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Structural and Electrophysiologic Outcomes in a Patient with Retinal Metallosis

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Report of a case

A 58 year old man presented reporting several years of blurred vision and “black and white” vision in his left eye only. He recalled a history of a small metallic intraocular foreign body (IOFB) entering his left eye 30 years prior while hammering bricks at work without protective eyewear. The IOFB was surgically extracted a number of years post-trauma. At the current visit his visual acuity was 20/20 and 20/25, for the right and left eyes, respectively. He read 15/15 Ishihara color plates with the right eye and 0/15 with the left. Visual fields were full to confrontation in both eyes. IOPs were normal (15, OD; 17, OS). There was no RAPD. Anterior segment exam was remarkable for well-positioned intraocular lenses, both eyes, and for a small round defect through the left iris. Dilated exam was unremarkable. Spectral domain optical coherence tomography (SD-OCT) revealed inner nuclear layer loss (INL), comparatively modest outer nuclear layer (ONL) thinning and loss of signal from the outer segment interdigitation zone (IZ)(Figure 1B, *arrows*). Full-field electroretinography (ffERG) showed reduced rod b-wave amplitude, an electronegative configuration of the mixed cone-rod response with minimally reduced photoreceptor a-wave amplitude but a dramatic b-wave loss, and barely detectable cone ERGs (Supplementary Figure 2).

Discussion

The patient reported herein presented with dyschromatopsia, which had been attributed to an anterior ischemic optic neuropathy. Severe inner retinal and cone dysfunction by ERGs were compatible with a diagnosis of ocular metallosis or siderosis (the exact composition of the IOFB was unknown) and provided an explanation for the patient's symptomatology.¹⁻² Retinal siderosis, a potentially devastating complication of IOFBs, presents weeks to years

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following the inciting trauma with an incidence ranging from 3-9%.¹ Ocular manifestations of siderosis include iris heterochromia, corneal endothelial changes, cataract, secondary glaucoma, retinal vasculopathy, retinal degeneration, and proliferative vitreoretinopathy, which may be in some cases the only clue to the presence of an unsuspected IOFB.¹ With the exception of the relatively minor retinal changes our patient had a favorable outcome.

The electrophysiologic abnormalities, and to a lesser extent, the visual sensitivity loss in ocular siderosis are well-documented in the literature. ERGs are the standard to monitor changes. The mechanisms mediating these changes, however, are not fully understood. Structural disorganization following an IOFB complicates the histopathology of human specimens available for study following enucleation.^{3,4} Reported histologic changes in retinal siderosis involve all retinal layers with a possible vitreal-to-RPE gradient of abnormalities as well as a perivascular predilection.³⁻⁵ Retinal imaging with SD-OCT in this patient presented a unique opportunity to examine mild structural changes in this eye with a favorable outcome post-IOFB extraction. There was INL thinning in the absence of other overt inner retinal abnormalities, modest ONL thinning and loss of the EZ band that coincided with the region of central NIR hyporeflectance and hypo-autofluorescence. To the best of our knowledge, this is the first quantitative description of the structural and functional abnormalities that result from a retained IOFB with the simultaneous use of multimodal imaging and electroretinography. Neuronal loss within the INL, possibly from loss of bipolar cells and/or Muller cell bodies, provide a structural background that underlies, at least in part, the severe loss of 'on' pathway function previously recognized by ERG in this condition.² Tropism of iron particles toward vascular elements in the inner retina observed *in-vivo* with adaptive optics in ocular siderosis is also consistent with this structural pattern.⁵ Outer retinal changes with a predilection for the posterior pole observed in this patient resembles the pattern induced experimentally after the administration of ferrous compounds in non-human primates and in some patients.⁴ Recognition of this pattern of structural and functional abnormalities should alert the clinician of the possibility of retinotoxicity from suspected or unsuspected metallic IOFBs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Acronyms

IOFB	intraocular foreign body
OD	right eye
OS	left eye
SD-OCT	spectral domain optical coherence tomography
INL	inner nuclear layer
ONL	outer nuclear layer
IZ	interdigitation zone
ffERG	full field electroretinography
NIR-REF	Near-infrared fundus reflectance
SW	short-wavelength
FAF	fundus autofluorescence

Figure 1.

Retinal structural abnormalities in ocular metallosis (presumed siderosis). **A.** *En-face* imaging using near-infrared fundus reflectance (NIR-REF), short-wavelength (SW) fundus autofluorescence (FAF), and SD-OCT imaging as maps of total central ($30^{\circ} \times 25^{\circ}$) retinal thickness are shown for the contralateral normal eye (top row) of the patient compared with data from the symptomatic eye (bottom row) (HRA/Spectralis system, Heidelberg Engineering, Heidelberg, Germany). Right eye images are converted to left eye orientation to facilitate region-specific comparisons and are black-level corrected to compensate for interocular differences in brightness of the *en-face* imaging raw data. Insets to the bottom right on NIR-REF images are NIR-FAF frames from in each eye of the patient compared to a normal (N, *inset to the left*). An ETDRS grid is superimposed on the retinal thickness maps. NIR-REF imaging shows central hyporeflectance in the left eye that contrast with the more homogeneous light gray normal appearance of the right eye; signal returns to a more normal appearance near the vascular arcades in nasal pericentral retina (*white arrows*). There is a transition from hypo-autofluorescence to hyper-autofluorescence on NIR-FAF imaging with a boundary that bisects the fovea; the hypo-autofluorescent region corresponds to the bluish area of outer retinal change and retinal thinning infero-temporal to the fovea in the SD-OCT retinal thickness maps. SW-FAF appears normal suggesting relatively intact retinal

pigment epithelium (RPE) and lipofuscin turnover from a functional outer retina. Central retinal thickness maps demonstrate overall retinal thinning in the left eye compared to the right eye. **B.** SD-OCT cross-sections extending 5.2 mm from the fovea (F) into temporal (T) retina in the normal eye (top row) compared to the affected eye (bottom row); magnified images from regions delimited within the white boxes (3 mm temporal retina) are shown to the right. Compared to the right eye the left eye showed overall retinal thinning (213 vs 273 μm ; normal $\pm 2\text{SD} = 258 \pm 29 \mu\text{m}$), a thinned INL (overlaid blue bars) (12 vs 35 μm ; normal = $28 \pm 12 \mu\text{m}$), modest ONL loss (45 vs 54 μm normal $\pm 2\text{SD} = 60 \pm 17 \mu\text{m}$), and attenuation or loss of the signal that corresponds to the interdigitation zone (IZ) between the photoreceptor outer segment tips and the apical RPE (arrows). Loss or attenuation of the IZ has been associated with a less reflective NIR-REF signal.