



# Clinical Reasoning: Acute-onset homonymous hemianopia with hyperglycemia

Seeing is believing

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## SECTION 1

**Case 1.** A 32-year-old woman with a history of bipolar disorder, polycystic ovarian syndrome, and hypertension and a 4-year history of uncontrolled type 2 diabetes mellitus (DM) presented with bifrontal headache, elevated blood sugars ( $>500$  mg/dL), and abrupt-onset left homonymous hemianopia upon awakening. Vital signs included temperature 98.0°F, blood pressure 160/89 mm Hg, and heart rate 67 bpm. Neurologic examination showed dense left homonymous hemianopia with macular sparing and without other focal findings.

**Case 2.** A 41-year-old woman with no medical history presented with bifrontal headache and vision deficit. After being started on oral prednisone for management

of asthma exacerbation 1 week prior, she reported severe polyuria, polydipsia, and 10-pound weight loss and subsequently was diagnosed with DM (fasting blood sugar  $>300$  mg/dL). In the days prior to presentation, she noted minor difficulty locating objects on her left side, which was acutely worse upon awakening the morning of admission. Vital signs included temperature 99.8°F, blood pressure 144/67 mm Hg, and heart rate 100 bpm. Neurologic examination confirmed dense left homonymous hemianopia without focal findings.

## Questions:

1. What diagnoses should be considered in the differential?
2. What initial workup should be performed?

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## SECTION 2

Vision loss is best organized into prechiasmal (e.g., monocular), chiasmal (e.g., bitemporal), or retrochiasmal (e.g., homonymous) deficits. The homonymous deficits observed in these cases localize retrochiasmatically, affecting the right optic tract, lateral geniculate nucleus, optic radiations, or visual cortex. The congruous homonymous deficits and macular sparing favor a more posterior or cortical lesion.

The timeline of onset is helpful in evaluating cerebral pathology. In these cases, acute onset of symptoms raises suspicion for a vascular etiology including ischemic or hemorrhagic stroke, venous sinus thrombosis with infarct, complicated migraine, or cerebral vasculopathy such as reversible posterior leukoencephalopathy syndrome (RPLS) or hyperglycemic hemianopia. Other secondary considerations include infection (i.e., cerebritis, encephalitis), inflammatory process (i.e., demyelinating lesion, sarcoidosis), or toxic/metabolic process (i.e., ictal or postictal phenomenon). Neoplastic, paraneoplastic,

hereditary, or degenerative pathology is not favored as these are more insidious in onset.

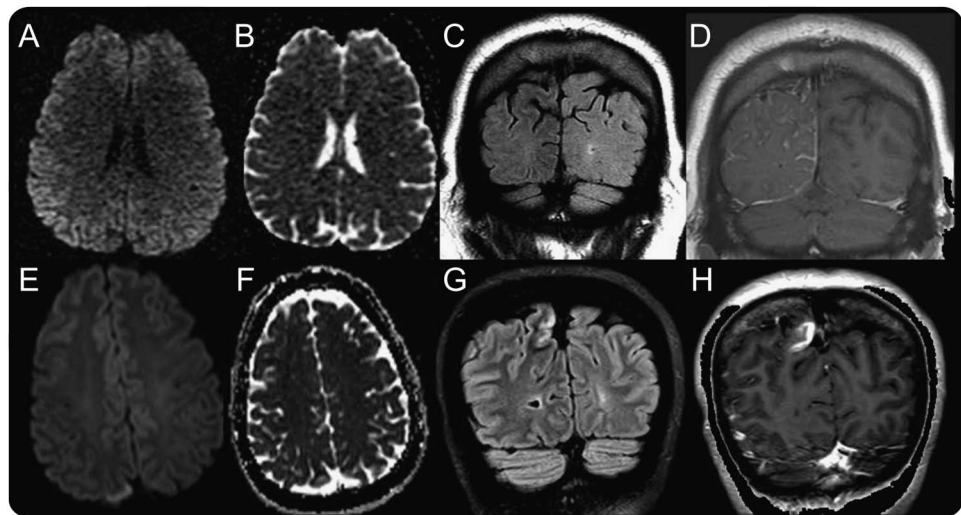
Noncontrast head CT ruled out intracranial hemorrhage. Laboratory investigation excluded leukocytosis, renal or liver dysfunction, and electrolyte disturbance except elevated blood sugars to 541 mg/dL (case 1) and 306 mg/dL (case 2). Brain MRI demonstrated subtle cortically based increased signal on diffusion-weighted sequences without corresponding decreased signal on apparent diffusion coefficient sequences (figure 1, A and B). Superimposed focal, pial (case 1), or cortical (case 2) gadolinium enhancement was observed, with adjacent subcortical hypointensity on T2-weighted imaging (T2WI) and fluid-attenuated inversion recovery (FLAIR) sequences (figure 1, C, D, G, and H).

### Questions:

1. Based on these imaging findings, what differential considerations are favored?
2. What further evaluation and initial management should be performed?

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**Figure 1** Neuroimaging findings in hyperglycemic hemianopia



MRI brain with and without contrast for cases 1 (A-D) and 2 (E-F). Axial diffusion-weighted sequences (A, E) show subtle right occipital and parietal increased signal with corresponding increased signal on the apparent diffusion coefficient for case 2 (F). Coronal fluid-attenuated inversion recovery (C, G) demonstrates subcortical hypointensity. Coronal T1-weighted gadolinium-enhanced images (D, H) demonstrate gyriform pial enhancement in case 1 (D) and focal cortical enhancement in case 2 (H).

### SECTION 3

MRI did not reveal restricted diffusion to suggest cerebral ischemic infarct. Subcortical T2WI hyperintensities that are characteristic of RPLS or demyelinating lesions were not present. In fact, subcortical T2WI and FLAIR hypointensity was observed. The differential for this finding is limited to viral encephalitis, meningitis, leptomenigeal metastasis, hemorrhagic infarct, hypoxic insult, and cerebral nonketotic hyperglycemia (NKH).<sup>1</sup> With the exception of NKH, these other conditions are associated with leptomenigeal enhancement, not focal cortical enhancement. Fever, leukocytosis, cancer history, or hypotension was not observed.

Initial evaluation showed no evidence of ketonuria or ketonemia in case 1 and large ketonuria with trace ketonemia in case 2. Hemoglobin A1c was 13.5% (case 1) and 12.1% (case 2). Both patients were managed for severe hyperglycemia with aggressive hydration and insulin. Rapid correction of blood glucose was achieved to 175 mg/dL (case 1) and 162 mg/dL (case 2) by discharge.

In case 1, the patient underwent unremarkable lumbar puncture (1 cell/mm<sup>3</sup>, protein 69 mg/dL, glucose 104 mg/dL, serum glucose 237 mg/dL). Additional studies did not reveal causative infectious or inflammatory conditions including normal viral PCR testing (e.g., enterovirus, herpes, varicella, Epstein-Barr, and cytomegalovirus), Lyme panel, Venereal Disease Research Laboratory testing, angiotensin-converting enzyme (ACE), cryptococcal antigen, and bacterial, fungal, and acid-fast cultures. CSF immunoglobulin G index was normal. CSF cytology was without neoplasia or lymphoma. Laboratory evaluation showed elevated sedimentation rate of 101 mm/h and C-reactive protein of 15.3 mg/L. Evaluation for systemic vasculitis or connective tissue disorder was negative including unremarkable rapid plasma reagin, antinuclear antibody, HIV

testing, double-stranded DNA testing, anti-Rho and La antibodies, antineutrophilic cytoplasmic antibodies, serum cryoglobulins, complement levels, ACE, cardiolipin antibodies, and lupus inhibitor. CT angiography of the head showed only right fetal-type posterior cerebral artery (fPCA).

In case 2, evaluation was similar, with normal lumbar puncture (0 cells/mm<sup>3</sup>, protein 36 mg/dL, glucose 100 mg/dL, serum glucose 162 mg/dL). CSF viral PCRs, cytology, and flow cytometry were unremarkable. Cerebral catheter angiogram excluded vasculitis but did demonstrate right fPCA. Transcranial Doppler ultrasonography was performed via transtemporal insonation of the bilateral middle cerebral arteries (MCAs). After 5 minutes of rest in the supine position, a baseline value for mean flow velocity was recorded. At baseline, slightly greater elevation of mean velocity was present on the right (99 cm/s) compared to left side (86 cm/s). To determine cerebrovascular reserve, a mixture of 5% CO<sub>2</sub> in air was then administered for 2–3 minutes via a nonbreathing face mask with continuous monitoring of MCA mean flow velocity. When the velocity response had reached a maximum, that value was recorded and monitoring continued until the velocity had returned to baseline. The difference between baseline and maximum response was divided by the baseline velocity to obtain the percentage change in response to this CO<sub>2</sub> challenge, with normal being a 30% or greater increase in mean flow velocity. Vasomotor reactivity was reduced on the right (20%) but normal on the left (38%).

#### Questions:

1. What is the final diagnosis?
2. What complications should be considered and monitored closely?
3. What is the prognosis and timeline of recovery?

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## SECTION 4

Presentation with severe hyperglycemia; lack of cerebrovascular infarction, neoplasm, demyelinating lesion, infectious source, or vasculitis on imaging; and the characteristic findings on T2WI, FLAIR, and contrast-enhanced images favor a diagnosis of hyperglycemic hemianopia.

The patient in case 1 developed visual obscurations consisting of colored orbs of light at times with associated left eye and head version and decreased responsiveness. Ictal EEG showed rhythmic alpha/theta evolving to rhythmic delta in the right temporal chains. These episodes resolved with levetiracetam and topiramate. The patient in case 2 was monitored closely for seizure without occurrence. Routine EEG showed only amplitude asymmetry (right hemisphere 15–20  $\mu$ V, left 25–40  $\mu$ V).

In case 1, visual symptoms resolved completely by subjective report but the patient had acute psychosis with resultant medication noncompliance, re-presentation with hyperglycemic crisis, and recurrent left homonymous hemianopia (figure e-1 on the *Neurology*<sup>®</sup> Web site at Neurology.org). Visual deficit persisted thereafter, with MRI brain at 1.5 years showing right temporal-occipital atrophy. In case 2, visual symptoms had improved to 70% by discharge and completely by visual field testing after 10 days.

**DISCUSSION** A spectrum of cerebral injuries has been described with severe hyperglycemia. Nonketotic hyperosmolar hyperglycemia (blood sugar >600 mg/dL, bicarbonate >20 mEq/L, pH >7.3, osmolality >320 mOsm/L, absent or small ketoacids) and diabetic ketoacidosis (blood sugar >400 mg/dL, bicarbonate <10 mEq/L, pH <7.2, normal osmolality, present ketoacids) occupy the ends of this spectrum. Specific CNS manifestations also include hyperglycemic hemichorea-hemiballismus, hemiparesis, hemianopia, and coma.

In hyperglycemic hemianopia, patients present with homonymous hemifield deficits and severe hyperglycemia, most often a nonketotic hyperosmolar state. MRI classically demonstrates T2WI hypointensity.<sup>1</sup> Seizures frequently complicate this illness. Symptoms are reversible with rapid correction of hyperglycemia.<sup>2</sup>

Mechanisms of cerebral injury from hyperglycemia are unclear and may include intracellular dehydration from hyperosmolarity, reactive oxygen species generation, altered neurotransmitter function, local cerebrovascular ischemia, or altered intracellular enzyme mechanics.<sup>3</sup> Arterial basal superoxide, nicotinamide adenine dinucleotide phosphate–stimulated superoxide, plasma ferritin, serum iron, and end-organ iron deposition are higher in animals exposed to chronic hyperglycemia.<sup>4</sup> Acidosis induced by NKH further increases unbound

iron due to acidosis-induced reductions in transferrin affinity and subsequent reactive oxygen species generation.<sup>5</sup> In acute hyperglycemia, where insulin deficiency leads to severe intravascular hyperglycemia, glycosuria, and varying levels of acidosis, intracellular dehydration may play a role in neuronal dysfunction and the characteristic imaging. Increased signal on diffusion-weighted sequences indicates cytotoxic edema typically associated with ischemia but also seen in osmotic dysfunction, hyperviscosity syndromes, or seizures. Seizures are frequent neurologic manifestations of NKH, leading some to suggest that the hemianopia in these patients may represent a post-ictal Todd paralysis. MRI in focal seizures, however, typically reveals T2WI hyperintensity. In contrast, subcortical T2WI hypointensity common to this condition has been associated with iron accumulation, early cortical ischemia, and cellular dehydration.<sup>6</sup> Further investigation is necessary.

Posterior predominance of pathology is known to occur in hyperglycemic hemianopia and RPLS. Sympathetic nerve innervation augments cerebral vascular tone in response to acute changes in cerebral hemodynamics. A pervading hypothesis has been that less abundant sympathetic innervation of the posterior circulation and pial collaterals results in the posterior predominance of these conditions.<sup>7</sup> Patients with DM are particularly susceptible to autoregulatory failure as a result of sympathetic dysautonomia, endothelial dysfunction, blood-brain barrier breakdown, and free radical release.<sup>8</sup>

Reduced cerebral vasomotor reserve by ultrasonography is interesting. The unilateral reduction in cerebral vasoreactivity in case 2 suggests a state of focal maximal cerebral vasodilation and reduced autoregulatory capacity in this region. Both patients presented here were found to have ipsilesional fPCAs. fPCA circuitry reduces MCA–posterior cerebral artery pial collateralization<sup>9</sup> and could predispose to such a unilateral reduction in vasomotor reactivity despite a systemic metabolic stress such as hyperglycemia. Mechanisms underlying focal cortical pathology in this condition have not been fully elucidated and further investigation is required.

Hyperglycemic hemianopia is an important consideration in patients with abrupt-onset hemianopia with hyperglycemia and can be further confirmed with characteristic imaging findings. Prompt treatment is important in this potentially reversible condition.

## AUTHOR CONTRIBUTIONS

Dr. Strowd: conception, manuscript preparation, generation of figures, and final revision and approval of manuscript. Dr. Wabnitz: manuscript preparation, revision, and approval. Dr. Balakrishnan: manuscript preparation, revision, and approval. Dr. Craig: manuscript preparation, revision, and approval. Dr. Tegeler: manuscript preparation, revision, and approval.

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## REFERENCES

1. Raghavendra S, Ashalatha R, Thomas SV, Kesavadas C. Focal neuronal loss, reversible subcortical focal T2 hypointensity in seizures with a nonketotic hyperglycemic hyperosmolar state. *Neuroradiology* 2007;49:299–305.
2. Lavin PJ. Hyperglycemic hemianopia: a reversible complication of non-ketotic hyperglycemia. *Neurology* 2005;65:616–619.
3. Kodl CT, Seaquist ER. Cognitive dysfunction and diabetes mellitus. *Endocr Rev* 2008;29:494–511.
4. Rowe PA, Kavanagh K, Zhang L, Harwood HJ Jr, Wagner JD. Short-term hyperglycemia increases arterial superoxide production and iron dysregulation in atherosclerotic monkeys. *Metabolism* 2011;60:1070–1080.
5. Selim MH, Ratan RR. The role of iron neurotoxicity in ischemic stroke. *Ageing Res Rev* 2004;3:345–353.
6. Ida M, Mizunuma K, Hata Y, Tada S. Subcortical low intensity in early cortical ischemia. *AJNR Am J Neuroradiol* 1994;15:1387–1393.
7. Ay H, Buonanno FS, Schaefer PW, et al. Posterior leukoencephalopathy without severe hypertension: utility of diffusion-weighted MRI. *Neurology* 1998;51:1369–1376.
8. Cotton F, Kamoun S, Rety-Jacob F, Tran-Minh VA, Nighoghossian N, Hermier M. Acute hypertensive encephalopathy with widespread small-vessel disease at MRI in a diabetic patient: pathogenetic hypotheses. *Neuroradiology* 2005;47:599–603.
9. Van Raamt AF, Mali WPTM, van Laar PJ, van der Graaf Y. The fetal variant of the circle of Willis and its influence on the cerebral collateral circulation. *Cerebrovasc Dis* 2006;22:217–224.

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