"Too Much Sugar is Bitter": An Important Cause of Reversible Inferior Quadrantanopia

Sir,

Visual field defects are commonly caused by structural lesions in the visual pathway, particularly those of a vascular origin or tumors. However, they can also occur without neuroimaging changes in conditions like occipital lobe seizures, migraine, nonketotic hyperglycemia (NKH), toxic/metabolic, and degenerative dementias.[1] Therefore, reversible causes need to be considered when structural abnormalities are not identified. Herein, we report a case of right homonymous inferior quadrantanopia due to NKH presenting as the first clinical manifestation of asymptomatic diabetes mellitus.

A 59-year-old male with no prior comorbidities presented with a 3-week history of episodic-positive visual phenomena. He described it as red- and blue-colored whorls (the pictorial representation is depicted in Figure 1) in the right inferior quadrant of his field. Initially, he had 1 to 2 episodes per day, lasting for 15 to 20 seconds each, which progressed to 15 to 20 per day, each lasting 5 to 10 minutes. Because of this, he had difficulty climbing downstairs and reading. He was completely aware and responsive during these events. There was no history of headache, other cranial nerve symptoms, motor weakness, involuntary movements of limbs, altered sensorium, or loss of consciousness. He did not give a history of frequent headaches or seizures in the past.

Neuroophthalmological examination revealed visual acuity of 6/6 bilaterally with briskly reacting pupils (4 mm each). He had right homonymous inferior quadrantanopia, confirmed by Humphreys visual field analyzer [Figure 2a]. Fundus examination was normal, and there were no other focal neurological deficits. General and systemic examination was noncontributory. The congruous right homonymous inferior deficits favored a left parietal or occipital cortical lesion. The acute onset of symptoms raised suspicion of a vascular etiology.

The metabolic profile revealed a high blood sugar of 576 mg/dL, serum osmolality of 326 mOsm/kg and HbA1c of 12.4% with negative urine ketones and normal arterial blood gas analysis. A brain MRI, including TOF imaging of intra and extracranial vessels, was normal. CSF analysis and video electroencephalography were normal. Vasculitic markers and other metabolic workup were also negative. A diagnosis of NKH was made, and the visual field defects and hallucinations were thought to be due to the hyperosmolar state. The patient was initiated on Insulin therapy and Oxcarbazepine 300 mg/day. His symptoms improved within a few days, and there was complete resolution of the visual phenomenon on follow-up 2 weeks later. Visual field analysis at the time of follow-up showed near-complete normalization, as shown in Figure 2b.

Nonketogenic hyperglycemia can have various neurological manifestations including coma, seizures, hemiparesis, and hemichorea.[2] It also can cause visual disturbances in the form of positive and negative phenomena including visual field defects.[3] Visual field defects associated with hyperglycemia are predominantly homonymous hemianopia followed by, superior and inferior quadrantanopia.[4]

Other etiologies of visual field defects without correlative structural lesions in neuroimaging include migraine, occipital lobe seizures, degenerative dementias (Alzheimer's, Lewy body dementia), Heidenhain variant of Creutzfeldt--Jacob disease, subtle occipital ischemia or hypoxia, and functional illness.[1] The timeline of onset of visual field defects helps evaluate cerebral pathology.

The pathophysiology of the visual phenomena in NKH is unclear and may be due to a hyperosmolar state which causes increased free radical generation and, as a result, a lowering in GABA, which leads to a reduction in seizure threshold [Figure 3]. In addition, the Krebs cycle and glucose utilization are reduced in hyperglycemic states, allowing other energy metabolism pathways to emerge, such as the conversion of GABA to succinic acid via the succinic-semialdehyde pathway (the GABA shunt), which provides up to 40% of the brain's energy needs.[5] The K-ATP channels which increase the neuronal excitability in a hyperglycemic environment have been recently shown to be important in hyperglycemia-induced seizure.

Our patient had elementary visual hallucinations of phosphenes---multicolored circles, that are typical of occipital lobe seizures. These moving circular patterns had the same onset regarding localization, and progression, they were mostly brief, lasting for seconds, with an abrupt onset and offset. Whereas, the visual aura of migraine with aura and acephalgic migraine begins with mainly flickering achromatic or black and white, linear, and zigzag patterns or light flashes in the center of visual field, gradually expanding over minutes towards the periphery of one hemifield and often leaves a scotoma.[6] They generally do not exhibit daily frequencies. The mechanism of visual field defects in NKH may be explained by postepileptic suppression of surrounding visual fields following focal awareness sensory seizure.[4] Traditionally, it was considered that positive symptoms like hallucinations occur during the ictal phase whereas negative symptoms of blindness/hemianopia occur in postictal phase. However, the demonstration of electrical correlate on EEG along with occipital hypermetabolism on brain FDG-PET scan suggest that ongoing seizure activity, rather than a post ictal phenomenon could be the underlying pathophysiology of homonymous hemianopia associated with NKH.[5]

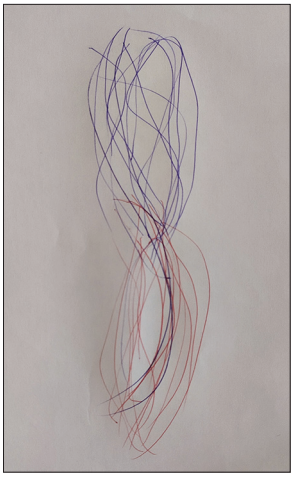

Figure 1: Visual hallucinations: drawn by the patient

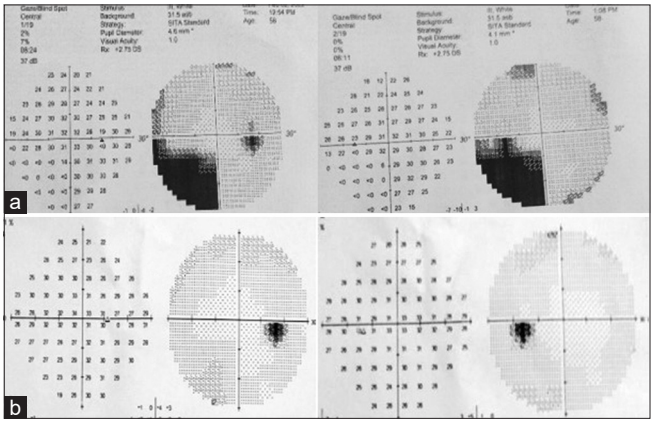

Figure 2: (a) Visual field on admission, (b) Visual field after 2 weeks (on follow-up after treatment)

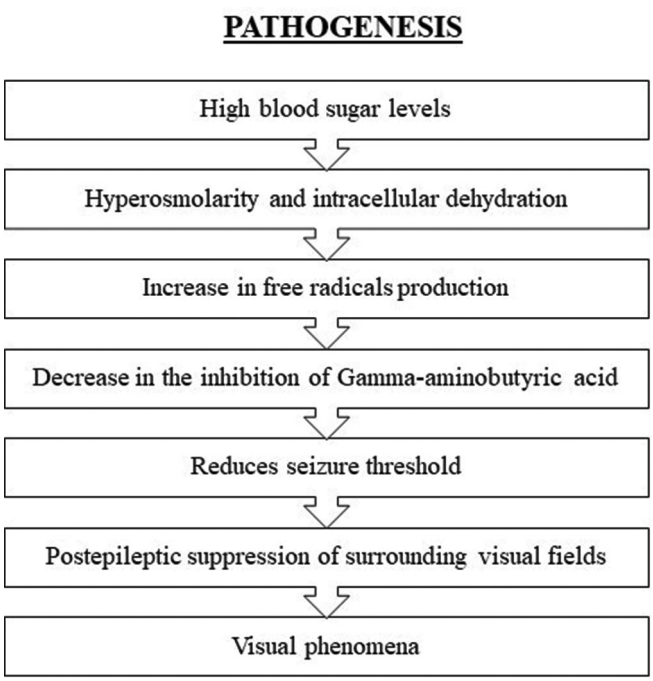

Figure 3: Pathophysiology of the visual phenomena in NKH

Given that the inferior quadrantanopia associated with positive visual phenomenon disappeared along with the normalization of serum glucose level in our patient, his visual symptoms may have been associated with NKH.

Brain MRI is abnormal in up to 85% of patients.[4] The most commonly described MRI findings associated with NKH include increased T1 and T2 signals on the side contralateral to symptoms.[7] The putamen is almost always involved with variable additional associated basal ganglia lesions. There are also reports of subcortical T2 hypointensity in the occipital white matter, gyral enhancement, and diffusion restriction.[8] However, in our case, Brain MRI demonstrated no restricted diffusion or focal parenchymal abnormalities. The video EEG, twelve hours after initiation of treatment, while the patient still continued to have symptoms was normal. Previous studies have reported epileptiform discharges in 61.1% of individuals.[4] CSF analysis was normal in previously reported cases.

Aggressive insulin therapy and adequate hydration are essential in management. Our patient was managed on the same lines. He was initiated on insulin therapy, with regular monitoring of blood sugars. Even though the EEG was normal, it is possible that the patient experienced visual seizures induced by NKH, and his transient inferior quadrantanopia was an ictal phenomenon or post ictal inhibition, similar to a Todd's phenomenon, and hence he was also given Oxcarbazepine 300 mg/day. It is not known whether drugs that enhance GABA will be more effective for seizures in the setting of NKH. Previously reported cases were found to have a good prognosis with a complete recovery in 97% of individuals with an interval of 2--16 days for remission.[4] Our patient also had complete remission in 14 days.

The case highlights the importance of considering nonstructural causes such as NKH in transient visual field defects, especially when associated with repetitive positive visual symptoms, and reiterates the importance of strict blood sugar control in the management.

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Conflicts of interest

There are no conflicts of interest.

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