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Left Homonymous Hemianopia: An Uncommon, Neuro-ophthalmological Presentation of Hyperglycemic Hyperosmolar State

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Abstract Spectrum of the neurological deficits in non-ketotic hyperglycemia and hyperosmolar hyperglycemic state (HHS) ranges widely among patients and can have any presentation from focal seizures, epilepsia partialis continua, chorea-hemiballismus syndrome, hemiparesis, hemianopia to mental obtundation and coma. Here we report a case of HHS which presented with Left Homonymous Hemianopia as the only initial presentation. Symptoms slowly resolved over the course of two weeks by administration of insulin and normalizing the glucose.

Keywords: *Homonymous Hemianopia, hyperosmolar hyperglycemic state, seizure, insulin*

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1. Introduction

Hyperglycemic Hyperosmolar State (HHS) is an acute complication of diabetes mellitus (DM) and carries significant morbidity and mortality. HHS is a syndrome defined by severe hyperglycemia, hyperosmolarity, and dehydration without ketoacidosis. Decreased cerebral perfusion from dehydration may cause neurologic signs such as focal neurologic deficits, visual acuity disturbances, delirium, and coma. Many etiologies have been described for the Homonymous Hemianopia (HH) in the literature, including infarction, hemorrhage, demyelination, neoplasm, inflammation and infection [1]. HH as a presentation of hyperglycemia or HHS is very uncommon and most of the reported cases have similarities, but major differences as well. Correcting the hyperglycemia remains the ultimate therapy for this condition.

2. Case Report

A 53 year-old African-American male with past medical history of essential hypertension presented to emergency room for acute onset of visual floaters and left visual field deficits upon awakening in the morning. Patient reported red white and blue puzzle-shaped particles in the far left vision of both eyes. Five days prior to admission patient was seen at the dermatology office for chronic contact dermatitis and furunculosis and he was started on prednisone 20 mg daily. Patient endorsed having large amount of sugary drinks in the days leading to his admission. Patient denied any headache, dizziness, speech and swallowing problem, limb weakness, numbness or tingling, gait abnormalities, difficulty hearing, urinary/bowel incontinence, previous similar complaints, history of stroke or head trauma. Furthermore, the patient denied any illicit drug use. At presentation, he was hypertensive at 150/84 mm-of-Hg, with otherwise normal vital signs. Triage finger-stick glucose (FSG) was 630 mg/dl.

On exam, he was awake, alert, oriented to time, place and person. Neurological exam was notable for subtle left sided ptosis and left sided homonymous hemianopia (HH), with otherwise normal cranial nerve exam. Visual acuity was 20/70 OS and 20/30 OD. Motor strength, sensory, reflexes, coordination exams were normal. Gait was assessed with caution due to left sided deficit, otherwise with intact heel to toe walking and tandem. Stroke code was initially called due to focal neurological deficits, but no tPA was administered as he was outside the treatment window. His NIHSS score was 3 (L homonymous hemianopia; subtle Left upper extremity pronator drift).

Labs were significant for Sodium of 129mEq/L, Anion gap of 14, bicarbonate of 26, pH 7.324 on ABG, Glucose 630 mg/dL, beta-hydroxybutyrate 1.0mmol/L, , creatinine 1.25 mg/dL, HbA1C 14.2% and serum osmolality 322mmol/kg. Urinalysis showed trace ketones (5 mg/dl) and Glucose of >1000 mg/dL. EKG and Chest X-ray were normal.

CT head as substantiated by MRI brain showed no acute but chronic microvascular ischemic changes and

mild cerebral atrophy. CT angiography of head showed no large vessel occlusion, high-grade stenosis, aneurysm or vascular malformation. Fetal origin of left PCA with hypoplastic P1 segment was noted. CTA of neck showed no significant stenosis according to NASCET criteria. Routine EEG was performed in the waking, drowsy and sleeping states and it was normal with no epileptiform discharges, and transthoracic echocardiogram showed normal LVEF, valves and chambers with no evidence of thrombi. Orbital MRI with contrast did not show any abnormality.

Our patient was admitted for HHS management from newly diagnosed diabetes and managed with aggressive hydration and insulin therapy. Ophthalmology was consulted and followed the patient throughout his stay. Initial exam by ophthalmology showed a congruent left homonymous hemianopia, suggestive of occipital lobe lesions. Final result showed scattered nonspecific superior visual field defects, dramatically improved from prior. Our patient's visual fields improved with glycemic improvement, and he was discharged with close neurology and ophthalmology follow up and primary care for new onset Diabetes. During ophthalmology follow up, on the same week of discharge, he reported near resolution of visual field defects.

3. Discussion

Homonymous Hemianopia has been previously reported as a rare complication of HHS or non-ketotic hyperglycemia. Many mechanisms of cellular injury caused by hyperglycemia are proposed which include hyperosmolar-induced dehydration, cortical ischemia, reactive oxygen species generation, neurotransmitter dysregulation and iron accumulation [2]. However none of these mechanisms quite explain the focal and specific finding of hemianopia in the hyperglycemic state. Many patients who present with HH in the setting of hyperglycemia have other symptoms such as headache, confusion or seizure (Table 1). Our patient's only presentation was the visual symptoms. Whether there is a correlation between the initial presentation and objective findings on MRI, EEG and PET/CT in these cases, needs to be studied further.

Mizuguchi *et al* [3] reported a case of a patient with HHS who presented with focusing deficit and reddish, greenish hallucinations and was found to have sharply demarcated inferior homonymous quadrantanopia. Interestingly the resolution of symptoms happened over the course of 8 days. Our patient's visual deficit improved slowly over the course of 4 days after accomplishing appropriate glycemic control in hospitalized patient (FSG 140-180). Similarly, significant improvement of symptoms did not happen up until 8 days after onset. As evident on Table 1, there is a variation in terms of the duration of symptoms in patients developing HH in the setting of hyperglycemia. Some patients had transient symptoms with quick recovery, while others did not have complete resolution of symptoms up until 1 or 2 weeks and in some cases even months. It would be interesting to investigate as to what exactly drives this variation in response, apart from time to normalization of blood glucose.

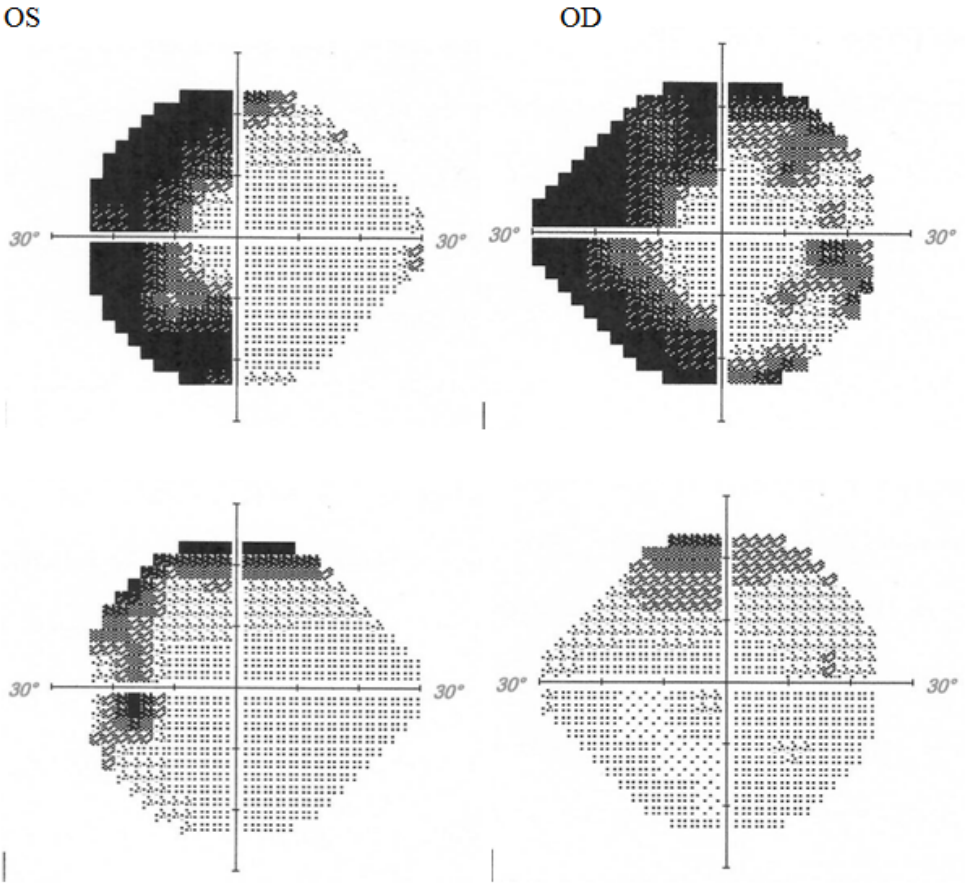

Figure 1. Upper panel: Left Homonymous Hemianopia on presentation. Lower panel: almost complete resolution of Left Homonymous Hemianopia by day 8

Table 1. Summary of the patients in current literature with homonymous hemianopia/quadrantanopia in the setting of hyperglycemia

Cases	Age/Gender	Comorbidities	Initial presentation	Other findings	Complete Resolution	Exam findings	CT/MRI findings	EEG
Strowd *et al* [2]	37, F	DM, Bipolar disorder, PCOS, HTN	Bifrontal headache, abrupt onset of L HH upon awakening	BG>500	Within days but with recurrence	Dense Left HH with macular sparing	R fPCA, superimposed focal, pial enhancement	Rhythmic alpha/theta evolving to delta
Strowd *et al* [2]	41, F	Asthma on steroids	Bifrontal headache and vision deficit	BG>300	10 days	Dense left HH without focal findings, unilateral reduction in cerebral vasoreactivity	R fPCA, superimposed cortical enhancement	Amplitude asymmetry
Mizuguchi *et al* [3]	60, M	DM, Obesity	Reddish & greenish hallucinations	BG 576	8-10 days	Discrete Homonymous Right inferior quadrantanopia, mild retinopathy	Unremarkable	Not performed
Stayman *et al* [6]	45, M	DM, HTN, OSA	Severe headache, blurred vision	BG 267	1-3 months	Dense Left HH, 30-sec speech/behavioral arrest	Right temporo-occipital cortical thickening, R hippocampus enhancement	Recurrent ictal discharges
Stayman *et al* [6]	60, M	Recent head trauma, HTN, Obesity, Asthma	Colored spots, loss of vision	BG 320	14 days	Left HH	T2 hyperintensity in R temporo-occipital cortex	Recurrent focal ictal discharges
Stayman *et al* [6]	69, M	Bulbar myasthenia gravis on steroids, obesity	Green circles in R lower binocular field	BG 487, SO 315	4 days	R HH	Unremarkable	Occipital lobe seizure
Kim *et al* [7]	65, F	DM	Intermittent L arm jerky movements, Blurred vision	NKH	Within 2 months	L HH	Focal cortical hyperintensity, delayed gadolinium enhancement of CSF on FLAIR	Data not available
Freedman *et al* [13]	72, F	DM	Multiple Visual deficits	NKH	Quick recovery	L HH	Unremarkable	Not performed
Nissa *et al* [15]	53, M	DM, HTN, CKD	Bilateral visual impairment and tonic-clonic seizure	BG 581	3 days	R HH	Hypointensity on T2WI and FLAIR	L occipital seizure
Gaballa *et al* [16]	65, M	DM, anxiety disorder, HTN	Intermittent confusion and visual disturbance, headache	BG 607, SO 303	10 days	Dense temporal visual field loss, unsteady gait	Chronic small vessel ischemic changes	Unremarkable
Lopez-Amoros *et al* [17]	62, F	DM, HTN, OSA, Afib, Hypothyroidism, RA, On steroids for Eczema	Headache, colors and flashes over visual field	BG 623	Quick recovery	L inferior homonymous quadrantanopia	Unremarkable	Not performed
Taban *et al* [18]	68, M	DM	Photopsia, visual hallucination, distorted vision	BG>600	Within days	L HH	Unremarkable	Not performed

Abbreviations: R, right; L, left; M, Male; F, Female; DM, Diabetes Mellitus; HTN, Hypertension; HH, Homonymous hemianopia; OSA, obstructive sleep apnea; PCOS, Polycystic ovary syndrome; fPCA, fetal-type posterior cerebral artery; CKD, chronic kidney disease; NKH, Nonketotic hyperglycemia; Afib, Atrial fibrillation; RA, Rheumatoid arthritis; CT, computed tomography; MRI, Magnetic resonance imaging ; EEG, electroencephalogram; T2WI, T2 weighted image; FLAIR, Fluid-attenuated inversion recovery; BG, Blood Glucose in mg/dL; SO, Serum Osmolality in mOsm/L.

Another observation in our patient is the presence of fetal origin of left PCA with hypoplastic P1 segment. Some authors [4,5], suggest that fetal variation of circle of Willis could be a risk factor for vascular insufficiency. In the two patients who presented with hyperglycemic hemianopia, Strowd *et al* [2] report that both had reduced cerebral vasomotor reserve confirmed by transcranial doppler ultrasonography due to the right fetal-type posterior cerebral artery (fPCA).

Extended video-EEG in a series of 3 patients with HH in the setting of non-ketotic hyperglycemia showed ictal discharges in the contralateral occipital quadrant. FDG-PET in 2 of those patients showed area of hypermetabolism in similar region [6]. Authors suggest ictal or post-ictal state as an underlying mechanism for HH. In some cases, seizure activity persisted, despite using anti-epileptic drugs [6]. Our patient had a normal EEG findings and also did not report any other symptoms such as severe headache, nystagmus or history of head trauma like the patients reported in that study. In one report, disrupted blood brain barrier (BBB) as evident on delayed gadolinium enhancement in FLAIR images, was suggested to play a role in seizure formation in this setting [7]. Sasaki *et al*, suggest that long-standing hyperglycemia, rather than HHS per say, is the trigger for seizure as their patient did not meet diagnostic criteria of HHS [8].

Despite the several proposed pathophysiological theories, the actual mechanism by which focal neurological deficits occur in the setting of HHS or hyperglycemia still remains unknown. What remains to be interesting is the timeline from onset to the resolution of symptoms which was around 8-10 days in our patient, suggesting possible underlying molecular mechanism which may be related to the role of insulin on neuronal membranes. In one study, expression of GABA(A) receptors on postsynaptic and dendritic membranes were increased by Insulin [9]. Many other studies have shown the physiological role of insulin in decreasing the excitability of neural networks [10,11]. In a recent study, low-dose intranasal insulin significantly reduced the duration and frequency of provoked seizures in mouse models [12]. Further investigation will be needed to clarify the underlying molecular mechanism for this phenomenon.

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