



Acute macular neuroretinopathy: is the name still appropriate?

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ABSTRACT

Background: Acute macular neuroretinopathy (AMN) is a rare but increasingly reported retinal disorder that predominantly affects young women and is characterized by acute-onset paracentral scotomas and distinctive parafoveal macular lesions. Following its first report in 1975 as an inner retinal disease, a considerable body of work has been produced, expanding on its clinical presentation and systemic associations. Aim of this review is to synthesize the current understanding of AMN, including existing controversies on nomenclature.

Methods: A literature search was conducted in PubMed/MEDLINE for English-language articles published up to 31 July 2025. Search terms included “acute macular neuroretinopathy” and “acute macular outer retinopathy”. Additional relevant sources were identified through manual screening of reference lists and targeted updating of the literature through 28 August 2025. Relevant articles were selected for inclusion in this narrative review based on the authors’ judgment of relevance to the review aims.

Results: Multiple cases of AMN in association with a variety of ocular and systemic conditions have been reported. Reported associations include viral illnesses such as influenza, Dengue fever, oral contraceptive use, vasoconstrictive agents, non-ocular trauma, and vaccination. An increased incidence of AMN was reported at a single center during the coronavirus (COVID-19) pandemic. Advances in multimodal retinal imaging, particularly optical coherence tomography (OCT) and OCT angiography, have led to a more precise localization and insight into the pathogenesis of the disease in the outer retinal layers. These findings have prompted some authors to suggest renaming the condition acute macular outer retinopathy (AMOR) to better reflect the anatomical involvement.

Conclusions: AMN appears to primarily affect the outer retinal layers, with current evidence suggesting a role for underlying vascular impairment in its pathogenesis. Although “AMOR” may offer a more anatomically precise description, AMN remains widely used in the academic literature and continues to be both appropriate and accepted. Further research is needed to elucidate the underlying pathophysiology, precisely localize the site of vascular impairment, and explore potential therapeutic strategies. In this context, consistent terminology is essential, and the continued use of the acronym “AMN” is supported by both clinical and historical considerations.

KEYWORDS

retina, white dot syndrome, acute macular neuroretinopathy, acute macular outer retinopathy, imaging, multimodal, hybrid imaging, optical coherence tomography

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INTRODUCTION

When Bos and Deutman first described acute macular neuroretinopathy (AMN) in 1975, they identified it as a condition characterized by sudden visual disturbances in young women taking oral contraceptives [1]. Patients typically reported paracentral scotomas that directly correlated to reddish-brown wedge-shaped lesions pointing toward the fovea, visible on fundus biomicroscopy. As the patients did not show signs of either retinal pigment epithelium or optic nerve dysfunction, the authors proposed that the lesions were localized to the superficial retinal layers [1].

Studies validated most of their original observations in subsequent decades. Two major literature reviews, published in 2003 [2] and 2016 [3], summarized the reported cases available at their respective publication periods and confirmed that the majority of patients found to have AMN are women in the third decade of life [2, 3]. These studies also broadened the spectrum of associated conditions and triggers. Aside from oral contraceptive use, the disease has been described following a flu-like illness or fever, use of vasoactive drugs, trauma, and hypotension. An increased incidence of AMN was reported at a single center during the coronavirus (COVID-19) pandemic [4]. Indeed, several reports and multiple case series also suggest a link between AMN and both COVID-19 infection [5, 6] and vaccination [7].

Recent advances in retinal imaging, especially the advent of high-resolution optical coherence tomography (OCT) imaging, further established that the disease affects the outer retina. It begins with transient outer nuclear layer (ONL) and outer plexiform layer (OPL) hyperreflectivity followed by outer segments abnormalities [8]. A hyperreflective lesion that follows the angulation of the Henle fiber layer, named angular sign of Henle layer hyperreflectivity (ASHH), has also been reported in the early phases [9]. To better reflect the anatomical site of pathology, some authors have suggested renaming the disease “acute macular outer retinopathy” (AMOR) [10]. However, only a limited number of works have adopted this proposed new terminology [11–13].

This review aims to summarize current concepts regarding the epidemiology, clinical presentation, pathophysiology, imaging characteristics, differential diagnosis, and clinical associations of AMN and to critically evaluate the proposed change in nomenclature.

METHODS

In this narrative review, an electronic search for relevant terms (“acute macular neuroretinopathy” and “acute macular outer retinopathy”) was conducted on the PubMed/MEDLINE database to identify English-language articles published up to 31 July 2025. The reference lists of the included papers were manually reviewed to identify additional relevant sources, and the literature was subsequently updated through 28 August 2025 to identify relevant newly published articles. Final article selection was based on the authors’ judgment of relevance to the aims of this narrative review rather than on a systematic or exhaustive selection process.

RESULTS and DISCUSSION

The initial search yielded 293 works on AMN. We included review articles, case reports, case series, and observational studies. Excluding the work that first proposed the term acute macular outer retinopathy [10], three articles were found that implemented the new terminology [11–13].

Epidemiology

Patients affected by AMN are more frequently young women [2, 3], although the disease can also be found in children [14] and the elderly [15, 16]. Oral contraceptive use was reported in 17 of 34 women (50%) in the 2003 literature review [2]. A wide range of additional associations have been reported [2, 3], most commonly a febrile illness, use of sympathomimetic agents such as epinephrine or ephedrine, use of cocaine [17], trauma, and hypotension following shock or blood loss [2, 3]. AMN has also been reported in association with migraine [18]. An increase in AMN incidence was reported at a single center during the COVID-19 pandemic [4]. Cases have also been reported in temporal association with COVID-19 infection (Table 1) and vaccination (Table 2).

While AMN had already been linked to viral illnesses such as dengue fever [99] and influenza [100] as well as influenza vaccination [101], some authors have questioned a causal relationship between AMN and COVID-19, given the anecdotal nature of the reports and the large scale of vaccinations [102].

Table 1. List of published original works featuring AMN following COVID-19 infection

Author (Year)	N	Age (Y)	Sex	Baseline VA / AMN involvement		Associated systemic condition
				status RE	LE	
Aidar et al. [19] (2021)	1	71	F	Unaffected	20/63	COVID-19 infection
An et al. [20] (2024)	78	29 ± 11	22 (M), 56 (F)	N/A	N/A	COVID-19 infection
Ayachit et al. [21] (2023)	17cases; AMN in 8/24 eyes	N/A	N/A	N/A	N/A	Post-COVID retinitis cohort
Azar et al. [4] (2021)	1	21	M	20/2000 (Amblyopia)	Unaffected	COVID-19 infection
	1	27	F	20/16	20/16	COVID-19 infection
	1	28	F	20/20	20/20	COVID-19 infection, OC use
	1	22	F	20/20	Unaffected	COVID-19 infection, OC use
Bi et al. [22] (2024)	1	30	M	Unaffected	20/32	COVID-19 infection
	1	24	F	20/20	20/40	COVID-19 infection
	1	28	F	20/63	Unaffected	COVID-19 infection
Cabral et al. [23] (2022)	1	20	F	20/20	20/25	COVID-19 infection, OC use
Capuano et al. [24] (2023)	1	37	F	20/20	20/20	COVID-19 infection
Yilmaz Cebi et al. [25] (2023)	1	29	F	20/40	20/30	COVID-19 infection
D'Souza et al. [26] (2023)	1	12	F	20/70	20/100	COVID-19 infection
David et al. [27] (2021)	1	22	F	20/20	20/20	COVID-19 infection, OC use, lisdexamfetamine use
Diafas et al. [28] (2022)	1	59	M	20/30	20/30	COVID-19 infection, DM
	1	24	F	20/20	20/20	COVID-19 infection
Dinh et al. [29] (2023)	15	24 ± 7.7	3 (M), 12 (F)	N/A	N/A	COVID-19 infection
Dovigo-Ane et al. [30] (2023)	1	34	F	20/20	20/20	COVID-19 infection
El Matri et al. [12] (2021)	1	75	F	N/A	N/A	COVID-19 infection
Fang et al. [31] (2024)	66	30.4 ± 6.7	12 (M), F (54)	N/A	N/A	COVID-19 infection
Feng et al. [32] (2024)	1	34	M	Unaffected	20/40	COVID-19 infection
	1	42	M	Counting fingers	20/100	COVID-19 infection
	1	37	M	Unaffected	20/25	COVID-19 infection
	1	39	F	20/20	20/32	COVID-19 infection
	1	32	F	20/25	20/25	COVID-19 infection
	1	34	F	20/25	20/20	COVID-19 infection
	1	21	F	20/20	20/400	COVID-19 infection
	1	16	M	20/25	20/800	COVID-19 infection
	1	40	F	20/20	20/20	COVID-19 infection
	1	36	F	20/20	20/20	COVID-19 infection
	1	41	F	20/25	20/40	COVID-19 infection
Ferkova et al. [33] (2023)	1	32	F	20/40	20/40	COVID-19 infection
Gascon et al. [34] (2020)	1	53	M	N/A	20/63	COVID-19 infection
Giacuzzo et al. [35] (2022)	1	23	F	20/20	20/20	COVID-19 infection
Goyal et al. [36] (2021)	1	32	M	20/20	Unaffected	COVID-19 infection
Guleser et al. [37] (2023)	1	27	F	20/20	20/20	COVID-19 infection
Guo et al. [38] (2025)	1	15	M	20/25	20/25	COVID-19 infection
	1	28	F	20/50	20/63	COVID-19 infection
Hawley et al. [39] (2022)	1	21	F	20/20	20/20	COVID-19 infection
Hu et al. [40] (2025)	1	42	M	12/20	Unaffected	COVID-19 infection
	1	16	F	6/20	6/20	COVID-19 infection
	1	13	M	N/A	N/A	COVID-19 infection
	1	29	F	N/A	N/A	COVID-19 infection
Huang et al. [41] (2024)	17	31.8 ± 10.8	6 (M), 11 (F)	N/A	N/A	COVID-19 infection
Jalink et al. [42] (2022)	1	21	F	Normal (not quantified)	Unaffected	COVID-19 infection, OC use
	1	29	F	Unaffected	Normal (not quantified)	COVID-19 infection, switch from OC to a hormonal intrauterine device
Karakosta et al. [43] (2023)	1	36	M	Unaffected	20/20	COVID-19 infection, double heterozygous mutation of the MTHFR gene
Koksaldi et al. [44] (2023)	1	32	M	20/25	20/20	COVID-19 infection
Liu et al. [5] (2023)	1	19	M	20/40	20/40	COVID-19 infection
	1	35	M	20/160	20/40	COVID-19 infection
	1	17	F	20/25	20/20	COVID-19 infection
	1	28	M	20/20	20/20	COVID-19 infection
	1	37	M	20/200	20/200	COVID-19 infection
	1	42	F	20/125	20/100	COVID-19 infection
	1	32	F	20/50	20/32	COVID-19 infection
	1	42	F	20/25	20/20	COVID-19 infection
	1	19	F	20/200	20/20	COVID-19 infection
	1	30	F	20/32	20/50	COVID-19 infection
	1	49	F	20/63	20/160	COVID-19 infection
	1	23	F	20/50	20/32	COVID-19 infection
	1	16	M	20/20	20/80	COVID-19 infection
	1	30	F	20/50	20/63	COVID-19 infection

Lu et al. [45] (2024)	15	31.36 ± 8.08	4 (M), 11 (F)	N/A	N/A	COVID-19 infection
Mace et al. [46] (2021)	1	39	F	20/20	20/20	COVID-19 infection
Masjedi et al. [47] (2021)	1	29	F	N/A	N/A	COVID-19 infection, diphenhydramine use
Mei et al. [48] (2025)	18	34.44 ± 12.04	9 (M), 9 (F)	N/A	N/A	COVID-19 infection
Mitamura et al. [49] (2023)	1	24	F	20/16	20/16	COVID-19 infection, OC use
Mohamad et al. [50] (2024)	1	24	F	20/30	20/30	COVID-19 infection
Pasol et al. [51] (2025)	1	44	F	20/20	Unaffected	COVID-19 infection, multiple sclerosis
Pineda-Garrido et al. [52] (2025)	1	27	F	Unaffected	20/20	COVID-19 infection
	1	23	F	20/20	Unaffected	COVID-19 infection
	1	28	F	20/25	20/25	COVID-19 infection, OC use
Preti et al. [53] (2022)	1	70	M	Unaffected	20/100	COVID-19 infection
Qiang et al. [54] (2025)	15	31.33 ± 7.96	4 (M), 11 (F)	N/A	N/A	COVID-19 infection
Reddy et al. [55] (2023)	1	24	F	Unaffected	20/70	COVID-19 infection, OC use
Sinha et al. [56] (2024)	1	26	F	20/20	20/20	COVID-19 infection
Song et al. [57] (2024)	33	30 (range: 13-49)	12 (M), 21 (F)	N/A	N/A	COVID-19 infection
Tang et al. [58] (2023)	1	27	M	20/20	20/20	COVID-19 infection
	1	25	F	Unaffected	20/20	COVID-19 infection
	1	27	F	20/63	20/63	COVID-19 infection
	1	29	F	20/160	20/50	COVID-19 infection
	1	29	F	20/20	20/20	COVID-19 infection
	1	32	M	Unaffected	20/20	COVID-19 infection
	1	16	F	Unaffected	20/40	COVID-19 infection
	1	54	F	Unaffected	20/25	COVID-19 infection, systemic lupus erythematosus
Vienne-Jumeau et al. [59] (2025)	1	48	F	20/20	Unaffected	COVID-19 infection, OC use
Virgo et al. [60] (2020)	1	32	M	Normal (not quantified)	Unaffected	COVID-19 infection, acephalgic migraine aura
von der Burchard et al. [61] (2024)	1	28	M	20/20	Unaffected	COVID-19 infection
	1	36	M	Unaffected	20/16	COVID-19 infection
	1	19	F	Unaffected	20/20	COVID-19 infection, OC use
	1	20	F	20/20	Unaffected	COVID-19 infection, OC use
	1	22	F	Unaffected	20/20	COVID-19 infection, OC use
	1	25	F	Unaffected	20/16	COVID-19 infection, OC use
	1	25	F	20/16	Unaffected	COVID-19 infection, OC use
	1	27	F	20/20	20/20	COVID-19 infection, OC use
Vu et al. [62] (2023)	1	60	M	Unaffected	20/20	COVID-19 infection, DM
	1	20	F	20/20	20/100	COVID-19 infection, uncontrolled DM
Wang et al. [63] (2024)	1	30	F	20/2000	20/32	COVID-19 infection
Wang et al. [64] (2023)	1	16	F	6/20	6/20	COVID-19 infection
Wei et al. [65] (2024)	23	N/A	N/A	N/A	N/A	COVID-19 infection
Weinberger et al. [66] (2024)	1	56	F	20/60	20/40	COVID-19 infection
Wu et al. [67] (2025)	1	12	F	N/A	N/A	COVID-19 infection
Xiong et al. [68] (2024)	1	20	F	20/32	20/50	COVID-19 infection
	1	23	M	Unaffected	20/200	COVID-19 infection
	1	36	F	20/25	20/40	COVID-19 infection
	1	16	F	20/20	20/40	COVID-19 infection
	1	19	M	20/32	Unaffected	COVID-19 infection
	1	27	F	Unaffected	20/50	COVID-19 infection
	1	21	F	20/32	20/100	COVID-19 infection
	1	31	F	Unaffected	20/200	COVID-19 infection
	1	23	F	20/200	Unaffected	COVID-19 infection
	1	27	M	20/2000	Unaffected	COVID-19 infection
	1	34	M	20/200	20/50	COVID-19 infection
	1	22	F	Unaffected	20/100	COVID-19 infection
	1	28	F	20/32	Unaffected	COVID-19 infection
	1	26	F	20/25	20/32	COVID-19 infection
Xu et al. [69] (2023)	1	27	F	Unaffected	20/20	COVID-19 infection
	1	23	M	Unaffected	20/20	COVID-19 infection
	1	30	F	Unaffected	20/20	COVID-19 infection
	1	35	F	20/50	20/100	COVID-19 infection
Zaheer et al. [70] (2024)	1	18	F	6/4	6/4	COVID-19 infection, OC use
	1	17	F	20/16	Unaffected	COVID-19 infection, OC use
Zamani et al. [71] (2021)	1	35	F	20/20	Unaffected	COVID-19 infection, acute myeloid leukemia
Zhang et al. [72] (2024)	1	49	F	20/50	20/50	COVID-19 infection (long COVID), Influenza A infection
Zubricky et al. [73] (2025)	1	24	F	Unaffected	20/25	COVID-19 infection

Abbreviations: AMN, acute macular neuroretinopathy; COVID-19, coronavirus disease 2019; N, number of patients; Y, years; VA, visual acuity; RE, right eye; LE, left eye; F, female; M, male; N/A, not available; OC, oral contraceptive; DM, diabetes mellitus; MTHFR, methylenetetrahydrofolate reductase. In the RE and LE columns, "Unaffected" denotes that the eye was not reported as clinically affected by AMN and is not a visual-acuity measurement. For group-level studies, age is presented as mean ± standard deviation unless otherwise specified.

Table 2. List of published original works featuring AMN following COVID-19 vaccination

Author (Year)	N	Age (Y)	Sex	Baseline VA / AMN involvement status		Associated systemic condition
				RE	LE	
Afonso et al. [74] (2023)	1	28	F	N/A	N/A	COVID-19 vaccination
Bellur et al. [75] (2023)	1	64	F	20/200	20/200	COVID-19 vaccination and infection
Bohler et al. [76] (2022)	1	27	F	Unaffected	20/20	COVID-19 vaccination, OC use
Bolletta et al. [77] (2021)	1	24	F	20/20	20/20	COVID-19 vaccination, OC use
Book et al. [78] (2021)	1	21	F	20/16	20/16	COVID-19 vaccination, OC use
Chen et al. [79] (2022)	1	21	F	Unaffected	20/20	COVID-19 vaccination, OC use
Diafas et al. [28] (2022)	1	54	M	Unaffected	20/20	COVID-19 vaccination, diabetes mellitus
Druke et al. [80] (2021)	1	23	F	20/20	20/20	COVID-19 vaccination, juvenile idiopathic arthritis, OC use
Fekri et al. [81] (2023)	1	18	F	20/20	20/20	COVID-19 vaccination
Franchi et al. [82] (2022)	1	19	F	20/20	20/20	COVID-19 vaccination
	1	31	F	20/20	20/20	COVID-19 vaccination, OC use
Gabrielle et al. [83] (2022)	1	25	F	20/20	20/20	COVID-19 vaccination, OC use, non-smoker
Girbardt et al. [84] (2021)	1	21	F	20/20	20/20	COVID-19 vaccination
Ikema et al. [85] (2023)	1	19	M	Unaffected	20/16	COVID-19 vaccination
Ishibashi et al. [86] (2022)	1	33	F	Unaffected	20/29	COVID-19 vaccination
Jalink et al. [42] (2022)	1	42	F	Normal (not quantified)	Unaffected	COVID-19 vaccination, OC use
	1	40	F	Normal (not quantified)	Unaffected	COVID-19 vaccination
Mambretti et al. [87] (2021)	1	22	F	20/20	Unaffected	COVID-19 vaccination, OC use
	1	28	F	20/20	Unaffected	COVID-19 vaccination, OC use
Marcus et al. [15] (2025)	1	79	M	N/A	N/A	COVID-19 vaccination
Mentes et al. [88] (2023)	1	65	F	Unaffected	20/200	COVID-19 vaccination
Michel et al. [89] (2022)	1	21	F	Unaffected	20/20	COVID-19 vaccination, OC use
Patel et al. [90] (2022)	1	26	F	N/A	N/A	COVID-19 vaccination
Pichi et al. [91] (2021)	1	N/A	N/A	Unaffected	20/400	COVID-19 vaccination
	1	N/A	N/A	N/A	N/A	COVID-19 vaccination
Priluck et al. [92] (2022)	1	20	F	20/20	20/20	COVID-19 vaccination, OC use
Protsyk et al. [93] (2023)	1	23	F	20/20	20/20	COVID-19 vaccination
Rennie et al. [94] (2022)	1	21	F	20/70	20/20	COVID-19 vaccination, OC use
Sanjay et al. [95] (2022)	1	25	F	20/20	20/20	COVID-19 vaccination, probable recent COVID-19 infection, β -thalassemia trait
Valenzuela et al. [96] (2021)	1	20	F	20/20	20/20	COVID-19 vaccination, vaginal birth control
Vinzamuri et al. [97] (2021)	1	35	M	20/20	20/20	COVID-19 vaccination
Zaheer et al. [98] (2022)	1	22	F	N/A	N/A	COVID-19 vaccination

Abbreviations: AMN, acute macular neuroretinopathy; COVID-19, coronavirus disease 2019; N, number of patients; Y, years; VA, visual acuity; RE, right eye; LE, left eye; F, female; N/A, not available; OC, oral contraceptive; M, male. In the RE and LE columns, "Unaffected" denotes that the eye was not reported as clinically affected by AMN and is not a visual-acuity measurement.

Clinical Presentation

Since the lesions do not typically involve the fovea, visual acuity (VA) is generally preserved and the most common presenting symptoms are paracentral scotomas that patients can accurately depict on an Amsler grid. However, reduced VA has been reported, particularly in cases with foveal involvement or concurrent ocular pathology [3, 22, 29]. While fundus examination may appear unremarkable, very subtle fundus changes may occasionally be noticed and small flame-shaped hemorrhages have been reported [9, 103].

OCT and near-infrared reflectance (NIR) imaging are the most sensitive imaging techniques for diagnosing and monitoring patients with AMN. NIR imaging shows characteristic wedge- or tear-drop-shaped hyporeflective lesions pointing toward the fovea (Figures 1 and 2). In the acute phase, OCT demonstrates focal hyperreflectivity of the ONL and OPL, followed by abnormalities of the external limiting membrane, ellipsoid zone, and photoreceptor outer segments; early OCT changes may precede the NIR lesions [7, 104]. An angular pattern of hyperreflectivity following the Henle fiber layer, termed ASHH, may represent early injury involving photoreceptor axons (Figure 2A) [9]. Fundus autofluorescence (FAF) and fluorescein angiography are usually unremarkable [2, 3].

Enlargement of the lesions over 2–4 weeks may be noted, and ONL thinning is observed in the late stages (Figure 1B) [8]. In the 2016 literature review, persistent scotomas were reported in 83 of 156 eyes (53.2%) at final follow-up, although follow-up duration varied [3]. No treatment with established efficacy has been identified [2, 3].

The temporal progression of OCT alterations suggests that the causative insult primarily affects the inner, proximal portions of the photoreceptors and subsequently extends to their outer segments [9].

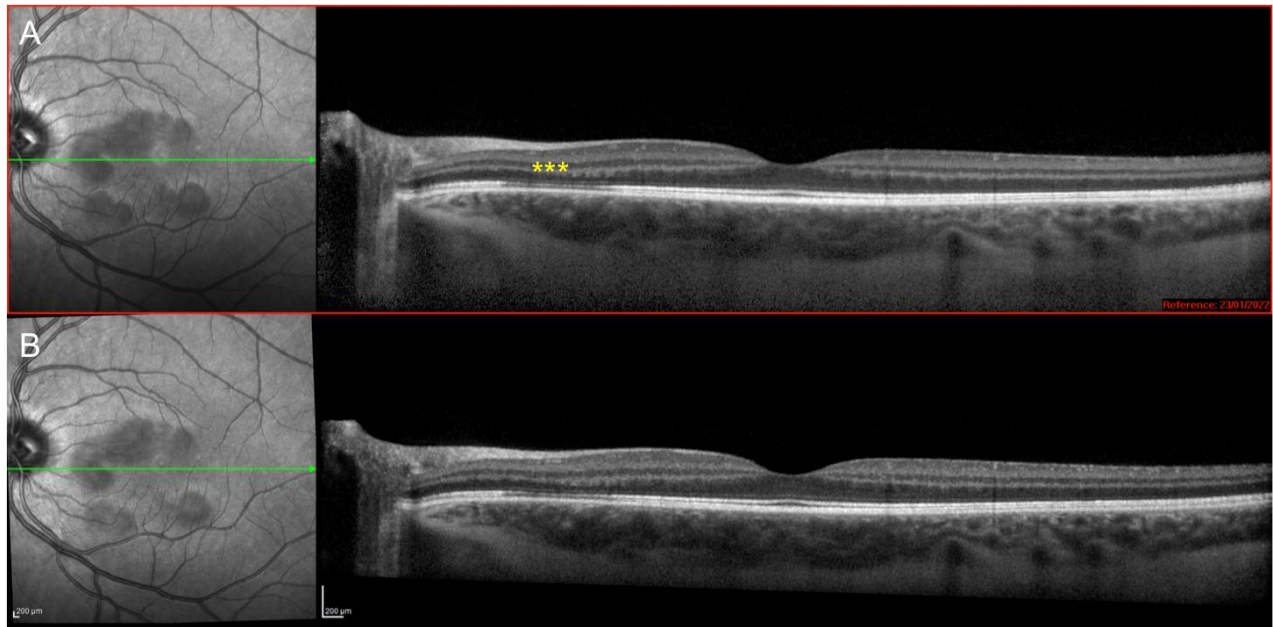


Figure 1. Representative case of acute macular neuroretinopathy (AMN) in the left eye of a 29-year-old woman presenting three weeks after onset of paracentral scotoma. At the onset of ocular symptoms, the patient reported a flu-like episode. (A) At presentation, near-infrared reflectance (NIR) imaging shows confluent wedge-shaped hyporeflective perifoveal lesions with attenuation of the ellipsoid zone and overlying thinning of the outer nuclear layer on the optical coherence tomography (OCT) scan (yellow asterisks). (B) Four weeks after presentation, follow-up imaging shows persistence of the hyporeflective perifoveal lesions on NIR and stable OCT findings. Imaging was acquired using the Heidelberg Spectralis OCT System (Heidelberg Engineering, Heidelberg, Germany).

Impairment of the retinal deep capillary plexus (DCP), which lies adjacent to the OPL, has been proposed as a potential mechanism and several studies have evidenced reduced DCP flow signals [32, 105, 106]. Conversely, other studies report choriocapillaris (CC) abnormalities on OCT angiography (OCTA) that colocalize with the structural OCT changes [107]. Notably, the persistence of the observed flow voids on OCTA despite resolution of the initial retinal hyperreflectivity on structural OCT argues against a shadowing artifact [108]. In some patients, vascular impairment has been found both in the DCP and the CC [109].

A proposed explanation for this apparent discrepancy might be found in an indocyanine green angiography study that highlighted how AMN lesions showed a topographical relationship with areas of lower choroidal vascularity. This suggests that AMN may develop within a dual-watershed zone: the watershed between the DCP and CC and the watershed between choroidal lobules [110].

Differential diagnosis

As a condition that primarily affects young women and is usually associated with unremarkable fundus examination, AMN should also be differentiated from neurological conditions such as retrobulbar optic neuritis. Color vision testing and pupillary reflex examination are useful for the differential diagnosis as they are usually affected in optic neuritis and not AMN [111, 112]. Lastly, it should be noted that cases of concomitant AMN and optic neuritis have been described—albeit with preponderant optic neuritis symptoms at presentation [113].

When considering the OCT findings of AMN, differential diagnosis of the disease includes paracentral acute middle maculopathy (PAMM), which appears as a focal hyperreflective band on OCT, but can be differentiated from AMN based on its more superficial retinal localization along the inner nuclear layer [16, 114]. Retinal artery occlusion (RAO) also manifests with hyperreflectivity and thickening of the ischemic inner retinal layers, with visual field loss corresponding to the affected retinal territory [115]. Similarities between AMN, PAMM, and RAO are consistent with ischemic mechanisms, although the pathogenesis of AMN remains incompletely established [3]. Indeed, cases of AMN concurrent with PAMM and central retinal artery occlusion have been described [116, 117].

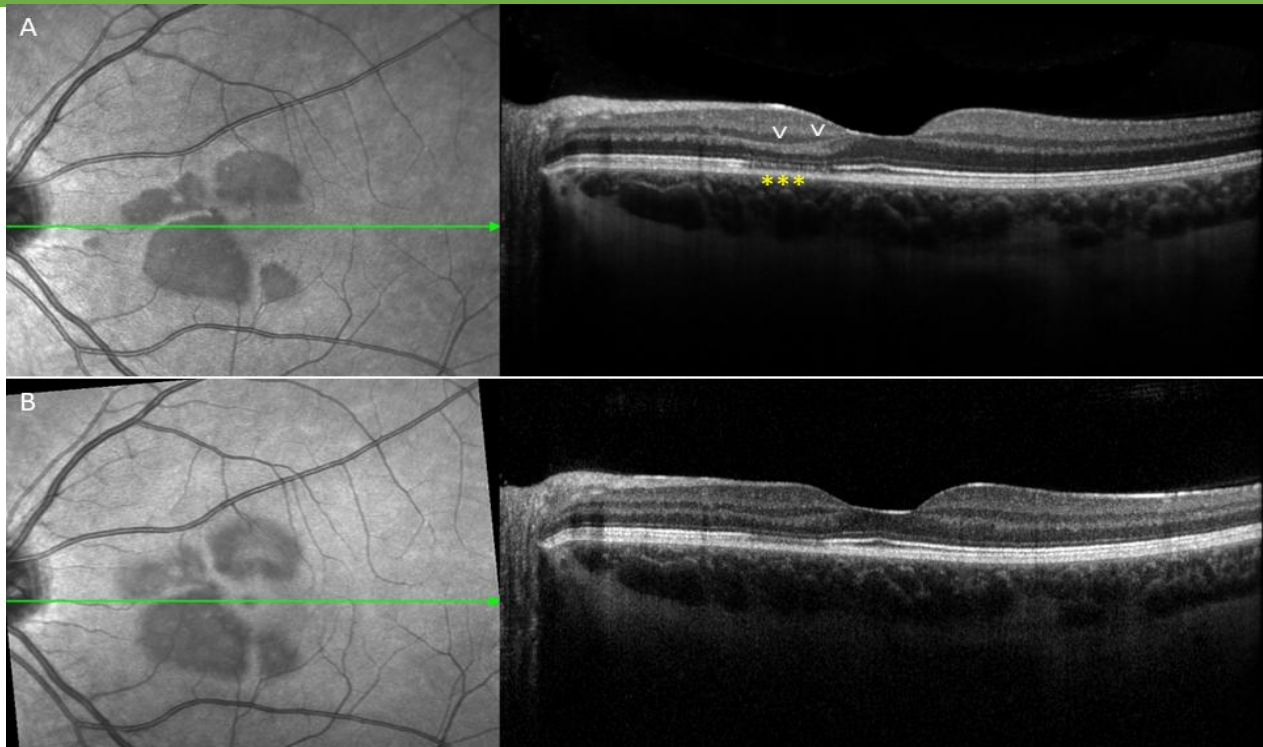


Figure 2. Representative case of acute macular neuroretinopathy (AMN) in the left eye of a 27-year-old woman presenting three days after the onset of a paracentral scotoma. (A) At presentation, near-infrared reflectance imaging reveals hyporeflective petaloid perifoveal lesions. A simultaneous spectral-domain optical coherence tomography scan passing through the AMN lesions demonstrates the angular sign of Henle fiber layer hyperreflectivity (ASHH; white arrowheads), with focal disruption of the ellipsoid zone (yellow asterisks). (B) Eight weeks after presentation, follow-up imaging shows persistence of the hyporeflective perifoveal lesions on near-infrared reflectance, resolution of the ASHH, and persistent ellipsoid-zone disruption. Imaging was acquired using the Heidelberg Spectralis OCT System (Heidelberg Engineering, Heidelberg, Germany).

Outer retinal lesions that disrupt the photoreceptor outer segments layers that may mimic AMN are inflammatory conditions such as multiple evanescent white dot syndrome (MEWDS) [118], acute posterior multifocal placoid pigment epitheliopathy (APMPPE), [119] and acute outer retinopathy (AOR) [120].

MEWDS primarily affects young women and may not be readily apparent on fundus examination [118]. Similarly to AMN, placoid lesions such as APMPPE may present with the ASHH sign [9]. However, placoids display distinctive FAF and angiography changes [119] that are not commonly observed in AMN—which, as stated, is usually unremarkable on retinal angiography and FAF [2, 3].

ASHH and photoreceptor disruption can also be observed at the onset of AOR. In this phase fluorescein and indocyanine angiography may also appear normal, yet unlike AMN, the AOR lesion shows increased autofluorescence and rapidly progresses to outer retina and retinal pigment epithelium atrophy [120].

Acute retinal pigment epitheliitis (ARPE) should also be considered on the differential for AMN as it presents among young adults with sudden-onset scotomas and focal ellipsoid zone disruption on OCT imaging. Although the central foveal localization and the absence of hyporeflective lesions on NIR may be useful in differentiating ARPE from AMN, it should be noted that a recent review questioned the very existence of ARPE, suggesting that most of the cases reported in literature may instead represent pachychoroid disease, MEWDS, or even AMN itself [121].

Nomenclature

A review of available literature evidences that AMN has consistently been considered as a disease of the retina rather than the optic nerve [2, 3]. The authors of the seminal paper believed the lesions to involve the superficial retina, based on their similarities in shape and distribution to superficial intraretinal hemorrhages observed in hypertensive retinopathy. However, they used the term “neuroretinopathy” to indicate the involvement of the neuroretina, as opposed to the retinal pigment epithelium [1]. The observation that the outer retina is the primary site of AMN had already been reported in 1978 [103], and yet the original name continued to be used. In 2009, with the advent of high-resolution OCT the name “acute macular outer

retinopathy” was proposed, to reflect the improved anatomical understanding of the disease [10], and was adopted by some authors [11–13]. Nevertheless, most of the published literature continued using the term AMN. Indeed, when Sarraf and colleagues first described the OCT findings of PAMM they referred to this new entity as AMN type 1, to highlight the connection (in terms of etiology and OCT appearance) to classical AMN, which they referred to as AMN type 2 [114].

The recent introduction of the entity known as “acute outer retinopathy” provides an additional reason to preserve the established name of AMN, as the similarity to the term “acute macular outer retinopathy” may result in confusion between two entities with different clinical features and outcomes [120]. The importance of standardized terminology in ensuring clarity and consistency is well-recognized in the field of medical retina, as reflected by efforts to standardize nomenclature for age-related macular degeneration [122, 123], OCT findings [124], and OCT-A features [125].

For a rare disease such as AMN, for which large-scale studies are lacking, insights derived from single case reports are particularly valuable. Maintaining terminological stability is therefore essential to ensure that relevant reports are not missed when performing systematic reviews and meta-analyses. In this review we presented the most recent observations on the pathogenesis and retinal imaging features of AMN. As a narrative review, this publication is not intended to be exhaustive. The articles included were selected based on the authors’ subjective assessment of relevance rather than a systematic search strategy. As a result, potentially relevant studies on AMN may have not been included and this may represent a limitation of this review. Further investigations are warranted to clarify the underlying pathophysiological mechanisms, accurately delineate the anatomical locus of vascular compromise, and evaluate potential therapeutic approaches. Within this framework, the adoption of consistent terminology remains essential, and the continued use of the term “AMN” is justified on both clinical and historical grounds.

CONCLUSIONS

Significant progress has been made in understanding AMN, and it is now established that the condition primarily affects the outer retinal layers, likely due to underlying vascular impairment. OCT alterations typically begin in the ONL and OPL and later involve the external limiting membrane, ellipsoid zone, and outer segments of photoreceptors. Although the impact on visual acuity is generally limited, the broad range of systemic associations should be considered when evaluating affected patients. Further research is needed to elucidate the underlying pathophysiology, precisely localize the site of vascular impairment, and explore potential therapeutic strategies. In this context, consistent terminology is essential, and the continued use of the term “AMN” is supported by both clinical and historical considerations.

ETHICAL DECLARATIONS

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