Case Report

Transient anisocoria after a traumatic cervical spinal cord injury: A case report

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Context: Autonomic dysreflexia and dysautonomia can be a common complication following spinal cord injury, especially at levels of T6 and above and can lead to complications associated with the pupil. In this case report, we review autonomic dysreflexia, the anatomy and physiology of the sympathetic nervous system of the eye, as well as review the clinical relevance in understanding autonomic and pupillary changes in response to autonomic dysfunction.

Findings: We present a patient with an incomplete C4 level injury who was found to have isolated anisocoria on two separate occasions during his acute inpatient rehabilitation stay.

Conclusion/Clinical Relevance: Anisocoria associated with abnormal sympathetic activation may be a clinical sign of dysautonomia.

Keywords: Anisocoria, Dysautonomia, Autonomic dysreflexia, Sympathetic dysfunction, Spinal cord injury

Introduction

Spinal cord injury (SCI) results in disruption of both the somatic and autonomic nervous system pathways. The effect on the somatic system may be noted on physical exam with motor and sensory changes. However, a detailed understanding of the autonomic pathways are necessary to diagnose and treat complications that may occur following SCI, such as Anisocoria. Anisocoria is a medical condition that is considerably influenced by the autonomic nervous system and is characterized by a difference in pupil size.^{1,2}

The autonomic nervous system regulates whole body homeostasis through complex sympathetic and parasympathetic pathways. Interruption to the pathways of the sympathetic nervous system can lead to autonomic dysreflexia, a life-threatening condition reported in individuals with injuries above T6 (however, it can sometimes occur lower). With the loss of supraspinal control, spinal autonomic circuits may respond with an exaggerated increase in sympathetic activity in response to a stimulus below the level of injury. This leads to an elevated blood pressure response with a baroreceptor-mediated reflexive

bradycardia and clinical changes above the level of injury which may include flushing, headache, diaphoresis, and piloerection.³ Autonomic dysreflexia can present within two to four weeks following the injury, and 90% of those with the condition will present within the first year. Moreover, up to 90% of complete cervical SCI and up to 25% of incomplete cervical SCI are at risk of autonomic dysfunction.^{4,5}

Clinical diagnosis of autonomic dysreflexia has historically been described as a rise in systolic blood pressure (BP) of at least 20 mmHg above baseline, noting the relative baseline hypotension in cervical SCI.⁶ These changes in BP put an individual at high risk of intracranial hemorrhage, seizures, cardiac arrhythmias, and death if not diagnosed and treated appropriately.⁷ Due to the already lowered projected life expectancy of those with SCI compared to the able bodied population, it remains crucial to have an understanding of autonomic mediated pathways which may produce less common clinical signs, such as the pupillary changes described in this case, that can lead to the increased morbidity and mortality associated with autonomic dysreflexia.^{7,8}

Case

A 64 year old male sustained a fall resulting in a C4-C6 cervical spondylolytic myelopathy with central cord syndrome. He underwent emergent C5 corpectomy and

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C4-C6 anterior arthrodesis with instrumentation due to progressive paralysis. On initial post-operative presentation, he was classified as having an incomplete tetraplegia according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) C4 level D.⁹ Twenty days post-SCI, the patient was noted to have anisocoria on routine morning rounds, which had not been noted prior. The right pupil was dilated to four to five millimeters (mm), while the left pupil was dilated at two mm. Both eyes were minimally reactive to light and no ptosis, anhidrosis, or flushing of the face was noted. Vital signs at that time were a BP of 124/78 and a pulse of 78, which were similar to his baseline of 128/71 following the SCI. Bladder catheterization revealed 1000 milliliters (mL), significantly above the adult normal of 300–400 mL, which can often contribute to autonomic dysfunction.¹⁰ The bladder was catheterized and fully emptied; however, due to persistent pupillary changes, recent trauma causing the initial injury, and lack of elevated BP changes to better confirm autonomic dysreflexia, a stat CT scan of the head was obtained. Imaging returned with no acute concerns and the patient's anisocoria resolved upon his return from radiology.

A second event occurred 18 days later by nursing staff on hourly rounds and shortly after by the physicians (now 38 days post-SCI), except it was noted in the opposite eye. During this event, the right pupil was 2 mm, while the left pupil was 5 mm. BP was mildly elevated at 135/66 with a pulse of 86. Again, no ptosis, anhidrosis, or flushing of the face was noted. Bladder catheterization revealed 200 mL volume and other common sources of noxious stimuli were ruled out with the exception of low lumbar discomfort from a cervical-thoracic orthotic. Immediate adjustments to this orthotic resulted in an improvement in pain and subsequently, anisocoria resolved.

These two isolated events of anisocoria with minimal to no elevation in BP were the only observed signs or symptoms to suggest autonomic dysreflexia in this patient. Due to this limited clinical presentation, it is important to understand the sympathetic supply to the pupil and how changes may occur with an acute change in sympathetic outflow. Further understanding of the pathophysiology may assist with a more accurate diagnosis, limiting unnecessary diagnostic tests, and effective treatment to remove noxious stimuli while closely monitoring autonomic response.

Sympathetic innervation of the eye

Preganglionic sympathetic fibers destined for the head and neck arise from neurons in the intermediolateral

cell column of the lateral horn of the upper five thoracic spinal segments (Fig. 1). These fibers ascend through the thoracic and cervical sympathetic trunk to reach the inferior, middle, and/or superior cervical ganglion.¹¹ Some preganglionic fibers synapse at the ganglia and their postganglionic fibers travel through gray rami communicates to access the cervical spinal nerves, while other preganglionic fibers course anteromedially to form the cardiac nerves.^{11,12}

The sympathetic innervation to the eye is from the superior cervical ganglion (Fig. 1). The superior cervical ganglion lies anterior to the transverse processes of the second and third cervical vertebra. Anterior to the ganglion lies the carotid sheath with the internal carotid artery, internal jugular vein, and vagus nerve, while the longus capitis muscle is found posterior to the ganglion. Postganglionic sympathetic fibers from the superior cervical ganglion are distributed onto the internal carotid artery and help to form the internal carotid nerve plexus, which ascends on the internal carotid artery into the carotid canal to enter the cranial cavity (Fig. 1).¹¹ Once in the cranial cavity, postganglionic fibers from the internal carotid nerve plexus travel on the nasociliary nerve of the ophthalmic division of the trigeminal nerve, while other fibers continue from the internal carotid nerve plexus as the sympathetic root of the ciliary ganglion.¹² The sympathetic root of the ciliary ganglion traverses the ciliary ganglion without synapsing (Fig. 1). These nerves then travel on the short ciliary nerves of the ciliary ganglion to the eye where they innervate the dilator pupillae muscle. Some of these postganglionic sympathetic fibers also travel on the long ciliary nerve, a nerve branch of the nasociliary nerve, to reach the eye (Fig. 1). Sympathetic activation of the dilator pupillae muscle dilates the pupil.^{11,12}

Conclusion/clinical relevance

To our knowledge, only two case reports discuss transient anisocoria after a cervical SCI.^{1,2} Cragg *et al.*,¹ reviewed a case where a patient with complete tetraplegia was found to have left-sided facial flushing and diaphoresis with contralateral miosis and anhidrosis, suggestive of a right-sided Horner's syndrome. These symptoms occurred simultaneously with a rise in systolic BP 150 mmHg above the patient's baseline. As the patient's bladder was emptied the symptoms resolved. A similar case by Wu *et al.*² reported a patient with incomplete tetraplegia who was found to have alternating anisocoria in response to noxious stimuli below the level of injury. This too was suggestive of autonomic dysfunction and the phenomenon

Figure 1 Sympathetic innervation of the eye. Preganglionic sympathetic fibers destined for the eye ascend from neurons in the lateral horn of the superior five thoracic spinal segments. These fibers travel through white rami communicantes to ascend through the sympathetic trunk to ultimately reach the superior cervical ganglion. Postganglionic sympathetic fibers arising from this ganglion are distributed onto the internal carotid artery to help form the internal carotid nerve plexus, which travels on the internal carotid artery into the cranial cavity. Postganglionic sympathetic fibers from the internal carotid plexus travel on the nasociliary nerve of the ophthalmic division of the trigeminal nerve, whereas other fibers continue from the internal carotid nerve plexus as the sympathetic root of the ciliary ganglion. The sympathetic root of the ciliary ganglion traverses the ciliary ganglion without synapsing. These nerves then travel on the short ciliary nerves of the ciliary ganglion to the eye where they innervate the dilator pupillae muscle. In addition, some of these postganglionic sympathetic fibers travel on the long ciliary nerve, a nerve branch of the nasociliary nerve, to reach the eye. Sympathetic activation of the dilator pupillae muscle dilates the pupil.

was coined 'seesaw dysautonomia'. Our case variant, isolated anisocoria, may be a form of dysautonomia following a SCI as our patient did not exhibit the typical elevation of BP to diagnose autonomic dysreflexia.

Hypotheses regarding the pathophysiology have been previously described.^{1,2} One proposed mechanism described an asymmetric increase in intramedullary pressure with a concomitant increase of intrasyrinx pressure within the spinal cord that selectively compromised sympathetic output and caused Horner Syndrome.¹ The second case report added that a contralateral noxious stimulus was often the culprit of the contralateral pupillary dilation and hyperhidrosis, understood by a previous mechanism caused by the decussation of afferent spinothalamic pathways within the spinal cord.² Our case suggests the possibility of pupillary dilation from an abnormal sympathetic response, in the setting of a stimulus below the level of injury. The alternating pupillary sizes, concerning for anisocoria, were likely a result of asymmetric changes in intramedullary pressure affecting sympathetic outflow.¹ One year following the injury, our patient self-reported no additional pupillary changes, nor signs or symptoms of autonomic dysreflexia; however, he was not formally evaluated with any additional ophthalmology evaluations.

Subtle autonomic changes should warrant clinical assessment of stimuli below the level of injury in the appropriate patient with SCI. A more focused clinical exam above the level of injury may lead to atypical findings of dysreflexia, such as isolated anisocoria with or without a true Horner's Syndrome. Reviewing the anatomy and relative physiology is the first important step for the clinician taking care of patients with SCI at high risk for autonomic dysreflexia. A better understanding of autonomic pathophysiology and associated exam findings may help to expedite treatment and avoid unnecessary testing.

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