Principles and Practice of Clinical Electrophysiology of Vision

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Birdshot Chorioretinitis and Related White-Dot Syndromes

Scott E. Brodie

Birdshot chorioretinitis is the term given to a group of diseases of unknown cause that affect the retina and choroid and are characterized by a peculiar pattern of oval depigmented lesions underlying the sensory retina. The condition was first described by Ryan and Maumenee[17] as "birdshot retinochoroidopathy." The term was chosen "because of the multiple, small, white spots that frequently have the pattern seen with birdshot in the scatter from a shotgun" (Fig 83–1, Plate 13.) They noted similarities to pars planitis, including a quiet eye, minimal anterior segment inflammation, chronic vitritis, retinal vascular leakage, and frequent cystoid macular edema. They distinguished the condition from pars planitis on the basis of absent vitreous "snowballs" or "snowbank" lesions overlying the pars plana and the cream-colored depigmented spots scattered throughout the fundus. They reported 13 cases, of which 2 seemed to show a definite response to corticosteroid therapy. Five patients demonstrated visual acuity of 6/60 (20/200) or worse at the last follow-up. No electrophysiological findings were reported.

Subsequently, Kaplan and Aaberg[12] reported four additional cases. They gave additional descriptions of compromised retinal physiology, including abnormalities of dark adaptation, the electroretinogram (ERG), and the electro-oculogram (EOG).

Gass[7] added 11 cases to the published record and used the term "vitiliginous chorioretinitis" to emphasize the depigmentation of the fundus lesions. He reported ERG abnormalites in 10 of 10 patients undergoing ERG testing and EOG abnormalities in 6 of 8 patients tested. He too stated that steroid treatment was of little if any benefit but offered the reassuring observation that of his 11 patients only 1 was legally blind and 9 retained 6/12 (20/40) or better acuity in at least one eye. Subsequent reports[3, 6, 20] have documented additional findings in occasional cases of birdshot chorioretinitis, including subretinal neovascularization, rhegmatogenous retinal detachment, rubeosis iridis, posterior subcapsular cataract, glaucoma, and anterior ischemic optic neuropathy.

Most patients with birdshot chorioretinitis present initially with reduced visual acuity, floaters, or occasionally photopsia. Patients may also report night blindness as an initial or subsequent symptom. Later in the course of the disease, abnormal color vision is frequently noted. Visual acuity fluctuates throughout the course of the disease.

Fluorescein angiography reveals findings suggestive of retinal inflammation, including vascular leakage, with cystoid macular edema seen in severe cases. The retinal blood vessels, which may appear attenuated clinically, are commonly hypofluorescent throughout the angiogram. The ERG is commonly reduced in a nonspecific fashion, and the EOG Arden ratio is often reduced, at least in one eye.

The specific mechanism of cellular dysfunction in birdshot chorioretinopathy is not known, although a significant inflammatory component is clearly present. Reports of a strong association between this disease and the HLA-A29 antigen (and also reactivity to retinal S antigen in affected patients) would seem to implicate an autoimmune etiology, possibly with a genetic component.[2, 16]

Results of electrophysiological testing in patients

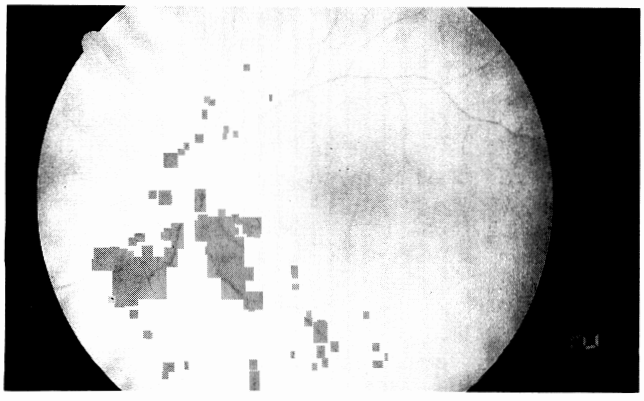

FIG 83–1.
Fundus appearance in birdshot chorioretinitis. Pale fundus lesions are neither raised nor depressed relative to the surrounding retina. (Courtesy of L. Yannuzzi, M.D.) **(See also Color Plate 13.)**

with birdshot chorioretinitis demonstrate ERGs that are rarely normal in the acute phase of the disease. Rod system dysfunction predominates. EOG testing results are frequently abnormal, but exceptions occur.

The diagnosis of birdshot chorioretinitis must be made on clinical grounds. The pale "birdshot" lesions are the defining element in the disease. These require differentiation from the white retinal lesions found in many other diseases. However, the birdshot lesions are larger and deeper to the retina than those of most of the "flecked retinas" and are much more prominent ophthalmoscopically than angiographically. Differentiation from Vogt-Koyanagi-Harada syndrome is occasionally difficult, particularly in the absence of retinal detachment, but a more generalized uveitis is to be expected in the latter condition as well as additional systemic findings. In the absence of visual loss or electrophysiological abnormalities, some confirmation of the diagnosis can be obtained if HLA-A29 is detected.

Recent reports have also described more than one additional syndrome characterized by white dots: Jampol et al.[10] reported 11 patients with a transient syndrome characterized by multiple white dots visible at the level of the retinal pigment epithelium, vitreal cells, granularity of the macular pigment epithelium, acutely reduced acuity, and abnormalities of the ERG. During the active phase of the disease, fluorescein angiography demonstrated hyperfluorescent lesions with late staining of the retina and optic disc. All patients were between 20 and 40 years old, and all but 1 was a woman. A "flulike" prodrome was reported by 5 patients. Symptoms resolved in 4 to 8 weeks, with substantial normalization of the fundus appearance and fluorescein angiogram and normalization of the ERG. The authors termed this syndrome "multiple evanescent white-dot syndrome" (MEWDS) (Fig 83–2, Plate 14). They differentiated the syndrome from birdshot chorioretinitis by virtue of unilateral presentation; smaller, less clear-cut retinal lesions; and a lesser degree of inflammation.

Electrophysiological testing of three of the original MEWDS patients was reported in *detail.*[18] During the acute phase, Ganzfeld ERGs indicated profound, diffuse abnormalities of photopic and scotopic function. In one patient, the ERG was virtually unrecordable acutely; 5 weeks later, the ERG in that individual was normal. The early receptor potential was substantially diminished during the acute stages, with excellent recovery that paralleled the clinical course. These findings were interpreted as evidence of dysfunction of the photoreceptor membranes, possibly reflecting insult to the retinal pigment epithelium. The report emphasized the unique nature of the reversibility of these severe ERG abnormalities.

Subsequent reports have established that MEWDS can occur bilaterally and may recur in the same patient.[7, 19, 25] MEWDS has been diagnosed in patients with acute macular neuroretinopathy[13] and idiopathic enlargement of the blind spot,[10] which suggests possible relationships with these conditions. Elevated serum levels of IgM and IgG have been detected during the acute phase of the disease in one patient, with partial normalization within 1 month.[11] Although this patient denied a prodromal illness, the immunoglobulin concentration elevations were interpreted as suggestive of an infectious etiology. Keunen and van Norren[13] performed foveal densito-

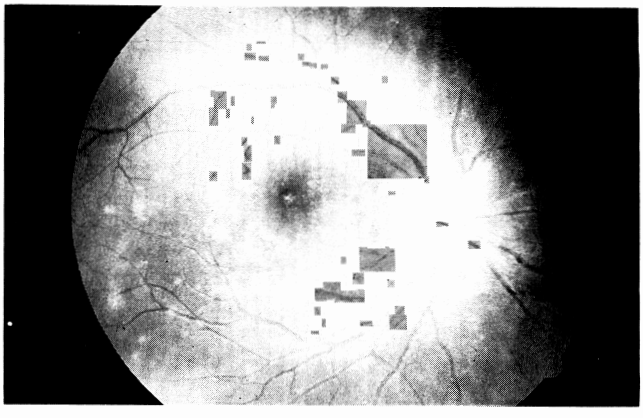

FIG 83–2.
Fundus appearance in MEWDS. (Courtesy of L. Jampol, M.D., and G. Fishman, M.D.) **(See also Color Plate 14.)**

metry on one MEWDS patient. They confirmed a profound loss of bleachable pigment during the acute phases, with complete normalization over the subsequent 8 weeks.

Yet another group of patients, apparently distinct from those described above, has also been tentatively identified by several authors.[15, 19] These patients evidence a relatively acute multifocal choroiditis characterized by discrete white lesions at the level of the retinal pigment epithelium, disc edema, mild vitritis, and visual loss. Recurrences are common, with new lesions developing adjacent to old ones. Subretinal neovascularization frequently occurs. The inflammation and neovascularization are reported to respond well to steroids by some authors, poorly by others.

Dreyer and Gass[5] reported electrophysiological studies in 29 affected eyes of 16 patients. ERGs were normal or nearly normal in 16 eyes, moderately impaired in 5 eyes, and severely abnormal in 6 eyes. The EOG light rise was normal in 2 patients and absent in a third (whose ERG was also extinguished). Electrophysiological test results have been only sporadically reported elsewhere and have shown no consistent pattern of abnormality. This clinical entity is at present less clearly delineated than birdshot chor*eoretinitis* or MEWDS, and no single name for the condition has been widely adopted.

The usefulness of electrophysiological testing in these entities appears limited since in acute phases the ERG and EOG are abnormal. However, the fairly rapid recovery of the ERG in MEWDS may provide a diagnostic parameter for distinguishing MEWDS from a number of causes of choroiditis.

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