EXTENDED REPORT

Macular microholes: pathogenesis and natural history

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Aims: To study the natural history and evaluate optical coherence tomography (OCT) and the retinal thickness analyser (RTA) in patients with macular microholes.

Methods: The medical records of 22 patients with a well demarcated red intraretinal foveal or juxtafoveal defect were reviewed. Fluorescein angiography (FA), RTA, and OCT were performed. The main outcome measures were visual acuity (VA), and OCT and RTA characteristics of microholes. Long term follow up was available in 13 eyes of 12 patients.

Results: The patients had a mean age of 50 years and a mean refractive error of -0.93 dioptres. The presenting symptom was a central scotoma in 14 eyes and metamorphopsia in eight eyes. All patients had a corrected VA ranging from 20/16 to 20/125, with 20 out of 24 eyes (83%) having a VA $\geq 20/40$. Symptoms remained stable or improved in 16 out of 22 patients (72%). OCT 2 findings were normal but an abnormality of the outer retina and/or a defect of the retinal pigment epithelium (RPE) were demonstrated on OCT 3 in 15 of 18 eyes (83%). The RTA topographic map demonstrated a defect at the site of the microhole in two out of 12 eyes.

Conclusion: Although biomicroscopic examination suggested an inner foveal defect, the OCT 3 scans demonstrated a localised abnormality of the outer retina and/or RPE which could not be resolved using OCT 2. Macular microholes have a favourable long term prognosis with stable VA. Bilateral involvement is uncommon.

Macular microholes have been described in patients presenting with mildly reduced visual acuity, a central scotoma, and metamorphopsia. The term "microhole" was coined by Cairnes and McCombe¹ who described a series of patients with an apparent foveal defect in the internal limiting membrane and neuroepithelium located near the centre of the capillary free zone of the fovea centralis. These lesions had a red appearance and well defined margins, but depth was difficult to determine. Reddy *et al* later described a series of 14 patients with small reddish 50–133 μm full thickness macular holes which they also termed microholes, and attributed these to acute anteroposterior vitreous traction with resulting avulsion of the central fovea, based on the presence of vitreofoveal separation (VFS) and a corresponding operculum.² More recently, normal OCT findings were reported by Douglas *et al* in four patients who presented with a foveal or juxtafoveal red single irregular lesion with sharply defined borders, these lesions were termed a "foveal spot".³ The lesion size was approximately 100 μm and appeared to be intraretinal.³ More importantly, the lesions described by Douglas *et al* differed from other foveal lesions such as macular holes or solar retinopathy.³ However, it is difficult to reconcile the sharply defined negative scotoma with a defect of the inner neuroretina.

We now describe the clinical findings of macular microholes in 22 patients with long term follow up in 12 patients. A focal defect of the outer band of high OCT signal indicating an abnormality of the outer retina and/or RPE are shown in the majority of patients using OCT 3.

PATIENTS AND METHODS

The medical records of a consecutive series of 22 patients who were diagnosed with a small, well demarcated intraretinal foveal or juxtafoveal red lesion were reviewed. Patients were invited to re-attend for further follow up examination; a detailed assessment of presenting symptoms including a description of the size and features of their scotoma, age, previous ocular history, and past medical history was

reviewed. Long term follow up was available in 12 out of 22 patients. The study was approved by the Moorfields Eye Hospital Research Ethics Committee and informed consent was obtained from each participating patient.

All patients received a complete ocular examination by two of the authors (HJZ and ZJG), including best corrected visual acuity using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart, slit lamp biomicroscopy, intraocular pressure measurement, and dilated fundus examination using a 78D Volk lens or a super 66 Volk lens. The recorded visual acuity was the Snellen equivalent of the smallest line read with one or no error, using chart 1 for the right eye and chart 2 for the left eye. All patients were tested using an Amsler chart to assess the location and size of the scotoma. The presence of a complete posterior vitreous detachment (PVD) was diagnosed if a Weiss ring was present on indirect binocular microscopy. The Watzke-Allen test was performed in all patients.

OCT (Carl Zeiss Ophthalmic Systems, Dublin, CA, USA) assessment was performed in 21 out of 24 eyes using OCT 2 and the Stratus OCT 3. The OCT scan is a two dimensional, cross sectional, high resolution retinal image, obtained by assembling multiple z-axis scans to generate each image. OCT 3 scans are obtained by assembling 512 z-axis scans, with an x-y plane resolution of 20 μm . Composite OCT images using OCT 2 consist of a linear array of 100 z-axis scans and have an x-y plane resolution of 50 μm (Schuman JS, American Academy of Ophthalmology, Subspecialty Day, 2002). OCT was also used to evaluate the vitreoretinal interface to detect VFS. Six radial OCT scans measuring 6 mm in length each were performed by one of the authors (PS). If no abnormality was found, a repeat examination using multiple horizontal scans was performed.

Abbreviations: FA, fluorescein angiography; OCT, optical coherence tomography; PVA, posterior vitreous detachment; RTA, retinal thickness analyser; VA, visual acuity; VFS, vitreofoveal separation.

RTA assessment using model 4.10 sp2 (Talía Technology Ltd, Neve-Ilan, Israel) was performed in 12 out of 24 eyes. RTA scans were centred on the fovea; the three dimensional topographic maps were examined specifically for a localised defect that would correspond to the observed macular microhole. FA was performed in four eyes of four patients.

RESULTS

The clinical characteristics of patients are summarised in table 1. Twenty four eyes of 22 patients of equal sex distribution were included in this series; two patients had bilateral involvement. The mean age of the patients was 50 years (range 28–77 years). The mean refractive error was -0.93 dioptres (range -5.25 to $+1.75$ dioptres). Corrected visual acuity ranged from 20/16 to 20/125 with a mean of 20/31 and 20 of the 24 eyes (83%) had a visual acuity $\geq 20/40$. Long term follow up was available in 12 patients and varied from 2 months to 8 years (mean 4 years).

A central scotoma was the presenting symptom in 14 eyes, and metamorphopsia in eight eyes. Upon further questioning, a total of 15 patients admitted having metamorphopsia, which was confirmed on Amsler chart testing. Micropsia and macropsia were present in two patients. Eleven patients had difficulty reading and two patients were asymptomatic (table 1). The duration of symptoms for all 22 patients varied from 2 months to 10 years, with a mean of 3 years.

Of 22 patients (72%), 16 became less symptomatic or remained unchanged. Three patients had worsening symptoms which were unexplained in patients 9 and 15 (patient 15 was diabetic with no visible retinopathy), and were associated with bilateral concentric visual field loss in patient 20, who is currently undergoing neuro-ophthalmic investigation. Three patients were subjectively worse as a result of mild cataract (patient 11), macular pucker (patient 12), and idiopathic intracranial hypertension (patient 21). In 12

patients with long term follow up, the scotoma was small and typically remained stable or became smaller over time.

We routinely enquired about sun gazing and direct trauma to the head or the eye. One patient gave a vague history of sun gazing as a child (patient 3). Two patients briefly glanced at a solar eclipse in the UK using protective eyewear (patients 6 and 10). The history and findings on examination were not consistent with a diagnosis of solar retinopathy in any of the above three patients. Patient 10 had a past medical history of meningioma excision with optic nerve compression 15 years prior to her current presentation. The patient made a full recovery following the neurosurgical intervention. Patients 15 and 18 suffered from non-insulin dependent diabetes without any retinopathy.

In 13 eyes of 12 patients with long term follow up, corrected VA at the first visit ranged from 20/16 to 20/80 with a mean of 20/34. Corrected VA at last follow up ranged from 20/16 to 20/125, with a mean of 20/33 in the affected eye (fig 1), and from 20/16 to 20/32 in the fellow (non-affected) eye with a mean of 20/19.

On examination, biomicroscopy suggested the presence of a red, well demarcated intraretinal foveal or juxtafoveal defect, measuring 50–100 μm (fig 2). None of the patients had a complete PVD. VFS was present in seven of the 21 eyes examined by OCT (fig 3). All patients were phakic. None of the patients demonstrated any retinal haemorrhage, lipid or exudate, full thickness macular hole, or operculum. The lesions did not change in appearance with long term follow up.

Fluorescein angiography (table 2) was performed in four eyes. Patient 19 had early hyperfluorescence superior to the anatomic centre of the macula, consistent with a small RPE window defect but not localised to the macular microhole. Three patients had normal FA. There was no evidence of vascular disease, no late leakage, and the RPE was healthy in all four eyes examined.

Table 1 Patient characteristics and clinical information

Patient	Age	Sex	Eye	Refraction	Initial VA	VA at follow up	Fellow eye	Duration follow up (months)	Presenting symptoms	Duration of symptoms	Other
1	53	F	R	-5.25	20/20	20/20		0	Metamorphopsia	12 months	
1	53	F	L	-5.25	20/20	20/20		0	Scotoma	5 years	
2	55	F	L	-1.0	20/30	20/30	20/20	0	Metamorphopsia	Asymptomatic	Idiopathic finding
3	31	M	R	0.0	20/16	20/16	20/16	36	Scotoma	10 years	Vague history of sun gazing during childhood
4	57	F	R	-1.25	20/30	20/25	20/16	96	Scotoma	7 years	
5	29	F	L	-0.5	20/30	20/16	20/16	27	None	Asymptomatic	Idiopathic finding
6	36	F	R	-0.5	20/40	20/32	20/20	42	Scotoma	4 years	Glanced at eclipse protected
7	28	M	L	0.0	20/30	20/30	20/16	0	scotoma	7 months	
8	51	M	R	0.0	20/40	20/25	20/20	34	Metamorphopsia	4 years	
9	57	F	L	0.75	20/40	20/63	20/25	7	Scotoma	3 years	
10	53	F	R	-0.5	20/60	20/50	20/16	3	Scotoma	12 months	Meningioma, glanced at eclipse protected
11	61	M	L	1.0	20/40	20/40	20/16	0	Scotoma	18 months	Cortical lens opacity
12	68	F	R	0.75	20/60	20/40	20/32	80	Metamorphopsia	8 years	Cortical lens opacity, macular pucker
13	30	F	L	-1.25	20/30	20/30	20/20	0	Metamorphopsia	36 months	
14	77	M	R	1.75	20/40	20/40	20/25	0	Scotoma	6 months	
15	49	M	L	0.0	20/30	20/40	20/16	80	Scotoma	10 years	NIDDM 2 years
16	53	M	R	-3.0	20/32	20/32	20/20	0	Scotoma	12 months	
17	50	F	R	1.25	20/80	20/40	20/20	2	Metamorphopsia, scotoma, and difficulty reading	5 months	
18	69	M	R	0.5	20/60	20/40	20/25	84	Metamorphopsia	4 years	NIDDM 4 years
19	48	M	R	-3.5	20/40	20/40	20/16	0	Metamorphopsia	11 months	
20	50	M	R	0.25	20/20	20/80		74	None	6 months	Unexplained bilateral visual field loss
20	50	M	L	0.75	20/30	20/125		74	Difficulty reading	7 years	
21	35	F	R	-1.5	20/30	20/30	20/16	0	Scotoma	12 months	IIH
22	69	M	R	-4.0	20/25	20/25	20/20	0	Scotoma	2 months	

F, female; M, male; L, left; R, right; NIDDM, non insulin dependent diabetes; IIH, idiopathic intracranial hypertension.

Figure 1 Scatter plot graph for 13 eyes of 12 patients with long term follow up. Visual acuity at last follow up versus VA at the initial presentation is shown. Nine out of 13 eyes (69%) achieved a VA of 20/40 or better at last follow up. Four eyes deteriorated (patients 9, 10, and 20 (both eyes)).

OCT (table 2) was performed in 21 eyes. Seven patients were examined using OCT 2. No abnormality was detected using OCT 2 in any of them (fig 3A). Five patients had a repeat examination using OCT 3, four of whom showed a defect of the outer band of high reflectivity suggestive of a defect of the outer retina and/or RPE (patients 3, 4, 8, and 10, fig 3).⁴ A total of 18 eyes of 17 patients were assessed with OCT 3. Fifteen of the 18 eyes examined by OCT 3 (83%) showed a similar abnormality with a defect of the outer retina and/or the RPE (figs 2 and 3).⁴ One patient was found to have a lamellar defect of the inner retina (patient 14).

RTA assessment (table 2) was performed in 12 eyes. The three dimensional topographic maps of the RTA scans were normal in nine eyes and abnormal in three eyes (fig 4). Two patients (patients 10 and 19) had a local depression adjacent to the anatomic fovea that corresponded to the location of the foveal microhole identified on clinical examination (fig 4). Patient 14 had a lamellar hole with an incompletely operculated flap on OCT and a corresponding abnormal RTA scan.

Figure 3 OCT scans of the right eye of patient 4. (A) OCT 2 shows the presence of vitreofoveal separation (VFS) but no outer retinal or RPE abnormality. (B) OCT 3 demonstrates VFS as well as a defect of the outer retina and/or RPE (arrow).

DISCUSSION

The diagnosis of a microhole can easily be overlooked without a careful history and examination. The majority of our patients presented with minimal symptoms, usually a central scotoma but occasionally metamorphopsia or reduced reading vision. Unless bilaterally affected, most patients were not significantly inconvenienced. Visual acuity was stable in the subgroup of patients with long term follow up. Clinical examination revealed a well defined red spot at the fovea or just off the anatomic centre of the macula; this clinical entity

Figure 2 Fundus photograph of the left (A) and right (C) eyes demonstrate a well localised, irregular, small red lesion at the centre of the fovea; the respective OCT scans (B and D) demonstrate a well demarcated defect (arrow) at the outer retina and/or RPE level (patients 11 and 3).

Table 2 Fluorescein angiography, optical coherence tomography, and retinal thickness analysis findings

Patient	FFA	OCT Model 2	OCT Model 3	RTA
1 (RE)		NAD*		
1 (LE)		NAD*		
2	NAD			
3	NAD	NAD†	Outer retina and/or RPE defect†	
4		NAD†	Outer retina and/or RPE defect†	
5		NAD*		
6		NAD†	NAD†	NAD
7				
8		NAD†	Outer retina and/or RPE defect†	NAD
9			Outer retina and/or RPE defect	
10		NAD†	Outer retina and/or RPE defect†	Depression adjacent to fovea
11			Outer retina and/or RPE defect	NAD
12			Outer retina and/or RPE defect	NAD
13			NAD	NAD
14			Lamellar hole, outer retina and/or RPE defect	Abnormal
15			Outer retina and/or RPE defect	NAD
16			Outer retina and/or RPE defect	NAD
17	NAD		NAD	
18			Outer retina and/or RPE defect	NAD
19	RPE window defect		Outer retina and/or RPE defect	Depression adjacent to fovea
20 (RE)			Outer retina and/or RPE defect	
20 (LE)			Outer retina and/or RPE defect	
21				
22			Outer retina and/or RPE defect	NAD

*Examined by OCT 2 only.
†Examined by OCT 2 and OCT 3.
RE, right eye; LE, left eye; NAD, no abnormality detected; RPE, retinal pigment epithelium.

is therefore similar to that described by other authors, without any haemorrhage, exudates, or retinal thickening.^{1 3} We did not observe any full thickness retinal defects. OCT 3 scans demonstrated a very well localised subtle defect probably indicating the presence of a gap in the photoreceptors, and/or an RPE defect consistent with the patients' presenting symptoms. The three dimensional topographic map of the RTA did not contribute any useful information,

although a localised depression at the site of the observed microhole was seen in two patients. The diagnosis of a macular microhole is a clinical diagnosis, which can be confirmed by OCT 3 in the majority of patients.

Similar clinical findings have been described in association with direct sun gazing, viewing an eclipse unprotected, and blunt trauma.⁵⁻⁸ Solar retinopathy however, is a well recognised clinical entity with a characteristic appearance and clinical course. RPE changes have been demonstrated on FA⁵ and on histopathology.⁹ Using OCT, reversible hyper-reflectivity of all retinal layers at the fovea after viewing an eclipse have been described^{10 11} Huang *et al* however demonstrated chronic OCT changes following photic exposure, and showed outer retinal defects and alterations of the RPE with cystic changes very similar to those described in our patients.¹² Patient 3 in our series gave a vague history of sun gazing as a child; his symptoms however, were unilateral, he gave no history of an acute onset and presented late with no evidence of parafoveal oedema. Patients 6 and 10

Figure 4 Three dimensional topographic map of the right eye of patient 19 using the RTA. A depression temporal to the fovea and corresponding to the microhole is shown (A; arrow). The three dimensional RTA map of the right eye of patient 8 is normal (B).

Figure 5 OCT scan of the right eye of patient 22. This demonstrates VFS but persistent attachment of the posterior vitreous face to the fovea. A localised cystic defect is present at the outer retina and/or RPE level (arrow).

had glanced briefly at the eclipse using protective eyewear and findings were not consistent with solar retinopathy. The salient differences between a microhole and solar retinopathy have been described elsewhere.¹

The patients described by Reddy *et al* presented with acute symptoms in 93% of cases, all lesions "appeared to be full thickness" and typically became extremely difficult to differentiate from the surrounding retina.² However, the patients described by Cairns *et al* presented with vague onset of symptoms, two out of 17 were asymptomatic, the level of the retinal lesion was difficult to determine, and its morphology remained unchanged throughout follow up.¹ Furthermore, the presence of a PVD was only mentioned in relation to one patient with a history of trauma in the series by Cairns *et al*,¹ but five patients had a complete PVD at the time of presentation in the series by Reddy *et al*, and in all patients within four weeks of follow up.² The uncertainty about the level of the lesion within the retina, and the state of the posterior hyaloid highlight the importance of high resolution imaging using OCT. Localised VFS at the macula may be missed on cursory examination of the macula but would be identified on OCT imaging. VFS supports the view that the pathogenesis of microholes may be associated with acute posterior vitreous detachment at the macula. OCT imaging permits longitudinal imaging to assess changes in morphology over time, and can rule out retinal cysts, traction, elevation, or thinning.

Douglas *et al* described a series of patients with mild visual disturbances and a corresponding red foveal lesion which appeared biomicroscopically similar to those described in the original series by Cairns *et al*.^{1,3} In addition, no patient in either study had any evidence of a full thickness macular hole and none of the lesions changed significantly in appearance during follow up.^{1,3} Although Douglas *et al* identified bilateral involvement in one third of their patients,³ bilaterality was present in <10% of other series including the present study.^{1,2} A favourable final vision was shown in the present study as 77% of eyes with long term follow up achieved a VA $\geq$ 20/50. Final visual acuity in other studies of microholes also showed a favourable long term prognosis as 63–100% eyes achieved a VA $\geq$ 20/50.^{1,2}

Our experience using OCT 2 showed normal cross sectional images of the central macula, as demonstrated by Douglas *et al*.³ The observed focal abnormalities on OCT 3 however, are likely to be the result of its improved axial (8 μ m) and longitudinal resolution (20 μ m) compared with previous versions of the same instrument (Schuman JS, American Academy of Ophthalmology, Subspecialty Day, 2002). The interpretation of the observed changes is difficult as OCT pseudocolour bands and light microscopy use different approaches to assess cellular elements.⁴ Furthermore, newer instruments using the same imaging principle with an axial resolution of 2–3 μ m¹³ represent a significant advance over commercially available OCT systems and may be more suitable to assess such defects.¹⁴

We have used the term microhole to describe these well defined foveal lesions because of the biomicroscopic appearance of an inner retinal abnormality; however the nature and the consistency of the patients' symptoms would suggest an outer retinal defect involving the photoreceptors and/or RPE. The absence of pigmentary changes on clinical examination and normal FA in the majority of patients indicates that this is not primarily a defect of the RPE. The localisation of the minute abnormality at the level of the outer retina and/or RPE, seen on the newer OCT with its improved resolution, would be consistent with the patients' symptoms. The absence of a full thickness retinal hole on OCT is consistent

with the clinical examination and absence of a positive Watzke-Allen test. The observed changes may be secondary to anteroposterior vitreofoveal traction as suggested by the presence of VFS in 33% of our patients.² In support of this theory, patient 22 had VFS in the macular area, with a flat trampoline-like configuration and a persistent attachment at the fovea (fig 5). OCT images of perifoveal vitreous separation in eyes with stage 1 and 2 macular holes have been described.¹⁵ The lack of progression of microholes is consistent with the lack of progression of stage 1 and 2 macular holes with vitreomacular separation.^{16,17}

The signs observed on OCT 3 in this series are most likely secondary to a primary event that affected the inner retina. Unlike the findings of other authors' series of microholes,² none of our patients had a complete PVD or a full thickness macular hole and we did not observe any subretinal fluid surrounding the small foveal lesions. This OCT appearance in isolation however, is not diagnostic given that a similar appearance can be observed following successful macular hole surgery (personal communication, A Gaudric) which may support the possibility of a gap in the photoreceptors. Typically, the presenting tiny central or paracentral scotoma, relatively good VA and absence of gross macular abnormality, full thickness hole, diffuse RPE abnormalities, yellow spots or rings, microaneurysms or haemorrhage on biomicroscopy, and/or FA should indicate the possibility of a macular microhole.

In conclusion, we presented a series of patients with a well defined foveal abnormality and corresponding visual symptoms. The benign nature of a microhole is indicated by the generally well preserved and stable visual acuity over time.

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