CASE REPORT

Acute Exudative Polymorphous Vitelliform Maculopathy Syndrome; natural history and evolution of fundal and OCT images over time

Patrick Murtagh, Maxwell Treacy, Kirk Stephenson, Ian Dooley

Department of Ophthalmology,
Mater Misericordiae University
Hospital, Dublin, Ireland

Correspondence to
Dr Patrick Murtagh,
murtagp@tcd.ie

Accepted 28 February 2018

SUMMARY

A 33-year-old man presented with a 10-day history of bilateral blurred vision on a background of a prodromal influenza-like illness. Ocular Coherence Tomography (OCT) and fundal examination coincided with a diagnosis of atypical central serous retinopathy. The patient's symptoms worsened during follow-up, and he was started on steroids. Subsequent fundal examination revealed yellow deposits in a honeycomb pattern and hard exudates in the perimacular region. Serial OCTs revealed progression of bilateral macular intraretinal and subretinal fluid. He was subsequently admitted to hospital for a full paraneoplastic workup. Liaison with our colleagues in other specialist retinal centres led us to a diagnosis of acute exudative polymorphous vitelliform maculopathy syndrome. We subsequently took fundal images to monitor disease progression and to monitor changes seen with autofluorescence in this rare disease entity.

BACKGROUND

Acute exudative polymorphous vitelliform maculopathy syndrome is an extremely rare fundal disorder associated with multifocal areas of exudation at the posterior pole. It is synonymous with polymorphous maculopathy syndrome. It was first described by Gass in 1988,¹ when he encountered two patients with similar symptoms. It is a seldom reported entity with only approximately 35 published cases to date.^{2,3} Fundal examination reveals yellowish debris at the posterior pole and multiple serous retinal detachments which can be observed using autofluorescence and optical coherence tomography (OCT) techniques.

The disease appears to have no predilection for age or sex. Typical presenting complaints include decrease in visual acuity, visual distortion and headache. Aetiology is unknown but many patients describe a prodromal influenza-like illness suggestive of an infective cause. Symptoms have been documented to respond to corticosteroids, which is indicative of an inflammatory basis for the disease.¹ The disease can also be associated with a paraneoplastic syndrome,⁴ termed *acute exudative polymorphous paraneoplastic vitelliform maculopathy*, and as such a neoplastic aetiology should always be excluded. The syndrome appears to have a benign course and usually resolves fully within 1–2 years of presentation.⁵

We here describe the findings in a 33-year-old white man, with reference to changes observed in fundal photographs, OCT, fundus autofluorescence and emphasis on further workup and treatment.

CASE PRESENTATION

A 33-year-old Caucasian man presented to the Eye Emergency Department of the Mater Misericordiae University Hospital in Dublin, Ireland, in May 2016 with a 10-day history of bilateral blurred vision. The patient described himself as a healthy individual with no previous ocular, medical or surgical problems. He had low myopia in each eye (−0.75, −0.5) and no history of trauma. The patient denied any chemical exposure or steroid use, is a non-smoker and there was no relevant family history of note. The patient did describe a influenza-like illness with severe sore throat, myalgia and fever of 1 week's duration ending 4 days prior to onset of his ocular symptoms. On examination, his unaided visual acuity was 6/5 in his right eye and 6/9 in his left eye. Anterior segment examination was unremarkable, showing no inflammatory sequelae and intraocular pressures were 16 mm Hg in each eye as measured by Goldmann applanation tonometry. The vitreous was clear with no inflammatory cells or evidence of posterior vitreous detachment. Fundal examination revealed multiple symmetrical confluent yellowish deposits at the level of the retinal pigment epithelium (RPE) extending from the macula to the vascular arcades (figure 1A,B). Autofluorescence imaging (AF, Optos plc, Scotland) delineated the extent of the serous detachments surrounding the macula and the optic nerve, appearing greater in the right eye than in the left (figure 1C,D). Spectral domain optical coherence tomography (SD-OCT Cirrus-4000, Carl Zeiss Meditec, Germany) revealed parafoveal subretinal fluid in both eyes with a small cyst of intraretinal fluid in the left eye (figure 1E,F).

INVESTIGATIONS

The patient underwent a full radiological and serological workup, including an extensive uveitis screen and all tests results were within the normal range or negative excluding occult malignancy and any obvious infectious or systemic inflammatory aetiology. Due to incomplete resolution of patient's signs and symptoms, he was admitted to hospital for a full workup for investigation from

To cite: Murtagh P, Treacy M, Stephenson K, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2018-224241

Figure 1 Fundal photographs (A and B, top), auto fluorescence (C and D, middle) and spectral domain ocular coherence tomography (E and F, bottom) of patient's right and left eyes, May 2016. ,

a paraneoplastic point of view. Input was received from the oncology, haematology, infectious disease, dermatology and urology to rule out any malignancy. CT thorax, abdomen and pelvis, secondary blood workup, ultrasound of testes and full dermatological examination were unremarkable.

DIFFERENTIAL DIAGNOSIS

The patient was given a provisional diagnosis of atypical central serous retinopathy (CSR) and reviewed in 3 weeks. At this stage in June 2016, the patient's visual acuity had deteriorated to 6/18 in his right eye and to 6/36 in his left eye. Autofluorescence revealed areas resembling honeycomb deposition and paramacular rings of intraretinal exudate in both eyes (figure 2A,B). SD-OCT revealed increased subretinal fluid and appearance of intraretinal fluid akin to a cystoid macular oedema (CMO) (figure 2C,D).

Fundus fluorescein angiography (FFA) was performed; however, this was unremarkable to the overall clinical picture (figure 2E,F). Considering the functional and anatomical deterioration, a decision to treat for an inflammatory aetiology was made. The patient was started on prednisolone 50 mg once daily. On review 2 weeks later in July 2016, his visual acuity was 6/9 in his right eye and 6/12 in his left eye. The intraretinal fluid had largely resolved with scant intraretinal cysts remaining. The subretinal fluid had also decreased but a substantial amount still remained (figure 3A,B). Acute posterior multifocal placoid pigment epitheliopathy was added to the differential, despite an atypical FFA pattern. Steroids were reduced by 5 mg weekly, and review was planned for

Figure 2 Auto fluorescence (A and B, top), SD OCT (C and D, middle) and fundus fluorescence angiography (E and F, bottom), June 2016.

3 months. On review in early October 2016, the vision remained stable from the last clinical appointment and SD-OCT revealed a slight improvement in subretinal fluid and resolution of intraretinal fluid despite withdrawal of steroid treatment (figure 3C,D).

TREATMENT

Patient was started on prednisolone as stated above. No other treatment was instigated.

Figure 3 SD OCT July (A and B, top) and October (C and D, bottom) 2016. SD OCT, spectral domain ocular coherence tomography.

Figure 4 Fundal photographs and swept source OCT December 2016 (top) and fundus fluorescein angiography December 2016 (bottom). OCT, ocular coherence tomography.

OUTCOME AND FOLLOW-UP

National and international opinions were sought by both patient and our team and subsequently a diagnosis of acute exudative polymorphous vitelliform maculopathy syndrome was reached. [Figure 4](#) depicts fundal photographs and swept source OCT from December 2016. Fundal photographs revealed multiple deep irregular vitelliform lesions spread throughout entire posterior pole in both eyes, forming a typical level of subretinal confluent lesions at the inferior retinal vascular arcades. OCT exposed a bilateral serous retinal detachment. There is a large and homogeneous thickening of hyper-reflective material at the level of the outer retinal layers and a thickened choroid. FA showed an extensive blocked fluorescence at the posterior pole ([figure 4](#)). Indocyanine green angiography revealed mild

Figure 5 Indocyanine green angiography December 2016.

Figure 6 Fundal photographs and autofluorescence of right and left eye from November 2016 (top), December 2016 (middle) and from September 2017 (bottom).

increased fluorescence of the choroid ([figure 5](#)). Serial fundus photographs and autofluorescence images were taken and to monitor natural progression and the fluctuant nature of the disease ([figure 6](#)). At last follow-up in September 2016, patient's vision was 6/6 bilaterally, and OCT imaging revealed perifoveal, hyper-reflective material beneath the RPE ([figure 7](#)).

DISCUSSION

Acute exudative polymorphous vitelliform maculopathy syndrome is a rare macular disorder. When this patient first attended our centre, a diagnosis of CSR was made due to the dome-like nature of the subretinal fluid on SD-OCT imaging and hyperopic shift which allowed the patient to see 6/5 in the right eye and 6/9 in the left eye unaided. Although bilateral CSR is relatively rare,

Figure 7 Right and left OCT images September 2017 demonstrating sub-RPE hyper-reflective material. Patient's vision is 6/6 bilaterally. OCT, ocular coherence tomography; RPE, retinal pigment epithelium.

reports have been described in the literature especially after high dose systemic steroid use.⁶ Contrary to the previously publicised reports on this condition, headache was not a feature in this case. At subsequent review, a marked decrease in visual acuity, increase in subretinal fluid and the onset of CMO were noted. It is therefore reasonable to assume that the disease can progress in the months postcommencement of symptoms. Although an improvement of CMO with corresponding increase in Best Correct Visual Acuity

Patient's perspective

Since the onset of the condition, the impacts on my vision have changed and evolved over time. Initially, the main symptom was numerous small areas of blurred vision across my field of vision. These blurred areas were quite fluid in their nature, and would constantly move around my field of vision.

With time this blurred vision subsided and was replaced by difficulties in dealing with light. Bright and sunny days would tire my eyes and leave me dazed, with objects in the foreground appearing as silhouettes, and losing their detail (eg, though I often can clearly see the outline of people, I cannot always decipher their facial features, particularly if they are set against a bright backdrop or do not have light projecting onto their face). On dark evenings and dull days, as well as within poorly lit spaces, it can be difficult to see certain objects, particularly if they are of dark colouration and set against other dark objects. Moving between environments of different levels and types of lighting also seems to confuse and tire my eyes, which struggle to respond to such changes in lighting conditions.

The severity of the above contrast and light sensitively has changed since the onset of the condition. In mid-2017 the adverse impacts on my vision practically ceased, and I felt that my vision was very close to being what it used to be before syndrome. However, in the last 4 months it has deteriorated again, and I continue to struggle with certain lighting conditions, though my vision is still reasonably sharp and defined (subject to there being sufficient light, I can carry out all the activities I did prior to having this condition).

Aside from the above impacts on my vision, I have experienced no pain or other symptoms.

Learning points

- Acute exudative polymorphous vitelliform maculopathy syndrome is a rare fundal disorder.
- A neoplastic basis for the disease should be excluded.
- Corticosteroids may be an option to improve visual acuity in the short term but are not suitable for extended periods; improvement may be spontaneous and unrelated to steroid therapy.
- The disease has a pathognomonic findings on multimodal imaging (spectral domain ocular coherence tomography, fundal photos and autofluorescence imaging). It may fit within the category of a 'virus induced disorder' but further research is required to determine the precise aetiology of the disease. Its rare incidence makes this condition difficult to diagnose, however, serial imaging and expert subspecialist ophthalmic opinion may help to reach a diagnosis at an early stage.
- Differential diagnosis includes Harada's disease, Best disease and paraneoplastic syndromes.

(BCVA) was noted, this was during a course of tapering steroids and the timing may be coincidental and long-term steroid use is not a feasible treatment option due to their side-effect profile. As the disease progressed, yellow deposits were noted to accumulate at the level of the RPE. These deposits tend to converge inferiorly and within a time frame of 1–2 years they usually disappear.⁷ This is the typical pattern of disease that has been reported in the literature. The hyperautofluorescent nature of the yellow deposits implies that they have a predominant lipofuscin composition.

Reports in the literature describe a prodromal influenza-like illness or upper respiratory tract infection leading many to hypothesise an inflammatory or autoimmune basis for the disease. Improvement with the use of corticosteroid supports this hypothesis. The primary concern in our opinion is when a patient is diagnosed with acute exudative polymorphous vitelliform maculopathy, a paraneoplastic component should be immediately ruled out. There have been cases described in the literature that have been associated with cutaneous melanoma, breast, testicular and lung carcinoma.⁸ It is imperative that malignancy be ruled out and specialist opinion, particularly oncology, be sought. An alternative pathogenesis of the disease describes the formation of antiretinal antibodies (peroxiredoxin 3) in particular those of a paraneoplastic nature.⁹

A recent meta-analysis and case series published by Barbazetto *et al* in 2018³ describes 18 patients with the syndrome. They deduced that symptoms and clinical findings may last from months to years. Half of their subjects had a prodromal symptoms and one of their patients developed choroidal neovascularisation. They concluded that younger patients who present with similar symptoms, especially those in their teens, should have genetic testing to rule out a genetic basis for the disease, especially a bestrophinopathy and that autofluorescent imaging remains one of the key diagnostic tests. Interestingly, they identified one patient who developed recurrence of the syndrome 2 years post complete resolution, a phenomenon which had not been previously described.

Acknowledgements We would like to thank Professor Nicolo, Genoa, for his kind use of the swept source OCT images.

Contributors After the diagnosis was made, it was ID who suggested that the case should be written up as a case report with the plan to publish. PM undertook the role of writing up the case under the guidance of ID and MT. MT and ID came up with the plan for the report and both reviewed the drafts, suggested corrections and ways to improve the report. KS supplied the fundal and OCT imaging. He also helped in editing the final report and to deem it fit for submission.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Gass JD, Chuang EL, Granek H. Acute exudative polymorphous vitelliform maculopathy. *Trans Am Ophthalmol Soc* 1988;86:354.
- 2 Massaro D, Pece A, Pichi F, *et al*. A case of acute exudative polymorphous vitelliform maculopathy: follow-up and wide-field spectral-domain optical coherence tomography. *Eur J Ophthalmol* 2015;25:91–4.
- 3 Barbazetto I, Dansingani KK, Dolz-Marco R, *et al*. Idiopathic Acute Exudative Polymorphous Vitelliform Maculopathy: Clinical Spectrum and Multimodal Imaging Characteristics. *Ophthalmology* 2018;125:75–88.
- 4 Grunwald L, Kligman BE, Shields CL. Acute exudative polymorphous paraneoplastic vitelliform maculopathy in a patient with carcinoma, not melanoma. *Arch Ophthalmol* 2011;129:1104–6.
- 5 Chan CK, Gass DJM, Lin SG. Acute exudative polymorphous vitelliform maculopathy syndromE. *Retina* 2003;23:453–62.

- 6 Gass JD, Little H. Bilateral bullous exudative retinal detachment complicating idiopathic central serous chorioretinopathy during systemic corticosteroid therapy. *Ophthalmology* 1995;102:737–47.
- 7 Chan CK, Gass JD, Lin SG. Acute exudative polymorphous vitelliform maculopathy syndrome. *Retina* 2003;23:453–62.
- 8 Grajewski RS, Schuler-Thurner B, Mauch C, *et al.* Ocular diseases in metastatic cutaneous melanoma: review of 108 consecutive patients in two German tertiary centers. *Graefes Arch Clin Exp Ophthalmol* 2014;252:679–85.
- 9 Koren L, He SX, Johnson MW, *et al.* Anti-retinal pigment epithelium antibodies in acute exudative polymorphous vitelliform maculopathy: a new hypothesis about disease pathogenesis. *Arch Ophthalmol* 2011;129:23–9.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow