Persistent Migraine Visual Aura  
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Keywords  
positive visual phenomena, persistent migraine aura, prolonged migraine aura, release phenomena, visual hallucinations

Objectives  
At the conclusion of this program, participants should be able to:  
1. Discuss non-migrainous causes of persistent positive visual phenomena.  
2. Apply the IHS criteria for persistent migraine aura to individual patients, and exclude alternate etiologies through selected investigations.  
3. Manage and counsel patients with persistent migraine aura

CME Questions  
1. What diseases may cause persistent positive visual phenomena?  
2. How long must an aura persist before meeting IHS criteria for persistent migraine aura?  
3. What are the typical characteristics of the visual phenomena in patients with persistent migraine aura?

Persistent positive visual phenomena (PPVP) are defined as the continuous or near-continuous presence of formed or unformed visual hallucinations. Formed hallucinations include shapes, figures, and people. Unformed hallucinations may include sparks, flickers, simple geometric shapes, and more complex visual symptoms such as metamorphopsia and palinopsia. Potential mechanisms may be direct stimulation of the afferent visual pathways (e.g., posterior vitreous detachment, irritative occipital lobe lesion), or deafferentation (“release hallucinations”). The differential diagnosis of PPVP is quite broad and may encompass lesions located from the vitreo-retinal interface to the visual cortex and visual association areas. In some cases, the etiology is obvious on the basis of history and examination, but in many cases there is no apparent etiology, even after exhaustive testing, and a presumptive diagnosis of persistent migraine aura is made. The diagnosis of persistent migraine aura is necessarily one of exclusion. This review will briefly cover the differential diagnosis of PPVP, and discuss the available literature regarding diagnosis and management of persistent migraine aura.

Non-migrainous Etiologies of Persistent Visual Phenomena  
1. Vitreo-retinal disorders:  
   Posterior vitreous detachments (PVD) and retinal tears/detachment (RD) may cause PPVP. The photopsias of PVD are most prominent in dim illumination and are often located in the temporal periphery. The photopsias associated with RD are more severe and may persist for weeks or months after successful treatment. They occur in less than 50% of patients with RD.

2. Photoreceptor degenerations:  
a. Photoreceptor degenerations may cause persistent, prolonged photopsias. The mechanism may be terminal discharges of dying photoreceptors or disinhibition of photoreceptors by other retinal elements. Paraneoplastic retinal degenerations such as Carcinoma-associated retinopathy (CAR) and Melanoma-associated retinopathy (MAR) may result in persistent visual phenomena. In CAR, both cones and rods are affected, and patients develop progressive loss of vision with bright, colorful photopsias, entopic phenomena, and photophobia. MAR affects only rods and is associated with shimmering or pulsating photopsias. Nyctalopia is a prominent symptom in MAR, and central vision is often spared. Clinical suspicion, electrophysiology, and serum autoantibodies confirm the diagnosis. One third of patients with Retinitis Pigmentosa may experience photopsias. These may be continuous, and assume the form of shimmering or rolling waves of light. Constricted visual fields, nyctalopia, and characteristic fundus changes usually make the diagnosis straightforward in most patients.

3. Toxic-Metabolic Retinopathies:  
a. Certain toxins and medications may cause prolonged positive visual phenomena. The visual symptoms are generally binocular and continuous. Digoxin may cause persistent flickering and scintillations, as well as hazy, snowy vision. Xanthopsia is a common symptom as well. Digoxin levels are usually toxic, but several patients have had normal serum levels, and the characteristic visual symptoms. Clomiphene has been associated with vibrating and shimmering in the periphery. Patients often describe difficulty with glare and photosensitivity.

4. Chorioretinal inflammatory disorders:  
a. Photopsias are a frequent and characteristic symptom of many of the enlarged blind syndromes, a heterogeneous group of related conditions including
Acute Zonal Outer Occult Retinopathy (AZOOR), Multiple Evanescent White Dot Syndrome (MEWDS), Acute Idiopathic Blind Spot Enlargement (AIBSE), and Multi-focal Choroidopathy (MFC). The exact frequency and characteristics of positive visual phenomena for each disorder is difficult to assess, due to overlap and lack of well-defined diagnostic criteria. However, when present, the photopsias are localized to the scotomatous area, and the presence of persistent visual phenomena within a scotoma should raise suspicion of one of these disorders. Diagnosis is secured by clinical suspicion, visual field and fundus examination, exclusion of alternate diagnoses, and electrophysiology.

5. Occipital lobe lesions:
   a. Toxic-metabolic disorders:
      i. Spontaneous, prolonged visual phenomena may occur secondary to moderate to severe, bilateral visual loss. This has been termed the Charles-Bonnet syndrome, after a Swiss philosopher who described visual hallucinations in his grandfather. The term “release hallucinations” specifically refers to spontaneous visual phenomena occurring in the setting of bilateral visual loss, which need not necessarily be severe. The phenomena may be simple, geometric forms or complex figures. The mechanism is not known, but may involve lack of inhibition following visual deprivation. The phenomena may resolve if visual loss is reversed (e.g., cataracts), resolve spontaneously, or persist indefinitely. Treatment with a variety of agents, including Haloperidol and Gabapentin, has been attempted, with variable success.

   Persistent Migraine Aura
   Some patients present with continuous, or nearly continuous positive visual phenomena, and no specific etiology is found, despite exhaustive investigations. Persistent migraine aura is often the final diagnosis, although this is usually arrived at only after excluding alternate diagnoses, such as those mentioned above. Persistent migraine aura is a specific diagnosis included in the 2nd edition of the International Headache Society Headache Classification. The IHS criteria are as follows:

   1.5.3: Persistent aura without infarction:

   **Diagnostic criteria:**
   1. Previous attacks fulfilling criteria for migraine with aura
   2. The present attack is typical of previous attacks but one or more aura symptoms persist for more than 2 weeks
   3. Not attributed to another disorder.

   The title and criteria emphasize the importance of excluded structural and vascular etiologies for persistent visual phenomena, but the lengths to which each clinician must go to satisfy the criteria is left unstated. The literature regarding persistent migraine aura is sparse. Most of the reports involve single patients or small case series, and it is not clear in all cases whether alternate diagnoses were adequately excluded. Liu et al reported the largest series of patients with persistent migraine aura. They described 10 patients (ages 9-67), all of whom had persistent visual phenomena lasting months to years. All of the patients had normal or non-contributory neuroimaging, normal examinations, no psychiatric disease, and no contributing medications or toxins. EEG and/or ERG were performed in most, and were normal when obtained. Three of the patients had a strong history of migraine with aura, with clear-cut temporal relationship between the headache and the persistent visual phenomena. Two patients had a history of migraine with aura, but a less clear temporal relationship between headache and visual symptoms. Five patients had a history of migraine headaches (2 with aura) but no relationship between
visual phenomena and headache. All of the patients described full-field visual symptoms, of varying forms. Haas\textsuperscript{18} reported two patients with “prolonged migraine aura status.” Both patients had a history of migraine with aura, and described prolonged positive visual symptoms, lasting 5 weeks in the first case, and 7 months in the second. Both patients had normal neurologic and ophthalmologic examinations. The first patient had CT of the brain and EEG, both of which were normal. Luda et al.\textsuperscript{19} reported a 65 year old woman with prolonged visual aura, manifesting as “scintillating geometric figures” in the right visual hemifield. The symptoms lasted 12 months and then remitted. Neurologic and ophthalmologic examinations were unremarkable, as were EEG and brain MRI. SPECT showed relative hypoperfusion in the left parieto-occipital and frontal regions.

The range of visual symptoms may be quite broad, but the limited literature suggests that many patients with persistent visual aura experience simple rather than complex visual phenomena. In Liu et al.’s series, phenomena such as palinopsia, micropsia, and formed hallucinations were exceptional. Most of their patients described features such as “TV static,” snow, lines of ants, dots, and rain. There may be greater awareness of these phenomena when looking at the sky or at a light-colored wall.

The mechanisms underlying migraine visual aura in general will be discussed in depth by other speakers, but relate to a decrease in cortical neuronal activity associated with decreases in cerebral regional blood flow.\textsuperscript{20} The mechanism by which visual aura persists indefinitely is unclear. The resolution of normal visual aura involves inhibition or modulation, resulting in suppression of neuronal activity, so it is possible that a failure of normal inhibition results in continuous, spontaneous cortical discharges, perhaps similar to release hallucinations.\textsuperscript{21,22} The concept that patients with migraine may have more “excitable” brains is not new. There is a prevailing theory that migraineurs have transient or persistent hyperexcitability of neurons in the cerebral cortex, particularly the occipital lobe. Although some studies have yielded conflicting results, data have consistently supported cortical hyperexcitability.\textsuperscript{23,24} Transmagnetic stimulation of the occipital cortex required to produce phosphenes is lower in migraine patients with aura than in controls.\textsuperscript{25} Battelli\textsuperscript{26} reported a lower phosphene threshold for transmagnetic stimulation over Brodmann’s area V5 in migraineurs, suggesting that hyperexcitability extended beyond the primary visual cortex (V1). Further studies, using magnetoencephalography and fMRI, have confirmed widespread regions of abnormal cortical excitability in patients with migraine.\textsuperscript{24} Cell membrane excitability appears to be the critical determinant for susceptibility to migraine attacks. There may be multiple factors that increase or decrease neuronal excitability and modulate the attack threshold and duration.

Although the hallmark of a migraine visual aura is complete reversibility, several studies have demonstrated that migraineurs may have interictal visual dysfunction. McKendrick et al.\textsuperscript{27} evaluated visual processing in 15 patients with a history of migraine with aura and 15 controls. Low-level spatiotemporal processing and motion processing were assessed. All migraineurs were at least 7 days after their most recent headache. The investigators identified cortical and pre-cortical visual dysfunction in migraine patients, suggesting that visual processing deficits may persist long after the aura has subsided. Other have found similar results in migraineurs, identifying deficits in spatial processing, motion detection, and contrast sensitivity.\textsuperscript{28,29}

Treatment of persistent migraine aura is generally unsatisfactory, although again, the literature on this subject is limited to case reports and small case series. In Liu et al.’s series, a variety of medications were attempted, largely without success. These included aspirin, verapamil, baclofen, carbamazepine, nifedipine, amitriptyline, gabapentin, phenobarbital, nortriptyline, and clonazepam. In one patient, sertraline reduced the visual phenomena by 50%. Chen and colleagues\textsuperscript{30} reported two patients with persistent migraine visual aura, lasting months to years. Both had normal examinations and imaging studies, although both demonstrated occipital hypoperfusion on SPECT. The visual symptoms resolved after treatment with lamotrigine. Rothrock described a single patient with persistent migraine aura arrested by valproate.\textsuperscript{31} Rozen reported two patients with prolonged migraine aura (visual aura in one patient) whose symptoms were completely relieved with intravenous prochlorperazine and magnesium sulfate.\textsuperscript{32} However, both patients had persistent migraine headache as well as persistent aura.

It is unclear how much further evaluation is necessary in a patient with a history of migraine with aura, thorough but non-contributory review of systems, and normal examination, including normal fundus and visual fields. Patients presenting with continuous photopsias require a careful headache and medication history, a complete ophthalmic examination (including visual fields and detailed evaluation of the peripheral retina), and in some cases, ancillary testing (such as neuroimaging, EEG, ERG). The extent to which ancillary investigations should be pursued must be left to the discretion of the physician, unless better data emerges. The relationship between psychiatric disorders such as depression and persistent migraine aura is unclear, but any identifiable, untreated psychiatric illness should be addressed. Many patients are concerned that they will eventually become blind, and reassurance that their examination is entirely normal may
be helpful. It is often worthwhile to discuss non-pharmacologic measures, such as minimizing excessive stress and sleep deprivation, eating regular meals, and physical exercise. Alternative therapies (biofeedback, relaxation, and acupuncture) have been used successfully in conjunction with conventional medical treatment for migraine headache, and may play a role in selected patients with persistent migraine aura. There are support groups accessible on the Internet, which may provide the patient with either information or misinformation, depending upon the site.

CME Answers
1. Persistent migraine aura, photoreceptor degenerations, visual seizures
2. Two weeks
3. Simple visual phenomena, such as dots, static, lines, etc.

References