214122, Jiangsu Province, China

Correspondence to: Zou Wenjun. Jiangnan University Medical Center; Wuxi No. 2 People’s Hospital, Wuxi 214000, Jiangsu Province, China; Wuxi School of Medicine, Jiangnan University, Wuxi 214122, Jiangsu Province, China. wenjunzou2022@163.com

Received:2026-04-07 Accepted:2026-09-07

Abstract

• Microcystic macular edema (MME) is a characteristic retinal imaging finding characterized by cystic changes within the inner nuclear layer (INL). It was first described in patients with optic neuritis associated with multiple sclerosis (MS). Subsequent studies have shown that MME is also present in a broad spectrum of neuro-ophthalmic disorders, including neuromyelitis optica spectrum disorder (NMOSD), non-arteritic anterior ischemic optic neuropathy (NAION), and hereditary optic neuropathies. Moreover, its presence is closely associated with disease severity and visual dysfunction. Current evidence suggests the occurrence of MME in neuro-ophthalmic diseases may be related to retrograde transsynaptic degeneration and vitreomacular traction. A deeper understanding of the clinical characteristics and pathophysiological mechanisms of MME may provide a new perspective and scientific basis for the clinical diagnosis, disease monitoring and prognosis evaluation of various neuro-ophthalmic diseases.

• KEYWORDS: microcystic macular edema; inner nuclear layer; neuromyelitis optica spectrum disorder; optical coherence tomography

Citation: Cui XQ, Zou WJ. Research progress of microcystic macular edema in neuro-ophthalmic diseases. Guoji Yanke Zazhi (Int Eye Sci), 2026,26(11):1932-1937.

0 引言

微囊样黄斑水肿(microcystic macular edema, MME)是一种主要累及黄斑中心凹旁视网膜内核层(inner nuclear layer, INL)的特征性眼底影像学表现,其在光学相干断层扫描(optical coherence tomography, OCT)下的典型征象为:局限于INL内多发、边界清晰的垂直走行囊样空腔,呈弱反射信号^[1-3]。随着近年来OCT成像技术的发展及对MME认识的不断深入,神经眼科领域关于MME的研究逐渐增多。目前MME已被纳入非血管源性囊样黄斑病变谱系的范畴,但其确切发生机制仍未完全明确^[4-5]。因此,进一步阐明MME的临床特征与发病机制具有重要意义,现就MME在神经眼科疾病中的研究进展作一综述。

1 神经眼科疾病相关MME的定义与疾病谱

2012年,Gelfand等^[6]首次在多发性硬化(multiple sclerosis, MS)相关视神经炎患者中报道了MME,该表现最初被命名为微囊样黄斑水肿(microcystic macular oedema, MMO),并发现其与疾病的严重程度相关。MME具有广泛的疾病谱,可见于多种疾病,包括不同病因导致的视神经萎缩,年龄相关性黄斑变性(age-related macular degeneration, ARMD)、糖尿病视网膜病变(diabetic

retinopathy, DR),以及黄斑前膜剥除术后等^[4,7-8]。2014年,Burggraaff等^[1]进一步细化了MME的诊断标准:MME是仅局限于黄斑中心凹周围INL的小的弱反射病变,不与邻近视网膜层的囊肿融合,且需与血管伪影区分^[1]。MME的存在形式主要分为3种:(1)纵向存在形式:间隔时间 ≥ 1 wk的两次黄斑扫描均检出;(2)瞬态/动态存在形式:至少在一次扫描中检出,先前或随访扫描未发现;(3)静态存在形式:所有间隔时间 ≥ 1 wk的多次扫描均持续可见^[1]。神经眼科疾病是MME的主要累及范畴,尤以神经脊髓炎谱系疾病(neuromyelitis optica spectrum disorder, NMOSD)最为常见,亦可见于MS相关视神经炎、非动脉炎性前部缺血性视神经病变(non-arteritic anterior ischemic optic neuropathy, NAION)、遗传性视神经病变、压迫性及外伤性视神经病变等^[9]。为系统总结神经眼科疾病相关MME的发病率、影像学特征及主要发病机制,现将相关研究结果整理如下,见表1。

2 神经眼科疾病伴发MME的病理机制

MME的发生机制尚未完全明确,目前认为其形成可能涉及多种病理过程,其中逆行跨突触变性、玻璃体黄斑牵引及Müller细胞功能障碍被认为是主要机制,此外炎症反应及微循环异常也可能参与其中^[24]。(1)逆行跨突触变性假说:视神经病变导致视网膜神经节细胞(retinal ganglion cell, RGC)丢失,并进一步引起内层视网膜神经元(如双极细胞)逆行跨突触变性,导致INL结构异常,出现微囊样改变。研究发现,MME形成早期可能伴随INL增厚,表明INL厚度变化可能反映MME发生过程中的早期影像学改变^[2,25]。(2)玻璃体黄斑牵引假说:微囊腔形成机制类似视网膜劈裂,RGC丢失会造成黄斑厚度下降,加之玻璃体黄斑异常黏连产生牵拉力,可诱发视网膜层间劈裂并形成微囊腔,这种机制可能会促进微囊腔形成,但并非产生的必要条件^[24,26-28]。(3)Müller细胞功能障碍:Müller细胞位于INL,表达水通道蛋白4(aquaporin-4, AQP4),参与维持视网膜水分运输和离子稳态,其功能异常可导致液体代谢失衡及微囊样空腔形成^[29]。在NMOSD及遗传性视神经萎缩等疾病中,Müller细胞损伤可能通过破坏视网膜内环境稳定促进MME发生^[30-31]。

(4)炎症:可能作为疾病背景相关调节因素参与MME的发生^[5]。早期研究基于MS患者提出,视网膜炎症反应、小胶质细胞激活及神经元损伤可能参与MME形成^[32]。然而,随后研究发现,非炎症性视神经病变患者同样可出现MME,提示炎症反应并非MME形成的必要条件,这表明MME的形成可能主要依赖于视神经损伤后的神经退变过程,而炎症反应可能在特定疾病背景下发挥调节作用^[33]。(5)异常血流动力学:MME好发于黄斑旁鼻侧象限及颞侧象限^[1],该区域血流相对较差,容易缺血缺氧,且有证据表明NMOSD患者的视网膜微血管系统发生了改变^[34-35]。此外,Brar等^[36]报道MME可表现出弥漫性荧光素渗漏,提示血-视网膜屏障(blood-retinal barrier, BRB)功能异常可能与MME形成相关^[6]。

3 神经眼科疾病伴发MME的影像学表现

MME并非一种独立的疾病实体,其影像学特征与传统意义上的囊样黄斑水肿(cystoid macular edema, CME)存在显著区别。CME是位于视网膜外丛状层的多囊状积液,常与炎症、视网膜静脉阻塞、DR及白内障术后相关^[37-39]。二者是不同的眼底表现,借助OCT与眼底荧光素血管造影(fluorescein fundus angiography, FFA)可实现有效鉴别,见表2。

MME的核心影像学特征为OCT下黄斑区INL内的弱反射微囊,可伴随INL局部增厚(图1),其分布位置可随原发疾病类型存在差异^[41]。在红外成像(infrared imaging, IR)中,MME可表现为与INL微囊对应的暗区,有助于显示病变范围及空间分布^[4]。FFA显示,MME多数情况下无显荧光素渗漏,表明其形成并非主要依赖血管渗漏机制;少数病例可出现荧光素渗漏,提示BRB功能异常可能参与其发生^[6]。OCTA进一步发现,部分MME患者存在SRCP和DRCP血管密度下降^[4]。AO成像可观察到与INL微囊对应的暗反射椭圆形区域,边界呈强反射改变。已有研究指出^[15],相较于OCT的B扫描,SLO成像对MME的检出兼具更高的敏感性与特异性,可作为OCT的重要补充。

4 神经眼科疾病相关MME

4.1 NMOSD Gelfand等^[10]研究发现,约20%的NMOSD

表1 神经眼科疾病相关MME的临床及影像学特征比较

疾病名称	发病率(%)	影像学表现	主要发病机制
NMOSD相关视神经炎	20-26 ^[10]	OCT:伴随RNFL及GCL变薄 ^[11] OCTA:SRCP、DRCP密度降低 ^[4]	逆行跨突触变性、Müller细胞功能障碍及异常血流动力学 ^[4,12-13]
MS相关视神经炎	5-6 ^[14]	OCT:主要累及黄斑鼻侧INL ^[15] SLO:黄斑区新月形暗区 ^[14]	炎症相关神经退变及轴突损伤 ^[16-17]
遗传性视神经病变	5-6 ^[18]	OCT:常伴随ONL增厚 ^[18] AO:黄斑区椭圆形暗区 ^[19]	线粒体功能障碍及Müller细胞异常 ^[19-20]
NAION	20 ^[9]	OCT:部分出现与视盘水肿相关的短暂性MME,边界清晰,局限于视盘周围 ^[21]	缺血性视神经损伤导致的Müller细胞功能障碍 ^[21]
压迫性视神经病变	18 ^[9]	OCT:MME多位于与视觉通路损伤区域拓扑对应的INL ^[22] SLO:黄斑区环形低反射区 ^[23]	压迫导致的直接逆行轴索变性 ^[22]
外伤性视神经病变	20 ^[9]	OCT:RNFL变薄,INL散在高反射点 ^[22] SLO:边界模糊的“C形”低反射区 ^[4]	外伤引发的神经元变性 ^[22]

注:ONL:外核层;OCTA:光学相干断层扫描血管成像;RNFL:视网膜神经纤维层;SRCP:浅层视网膜毛细血管丛;DRCP:深层视网膜毛细血管丛;AO:自适应光学;SLO:扫描激光检眼镜。

表 2 MME 与 CME 的影像学鉴别

影像学检查	MME	CME
OCT	主要累及 INL,为微小、离散的腔隙性弱反射信号,大小约为 20 μm×30 μm-70 μm×90 μm;多集中于黄斑中心凹 500-1 800 μm ^[7,40]	位于视网膜外丛状层,囊腔尺寸较大,以黄斑中心凹为中心,呈花瓣样多囊分布 ^[7,40]
FFA	大多数无异常荧光表现,仅 1/4 患者可见晚期轻微荧光素渗漏 ^[10]	早期视网膜血管渗漏,晚期黄斑区呈典型花瓣样荧光积存 ^[7]

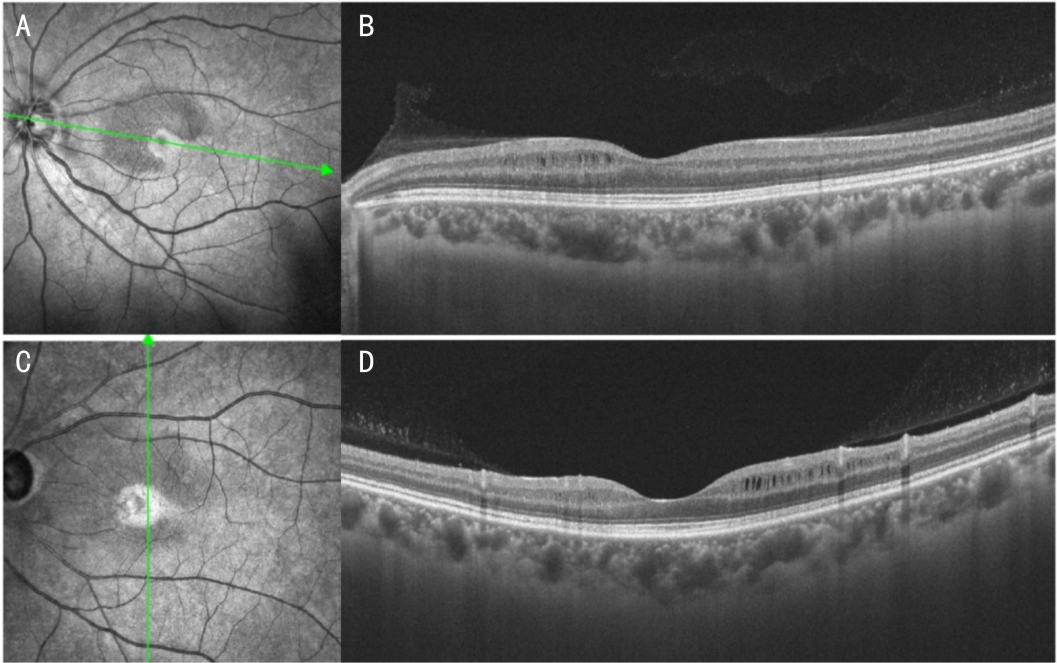


图 1 NMOSD 伴 MME 患者的 OCT 图像 A、B:病例 1,女,48 岁,左眼,病程 33 mo,最佳矫正视力 0.02;C、D:病例 2,女,33 岁,左眼,病程 19 mo,最佳矫正视力 0.4;A、C:黄斑区可见特征性暗区,绿色箭头示 OCT 扫描定位线;B、D:可见 INL 内微囊样改变,伴局部视网膜增厚。

患者存在 MME,且仅见于有视神经炎病史的患眼。后续研究进一步显示,NMOSD 患者 MME 发生率约为 20%~26%,明显高于 MS 患者;在 AQP4-IgG 阳性的 NMOSD 相关视神经炎患眼中,MME 发生率可达约 40%^[12]。此外,NMOSD 患者的 MME 与 RNFL 和神经节细胞层(ganglion cell layer,GCL)厚度减少及视功能损害相关,它可能反映了视神经的损伤程度^[11]。OCTA 显示,SRCP 及 DRCP 血管密度下降,且部分微血管改变可能早于 MME 出现^[13]。目前,NMOSD 相关 MME 的具体发病机制尚未完全明确,可能涉及视神经损伤后的逆行性神经退变、视网膜免疫炎症反应以及 BRB 功能异常等多个过程^[12]。AQP4-IgG 介导的 Müller 细胞功能异常可能导致视网膜内液体稳态失衡,而视神经损伤后的 RGC 丢失可进一步诱导跨突触变性及胶质细胞激活,共同促进 INL 微囊样改变形成^[13]。

4.2 MS MS 患者的 MME 几乎仅见于有视神经炎(optic neuritis, ON)病史的患眼(90.5%),这表明 MME 与既往视神经炎导致的视神经损伤密切相关,并且 MS 伴 MME 患眼 INL 厚度较对侧眼增加,可能是 ON 相关眼部炎症的结果^[15,42]。Kaufhold 等^[15]研究发现,较薄的视盘周围视网膜神经纤维层(peripapillary retinal nerve fiber layer,pRNFL)厚度与 MME 发生风险增加相关,其中 pRNFL 厚度低于 64.6 μm 时发生 MME 的风险显著升高(odds ratio=13.6)。有研究推测,MS 患者 MME 的发病机制与视

网膜神经元、轴突等无髓鞘区域的紧密连接结构破坏有关,进而引发局部小胶质细胞激活及炎症反应^[15,43],导致视网膜内液体积聚形成囊样异常,同时可能伴随 BRB 局部破坏^[16-17]。MS 患者的 MME 呈现时间动态性,多数病例基线无微小囊样异常,与未发生 MME 的患眼相比,最终发生 MME 的 MS 患眼在基线时就存在视网膜 INL 增厚的表现^[10,15]。

4.3 遗传性视神经病变 Carbonelli 等^[18]的研究指出,线粒体视神经病变(mitochondrial optic neuropathy, MON)中 MME 的患病率约为 5%-6%,且常伴随 ONL 增厚。既往研究表明,在合并 MME 的 MON 患者中,可能以玻璃体黄斑牵引为驱动力,在视网膜内层变薄的基础上产生反向机械力,导致 ONL 增厚及牵拉性微囊腔形成,逆行性跨突触变等因素发挥协同作用^[18,20]。常染色体显性遗传性视神经萎缩(autosomal dominant optic atrophy, ADOA)为 MON 的常见类型^[44]。ADOA 以双侧视力下降为特征,伴中心暗点、视盘颞侧苍白及色觉异常,23%的患者可出现 MME,且该病变更常见于视力中度下降、RNFL 更薄的年轻患者^[19];在基因型方面,剪接突变在合并 MME 的患者中更常见;MME 在 AO 下表现为椭圆形暗区,与 IR 图像的弱反射区相吻合^[19,45]。

4.4 NAION NAION 患者中存在两种性质不同的微囊性改变,分别为可逆性急性微囊样改变和永久性微囊样改

变,这类病变的形成均与 Müller 细胞功能障碍相关,但机制各异^[21]。可逆性急性微囊样改变是 BRB 及类淋巴系统受损致液体渗出、Müller 细胞重吸收超负荷形成的暂时性改变,随视盘水肿消退可逐渐恢复^[46-48];而永久性微囊样改变则由 RCG 显著丢失引发逆行跨突触变性,导致 Müller 细胞异常或变性,其遗留空泡液体积聚形成,与神经纤维层/神经节细胞复合体变薄相关^[21,49-50]。Chapelle 等^[51]研究发现 NAION 中视网膜液体的存在与 6 mo 视功能结局没有显著相关,提示 NAION 相关 MME 可能是视神经缺血损伤后继发的组织反应性改变,而非独立的视功能预后因素。

4.5 压迫性视神经病变 2016 年, Pott 等^[22]的前瞻性研究显示,在非视神经炎源性视神经萎缩的患者中, MME 的发生率为 20.4%,以压迫性视神经病变为首要病因,其中垂体瘤、视神经胶质瘤压迫较为常见^[26,52]。MME 的出现常早于视觉功能异常,可作为“早期预警信号”^[23,53]。OCT 示 MME 多位于与视觉通路损伤区域拓扑对应的部位,如垂体瘤压迫视交叉导致颞侧视野缺损时, MME 位于黄斑鼻侧 INL;视神经胶质瘤压迫视神经导致鼻侧视野缺损时, MME 位于黄斑颞侧 INL,且 INL 厚度与压迫持续时间正相关。SLO 可见黄斑区低反射区呈环形^[23]。直接逆行轴索变性作为与压迫性病变相关的重要病理类型,由前视觉通路(如视束)直接受损诱发,具有进展迅速、破坏性显著的特征^[22]。

4.6 外伤性视神经病变 外伤性视神经病变相关 MME 多发生于外伤后 6-12 mo,其原发损伤以视神经挫伤、视神经管骨折为主要类型^[22]。MME 多出现于患眼视力稳定后,部分伴随轻度视力波动。OCT 显示患眼 RNFL 完全缺失或显著变薄, MME 所在区域 INL 局部增厚,且病变周围可见散在强反射点,其分布范围超出 MME 病变区域,可能与外伤引发的 INL 神经元急性变性(如细胞碎片聚集)相关。SLO 下 MME 多呈边界模糊的“C 形”弱反射区,因外伤多为单侧、局部撞击, RGC 丢失呈非对称性,进而导致 MME 呈弥漫性分布^[4,22]。

4.7 其他视神经病变 其他可并发 MME 的视神经病变还包括慢性复发性炎性视神经病变(chronic relapsing inflammatory optic neuropathy, CRION)^[54]、感染性视神经病变^[55]、中毒性视神经病变^[56],以及脑积水^[57]、视盘玻璃膜疣^[9]、视盘小凹^[58]、颅内高压所致视神经病变^[9]等。Hipolito-Fernandes 等^[55]报道 1 例 51 岁男性在病毒性上呼吸道感染后出现双侧感染性视神经炎,随访 5 mo 时 OCT 示双眼 RNFL 厚度减少, MME 多呈黄斑旁环形分布且黄斑鼻侧象限多见。Balk 等^[33]在 1 例 CRION 患者中观察到 MME, OCT 表现为远离视网膜内血管区的多发弱反射囊性区域,伴患眼视觉诱发电位(visual evoked potential, VEP) P100 波潜伏期显著延迟,脑部及脊髓磁共振成像(magnetic resonance imaging, MRI)可见患侧视神经炎症。视盘小凹患者的 MME 多为偶然发现,常伴随累及乳头黄斑束的 RNFL 缺损(小凹多位于视盘颞侧缘),推测 MME 继发于神经纤维萎缩,由神经节细胞跨突触逆行变性及 Müller 细胞功能障碍共同导致^[58]。

5 小结与展望

MME 是定位于 INL 的特征性囊性改变,并非某一特定疾病的专属体征,可见于多种神经眼科疾病。通过 OCT、OCTA、SLO、IR 等影像学检查可明确识别。其发生

机制目前认为主要与逆行跨突触变性以及玻璃体黄斑牵引相关。MME 的出现不仅反映潜在的视网膜结构损伤,也可能提示疾病进展及视觉功能损害风险,因此在临床管理中具有重要的辅助评估价值。例如,在 MS、NMOSD 中, MME 可作为疾病严重程度评估和长期随访的重要影像学指标,但尚缺乏特异性治疗策略,临床处理主要围绕原发病控制^[13,59-60]。目前国内神经眼科领域关于 MME 的临床研究仍较为有限,现有研究主要集中于黄斑疾病。研究显示,特发性黄斑前膜患者术前 MME 发生率约为 35%-51%,其发生与黄斑前膜分期较晚及病程延长相关;术后 MME 可持续存在或新发,并可能影响视觉恢复^[8,61]。然而,当前 MME 研究仍存在诸多不足,包括缺乏评估其长期视觉功能影响的大样本循证医学证据,不同疾病背景下 MME 形成的特异性病理生理机制尚未完全明确,以及针对 MME 相关结构改变的精准干预策略仍较缺乏。随着影像人工智能(artificial intelligence, AI)技术的发展,基于深度学习的 OCT 影像分析方法已在多种视网膜疾病的自动识别、定量评估及风险预测中展现出潜力,未来可进一步用于 MME 的自动化检测及预后评估^[62-63]。同时,结合多模态影像分析和纵向研究,将有助于深入阐明 MME 的临床价值,并推动其向疾病监测和个体化治疗相关影像学生物标志物转化^[64-65]。

利益冲突声明: 本文不存在利益冲突。

作者贡献声明: 崔雪晴论文选题与修改,初稿撰写,文献检索,数据分析;邹文军选题指导,论文修改及审阅。所有作者阅读并同意最终的文本。

参考文献

[1] Burggraaff MC, Trieu J, de Vries-Knoppert WA, et al. The clinical spectrum of microcystic macular edema. Invest Ophthalmol Vis Sci, 2014,55(2):952-961.
[2] Saidha S, Sotirchos ES, Ibrahim MA, et al. Microcystic macular oedema, thickness of the inner nuclear layer of the retina, and disease characteristics in multiple sclerosis: a retrospective study. Lancet Neurol, 2012,11(11):963-972.
[3] Govetto A, Virgili G, Rodriguez FJ, et al. Functional and anatomical significance of the ectopic inner foveal layers in eyes with idiopathic epiretinal membranes: Surgical Results at 12 Months. Retina, 2019,39(2):347-357.
[4] Carlà MM, Ripa M, Crincoli E, et al. The spectrum of microcystic macular edema: Pathogenetic insights, clinical entities, and functional prognosis. Surv Ophthalmol, 2025,70(5):982-994.
[5] Gaudric A, Audo I, Vignal C, et al. Non - vasogenic cystoid maculopathies. Prog Retin Eye Res, 2022,91:101092.
[6] Gelfand JM, Nolan R, Schwartz DM, et al. Microcystic macular oedema in multiple sclerosis is associated with disease severity. Brain, 2012,135(Pt 6):1786-1793.
[7] Govetto A, Francone A, Lucchini S, et al. Microcystoid macular edema in epiretinal membrane: not a retrograde maculopathy. Am J Ophthalmol, 2025,272:48-57.
[8] 吕喆, 岑金儿, 陆洋, 等. 特发性黄斑前膜手术前后黄斑微囊样水肿的临床观察. 中华眼底病杂志, 2022,38(10):805-810.
[9] Coutureau T, Butterworth J, Biotti D, et al. Microcystic macular edema caused by non - glaucomatous optic atrophy: a single - center, retrospective, cohort study in France. Vision (Basel), 2024,8(3):52.
[10] Gelfand JM, Cree BA, Nolan R, et al. Microcystic inner nuclear layer abnormalities and neuromyelitis optica. JAMA Neurol, 2013,

70(5):629-633.

[11] Borruat FX. *In vivo* identification of morphologic retinal abnormalities in neuromyelitis optica. *Neurology*, 2014,82(2):188-189.

[12] Reichenbach A, Wurm A, Pannicke T, et al. Müller cells as players in retinal degeneration and edema. *Graefes Arch Clin Exp Ophthalmol*, 2007,245(5):627-636.

[13] Li J, Chen YH, Zhang Y, et al. Visual function and disability are associated with microcystic macular edema, macular and peripapillary vessel density in patients with neuromyelitis optica spectrum disorder. *Front Neurol*, 2022,13:1019959.

[14] Bennett JL, de Seze J, Lana-Peixoto M, et al. Neuromyelitis optica and multiple sclerosis: Seeing differences through optical coherence tomography. *Mult Scler*, 2015,21(6):678-688.

[15] Kaufhold F, Zimmermann H, Schneider E, et al. Optic neuritis is associated with inner nuclear layer thickening and microcystic macular edema independently of multiple sclerosis. *PLoS One*, 2013,8(8):e71145.

[16] Frahm N, Ellenberger D, Stahmann A, et al. Treatment switches of disease-modifying therapies in people with multiple sclerosis: long-term experience from the German MS Registry. *Ther Adv Neurol Disord*, 2024,17:17562864241239740.

[17] Klinkenbusch A, Kern M, Kohnen T. Microcystic macular edema as biomarker for multiple sclerosis. *Ophthalmologie*, 2026,123(2):147-149.

[18] Carbonelli M, La Morgia C, Savini G, et al. Macular microcysts in mitochondrial optic neuropathies: prevalence and retinal layer thickness measurements. *PLoS One*, 2015,10(6):e0127906.

[19] Eckmann-Hansen C, Bek T, Sander B, et al. Prevalence of macular microcystoid lacunae in autosomal dominant optic atrophy assessed with adaptive optics. *J Neuroophthalmol*, 2022,42(3):328-333.

[20] Wang D, Liu HL, Du YY, et al. Characterisation of thickness changes in the peripapillary retinal nerve fibre layer in patients with Leber's hereditary optic neuropathy. *Br J Ophthalmol*, 2021,105(8):1166-1171.

[21] Chapelle AC, Rakic JM, Plant GT. Nonarteritic anterior ischemic optic neuropathy: cystic change in the inner nuclear layer caused by edema and retrograde maculopathy. *Ophthalmol Sci*, 2023,3(1):100230.

[22] Pott JW, de Vries-Knoppert WA, Petzold A. The prevalence of microcystic macular changes on optical coherence tomography of the macular region in optic nerve atrophy of non-neuritis origin: a prospective study. *Br J Ophthalmol*, 2016,100(2):216-221.

[23] Goel N. "Doughnut appearance" of macular microcysts due to optic atrophy on optical coherence tomography angiography. *Retin Cases Brief Rep*, 2026,20(5):688-690.

[24] Barboni P, Carelli V, Savini G, et al. Microcystic macular degeneration from optic neuropathy: not inflammatory, not trans-synaptic degeneration. *Brain*, 2013,136(7):e239.

[25] Monteiro ML, Araújo RB, Suzuki AC, et al. Homonymous hemianopic hyporeflective retinal abnormality on infrared confocal scanning laser photography: a novel sign of optic tract lesion. *J Neuroophthalmol*, 2016,36(1):46-49.

[26] Monteiro MLR, Sousa RM, Araújo RB, et al. Diagnostic ability of confocal near-infrared reflectance fundus imaging to detect retrograde microcystic maculopathy from chiasm compression. A comparative study with OCT findings. *PLoS One*, 2021,16(6):e0253323.

[27] Govetto A, Su D, Farajzadeh M, et al. Microcystoid macular changes in association with idiopathic epiretinal membranes in eyes with and without glaucoma: clinical insights. *Am J Ophthalmol*,

2017,181:156-165.

[28] Brandt AU, Oberwahrenbrock T, Kadas EM, et al. Dynamic formation of macular microcysts independent of vitreous traction changes. *Neurology*, 2014,83(1):73-77.

[29] Goodyear MJ, Crewther SG, Junghans BM. A role for aquaporin-4 in fluid regulation in the inner retina. *Vis Neurosci*, 2009,26(2):159-165.

[30] Abegg M, Dysli M, Wolf S, et al. Microcystic macular edema: retrograde maculopathy caused by optic neuropathy. *Ophthalmology*, 2014,121(1):142-149.

[31] Wolff B, Azar G, Vasseur V, et al. Microcystic changes in the retinal internal nuclear layer associated with optic atrophy: a prospective study. *J Ophthalmol*, 2014,2014:395189.

[32] Liu CX, Xiao H, Zhang XY, et al. Optical coherence tomography angiography helps distinguish multiple sclerosis from AQP4-IgG-seropositive neuromyelitis optica spectrum disorder. *Brain Behav*, 2021,11(5):e02125.

[33] Balk LJ, Killestein J, Polman CH, et al. Microcystic macular oedema confirmed, but not specific for multiple sclerosis. *Brain*, 2012,135(12):e226.

[34] Chen YH, Shi C, Zhou LL, et al. The detection of retina microvascular density in subclinical aquaporin-4 antibody seropositive neuromyelitis optica spectrum disorders. *Front Neurol*, 2020,11:35.

[35] Kwapong WR, Peng CL, He ZY, et al. Altered macular microvasculature in neuromyelitis optica spectrum disorders. *Am J Ophthalmol*, 2018,192:47-55.

[36] Brar M, Yuson R, Kozak I, et al. Correlation between morphologic features on spectral-domain optical coherence tomography and angiographic leakage patterns in macular edema. *Retina*, 2010,30(3):383-389.

[37] Hosseini F, Asadi F, Rabiei R, et al. Applications of artificial intelligence in diagnosis of uncommon cystoid macular edema using optical coherence tomography imaging: a systematic review. *Surv Ophthalmol*, 2024,69(6):937-944.

[38] 唐树泽, 杨宇. 黄斑水肿的发病机制及治疗方式研究进展. *临床医学进展*, 2023,13(12):19769-19777.

[39] Abou-Jokh Rajab B, Doncel-Fernández C, Sánchez-Liñan N, et al. Assessment of the retinal ganglion cell layer after uncomplicated cataract surgery. *J Clin Med*, 2024,13(12):3579.

[40] Yang XH, Wang ZY, Yu YP, et al. Clinical features and prognosis in idiopathic epiretinal membranes with different types of intraretinal cystoid spaces. *Retina*, 2022,42(10):1874-1882.

[41] Arora S, Zur D, Iovino C, et al. Peripapillary fluid: obvious and not so obvious!. *Surv Ophthalmol*, 2024,69(3):311-329.

[42] Burguet Villena F, Sellathurai S, Schoenholzer K, et al. Case Report: Progressive visual decline after optic neuritis associated with microcystic macular oedema. *Front Neurol*, 2026,17:1772551.

[43] Antony BJ, Lang A, Swingle EK, et al. Simultaneous segmentation of retinal surfaces and microcystic macular edema in SDOCT volumes. *Proc SPIE Int Soc Opt Eng*, 2016,9784:97841C.

[44] Ai C, Li HY, Wang CY, et al. Vitamin A treatment restores vision failures arising from Leber's hereditary optic neuropathy-linked mtDNA mutation. *JCI Insight*, 2025,10(8):e188962.

[45] Gocho K, Kikuchi S, Kabuto T, et al. High-resolution en face images of microcystic macular edema in patients with autosomal dominant optic atrophy. *Biomed Res Int*, 2013,2013:676803.

[46] Delle C, Wang XW, Nedergaard M. The ocular glymphatic system-current understanding and future perspectives. *Int J Mol Sci*, 2024,25(11):5734.

[47] Uddin N, Rutar M. Ocular lymphatic and glymphatic systems;

implications for retinal health and disease. *Int J Mol Sci*, 2022,23(17):10139.

[48] Wang XW, Delle C, Nedergaard M, et al. Glymphatic transport and ocular diseases. *Prog Retin Eye Res*, 2026,110:101433.

[49] Zhang W, Sun XQ, Peng XY. Macular ganglion cell complex injury in different stages of anterior ischemic optic neuropathy. *World J Clin Cases*, 2021,9(21):5830–5839.

[50] Fouad YA, Hamza MN, Wessam MM. Prevalence and distribution of macular fluid with central retinal artery occlusion and anterior ischemic optic neuropathy. *Clin Ophthalmol*, 2024,18:887–893.

[51] Chapelle AC, Rakic JM, Plant GT. The occurrence of intraretinal and subretinal fluid in anterior ischemic optic neuropathy; pathogenesis, prognosis, and treatment. *Ophthalmology*, 2023,130(11):1191–1200.

[52] Bhatti MT, Mansukhani SA, Chen JJ. Microcystic macular edema in optic nerve glioma. *Ophthalmology*, 2020,127(7):930.

[53] Mahroo OA, Shalchi Z, Williamson TH, et al. Re: Bhatti et al.: Microcystic macular edema in optic nerve glioma (*Ophthalmology*. 2020; 127: 930). *Ophthalmology*, 2021,128(1):e9.

[54] Petzold A, Pittock S, Lennon V, et al. Neuromyelitis optica–IgG (aquaporin–4) autoantibodies in immune mediated optic neuritis. *J Neurol Neurosurg Psychiatry*, 2010,81(1):109–111.

[55] Hipolito – Fernandes D, Elisa – Luís M, Trigo M, et al. Parainfectious opticneuritis followed by microcystic macular oedema. *BMJ Case Rep*, 2019,12(9):e231442.

[56] Halder S, Mukherjee R, Elston J. Microcystic macular edema in a case of tobacco – alcohol optic neuropathy. *Can J Ophthalmol*, 2017, 52(1):e19–e22.

[57] Tawse KL, Hedges TR 3rd, Gobuty M, et al. Optical coherence

tomography shows retinal abnormalities associated with optic nerve disease. *Br J Ophthalmol*, 2014,98(Suppl 2):ii30–ii33.

[58] Dwivedi A. Microcystic macular edema in a case of optic disc pit. *Ophthalmol Retina*, 2022,6(2):178.

[59] Huang TL, Wang JK, Chang PY, et al. Neuromyelitis optica spectrum disorder: from basic research to clinical perspectives. *Int J Mol Sci*, 2022,23(14):7908.

[60] Tardo L, Salter A, Truong–Le M, et al. A narrative review of neuro–ophthalmologic disease in African Americans and Hispanics with multiple sclerosis. *Ther Adv Chronic Dis*, 2023,14:20406223231202645.

[61] Lee DH, Park SE, Lee CS. Microcystic macular edema and cystoid macular edema before and after epiretinal membrane surgery. *Retina*, 2021,41(8):1652–1659.

[62] Shao Y, Lou Y, Gao Y, et al. Expert consensus on the application of artificial intelligence in neuro–ophthalmic diseases. *Visual Neurosci*, 2025,42:e019

[63] Wang RY, Hu XY, Sun L, et al. Artificial intelligence applications in ophthalmic optical coherence tomography: a 12 – year bibliometric analysis. *Int J Ophthalmol*, 2024,17(12):2295–2307.

[64] Tilgner E, Dalcegio Favretto M, Tuisl M, et al. Macular cystic changes as predictive factor for the recurrence of macular oedema in branch retinal vein occlusion. *Acta Ophthalmol*, 2017, 95 (7): e592–e596.

[65] Munk MR, Ceklic L, Stillenmunkes R, et al. Integrated assessment of OCT, multimodal imaging, and cytokine markers for predicting treatment responses in retinal vein occlusion associated macular edema: a comparative review of anti – VEGF and steroid therapies. *Diagnostics (Basel)*, 2024,14(17):1983.