Strabismus and Ocular Motility Deficits in a Patient with ZC4H2-Associated Rare Disorder (ZARD1)

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INTRODUCTION

This case presents the ocular findings in a female child diagnosed with ZC4H2-Associated Rare Disorders (ZARD1), an "ultra-rare" genetic condition that results in multiple musculoskeletal and neuromuscular abnormalities. Ocular manifestations of this condition most commonly include ptosis, strabismus and oculomotor apraxia. This case report adds to the current literature regarding ZARD1 and will consider the possible therapeutic benefits of vision therapy to improve ocular motility.

INITIAL EXAMINATION

A 20-month-old female diagnosed with a ZC4H2 genetic mutation presented for strabismus evaluation. Her parents report an inward eye turn, possibly OS>OD; however, it does alternate between the two eyes. Her vision appears clear, and she shows interest in objects placed in front of her. Her medical history included a repaired craniosynostosis and multiple contractures of fingers and toes. She was enrolled in speech therapy, physical and occupational therapy working on relaxing tight muscles of fingers and toes to improve reaching, grasping and use of her fingers in addition to increasing muscle tone for improved core strength and mobility.

On examination, the patient was diagnosed with strabismus along with ocular motility deficits, including bilateral abduction deficits, bilateral infraduction deficits and hypometric saccades. Smooth pursuit eye movements appeared intact. Initially, there was concern over visual field restriction inferiorly; however, patient appeared to be aware of objects in the inferior periphery OU but unable to make full infraversion eye movements, resulting in delayed response to objects in her inferior field. The patient had a (+) OKN response OD and OS, normal pupillary responses and no nystagmus in any position of gaze. Her refractive error and ocular health evaluation were unremarkable.

Summary of abnormal exam findings:

- 35-45Δ CAET, OD fixation preference
- Bilateral abduction deficits, OS>OD
- Bilateral infraduction deficits
- Hypometric saccades (see below)

Description of saccadic eye movements:

Head movements guided saccadic eye movements, both to the left and to the right. Low amplitude saccades were initiated via the vestibular system in response to quick head movements. Multiple head movements/saccades needed to move gaze from side to side when a visual or auditory stimulus was used.

After a discussion of goals and treatment options, the patient's parents elected to begin home vision rehabilitation exercises emphasizing improved abduction OS>OD, infraduction OU and saccadic eye movements. Her parents were instructed to begin working on monocular duction exercises and to position the patient to either the right or left side during dinner and other therapeutic activities to force her into extreme gazes. Additionally, eye-hand coordination activities were added to her other therapies, both along and off midline.

THREE MONTH FOLLOW UP

At follow up three months later, the patient's parents noted progress from all home-based therapies. She was able sit on her own, though unable to catch herself from falling backwards, and she had recently taken her first steps with a gait trainer. They reported noting an improved range of motion on duction work; however, were aware of cross-fixation when the patient was binocularly viewing in extreme lateral gazes.

The patient's esotropia showed more frequent alternation between the right and left eyes, with improved OS abduction. She continued to demonstrate difficulties with infraduction and saccadic eye movements (head movements guided eye movements). However, given the progress noted on abduction, her parents were instructed to continue home vision rehabilitation. She will continue to be monitored over time.

DISCUSSION

ZC4H2 gene expression is hypothesized to be an important factor during neurodevelopment, and mutations result in a variety of neuromuscular abnormalities. This case of ZARD1 presented with strabismus (constant alternating esotropia), bilateral abduction deficits, bilateral infraduction deficits and hypometric saccadic eye movements that were primarily elicited via the vestibular system following brief head movements. Current therapies for ZARD1 are primarily supportive; however, recent reports from The ZC4H2 Research Foundation have identified favorable outcomes with early therapeutic interventions. Treatment in this case is aimed at improving the patient's ocular motility skills by employing home-based vision rehabilitation exercises. Early outcomes appear promising and may add to anecdotal evidence in support of therapeutic interventions for patients diagnosed with this rare disease.

CONCLUSION

This case adds to the current literature regarding the ocular manifestations of ZC4H2-Associated Rare Disorders. Though long-term follow ups and future case reports are needed to understand the full efficacy of vision therapy to treat these conditions, early indications support optometry's role in the management of this "ultra-rare" disease.

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