

## Normal S cone electroretinogram b-wave in Oguchi's disease

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### Abstract

**Aim**—The short wavelength sensitive (S) cone electroretinograms (ERGs) were examined in two patients with Oguchi's disease to study S cone function.

**Methods**—Ganzfeld colour flashes under bright white background illumination were used to elicit S cone, and mixed long (L) and middle (M) wavelength sensitive cone ERGs.

**Results**—The S cone ERG b-wave was normal with short wavelength stimuli with normal L and M cone responses in both patients.

**Conclusions**—These ERG results indicate that the S cone system as well as the L and M cone system is not defective in Oguchi's disease, while the S cone responses are not detectable in the complete type of congenital stationary night blindness as reported previously. The results imply that there is a significant difference in the way the S cone system is affected in different forms of stationary night blindness, and that the S cone and rod do not share the same arrestin system.

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Oguchi's disease is a stationary form of congenital night blindness, in which a characteristic golden yellow or grey-white discoloration of the fundus and elevated dark adaptation threshold can be normalised after prolonged dark adaptation.<sup>1-4</sup> Many investigators have postulated that this disorder is due to retarded resynthesis of visual pigments; however, normal rhodopsin kinetics have been reported and defects in bipolar cell layer have been suggested.<sup>5</sup> Recently a homozygous deletion in the arrestin gene has been detected in Japanese patients and abnormalities in the rod phototransduction have been implicated.<sup>6,7</sup> In the complete type of Schubert-Bornschein type congenital stationary night blindness (CSNB), in which exclusive defects of the 'on' pathway in the bipolar region have been postulated, the short wavelength sensitive (S) cone electroretinogram (ERG) b-wave is not detectable.<sup>8,9</sup> We now report two patients with Oguchi's disease whose S cone ERGs were normal.

### Patients and methods

#### REPORT OF CASES

##### Case 1

A 35-year-old woman complained of night blindness of long duration. There was no con-

sanguinity. No other family member has noticed night blindness. Her visual acuity was 20/25 with a correction of -4.0 dioptres in both eyes. Ophthalmoscopically, a golden yellow glistening colour was observed throughout the retina in both eyes. Retinal vessels stood out in marked contrast. This fundus appearance became almost normal after 2 hours of dark adaptation confirming the presence of a Mizuo's phenomenon. She had normal colour vision on the Farnsworth Panel D-15. A molecular genetic study has not yet been performed.

##### Case 2

A 55-year-old woman also complained of night blindness since early childhood. Her parents were not consanguineous. The family history was not remarkable. Her visual acuity was 20/20 without correction in both eyes. On ophthalmoscopic examination, a golden yellow, metallic reflex was observed throughout both fundi. The Mizuo's phenomenon was also observed at the end of 12 hours of dark adaptation. Dark adaptometry showed that a normal rod final threshold was reached only after 12 hours of dark adaptation. Her colour vision tested by the Panel D-15 was also normal. Molecular genetic analysis has not been performed.

#### ELECTRORETINOGRAPHY

The method for ERG recordings was previously described.<sup>8</sup> The ERGs were recorded using a Burian-Allen contact lens electrode. The patients' eyes were fully dilated with tropicamide eyedrops. A Ganzfeld stimulator provided full field flash stimuli and white background illumination. Light flashes were produced by a Grass PS22C strobe that has been placed into a metal box mounted on the Ganzfeld above the head of the subject. The white flash intensity was 5.0 cds/m<sup>2</sup>. Cone ERGs were recorded to white stimuli presented at 5 Hz on a white background light (50 cd/m<sup>2</sup>). Kodak Wratten colour filters were placed before the strobe in order to obtain defined colour stimuli. The following filters were used on the same white background illumination: 98 (450 nm), 48 (471 nm), 61 (534 nm), 21 (593 nm), and 29 (633 nm). We routinely obtained responses using the maximum flash intensity available at 450 nm and then dimmed the other stimuli with neutral density filters to produce approximately equal L, M cone b-wave, because all longer wavelength stimuli had more effective energy for the L and M cones. The stimulus rate was 5 Hz

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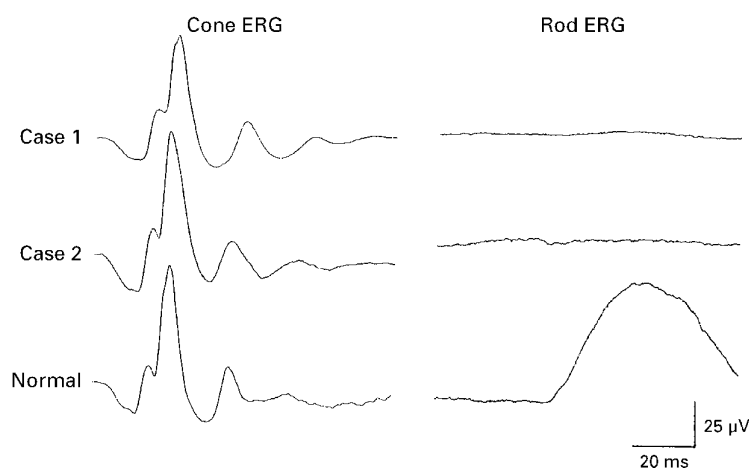


Figure 1 Cone ERGs to white flashes on a bright white background illumination (left), and averaged rod ERGs to dim blue flashes (right), after 2 hours of dark adaptation in case 1, after 12 hours of dark adaptation in case 2, and after 30 minutes of dark adaptation in a normal subject.

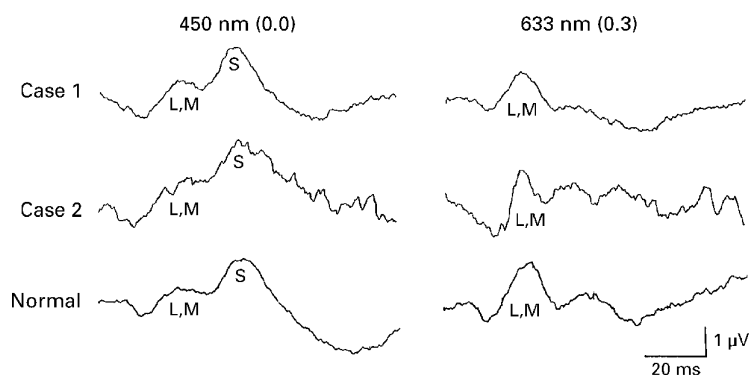


Figure 2 Cone ERGs to 450 nm stimuli (left) and to 633 nm stimuli (right) were recorded in the presence of a bright white adapting light. Numbers in parentheses indicate the neutral density filter used to adjust the energies of the flashes to produce approximately equal early (L, M cone) b-waves. S signifies the S cone b-wave, and L, M indicates the L, M cone b-wave.

and 500 responses were averaged. Rod ERG was recorded to dim blue flashes after 2 hours of dark adaptation in case 1 and after 12 hours in case 2, and averaged 20 times at 0.9 Hz.

### Results

The cone ERGs to white flash stimuli were normal in both patients (Fig 1). The averaged rod ERGs to dim blue stimuli after long dark adaptation, 2 hours in case 1 and 12 hours in case 2, were undetectable (Fig 1).

In normal subjects, the S cone ERG elicited by short wavelength stimuli (450 nm) appeared as a separate b-wave riding on an earlier b-wave of the L, M cone ERG (Fig 2). The range for the S cone ERG amplitude was 0.54–2.46 µV in normal controls in our laboratory. To long wavelength stimuli (633 nm), only the L, M cone b-wave appeared. The S cone ERG and the L, M cone ERG b-waves were both normal in amplitude and waveform in all patients (Fig 2).

### Discussion

Our patients demonstrated a characteristic golden yellow, glistening fundus colour associated with the Mizuo's phenomenon, normal

rod threshold only after prolonged dark adaptation, and undetectable averaged rod ERGs. Although Gouras<sup>1</sup> reported that the first response to a single flash after dark adaptation showed the presence of rods, we could not detect the rod response because of an artefact caused by a blink in both patients. The cone ERGs to white stimuli were normal in our patients, as have been reported previously.<sup>3,4</sup> The S cone ERG elicited by short wavelength flashes was also normal, implying that the S cone pathway was not affected in Oguchi's disease.

Early investigators had thought that an abnormality in the resynthesis of rhodopsin might be the reason for the prolonged dark adaptation in Oguchi's disease. However, Carr and Ripps<sup>5</sup> reported that the concentration and regenerative properties of rhodopsin, tested by means of fundus reflectometry in one patient with Oguchi's disease, were entirely normal, suggesting that this disease might be related to the abnormalities in the bipolar cell region. Such a defect would imply that normal rod a-waves might be detectable in this disease but this has not been described. Recently, a homozygous defect in the arrestin gene has been discovered in Japanese patients with Oguchi's disease.<sup>6,7</sup> Arrestin is known to bind to phosphorylated rhodopsin and to prevent it from activating transducin. These authors suggested that arrestin deficiency would result in prolonged activation of transducin and rod cGMP specific phosphodiesterase upon light stimulation of photoreceptors, which delay normal dark adaptation.<sup>7</sup>

It is well known that the rod system has only 'on' bipolars and involves an intermediary amacrine cell pathway. In the S cone pathway, there has been some evidence that there is a preponderance of S cone 'on' units at the ganglion cell level.<sup>10</sup> We have reported that the S cone ERG b-wave is undetectable, as well as the rod b-wave, in the complete type of CSNB.<sup>8</sup> The defect in the complete type of CSNB may involve the 'on' pathway exclusively and therefore have a more profound effect on both the S cone and rod bipolar systems.<sup>11</sup> A similar type of acquired nyctalopia has been described in the so called cutaneous melanoma syndrome,<sup>12</sup> which also lacks an S cone ERG.<sup>9</sup> In this case immunohistochemistry reveals the bipolar cells as the site of the defect.<sup>13</sup> However, the S cone ERG b-waves are normal in patients with Oguchi's disease, implying that the S cone bipolar system is not affected in this disease. This clearly distinguishes it from the complete type of CSNB. The S cone ERG may be a useful tool to assess cone 'on' bipolar function and to distinguish different forms of congenital night blindness. Our results also imply that rods and S cones do not share the same arrestin system, although similar physiological properties have been reported in these photoreceptors in terms of slow response time and 'on' pathway predominance.

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