Central Serous Chorioretinopathy

Bilateral Multifocal Electroretinographic Abnormalities

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Objectives: To assess retinal function topographically in the posterior pole of affected and fellow eyes with central serous chorioretinopathy.

Participants and Methods: Multifocal electroretinograms (MERGs) were recorded from 6 patient with active central serous chorioretinopathy and 5 normal control subjects. Two patients also had full-field conventional ERGs. The MERG responses were averaged in rings radiating out from the foveal center.

Results: All of the patients had central macular detachments in the affected eyes, while the fellow eyes were normal except for a few small retinal pigment epithelial abnormalities. The MERG was not only depressed in areas of detachment as expected, but was also reduced beyond the area of detachment in affected eyes and throughout the posterior pole of the fellow eyes. Full-field ERGs were normal.

Conclusions: The MERG findings show that there is broad retinal functional disturbance in central serous chorioretinopathy involving both eyes and areas beyond the zone of detachment. These data strongly suggest that diffuse and possibly systemic pathologic conditions underlie this disease and that the leak itself may be a somewhat incidental event. The MERG may prove useful as a clinical marker for susceptibility to serous detachment.


CENTRAL SEROUS chorioretinopathy (CSC) is an idiopathic syndrome of young-to-middle-aged adults, in which a serous detachment forms in one eye. Fluorescein angiography usually shows a relatively focal source of dye leakage into the detachment. Although attacks are generally unilateral, some retinal pigment epithelial (RPE) changes are often seen in the other eye. Men are affected more than women, and there is frequently a history of recent stress or type A personality. The etiology of this disorder is unknown. A small RPE detachment may precede or underlie the site of leakage, but there is an increasing body of clinical evidence that the focal leak is not the primary disease. For example, detachments may recur or appear in the fellow eye; RPE changes are often seen in both eyes, which suggests a diffuse or multifocal pathologic condition; and indocyanine green angiography has shown choriocapillary insufficiency and capillary hyperperfusion involving areas of the macula much larger than the site of leakage.

Physiologic studies on the RPE also argue for a pervasive rather than pinpoint ocular basis for CSC. The RPE has a very high capacity for removing subretinal fluid, even when it contains serum proteins, and it seems doubtful that a healthy RPE transport system would fail to handle the amount of fluid that leaks from a tiny focal source. Furthermore, opening the tight junctions of the RPE (mechanically or with a toxin) does not cause serous detachment experimentally, but rather allows fluid to leave the subretinal space even more quickly under the influence of intraocular pressure and choroidal osmotic pressure. These data suggest that there is broad dysfunction of the RPE transport system in CSC that sets the stage for fluid to accumulate in the subretinal space, if and when leakage occurs. The cause of such transport dysfunction still remains unknown, and may well derive from underlying disease of the choroid and choriocapillaris. Multifocal serous detachments can be induced in animals by long-term administration of systemic adrenalin and corticosteroids, and both psychologic stress and corticosteroid administration are risk factors for CSC in humans. Chronic hormonal effects on the choroidal vasculature may lead to the changes that are seen on indocyanine green angiography, and the vascular changes may then secondarily affect the RPE and its ability to transport fluid.

Many studies have examined functional deficiencies of the detached retina in CSC. Even when visual acuity is reasonably good (correcting for the retinal el-
PATIENTS, SUBJECTS, AND METHODS

Six patients with CSC were studied, of which 4 were men and 2 were women, aged from 34 to 52 years (Table). All had central macular serous detachments at the initial visit, with visual acuities ranging from 20/20 to 20/50. Electroretinographic recordings were performed 1 to 10 weeks later when 3 of the detachments had flattened, but 3 were still elevated to some degree. None of these patients had a history of CSC attacks in the fellow eye or showed any pathologic condition in the fellow eye other than a few local RPE abnormalities.

Patients underwent a conventional ophthalmologic examination, and the diagnosis of CSC was confirmed by fluorescein angiography (Figure 1). None of the patients received laser photocoagulation, and all of the detachments ultimately resolved with a return of good visual acuity. All patients were in good general health with no underlying medical problems or drug usage relevant to CSC.

Five control subjects (3 men, 2 women; aged 24 to 73 years) were studied during the same period. All were in good general health, had 20/20 OU visual acuity, and had no known retinal disease.

All the patients and control subjects had MERGs using the system developed by Sutter and Tan. We used recording equipment (VERIS System; Tomey Corporation, Nagoya, Japan), and analyzed data using a specialized software (VERIS Science; Electrodiagnostic Imaging Inc, San Mateo, Calif). For MERG, subjects sat 30 cm from a television monitor that displayed a 103- or 241-element hexagonal grid, the elements of which flashed on and off in a computer-controlled, pseudorandom sequence. Segment brightness was 200 candelas per meter squared (cd/m²) and contrast was greater than 90%. Electroretinograms were recorded with Burian-Allen (Hansen Instruments Inc, Iowa City, Iowa) or GoldLens (Doran Instruments, Littleton, Mass) bipolar contact lens ERG electrodes. The pupils were dilated with a combination of 1% tropicamide and 2.5% phenylephrine hydrochloride, and topical anesthetic was instilled. Each subject was refracted for the test distance and appropriate corrective lenses were placed in front of the eye. The recording time was 8 minutes, divided into 30-second intervals. Amplifier filter settings were 0.3 to 300 Hz. Conventional full-field ERGs (UTAS System; LKC Technologies Inc, Gaithersburg, Md) were performed on 2 of the patients with CSC (cases 3 and 4), under recording conditions that conformed to the International Standard for Clinical Electroretinography.

Results

An array of MERG wave forms from a normal subject is shown in Figure 2. Note that the responses are larger in the center of the macula than in the periphery 20° off-center. The wave form of the normal MERG is a negative deflection followed by a positive deflection that resembles a conventional ERG. Although the MERG wave forms are not strictly equivalent to the full-field ERG, the major negative and positive deflections have been shown to be roughly homologous to ERG A and B waves, and this terminology will be used for ease of description.

Multifocal electroretinograms from a patient with CSC are also shown in Figure 2. As might be expected, the central responses from the eye with detachment were markedly depressed. The responses from the fellow eye were also depressed centrally relative to the periphery. This was true for all 6 patients studied. However, the full-field ERG was normal in both eyes of the patients (cases 3 and 4) in whom it was recorded.

To compare MERG responses from different eccentricities of the macula, MERG responses were averaged in rings from the center outward. Ring data from a nor-

<table>
<thead>
<tr>
<th>Patient No./Symbol* / Sex/Age, y</th>
<th>Interval, wk†</th>
<th>Initial Visit</th>
<th>MERG Visit</th>
<th>Fellow Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/□/M/34</td>
<td>4</td>
<td>20/40, elevated detachment</td>
<td>20/15, flat</td>
<td>20/20, tiny parafoveal RPE defect</td>
</tr>
<tr>
<td>2/x/M/36</td>
<td>1</td>
<td>20/20, low detachment</td>
<td>20/15, normal</td>
<td>20/15, normal</td>
</tr>
<tr>
<td>3/ Marathon Reken/37</td>
<td>1</td>
<td>20/60, elevated detachment</td>
<td>20/20, small paracentral RPE detachment</td>
<td>20/20, normal</td>
</tr>
<tr>
<td>4/□/F/39</td>
<td>2</td>
<td>20/25, elevated detachment</td>
<td>20/20, detached</td>
<td>20/20, normal</td>
</tr>
<tr>
<td>5/Δ/F/40</td>
<td>10</td>
<td>20/50, large detachment</td>
<td>20/30, flat</td>
<td>20/20, small RPE defect</td>
</tr>
<tr>
<td>6/O/M/52</td>
<td>1</td>
<td>20/40, shallow detachment</td>
<td>20/20, very low detachment</td>
<td>20/20, small RPE defect</td>
</tr>
</tbody>
</table>

* Symbol identifying each patient in Figures 4 through 6.
† Interval between initial visit and time of multifocal electroretinographic recording.
‡ Snellen visual acuity and appearance of the macula. MERG indicates multifocal electroretinogram; and RPE, retinal pigment epithelium.
A normal control and patient with CSC are shown in Figure 3. Ring 1 represents the central stimulus hexagon, ring 2 is the average response from the ring of hexagons just outside the center, and the subsequent rings move out peripherally. The responses were not only depressed severely in amplitude in the central zones of the eye with CSC, but they were depressed as well in the fellow eye. The timing of the B-wave peak in this patient was quite delayed in the region of detachment relative to the fellow eye and to normal controls.

Figure 4 shows A- and B-wave times-to-peak from all 6 patients, plotted by degrees from the center of the retina. The dotted lines enclose the range of values observed for the normal subjects. In general, the times-to-peak were slightly delayed everywhere in both eyes of the patients with CSC. The B waves were more prominently delayed in the area of active detachment than in the center of the fellow eyes.

Figure 5 and Figure 6 show A- and B-wave amplitudes as response density from each stimulus hexagon (nanovolts per degree, squared). As in Figure 5, the dotted lines enclose the range of normal responses. Both A- and B-wave amplitudes were severely depressed in the central retina of the affected eyes, but subnormal responses were present beyond the area of detachment in the affected eye and across the entire posterior pole of the fellow eye as well.

Our MERG results showing ERG depression in the area of active or recent detachment in CSC are consistent with previous studies.\textsuperscript{15,16,20} The focal ERG is subnormal in affected regions,\textsuperscript{15,16} and an MERG report on affected eyes,\textsuperscript{20} that was published simultaneously with ours,\textsuperscript{21} found similar results. These electrophysiological abnormalities mirror the wide range of visual and functional difficulties that have been found in serous detachments.\textsuperscript{12-14} These functional defects have generally been attributed to the retinal separation, which affects the transport of nutrients and visual pigments and also

\textbf{COMMENT}

\textit{Fluorescein angiograms from a representative patient (case 5). Classic smokestack leakage of dye is present in the left eye (which has the serous detachment), and a small retinal pigment epithelium defect is present on the temporal side of the right macula.}

\textit{Multifocal electroretinographic arrays for a normal subject and a patient with central serous chorioretinopathy (case 4). Suppression of the central signals is evident in both eyes of the patient with central serous chorioretinopathy. Note that the amplitude scales are different, so that the normal responses are actually larger than they appear, relative to the patient.}
may allow some disruption of photoreceptor orientation. However, evidence is increasing (see “Introduction”) that CSC involves pathologic changes over a larger area than the detachment itself, in which case some of the functional or ERG abnormalities may originate from underlying choroidal or RPE dysfunction. Electroretinographic data in CSC have been ambiguous concerning diffuse or bilateral abnormalities. Most authors have reported no full-field ERG changes in CSC [eg, Francois et al22], but subtle and somewhat variable abnormalities have been seen in a few studies.23-25 The fellow eye has not been compared with normal subjects using either focal ERG or MERG. Our results show clearly that macular electrical function is abnormal both beyond the area of detachment in the affected eye, and throughout the posterior pole of the unaffected eye.

These MERG changes were much more pervasive than might have been predicted based on the healthy fundus appearance beyond the area of detachment and the normal vision in the fellow eye, and they strongly suggest that CSC involves a broad and bilateral physiological dysfunction of the macula. The normal full-field ERGs in our patients rule out severe peripheral damage, and

Figure 3. Averaged wave forms from rings of multifocal electroretinographic responses at different degrees of eccentricity from the center of the fovea. Signals from a normal subject and a patient with central serous chorioretinopathy (case 1) are compared. The responses from the patient with central serous chorioretinopathy are subnormal in all locations of both eyes and show a delay of the B-wave peak in the central (detached) area of the affected eye. Dots mark the A-wave troughs and B-wave peaks.

Figure 4. Times-to-peak of the A and B wave of the multifocal electroretinogram at different eccentricities from the fovea. These data were derived from ring averages as illustrated in Figure 3. The dotted lines enclose the envelope of normal control responses. The A and B waves appear to be slightly delayed in both eyes of most patients with central serous chorioretinopathy relative to normal subjects. In the patients with central serous chorioretinopathy, there was a more prominent delay in the B wave from the central zones of affected eyes relative to fellow eyes. Each symbol represents a patient in the Table.

Figure 5. A-wave amplitude of the multifocal electroretinogram in affected and fellow eyes in central serous chorioretinopathy. Data are plotted as in Figure 4 to show values at different eccentricities from the fovea. Dotted lines enclose the envelope of normal responses. The A wave is severely depressed in the central (detached) area of the eyes affected by central serous chorioretinopathy, but is also subnormal in most of the affected eyes outside the detached area and across the posterior pole of the fellow eye.
make it likely that the pathologic condition in CSC is primarily in the posterior pole. Since there is a considerable range of normal values for the full-field ERG, it is also possible that the full-field ERG signals recorded in our patients were depressed from baseline levels. The finding of diffuse bilateral macular dysfunction in CSC is consistent with the concept that this disease is conditioned by systemic humoral factors such as adrenaline and corticosteroids, or by diffuse underlying choroidal vascular disease. It is also consistent with recent indocyanine green angiography findings of Iida et al., who have shown early hypoperfusion and late hyperperfusion not only beyond the leakage site of affected eyes, but also in the posterior pole of fellow eyes. The appearance of leakage from a focal source in CSC may well be a relatively incidental event, or perhaps a secondary effect of underlying vascular pathology that compromises a few RPE cells to the point of blood-retinal barrier decompensation. The reason for a macular predilection in this disease is unknown, as it is for most macular diseases. However, the fact that the physiologic disturbance in CSC (including presumably an impairment of RPE transport) is greatest in the center of the macula may help explain why serous detachments tend to gravitate toward the posterior pole even when the leakage site is eccentric.

The finding of bilateral and diffuse retinal dysfunction in CSC helps to explain some of the characteristics of this syndrome. The frequent finding of bilateral RPE abnormalities is no longer surprising, nor is the propensity for recurrence (since the underlying pathophysiologic condition, that leads to a diffuse insufficiency of RPE water transport, is not corrected by sealing the leak, whether spontaneously or with laser photoagulation). If further studies show the MERG to be a reliable correlate of RPE functional capacity in CSC, this test might prove clinically useful in several ways. It could help to monitor the effects of drugs such as acetazolamide or adrenergic antagonists, and to evaluate whether stress reduction can reduce the predisposition to CSC. It could also help to judge the functional status of the RPE transport system (and the risk of serous detachment) in patients recovering from a CSC attack or in patients with systemic ischemic diseases that predispose to serous detachment such as hypertension, lupus erythematosus, or preeclampsia.

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