

Case reports

Speech-language disorders in CADASIL: a case report

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ABSTRACT

The purpose of this study was to report the main speech-language disorders in a patient with CADASIL diagnosis, attending the Speech Therapy School Clinic of a Higher Education Institution from 2008 to 2013. Clinical evaluation of the speech organs was carried out, verifying reduced mobility and tonus of lips, tongue and cheeks, with major repercussions on deglutition in the last two years of care. Multiple swallowing were observed for pasty consistency, and coughing, for the liquid one, with “wet” vocal quality and cervical auscultation without alterations, after multiple swallowing. A hoarse vocal quality with asthenia, weak loudness, hypernasal resonance and imprecise articulation were observed regarding the patient’s voice. The speech therapy aimed at maintaining food intake and communication, improving the patient’s quality of life.

Keywords: CADASIL; Speech, Language and Hearing Sciences; Deglutition Disorders; Dysarthria; Dysphonia

INTRODUCTION

The acronym CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) refers to a genetic disease hereditarily transmitted in an autosomal dominant way, caused by a mutation of the NOTCH3 gene¹.

Such a gene encodes a protein whose main function is to maintain structural and functional vascular stability. Pathogenic mutations result in accumulation of this protein in smooth muscle cells lining small cerebral and extracerebral vessels, mainly leading to small infarcts and the progressive increase of demyelination areas^{1,2}.

An accumulation of infarctions leads to progressive worsening of neurological symptoms and may appear in outbreaks, combining cognitive disorders (changes in executive and attention functions), gait and balance disorders, and in later stages dementia, pseudo-bulbar syndrome (dysarthria, dysphonia, dysphagia), and urinary sphincter dysfunction (incontinence or retention, recurrent infections)¹. Death usually results from complications, especially malnutrition and infectious diseases such as aspiration pneumonia², but unexpected sudden death may also occur^{3,4}. The clinical manifestations of the disease are independent of gender and occur around the third or fourth decade of life⁵, which does not enable early diagnosis.

CADASIL diagnosis requires careful clinical evaluation based on typical symptoms, family history, imaging, molecular study and cutaneous biopsy. Magnetic resonance imaging (MRI) can show white matter lesions and lacunar infarcts which are very characteristic, whereas the mutation of the NOTCH3 gene is confirmed in the molecular study, favoring the definitive diagnosis².

Family history is almost always present; however, its absence does not exclude the diagnosis. Isolated cases of spontaneous genetic mutation which occurs

for unknown reasons have been described³. In addition, some individuals with the gene mutation may remain asymptomatic for long periods, even with well-defined lesions detected in MRI, while others only exhibit some major features of the disease such as migraine with aura, depression, or cognitive impairment².

As no treatment to modify disease progression is available, it is necessary to control symptoms and vascular risk factors with medication⁶ and the support of a multidisciplinary team. The team should be composed of a physician, speech therapist, physiotherapist, occupational therapist, nutritionist, social worker and psychologist. Psychological support should mainly extend to the family given the hereditary nature of the disease¹.

This arteriopathy is reported in some countries in all continents, and is one of the most dynamic and leading research fronts of neurogenetics⁷, with a prevalence of NOTCH3 mutations estimated at 4.15 per 100,000 adults in a Scottish study⁸. However, publications on this disease in South America are scarce⁶.

Considering its consequences for adults, the importance of diagnosis and care, and in order to minimize the limitations and disadvantages that the disease entails, the present study aims to report the case of a patient with CADASIL, by describing the main speech-language disorders found.

CASE PRESENTATION

This study was approved by the Institutional Research Ethics Committee of the Guararapes Memorial Hospital under protocol number 1.540.014/2016. The data of the consultations were collected from the patient's chart from the beginning of her treatment in 2008, until her release in 2013 (Figure 1). The codename "Flora" was chosen in order to guarantee anonymity without distancing her from her human presence.

Aspects investigated	2008	2009	2010	2011	2012	2013
Main complaint	Sporadic choking during feeding and incomprehensible speech.	Forgetfulness; Motor incoordination during writing; Visual impairment.	Maintenance of memory, speech and writing complaints.	Dependence on some activities of daily life; Speech and memory very compromised; Gagging for solid consistency.	Worsening dependence on daily life activities; Locomotor difficulty; Somnolence; Loss of appetite; Social isolation.	Maintenance of previous complaints; Urinary incontinence; Gagging in liquid consistency.
Orofacial Musculature	Decreased tone and muscle strength on the left side of the face; Difficulty in lips, tongue and cheeks mobility; Mentalis muscle hypercontracted during lip sealing.	Discrete tonus enhancement and mobility of the lips, tongue and cheeks.	Decreased tonus and muscle strength on the left side of the face; Deepest nasogenian sulcus on the right; Lower left commissure; Difficulty in lips, tongue and cheeks mobility.	Maintenance of previous pattern.	Mobility aspects improved, but the hypotonic pattern remained with the same degree of alteration.	Maintenance of previous pattern.
Chewing and swallowing	Bilateral chewing with predominance to the left side, with adequate speed and rhythm; Absence of coughs and/or gagging; Residue in oral cavity after swallowing.	Maintenance of the same chewing pattern; Efficient swallowing.	Maintenance of the same chewing pattern; Accentuated contraction of the periorbicular and mentalis musculature during swallowing.	Maintenance of previous pattern, but with escape of food through lip commissure; Cough episodes for all consistencies; Residue in oral cavity after swallowing.	Maintenance of previous pattern, but with frontal saliva escape during rest; Needing liquid to form bolus during ingestion of solids.	Salivary stasis in oral cavity; Multiple swallowing for pasty consistency; Presence of coughing and wet voice, after swallowing liquids.
Breathing and voice	Upper breathing type and oronasal breathing mode; Hoarse voice, unstable, with discrete degree, and imprecise articulation.	Mixed breathing type and nasal mode; Harsh, unstable, voice, with discreet degree, weak loudness and improved articulatory inaccuracy.	Maintenance of the same breathing pattern; Same vocal quality, however, with improved instability.	Maintenance of the same breathing pattern; Maximum phonation times reduced; Hoarse and breathy vocal quality of moderate to severe degree, with presence of asthenia.	Maintenance of previous pattern.	Maintenance of previous pattern. Hypernasal resonance of slight degree noticeable.

Figure 1. Speech-language disorders observed in the case, over the years

Patient Flora, a 56-year old female, with a complete higher education, married, a mother of three children, attended the Orofacial Motricity outpatient clinic of the Professor Fábio Lessa Speech Therapy Clinic of the Federal University at Recife, PE, Brazil, reporting sporadic choking when eating, and that her speech was not understood by family and friends. She was referred by a physiotherapist with the diagnosis of Multiple Sclerosis (MS), given in 2002 by a neurologist. According to the patient, the cause of her mother's death was decisive for her diagnosis, since she had died diagnosed with MS years before. However, in the second half of 2011, a new neurologist requested a molecular study, diagnosing Flora with CADASIL.

Flora began speech therapy sessions in a public hospital in 2004, but discontinued them three years later, and then she attended the school clinic in 2008 reporting worsening symptoms. During anamnesis, she was also referred to psychiatric follow-up for depression as well as endocrinological follow-up for hypothyroidism, with medication usage to control symptoms.

Other medications to reduce the risk of ischemic attacks, relieve symptoms related to urinary incontinence and memory were also used. At first, complaints were related to swallowing and voice; then, changes in vision, motor coordination, and tiredness when performing activities which require effort and memory had arisen.

Speech assessment was performed according to the protocols proposed in the literature^{9,10}. Photos of Flora were taken standing, behind the symetograph in front, lateral and posterior views to evaluate body posture. In the early years, she only had slight elevation of her right shoulder; later, a forward and to the left side inclination of the whole body was also observed due to balance limitations. Asymmetries were observed regarding her face with deviations to the right side, being the side of greater facial expression. The left side of the face was hypotonic, more elongated, while the right side was shorter, hypertonic, with the deepest nasogenic fold on the right. Her lips are united, with lower left labial commissure.

It was possible to evaluate the intraoral region through photos taken with cheek retractors and a flashlight. The teeth were in good state of preservation, 08 in the upper arch, using fixed dental prosthesis with replacement of three teeth, and 10 in the lower arch, with fewer teeth to the right and without the use of prosthesis. The mucosa was free of wounds or bite marks. Normal color gums. Palatine tonsils in appropriate sizes and shades. Hard palate without alterations and symmetrical soft palate. Hypotonic tongue, but with adequate longitudinal fold.

Flora presented some limitations in her mobility of lips, tongue and cheeks. She could protrude and retract her lips, vibrate and pop into protrusion. Her tongue mobility was adequate when in the direction of the four cardinal points and in crackling; however, she performed vibration with difficulty. Regarding her cheeks, she was able to inflate and suck, but had difficulty in alternately inflating the sides, inflating only the right side. She performed emission with good mouth opening, but with deflection.

Solid (bread), pasty (firm consistency - yogurt/ pudding) and liquid (water) foods were used to evaluate her chewing and swallowing functions. The volume varied according to her acceptance. It was verified that food incision was performed by the central incisors and grinding by the posterior teeth. She showed an alternate bilateral chewing pattern with a predominance to the left side. The velocity and rhythm were adequate during chewing and swallowing with labial sealing, but with marked contraction of the orbicular and mental musculature.

Flora began to present salivary stasis in the oral cavity, food escape by the labial commissure and food residues in her mouth vestibule, after deglutition, in the last two years, not being perceived by her, which

demonstrated a lack of sensitivity in the region. There was also a discreet upward compensatory movement during swallowing and coughing for liquid consistency. There were no noises during cervical auscultation suggestive of laryngeal penetration of saliva and/or food after multiple swallowing.

In order to evaluate her voice, Flora was asked to issue the vowels / a /, / e / and / i / sustained, sing "happy birthday to you", give a spontaneous statement and repeat a list of words said by the therapist. In the perceptual-auditory analysis, we initially detected hoarse and breathy vocal quality to a discrete degree, with emission instability. The patient subsequently presented a moderate to severe degree of hoarseness and breathiness, presence of asthenia and weak loudness. The maximum phonation times were reduced. Articulation became more inaccurate, with limited movements in her lips and jaw. Her resonance had become hypernasal in a slightly perceptible degree in the last year, characterizing a condition of dysarthrophonia.

Therefore, the speech-language diagnosis was established as flaccid dysarthrophonia, being associated with mild oropharyngeal dysphagia with the disease's advancement. Regarding the results of the myofunctional orofacial disorder evaluation, the patient had scores close to the best results despite the presented limitations, being classified with a degree of mild alteration. The most stressed axes were extraoral aspects, mobility, tone and swallowing.

Although cognitive and mental status assessment protocols were not applied, it was possible to observe a gradual impairment in the patient's attention, memory and temporal abilities during therapeutic activities, manifested by forgetfulness in relation to recent events when asked about facts from the previous day, being unable to tell where she was at the time of therapy and what the date was; these characteristics were also observed her relatives in the patient's daily life according to their testimony.

Flora performed speech therapy twice a week, aimed at maintaining stomatognathic functions and improving her quality of life. Extra and intra-oral manipulations were performed for warming-up, loosening, vascularization and activation of motor zones; tactile and thermal sensory stimulation; isometric, isotonic myofunctional and counter-resistance exercises for the lips, tongue and cheeks; functional therapy using food in different consistencies with the aid of facilitating maneuvers; vocal therapy with facilitator sounds, glottic

firmness, over-articulation; as well as facilitating therapy with memory stimulating games, reasoning and attention (memory games, crosswords, word hunting, dominoes, songs).

In the year 2013, Flora presented greater motor limitations, urinary incontinence, dependence to perform some daily life activities, was more depressive, avoiding speaking. Complaints of gagging became more frequent for liquid consistency. There were multiple swallowing for pasty consistency and cough presence for liquids in the evaluation, also with a “wet” vocal quality, suggesting laryngeal penetration. She presented cervical auscultation without alterations after multiple swallowing, demonstrating a possible clearance of the pharyngolaryngeal region. Adjustments were made for food consistency: liquid thickening was indicated and videofluoroscopy of swallowing was requested for a better follow-up, but it was not performed. Continuous care was necessary at home due to the worsening of her problems, as this was more comfortable and beneficial for the patient, and then Flora voluntarily quit attending the school clinic.

She was also accompanied by a physiotherapist, an occupational therapist, a psychologist, a psychiatrist and a neurologist. Opinions were exchanged in order to integrate practices for follow-up.

RESULTS

Patient care period comprised from March 19, 2008 to September 6, 2013, twice a week, totaling 257 sessions. Flora was attended by a different trainee every year, considering that it is a school clinic and the internship lasted two semesters, according to the academic calendar.

Improvements were perceived when she performed the exercises at home during the week and during periods of academic recess in order to continue the therapy. Flora managed to improve aspects of facial mobility, responding better to isotonic exercises; however, her responses to isometric and isokinetic exercises were limited, with no noticeable improvement in tone and muscle strength, especially on the left side of her face. Swallowing was only safe with volume and speed control. Her voice was more projected and her speech was with precise articulation.

However, her clinical status varied according to the disease progression and the occurrence of small infarctions and hospitalizations. Adjustments were made to

the objectives and proposed activities over the years due to the emergence of new limitations.

Tactile and thermal stimulation, as well as the simple verbal command to swallow, enabled better motor response, avoiding salivary and alimentary stasis. The use of facilitating maneuvers and adjustments in food consistency minimized the risk of bronchoaspiration, providing safer deglutition. Vocal exercises, especially those focused on glottal coadaptation, aided this safety and entailed better pneumophonic coordination, higher loudness and greater evidence of oral component in her resonance.

DISCUSSION

CADASIL may be one of the most common genetic neurological conditions, however it is probably under-diagnosed. In the unavailability of the genetic test for CADASIL, many cases (like Flora’s and probably her mother’s), were diagnosed as MS, Alzheimer’s or other neurodegenerative diseases^{3,4}.

There is always aggravation in the course of the disease, but at short intervals. The evolution is very variable, with periods of rapid deterioration, clinical stability, or occasionally improvement⁵. These fluctuations and variability in the symptoms observed in Flora’s case can be explained by the possible transient or established ischemic cerebral accidents¹. Hence, the importance of studies describing the clinical findings of this pathology.

As described in the results and verified in the data collected (Figure 1), Flora presented some of the most prevalent symptoms described in the literature, such as cognitive disorders with memory alterations, depression, gait and balance disorders, urinary sphincter dysfunction, dysarthria and dysphagia^{1,2,4}. These symptoms were more intense in the last year due to the progression of the disease⁵.

Cognitive disorders associated with depression have a direct consequence on the patient, family member and/or caregiver life quality. Memory impairment is probably related to different causes due to white matter infarctions, mainly in the frontal lobe and primary cortex. Ischemic events may also involve the optic nerve and retina⁴, which may justify Flora’s visual complaints.

Despite the pathophysiological distinction of the discussed disease, it is possible to observe that the speech-language pathological peculiarities (according to the reports of the literature and the clinical characteristics presented by the described patient) tend to present in a similar way to the findings in individuals

with central nervous system degenerative disease. The presence of pseudobulbar syndrome is described in CADASIL, which is due to the supranuclear lesions of the corticobulbar and corticopontin pathways, affecting articulation, phonation, swallowing, chewing and tongue movements¹¹.

The dysarthria and dysphagia in Flora's case resemble the great variety of symptoms of MS, such as the presence of coughing and/or gagging during eating, greater difficulty with liquid foods than with solids, difficulty in bolus formation and multiple swallowing. Motor alterations of the tongue, lips, palatine veil and pharynx are also observed, as well as difficulty in glottic closure¹², which implied the patient's vocal repercussions.

Regarding the stomatognathic system structures, Flora was able to improve her mobility aspects during therapy; however, muscle tone and strength remained unchanged. Although they are interrelated, it cannot be said that the reduction of tonus necessarily impairs mobility¹³. In addition, the degenerative nature of CADASIL may explain the apparent non-response to the applied isometric exercises, and a positive effect of these in delaying the deleterious consequences of the disease itself on tone and muscle strength can be considered^{1,2}.

Although Flora showed greater motor deficit and tonus to the left, masticatory predominance was observed on this side, which may be justified by the greater presence of teeth in the two hemiarches, providing a better performance during food grinding. In addition, her body posture may have favored directing the food to the predominant side.

Concerning her voice, Flora presented characteristics compatible with flaccid dysarthrophonia, with repercussions on the parameters of roughness, breathiness, reduced intensity, hypernasality and imprecise articulation related to muscle weakness patterns¹⁴. As observed in degenerative diseases of the nervous system, the manifestations are unpredictable, including different types of dysarthrophonia or even combinations between them, as in cases of mixed dysarthrophonia. Several factors can lead to such swallowing and voice changes, such as involvement of corticobulbar and cerebellar tracts, brain stem dysfunctions and cognitive alterations^{12,14,15}.

For multidisciplinary treatment¹, the importance of the speech-language pathologist in evaluating stomatognathic functions and the control of symptoms regarding voice and speech, but mainly to swallow,

considering the respiratory and nutritional complications of dysphagia, is evident.

Other speech-language studies on this subject are necessary as this was only a single case and considering there are multifocal issues with polymorphism of the symptoms. It is important to know the signs and symptoms of CADASIL related to communication and stomatognathic system functions for accurate diagnosis and adequate therapeutic conduction.

FINAL CONSIDERATIONS

In the clinical case herein presented, there were changes in the stomatognathic system regarding posture, reduced mobility and tonus of lips, tongue and cheeks, dysarthrophonia and signs of oropharyngeal dysphagia, with greater repercussions in the last two years of care. There were multiple swallowing for the pasty consistency and coughing in liquid consistency, with "wet" vocal quality, performing clearing of the pharyngolaryngeal region, after multiple swallowing with cervical auscultation without alterations. Her voice presented a hoarse and breathy vocal quality, asthenia, weak loudness, hypernasal resonance and speech with imprecise articulation.

Reports of speech-language disorders in CADASIL, in the literature, are still scarce. The studies are generally directed to pathogenesis, addressing the molecular aspects, their genetic variabilities and the diagnostic strategies. The case report described in the present study, may provide an understanding of CADASIL characteristics of interest to speech therapy, guiding the action approach. This enables implementing interdisciplinary intervention, in order to minimize the difficulties described and provide a better quality of life to patients presented with this condition.

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