

# Cri du Chat Syndrome: Case Presentation and Review

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## Abstract

**Background:** Patients with Cri du Chat syndrome (CdCs) often present with hallmark signs of the condition including craniofacial malformations, varying degrees of mental retardation, and language/communication delays. They are often previously diagnosed and under the care of other medical professionals. However, significant ocular, developmental, and visual-spatial concerns for which CdCs patients are pre-disposed must be identified and treated. The following case study presents a patient with CdCs, and further investigates the occurrence of the syndrome and methods of diagnosis, management, and prognosis of associated ocular sequelae.

**Case Report:** A six-year-old female presented for an examination. Her parents wanted advice on incorporating vision therapy to help reduce the daughter's eye turn. She had been diagnosed with CdCs at birth and accommodative esotropia at the age of two. She was wearing moderate plus lenses for several hours a day while doing near work. Characteristic signs of CdCs were evident including micrognathia, high-pitched voice, severe developmental delays, and strabismus. The examination consisted of qualifying and quantifying the strabismus, visual acuity estimation, extraocular muscle testing, and patient observation using gross motor movements.

**Conclusion:** While most CdCs patients will present with a history of diagnosis and management by other health care professionals, the responsibility of identifying ocular abnormalities and visual-spatial deficiencies remain an essential part of the examination. Signs of amblyopia (the leading cause of vision loss in patients with CdCs), strabismus, high refractive error, cataracts, lid/adnexal disease, optic nerve atrophy and/or dysplasia, and poor kinesthetic/spatial awareness may be subtle and challenging to obtain, but must not go overlooked when caring for patients within this population.

## Key Words

*Cri du Chat, craniofacial malformations, developmental delay, sensorimotor, strabismus*

Patients with Cri du Chat syndrome (CdCs) often present with characteristic signs of the condition including craniofacial malformations, varying degrees of mental retardation, language and communication delays, and a hallmark high-pitched cry during infancy. CdCs is a genetic disorder, and patients are often previously diagnosed and under the care of other medical professionals. Patients affected by the syndrome typically present with epicanthal folds and telecanthus. A higher risk of strabismus has also been documented.<sup>1</sup> However, developmental and cognitive delays, poor spatial awareness, impaired ambulation, and poor sensorimotor skills that accompany the diagnosis must be addressed during a comprehensive functional vision evaluation.

## Case Report

AT presented for an examination with her mother, who was seeking advice on incorporating vision therapy to help reduce the patient's eye turn. The patient, a six-year-old white female, was diagnosed with CdCs at birth. Her mother reported she was delivered by Caesarian section at 37 weeks, and weighed six pounds, two ounces. She spent the first few weeks in the neonatal intensive care unit, but received no oxygen during this time. AT was seen by an ophthalmologist for the eye turn when she was one year old, and was given moderate-plus glasses that have decreased in power over time. Her mother reported her daughter's eye turn manifested itself mostly in the right eye and was present most of the time. Her mother stated that AT began to crawl at 18 months, and was able to walk

without support at four years of age. She showed signs of oral fixation, and often explored her world by putting unfamiliar objects in her mouth. AT was otherwise healthy and was taking only Prevacid as needed.

AT manifested several developmental delays (physical, mental, sensorimotor, and social). She was enrolled in speech, physical, and occupational therapy at school and at a local children's hospital. Much of the physical therapy focused on developing core and large muscle strength, while occupational therapy focused on improving fine motor skills. She had completed three hours of physical and occupational therapy earlier in the day before coming in for her examination, and her mother explained that she was likely tired and hungry. For this reason, the case history and data gathering was shared over two separate encounters.

## First Visit

AT presented with an obvious and constant esotropia that appeared to alternate but manifested as right eye dominant. During the course of the examination, as she looked around the room, her eyes appeared to be momentarily aligned, showing no eye turn. While AT was unwilling to wear her glasses, the prescription measured was appropriate for alleviating the eye turn. Extra-ocular motilities were full, and she was able to fixate and follow targets easily. The patient's habitual prescription was found to be OD: +2.00-0.50x160; OS: +2.00-0.75x045. While the patient's tolerance for her glasses was limited, her mother ensured the use of lenses during the few

hours a day the patient spent playing near-point games and tending to desk tasks.

AT showed a preference for using her left hand, and her mother explained that she often used her left hand when given the option. When playing with blocks, she used more tactile sensory feedback than visual/motor feedback to place blocks into a container. AT tended to “rake,” using her left hand and bending her elbow to gather blocks on the floor. She grasped with all four fingers and showed no voluntary pincer grasp. She showed the ability to stack one block atop another. She was unable to perform the three-form board task, although her mother said she had a similar puzzle at home with knobs on the pieces with which she usually performed well. (The three-form board is a puzzle consisting of square, circle, and triangle shapes that fit into corresponding holes. It is often used to assess functional development.)

Testing and observation performed at this examination confirmed the presence of developmental delay; however, the exact stage of development was unable to be determined. Esotropia was observed as nearly constant and almost always in the right eye, in addition to having an accommodative component. At times when the patient was seated or lying supine on an exercise ball while engaged in bilateral push and pull motion with the attending doctor, the patient’s eyes intermittently aligned. AT’s physical and mental status was consistent with that of CdCs.

It was recommended that AT continue with her physical, occupational, and speech therapies. Emphasis was to be placed on motor activities incorporating sensory integration techniques. Consultation with attending doctors led to suggesting bilateral activities that incorporated vestibular stimulation (eg: rolling, making angels in the snow, spinning, using a swing). These were especially encouraged to develop sensorimotor skills and a better sense of physical and visual awareness of body positioning in space. Activities while lying prone and/or supine, as well as seated on an exercise ball, would provide stimulation to improve balance and kinesthetic awareness. Further, the patient’s mother was educated that she should encourage the patient to seek objects from the right side of her body and to hand toys and tools to her daughter from this side to reinforce opening up her visual field. She should be allowed to sleep with her right side toward the center of her bedroom to invite right side stimulation. The patient should also trace or draw on a chalkboard to encourage use of her full visual field and to receive tactile stimulation with movement.

## Second Visit

AT arrived for her examination with her mother after attending school but having had time to eat lunch and relax before her appointment. The patient did not wear spectacle correction during the exam. OKN drum testing was performed with the patient seated quietly in her stroller with the drum placed 50 cm away. She showed equal resistance to occlusion with each eye. She exhibited little to no attention to the drum or movements. No tracking of the lines was observed. Preferential looking with Lea gratings was performed at 50 cm. The patient showed intermittent interest in the 0.25 cycles-per-minute paddle (widest lines – lowest spatial frequency), with little reliability OU. AT attempted to reach out to touch the paddles, but with no consistent preference for the striped paddle.

Near retinoscopy was performed, showing approximately +0.75 DS OD and, OS, while the patient fixated on her pacifier with a penlight at Harmon distance. Hirschberg and Bruckner testing showed equally bright and full reflexes OD and, OS, with corneal reflexes in gross alignment. The patient was able to fixate and follow a target at near, showing full range of motion of extraocular muscles. The patient was also able to observe and place her hand on the spot cast by a laser pointer on the floor, her lap, and a magazine, showing a left hand preference with gross motor tapping with the hand in a thumb-adducted position (thumb touching all four fingers). A large angle (40-50 prism diopters) constant right esotropia was observed at all distances during normal viewing. As in the previous encounter, the patient was able to exhibit ocular alignment, albeit brief and variable, during gross motor skills. Alignment occurred while she was on an exercise ball and not focused on a specific near target. Three-piece form board testing was attempted, but resulted in the patient placing blocks in her mouth and tossing them aside with her left hand.

The examination concluded with a discussion of the possibility of further incorporating basic visual tasks into home exercises. It was decided that the patient’s mother would return to speak with a faculty member in the vision therapy department to discuss specifically the types of sensory stimulation tasks that could be easily translated into other therapy modalities, and from which AT would most likely gain maximum benefit. Unfortunately, after weeks of scheduling attempts, the patient’s mother informed us she was no longer interested in those services.

## Review of Diagnosis

Geneticist Jerome LeJuene first described the karyotype abnormality that was later linked to CdCs (also known as “5 p minus” syndrome) in 1963.<sup>2</sup> He observed that the deletion of the short arm of chromosome five consistently resulted in craniofacial malformations and developmental delays, and that up to 85% of all presentations of CdCs result from “de novo” deletions (the chromosomal abnormality is not inherited from parents).<sup>3</sup> Approximately one patient among every 15,000-50,000 live births is diagnosed with CdCs.<sup>4</sup> More recent research shows that the extent of chromosome deletion (ie: partial or total) determines the multitude and severity of presenting signs and symptoms, and that another gene is likely responsible for the larynx malformation causing the high-pitched cry.<sup>4,5</sup>

Most cases of CdCs are diagnosed at birth or shortly thereafter and show common signs of physical manifestations and psychomotor retardation in varying degrees (Table 1). Not all patients exhibit every characteristic, but have a predilection for developing some traits over time (Tables 2 and 3). Diagnosis usually consists of genetic testing using high-resolution chromosome analysis after gross observation of cranial facial dysmorphisms (“facial gestalt”), low birth weight, and high-pitched cry.<sup>3,4</sup> Patients typically reach milestones, especially those of speech and ambulation, at delayed ages. These delays can be attributed to not only physical malformations and altered growth of speech and skeletal structures, but also impaired ability to explore and take part in skill-building stimuli and life experiences.<sup>6,7</sup> This plays an important role in patient management, as one must consider both perceptual and physical limitations in ambulation, sensorimotor abilities, and spatial action.

**Table 1. Signs of Cri du Chat Syndrome\*<sup>2-4,6-8</sup>**

High-pitched monochromatic cry during infancy (95%)	Wide nasal bridge (87%)
Round face (83%)	Hypersensitivity to sensory stimulation (81%)
Downturned mouth present at birth (81%)	Impaired and/or delayed walking ability (80%)
Inability or reduced ability to express needs (verbally or through signing) (80%)	Low-set ears (70%)
Self-injurious behavior, repetitive movements (70%)	Cardiac defects (malformations most common) (30%)
Psychomotor retardation presenting within first year of life	Low birth weight (average birth weight =2614g)
Microretrognathia (small, posteriorly-positioned mandible), with or without a high palate	Varied neural and renal malformations (poor hearing, recurrent renal and intestinal infections)
Microcephaly	Age-appropriate gross-motor hand movements (ball catching/throwing, waving, rudimentary signaling)
Hypotonism	Transverse flexion (Simian) crease

**Table 2. Developmental traits and complications\*<sup>4,6,8</sup>**

Milestone completion ranges from age-appropriate to up to six years of delay
Clear discrepancy in pattern of language function (moderate to severe impairments in expressive language skills with normal to moderately decreased receptive language skills)
Friendly, affectionate disposition when in comfortable environment
Emergence of elongated philtrum (87%), often with full lower lip (45%)
Narrowing of face (70%)
Walking reasonably well by age three (50%), with all developing walking skills over time
Ability to speak in short sentences (5.5 years of age), with nearly all speaking sentences by age 10
Hyperactive behavior (50%)
Musculoskeletal abnormalities (scoliosis, diastasis recti, flat feet)
Microcephaly becomes more prominent
Hypotonism often becomes hypertonicism
Possible atrophy of brain stem (poor feeding and appetite with lower than average norms for weight)
Possible atrophy of cerebellar white matter (balance and posture abnormalities)

**Table 3. Ocular manifestations and considerations\*<sup>1,4,9-11</sup>**

Epicanthal folds (90%)
Hypertelorism (81%)
Downward slanting palpebral fissures (57%), with 70% becoming more horizontal over time
Hypersensitivity to methacholine with resistance to mydriatics (dilator muscle defect)
Divergent strabismus (44% in one study)
Optic atrophy
Tortuosity with or without dilation of retinal vasculature
Congenital cataracts (one case involved additional microspherophakia diagnosis)

**Table 4. Treatment and management\*<sup>7,8</sup>**

Identify intubation and anesthesiological complications soon after birth
Appropriate sensory testing, particularly visual and auditory evaluation
Early educational intervention, encouraging family involvement and social support programs
Suckling therapy within first few months of life, especially if difficulty with breastfeeding
Establishment of home support to increase likelihood of independence in self-care skills, communication and speech, and increased mobility)
Stable living and learning environment (to decrease emotional and mental stress with translocation)
Consider receptive versus expressive language skills – patients are likely to understand speech and signing better than expressive skills can suggest)

\* Percentages refer to patients with Cri du Chat syndrome diagnosis presenting with sign, when applicable

Figure 1. Patient with Cri du Chat syndrome. Notice telecanthus, epicanthal folds, low-set ears, microretrognathia.



While CdCs often presents with symptoms affecting multiple organ systems, those pertaining to the eye and visual system are of most importance in this setting (Table 1 and Figure 1). Approximately half (44-66%) of patients with CdCs develop strabismus (exotropia more likely than esotropia), which carries with it an additional host of visual perceptual concerns.<sup>4,10,11</sup> In addition, Cornish<sup>6</sup> showed that four of every five patients affected by the syndrome harbor some degree of hypersensitivity to sensory stimulation. In essence, not only are affected patients likely to be overwhelmed by visual and other sensory input, they also lack the receiving and processing skills to interpret such input comfortably and meaningfully.

Delayed or impaired development, regardless of the cause, often results in deficiencies in locomotion, communication skills, and cognition. These characteristics combined with strabismus set the stage for several significant visual sequelae, including decreased spatial awareness and localization skills, perception of a distorted environment, amblyopia, ocular-motor dysfunction, and poor fixation.<sup>12-14</sup> Studies show that over 90% of patients with strabismus develop some degree of spatial uncertainty and distortion, with increased angle of eye turn correlating with increased severity and frequency of such traits.<sup>13</sup> The early establishment of localization defects and spatial precision becomes a weak and faulty foundation upon which to build sensory and motor skills.<sup>12,14</sup> Patients diagnosed with strabismus that present with no remarkable karyotypes can often benefit from long-term therapeutic intervention.<sup>13,14</sup> How much more, then, can patients with genetic predisposition to intellectual and physical deficiencies benefit from whole-body perceptual, developmental, and behavioral therapies?

This case presentation represents just one encounter with a severely developmentally delayed child with CdCs. History and experience unique to the individual must be considered when approaching similar cases. For example, this patient has a unique history in that she was delivered by Caesarean section. Bartlett,<sup>15</sup> among others, showed that primitive reflexes are stimulated by the individual's passage through

the birth canal. Without this experience, reflexes (especially the Moro reflex) are more likely to linger and prevent proper progression to postural reflexes at appropriate ages. Long-standing strabismus, poor muscle development and strength, and the likely persistence of primitive reflexes all contribute to AT's overwhelming perceptual deficiencies.

While patients with CdCs are often diagnosed and under the management of several health care professionals at the time they seek optometric and therapeutic care, we must not neglect to address whole body presentation of the syndrome. Physical limitations, developmental age, and parent/family communication are all of significant importance, especially when considering therapeutic intervention (Table 4). Pizzamiglio et al.<sup>16</sup> showed that patients with CdCs can benefit from improved visual-motor coordination with computerized training. However, in this case, the patient was already participating in almost eight hours of different therapies (speech, swallowing, hand, occupational, and physical) per week, as well as attending day school. In addition, with a developmental age of only 18 months, the chance of successfully implementing an active vision therapy protocol was limited. We felt that at this time the patient would receive the most benefit from incorporating vestibular, spatial, and fixation stimulation into existing physical and occupational therapy sessions. Using exercise ball and suspended swing tasks would afford the patient the chance to improve visual field awareness and encourage the alignment of the strabismic eye. In cases such as this, physical limitations need to be defined so as not to push the patient beyond his or her means.

## Conclusion

Patients with CdCs may not only present with abnormalities of ocular health, visual development, and perceptual processing, but may also manifest significant multi-system conditions. The diagnoses of strabismus, delayed visual development, and perceptual processing deficiencies carry a host of management implications. However, when these diagnoses are compounded with CdCs, therapeutic expectations and prognosis should be tailored to the patient's abilities. It is important to recognize that while the patient may be under the direct care of other specialists for certain diagnoses, behavioral optometric management and therapy can affect other medical treatments. Just as we must consider the whole patient when diagnosing and providing treatment, we must see the whole picture, including meeting the needs of the family and professional support system to establish the most appropriate care for these extraordinary patients.

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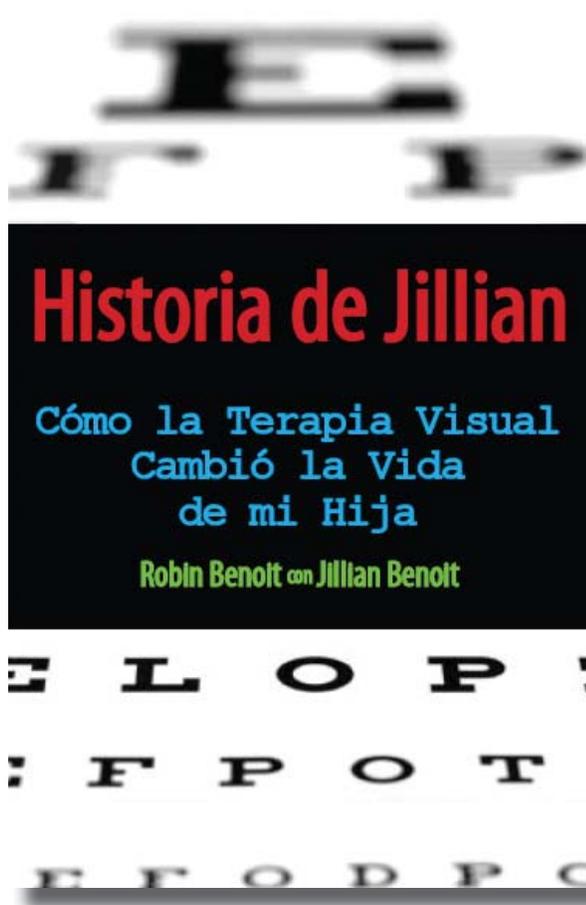
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