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Idiopathic Acute Exudative Polymorphous Vitelliform Maculopathy

Clinical Spectrum and Multimodal Imaging Characteristics

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Purpose: To describe clinical findings in patients with acute exudative polymorphous vitelliform maculopathy (AEPVM).

Design: Retrospective, observational, multicenter case series review.

Participants: Consecutive patients diagnosed with idiopathic AEPVM.

Methods: Review of clinical charts, multimodal imaging, electrophysiologic findings, and genetic findings in previously unpublished patients and review of the literature.

Main Outcome Measures: Clinical features of idiopathic AEPVM and differential diagnosis.

Results: Eighteen patients (age range, 21–74 years) with typical features of AEPVM, including initial localized, serous detachments followed by the development of characteristic yellow-white deposits in the vitelliform space. Over time, this hyperautofluorescent material gravitated within the larger lesions, resulting in typical curvilinear deposits characteristic of later stages. Symptoms and clinical findings lasted from weeks to several years. Some patients showed previously undescribed features such as fluorescein-negative intraretinal cystic changes, choroidal neovascularization, serous retinal elevations mimicking retinal folds, increased choroidal thickness, lack of rapid visual recovery, and recurrence years after complete resolution of initial manifestations.

Conclusions: Acute exudative polymorphous vitelliform maculopathy can present with a more variable natural course than previously described. Paraneoplastic retinopathy and autosomal recessive bestrophinopathy closely resemble AEPVM, necessitating medical and hereditary evaluation to exclude these clinical possibilities. This series of patients with AEPVM expands the clinical spectrum of the disorder, including demographics, clinical manifestations, imaging features, natural course, and visual prognosis. *Ophthalmology 2017;■:1–14 © 2017 by the American Academy of Ophthalmology*

The first description of vitelliform changes in the macula has been attributed to Adams,[1] who published in 1883 a case report describing "peculiar macular changes." In 1905, Friedrich Best[2] described for the first time a similar condition segregating in a family and affecting 8 members. However, the term *vitelliform* (Latin *vitellum*, meaning egg yolk) was not introduced until the early 1950s by Zanen and Rausin[3] in their publication "Kyste vitelliforme congénital de la macula." Over the years, it has become apparent that vitelliform lesions are not exclusive to Best disease, but rather that a variety of other conditions can present with similar shallow, yellowish-appearing photoreceptor detachments in the posterior pole. These include familial disorders, dystrophies, vitreoretinal traction, retinal pigment epithelium (RPE)–choroid degenerations, and paraneoplastic syndromes (Table 1).

Acute exudative polymorphous vitelliform maculopathy (AEPVM) is a rare condition first described in 2 patients by Gass et al[4] in 1988. Only 15 additional idiopathic cases have been reported in the literature to date, but other cases associated with different tumors have been reported. The disorder is characterized by acute vision loss associated with multiple, yellow-white, morphologically variable lesions at the level of the RPE and serous macular detachments. In contrast to the macular detachments, numerous small bleb-like lesions, scattered along the arcades and encompassing the macula, may develop in a honeycomb pattern.[4] During the course of the disease, patients typically develop polymorphous subretinal yellowish deposits in the form of a meniscus simulating the appearance of vitelliform macular dystrophy. Patients experience gradual visual recovery over months to years, but electrophysiologic abnormalities may persist.[5] The findings on fluorescein angiography (FA), indocyanine green angiography (ICGA), optical coherence tomography (OCT), and recently fundus autofluorescence (FAF) have been described in several case reports and small case series.[4–13] Although the clinical features of AEPVM are well described, there is little information available regarding its pathogenesis, natural course, or response to treatment. Although the disorder shows similarities with vitelliform macular dystrophy, no patient with AEPVM has been

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Table 1. Spectrum of Conditions Featuring Vitelliform Detachments

Best disease
Multifocal vitelliform dystrophy
Sjögren-Larsson syndrome
Pattern dystrophies/systemic diseases associated with pattern dystrophies
Adult-onset pigment epithelial dystrophy (pattern dystrophy group 1)
Kjellin syndrome
Myotonic dystrophy
McArdle's syndrome
Cuticular drusen
Reticular pseudodrusen
Drusenoid pigment epithelium detachment
Acute exudative polymorphous vitelliform maculopathy
Pseudoxanthoma elasticum
Vitreomacular traction syndrome
Macular telangiectasia type 2
Central serous choroidopathy
Paraneoplastic syndromes
Mitogen-activated protein kinase inhibitor toxicity

reported in a vitelliform pedigree or has shown positive results for mutations in *BEST1* or *peripherin/RDS*.

The purpose of this study was to examine the clinical presentation and course of AEPVM in 18 new patients and to compare these findings with those in previously reported cases. The aim of this meta-analysis was to gain a better understanding of the clinical heterogeneity of the disease and to help differentiate it from other phenotypes with single or multiple vitelliform lesions in the macula as well as masquerading disorders.

Methods

The study was conducted with approval of the Institutional Review Board of Columbia University (identifier, IRB-AAAD8689). Diagnosis of AEPVM was confirmed based on clinical and available imaging information. Clinical diagnostic criteria included the presence of bilateral and symmetric serous retinal detachments with evolving vitelliform material or the presence of bleb-like lesions along vascular arcades, as well as an absence of known genetic mutations or a family history and absence of known malignancy.

The literature was reviewed by way of a PubMed search using search terms including *acute exudative polymorphous vitelliform maculopathy*, *vitelliform maculopathy*, *best-like maculopathy*, and *pseudovitelliform maculopathy*. Paraneoplastic cases were excluded, and only idiopathic cases were included in the final analysis.

Eighteen previously unpublished patients with the diagnosis of AEPVM were included in this review from different settings: Vitreous Retina Macula Consultants of New York (New York, New York), the University of Ancona (Ancona, Italy), the University of Genova (Genova, Italy), and Vanderbilt Eye Institute (Nashville, Tennessee). Patients were selected from a group of 31 patients with multiple vitelliform detachments reminiscent of AEPVM at presentation. Ten patients were excluded from the study after additional workup: 6 patients had a known history of cancer or were diagnosed with a malignancy during workup and were excluded on the basis of possible paraneoplastic cause; 3 patients, all younger than 21 years, were found on genetic testing to have autosomal recessive bestrophinopathy; and 1 patient was excluded for showing positive results for a mutation in *BEST1*.

Patients underwent a complete ophthalmic examination, including determination of best-corrected visual acuity; slit-lamp and fundus assessment; color photography, and time-domain or spectral-domain OCT (Stratus or Cirrus OCT [Carl Zeiss Meditec, Inc., Dublin, CA] or Spectralis HRA-OCT [Heidelberg Engineering, Dossenheim, Germany]). In selected patients, FA, ICGA (TRC 50IX fundus camera; Topcon Medical Systems, Tokyo, Japan), and electrophysiologic testing were also performed. Fundus autofluorescence imaging was carried out, where available, using either a modified fundus camera (Topcon USA, Paramus, NJ) with an excitation filter centered at 580 nm (bandwidth, 500−610 nm) and

Table 2. Summary of Acute Exudative Polymorphous Vitelliform Maculopathy Patients in

Patient No.	Age (yrs)	Gender	Race	Family History	Viral Prodrome	Headaches	Visual Symptoms	Visual Acuity		Curvilinear Deposits	Cysts on OCT	Serous Macular Detachment	Honeycomb
								Right Eye	*Left Eye*				
1	52	F	White	N	N	N	Y	20/40	20/40	Y	N	Y	N
2	35	F	White	N	N	N	Y	20/25	20/25	Y	N	N	N
3	34	F	White	N	N	N	Y	20/40	20/20	Y	N	N	N
4	36	M	White	N	Y	Y	Y	20/25	20/25	Y	N	Y	
5	54	F	White	N	N	N	Y	20/25	20/20	Y	N	Y	N
6	35	F	White	N	Y	Y	Y	20/20	20/40	Y	N	N	N
7	34	M	White	N	N	Y	Y	20/25	20/25	Y	Y	Y	N
8	26	M	White	N	N	N	Y	20/80	20/80	N	Y	Y	Y
9	29	M	Hispanic	N	N	N	Y	20/30	20/30	Y	Y	Normal	
10	32	M	White	N	N	N	Y	20/30	20/30	Y	Y	NA	
11	35	M	White	NA	NA	NA	Y	20/40	20/40	Y	Y		
12	74	F	Black	N	N	N	Y	20/50	20/100	Y	Y	Y	
13	36	M	White	N	N	N	N	20/20	20/20	N	N	Y	Y
14	21	M	White	N	Y	N	Y	20/20	20/20	Y	N	Y	N
15	72	F	White	N	NA	NA	Y	20/60	20/70				
16	42	M	White	N	N	Y	Y	20/40	20/30	Y	NA	NA	N
17	38	F	Native American	N	N	N	Y	20/60	20/80	Y	N	Y	N
18	32	M	White	N	Y	N	Y	20/70	20/50	Y	Y	Y	N

F = female: M = male; N = no; NA = not applicable; Y = yes.