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Case Report

Stress-Induced Oculogyric Crisis in Septo-Optic Dysplasia: Case Report

Phillip Keys[a] Pamela Davila-Siliezar[b] Noor Laylani[b] Andrew G. Lee[a, b, c, d, e, f]

[a]Department of Ophthalmology, University of Texas Medical Branch School of Medicine, Galveston, TX, USA; [b]Department of Ophthalmology, Blanton Eye Institute, Houston Methodist Hospital, Houston, TX, USA; [c]Departments of Ophthalmology, Neurology, and Neurosurgery, Weill Cornell Medicine, New York, NY, USA; [d]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [e]Texas A and M College of Medicine, Bryan, TX, USA; [f]Department of Ophthalmology, The University of Iowa Hospitals and Clinics, Iowa City, IA, USA

Keywords
Oculogyric crisis · Septo-optic dysplasia · Dystonia · Hypothalamic-pituitary axis · Case report

Abstract
Introduction: Oculogyric crisis (OGC) is a dystonic movement disorder of varying durations that manifests as bilateral paroxysmal upward eye deviation accompanied by involuntary blinking, tongue protrusion, and autonomic symptoms. Separately, septo-optic dysplasia (SOD) is a congenital disorder involving hypoplasia of the optic nerve as well as hypothalamic and pituitary abnormalities. In the presented case, we report a case of OGC in the setting of SOD with proposed pathogenesis. ***Case Presentation:*** A 27-year-old female presented with a history of SOD (optic nerve hypoplasia and hypopituitarism) with acute, recurrent, painless, bilateral, intermittent, simultaneous tonic conjugate upward eye deviation (i.e., OGC) and dystonic body posturing. She experienced her first episode upon meeting her biological sister for the first time at a loud, crowded public restaurant with continued episodes of OGC increasing in frequency and duration over the subsequent months. She later responded well to treatment with carbidopa/levodopa. ***Conclusion:*** Based on our current understanding of OGC, we hypothesize that acute stressful life events in the setting of prior hypothalamic-pituitary axis dysfunction secondary to SOD could lower the threshold for developing OGC. Although most cases of OGC are idiopathic, various etiologies including medications, stress, and hormonal imbalance have been postulated as possible pathogenic mechanisms. We describe a case of SOD with OGC, and based upon our review of the English language ophthalmic literature, we believe that our case is novel.

Correspondence to:
Andrew G. Lee, aglee@houstonmethodist.org

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Introduction

Septo-optic dysplasia (SOD) is a congenital disorder characterized by optic nerve hypoplasia and other midline hypothalamic and pituitary abnormalities (e.g., absence of the septum pellucidum and pituitary hypoplasia) [1]. Although many cases are idiopathic, young maternal age, maternal drug consumption, viral infections, and genetic predispositions have been reported in SOD [2]. Initially described in 1956, the incidence of SOD is estimated at 1 in 10,000 live births [1, 2]. The visual loss in SOD is variable, and hypopituitarism is the main risk of morbidity and potential mortality in SOD.

Oculogyric crisis (OGC) is a nonrhythmic, dystonic ocular movement disorder lasting minutes to hours during which the eyes develop a bilateral paroxysmal, conjugate, and upward deviation without loss of consciousness [3]. Involuntary blinking, tongue protrusion, neck dystonia, and a number of potential autonomic symptoms may accompany the OGC [3]. Although OGC is often a side effect of medications (e.g., antiemetics, neuroleptics, antipsychotics, anticonvulsants, and antidepressants), neurodegenerative movement disorders and other brainstem pathology have been reported with OGC [3, 4]. We describe OGC in a patient with SOD and propose a possible hypothesis for pathogenesis. To our knowledge and based upon a review of the English language ophthalmic literature, we believe our case to be novel.

Case Report

A 27-year-old white female had congenital SOD. She presented with new, acute, recurrent, painless, bilateral, simultaneous, intermittent, stereotyped tonic conjugate upward eye deviation. The episodes of OGC were sometimes associated with dystonic body posturing. The initial episode was precipitated by a stressful psychosocial event where she met her biological sister for the first time in a loud and crowded restaurant. Thereafter, the OGC events were increasing in frequency and duration over the next few months. She retained consciousness and sphincter function and had no seizure activity during the episodes. The OGC events lasted several minutes to hours at a time and occurred 2–3 times per week. She had no bradykinesia, autonomic dysfunction, or orolingual dyskinetic movements.

Past medical history included intrauterine brain hypoxia secondary to maternal diabetes and cocaine use during pregnancy in her biological mother. The family history was otherwise unknown because the patient was adopted at birth. Neuroimaging showed a stable arachnoid cyst in the middle cranial fossa without hydrocephalus and pituitary hypoplasia. She had stable hypopituitarism on hormone replacement therapy with endocrinology. She had stable migraine without aura. Her medications include levothyroxine, clonazepam, estradiol, hydrocortisone, metoprolol, nitroglycerin, and progesterone. Serial magnetic resonance imaging of the brain showed absence of the olfactory bulb, the tuber cinereum, and the anterior commissure in addition to optic nerve hypoplasia. Electroencephalography was normal, and she had no seizure clinically. The endocrinologic evaluation showed a thyroid-stimulating hormone level of 0.01 mIU/L consistent with normal suppression after levothyroxine replacement for hypothyroidism. The patient had normal cortisol and estrogen levels consistent with replacement therapy.

On neuro-ophthalmic examination, visual acuity was count fingers at 3 feet in the right eye (OD) and 20/400 in the left eye (OS) which was unchanged from previous documentation of her baseline from childhood. She had pendular congenital nystagmus and superimposed roving eye movements. She showed a −1 impairment in abduction and adduction in both eyes (OU). Her visual field was reduced to 10° OD and 30° OS. Her pupils were isochoric but poorly

reactive OU. The anterior segment was unremarkable OU. Dilated fundus exam showed a small optic nerve bilaterally. The cup-to-disk ratio was 0.7 OU. There was flat hyperpigmentation on the left optic nerve suggestive of congenital hyperpigmentation, but a disk melanocytoma was in the differential diagnosis (Fig. 1).

The patient was diagnosed with OGC and treated with carbidopa/levodopa with a marked reduction in her episodes of OGC at last follow-up. A repeat magnetic resonance imaging of the head showed no acute intracranial abnormality, and follow-up endocrinologic evaluation was stable. She was thoroughly pleased with the care she received and continues to follow up with neuro-ophthalmology.

Discussion

Our patient experienced multiple, recurrent episodes of stereotyped, tonic, conjugate deviation of her eyes, episodes lasting minutes to hours, and the maintenance of consciousness throughout the episodes consistent with OGC [3]. Although the precise pathogenesis of OGC is multifactorial and is incompletely understood, disruption of the nigrostriatal pathway has been hypothesized to be partially causative [4]. The differential diagnoses of OGC include versive seizures, paroxysmal tonic upward gaze, encephalopathy, and ocular dyskinesias or tics [4]. Table 1 lists the proposed associations of OGC in the literature. This patient had an acute onset of OGC with subsequent recurrences after an emotionally charged event. She had not complained of any similar previous episodes, and she did not have any psychiatric history. She was not taking any drugs reported in the literature to be related to OGC episodes.

Patients with SOD and hypopituitarism are at risk for endocrine disturbance following stress. This "stress response" includes increased demand for corticosteroids via corticotropin-releasing factor and adrenocorticotropic hormone secretion. Additionally, a hyperdopaminergic state has been purported to result in response to acute stress [5]. OGC is commonly posited to occur secondary to a hypodopaminergic state, however, and empiric treatment with levodopa/carbidopa has improved some patients [6]. Abortive treatment options include diphenhydramine, clonazepam, and various anticholinergics [3, 7, 8]. Patients with SOD characteristically demonstrate variable pituitary dysfunction and can present with abnormal hormonal responses (or lack thereof) to stressful stimuli [1].

Stress is not limited to an effect on the hypothalamic-pituitary axis (HPA) axis but instead elicits a systemic response that remains to be entirely defined. In fact, Mahal et al. [3] described preceding anxiety/discomfort as supportive criteria for an OGC diagnosis. Recently reported by Kim et al. [9], in response to stressful external stimuli serotonergic neurons induce excitement of the centromedial/centrolateral thalamus, thus decreasing the threshold for dystonia onset. We hypothesize that the lack of dopamine secondary to a dysfunctional HPA axis in the setting of SOD as well as a serotonergic lowering of the dystonic threshold in response to acute stress may have been a precipitating factor for OGC.

SOD is a congenital disorder associated with visual loss and endocrinopathy. Although congenital, lifelong endocrinologic monitoring is recommended for patients with hypopituitarism. Stress dosing of hormones (e.g., cortisol) may be necessary in such patients. We hypothesize that pre-existing HPA dysfunction due to SOD was a predisposing factor in our patient and that a stress-induced serotonergic and dopaminergic imbalance may have been the precipitating factor for OGC. The precise mechanisms for OGC in this and other reported cases in the literature remain ill-defined, and further study is necessary to determine whether our case was causal or coincidental. Ophthalmologists should be aware however that children with congenital SOD and optic nerve hypoplasia may be at risk for future endocrinopathy as

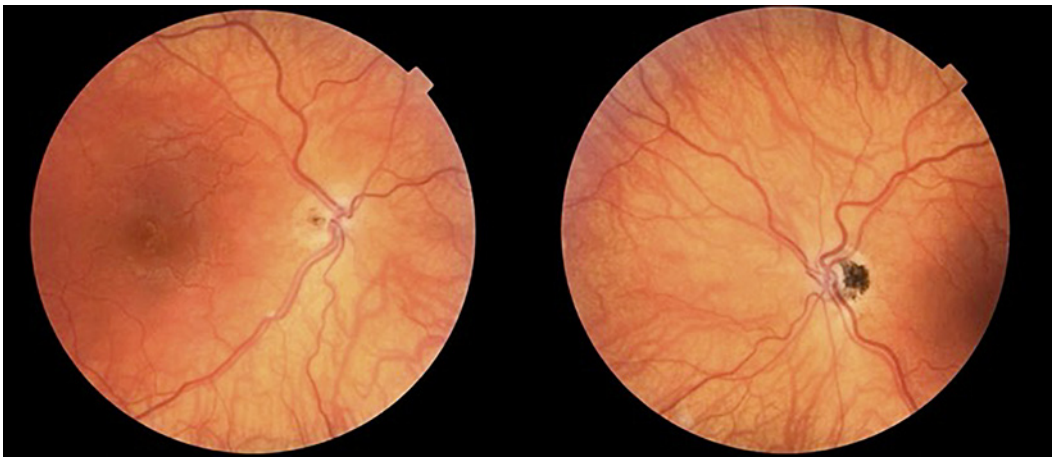

Fig. 1. Fundus photos demonstrating bilateral optic nerve hypoplasia. There was a flat hyperpigmentation on the left optic nerve (although melanocytoma could not be excluded).

Table 1. Various pathologies and medications share an established association with OGC episodes

Pathology and medication associations with OGC [3]	
Neurometabolic movement disorders	**Antipsychotics**
Hereditary dopamine transporter deficiency	1st and 2nd generation
Wilson's disease	**Antiemetics**
Neurodegenerative movement disorders	Metoclopramide
Parkinson's disease	**Anticonvulsants**
Neuronal intranuclear hyaline inclusion disease	Carbamazepine
Rett syndrome	Lamotrigine
Brain lesions	Gabapentin
Periaqueductal	**Antidepressants**
Midbrain tegmentum	Imipramine
Brainstem	Escitalopram
Substantia nigra	Fluvoxamine

adults. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000534493).

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. This report does not include any identifying patient information. All actions related to this study were performed in accordance with the World Medical Association Declaration of Helsinki. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

Phillip Keys, Pamela Davila-Siliezar, Noor Laylani, and Andrew G. Lee declare that they have no conflict of interest.

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Author Contributions

Phillip Keys drafted and edited the manuscript. Andrew Lee, Pamela Davila-Siliezar, and Noor Laylani performed the medical treatment, conducted the follow-up of the patient, and critically reviewed the manuscript. All authors were involved in the conception and design of the manuscript as well as the acquisition and interpretation of data, approved the final version of the manuscript, and attested to meeting ICMJE criteria for authorship.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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