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The presence of dysphagia in patients with cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS): a subjective and objective study

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Abstract

Purpose The aim of this study was to determine the prevalence of dysphagia in patients with cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS), characterizing this condition, both in its objective dimension and in terms of quality of life (QoL).

Methods A cross-sectional study was developed in 11 patients diagnosed of CANVAS. In all patients, clinical records were reviewed and the Eating assessment tool 10 (EAT-10) was performed as screening of oropharyngeal dysphagia. To evaluate the QoL impairment secondary to dysphagia, we applied the swallowing quality of life questionnaire (SWAL-QOL) and the MD Anderson Dysphagia Inventory (MDADI). To evaluate the deglutition mechanisms impaired, two objective-instrumental studies were performed: the volume-viscosity swallow test (V-VST) and the fiberoptic endoscopic evaluation of swallowing (FEES).

Results 82% of the patients presented an abnormal EAT-10 score. A correlation was found between the EAT-10 and MDADI and between both QoL questionnaires. After the FEES and V-VST analysis, all 11 patients presented some degree of swallow effectiveness impairment, and most of them safety alterations as well.

Conclusion CANVAS remains an underestimated and underdiagnosed condition and the prevalence of swallowing disorders in those patients is higher than expected. Despite the possibility that EAT-10 works as a useful screening test to predict the results in the QoL questionnaires, the absence of correlation between QoL test and instrumental results suggests that to properly evaluate the patients swallowing status, objective instrumental procedures must be conducted.

Keywords CANVAS · Dysphagia · Quality of life · FEES · V-VST

Introduction

Cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS) is a neurodegenerative multisystemic disorder characterized by the progressive impairment of the three neurological pathways responsible for balance: the cerebellar, the vestibular and the proprioceptive systems [1]. The majority of cases of CANVAS have been found in individuals of European ancestry and its real prevalence remains unknown [2, 3].

Until recently, CANVAS diagnosis was based on clinical history and radiological findings and after excluding commons forms of ataxia. However, Cortese et al. [4] and Rafehi et al. [5] have found that CANVAS is associated with the biallelic inheritance of a previously undescribed expanded intronic pentamer $(AAGGG)_{exp}$ in the gene encoding

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Replication Factor C subunit 1 (*RFC1*) [6, 7]. There are patients who are carriers of the genetic alteration but have not yet clinically manifested the disease. Although so far is considered a rare disease, the description of genetic diagnosis potentially will increase the total number of cases.

Typical features of CANVAS are gait imbalance, lower limb dysesthesia, oscillopsia, dizziness and intrinsic falls. Moreover, a high prevalence of autonomic dysfunction has been found in CANVAS patients, leading to consider autonomic dysfunction as an important feature of this condition [8–10].

Apart from the described symptoms, an unexplained spasmodic dry cough without apparent trigger was reported in over 60% of patients [11] and most of them report some degree of dysphagia when asked about it. Dysphagia can arise as a consequence of pharyngeal incoordination, as seen in patients with pure cerebellar syndromes and/or sensory impairment, secondary to reduced trigeminal, chorda tympani, glossopharyngeal and pharyngeal branch of the vagus nerve input [10]. Impaired swallowing could cause significant long-term morbidity in these patients.

The aim of this study was to determine the real prevalence of dysphagia in this group of patients, as well as to characterize this condition, both in its objective dimension and in terms of quality of life (QoL), establishing its severity and the need to implement measures aimed at preventing potentially complications. The ultimate goal of this approach was to try to improve the QoL of patients with this poorly understood and highly debilitating condition.

Patients and methods

We reviewed the clinical records of 11 patients with clinical and genetic diagnosis of CANVAS. Medical records were retrospectively examined, following institutional review board guidelines. Written informed consent was obtained from each patient. This study was approved by Institutional Ethics Committee. Only patients with the concomitant existence of the genetic alteration (the biallelic AAGGG repeat expansion in RFC1) and the clinical-radiological manifestations associated with CANVAS were included in the study [4].

The clinical variables studied were family history, age, sex, debut symptoms, presence of autonomous dysfunction, evolution and follow-up, as well as the existence of an initial clinical diagnosis.

The Eating Assessment Tool 10 (EAT-10) was used for screening oropharyngeal dysphagia [12]. The EAT-10 is a self-administered questionnaire that includes ten questions about the severity of symptoms of oropharyngeal dysphagia. Each question will be scored from 0 to 4 (“no problem” to “severe problem”). The total EAT-10 score is calculated by adding up the scores of each question, and higher scores indicate a self-perception of a high level of dysphagia severity. An EAT-10 score of 3 or higher is abnormal and higher scores indicate a greater perception of dysphagia.

Two validated survey tools, the Swallowing Quality Of Life Questionnaire (SWAL-QOL) and the MD Anderson Dysphagia Inventory (MDADI), were used to evaluate swallowing-related QoL. The spanish versions of both questionnaires were used in this study. Their reliability and validity has been verified in previous studies [12, 13].

SWAL-QOL (44 items) consists of 10 scales (30 items) and a 14-item dysphagia symptom battery for assessing the severity of dysphagia symptoms. The patients were asked to respond to each item based on their experiences during the past month. The ten scales of the SWAL-QOL are: food selection, burden, mental health, social functioning, fear, eating duration, eating desire and communication. The first eight scales are dysphagia specific, whereas the last two are generic QoL scales [14]. The responses to each SWAL-QOL item are provided on a 5-point Likert scale. The items were averaged and the linearly transformed to a score of 0 to 100, with lower scores indicating greater impairment [14, 15].

The MDADI questionnaire is a self-administered questionnaire to evaluate the impact of dysphagia on QoL and includes 20 statements stratified into 4 subscales: global (GS) allows a general assessment of QoL related to dysphagia, emotional (ES) investigates the impact of dysphagia in the relationship with others, functional (FS) evaluates the impact of dysphagia on daily activities, and physical (PS) investigates patient´s perception of the swallowing problem. The composite subscale (CS) is a weighted average of the previously described subscales. The mean score of each subgroup is multiplied by 20 to obtain a score between 20, extremely low functioning, and 100, high functioning [13, 16].

To understand the specific deglutition mechanisms impaired in patients with CANVAS, we performed two tests. The volume-viscosity swallow test (V-VST) is useful in identifying clinical signs of oropharyngeal dysphagia. It is based on reducing the volume of the bolus and increasing viscosity thus improving swallowing safety. To assess swallowing we administered boluses of 5, 10 and 20 cc of syrup, pudding and liquid consistency, after mixing liquid with thickener (Resource Powder®). If the patient showed any signs of impaired swallowing, the test was considered positive. Otherwise the test was considered negative. An instrumental swallowing evaluation with fiberoptic endoscopic evaluation of swallowing (FEES) was performed to evaluate airway protection to detect and manage dysphagia. During the FEES study, oropharyngeal swallowing function was evaluated during swallowing of 5, 10 and 20 cc of blue-dyed syrup, honey, pudding and liquid consistency. The parameters studied were oral and pharyngeal residue

and piecemeal deglutition (effectiveness of swallow) and decrease in oxygen saturation, penetration and aspiration (impaired safety of swallow). These parameters were analyzed and scored as either "absent" or "present". Identification of at least one of these signs was considered as an impairment of the effectiveness or safety of swallowing.

Impaired effectiveness and impaired safety data obtained in both V-VST and FEES were analyzed together and scored according to the number of altered variables as represented in Fig. 1. Taking into account the parameters evaluated, the results obtained by V-VST and FEES were combined in a single score to determine the degree of swallowing disorder. The degrees of effectiveness impairment would be: normal (when no alterations were identified), mild (with 1 alteration), moderated (2 or 3 alterations) and severe (when 4 alterations were identified). In the same way, the degrees of safety impairment would be: normal (when no alterations were identified), mild (with 1 alteration), moderate (2 or 3 alterations) and severe (when 4 alterations were identified or in those cases in which an aspiration was detected). From the data obtained from these two scores, it was determined the safest and most effective volume.

All statistical analyses were performed using IBM SPSS statistics software version 22 for MacOS. $p < 0.05$ was considered statistically significant for all comparisons.

Results

The clinical characteristics of the patients are shown in Table 1. Our sample was comprised by seven women (63%) and four men (37%) with a mean of 68 years (range 60–74 years). Two affected sibling pairs were identified in two unrelated families: case 4 and 5 and cases 8 and 9 were siblings and the age of onset of the symptoms was similar within each family. The remaining patients did not refer any other relatives with similar complaints. 4 of the patients had not been diagnosed with CANVAS because they did not meet the required clinical symptoms [17] but they had the specific genetic alteration.

Fig. 1 Variables of altered effectiveness and safety swallowing assessed with V-VST and FEES. Score of disorder

Effectiveness variables	V-VST	FEES	Score of the disorder according to the number of altered variables
Incompetent labial seal	X		0: none 1 (Mild): 1 variable 2 (Moderate): 2 or 3 variables 3 (Severe): all
Oral residues	X		
Pharyngeal residues		X	
Fractional swallowing*	X	X	
Safety variables			
Cough	X		0: none 1 (Mild): 1 variable 2 (Moderate): 2 or 3 variables 3 (Severe): 4 variables or aspiration
Wet voice	X		
O_2 desaturation*	X	X	
Penetration		X	
Aspiration		X	

*These variables can be evaluated with both tests: V-VST and FEES

Table 1 Summary of clinical data

Case	Sex	Age/Age of onset	Initial symptoms	Autonomic dysfunction	Cough	Cerebellar ataxia	Peripheral neuropathy	Vestibular areflexia	Clinical diagnosis*	Genetic diagnosis	Familiar history
1	M	74/62	LLD	No	Yes	+	+	+	+	+	No
2	F	67/61	LLD	No	Yes	+	+	+	+	+	No
3	M	62/56	Gait imbalance	Dry mouth, cold fet	Yes	+	+	+	+	+	No
4	F	70/65	Gait imbalance	Constipation	Yes	+	+	+	+	+	Yes (sibling of case 5)
5	M	60/59	LLD	Syncope	Yes	+	+	+	+	+	Yes (sibling of case 4)
6	F	70/69	LLD	Hypotension	Yes	–	+	+	–	+	No
7	F	70/69	LLD	UI	No	–	+	+	–	+	No
8	M	70/68	Gait imbalance	Cold fet	Yes	+	+	+	+	+	Yes (sibling of case 9)
9	F	73/70	LLD	No	Yes	+	+	+	+	+	Yes (sibling of case 8)
10	F	71/67	Gait imbalance	Hypotension	Yes	+	+	–	–	+	No
11	F	68/62	LLD	UI	Yes	–	+	–	–	+	No

LLD lower limb dysesthesia, *UI* urinary incontinence

*Met the diagnostic criteria for definitive CANVAS disease by Szmulewicz et al. [17]

Common symptoms at onset of illness were lower limb dysesthesia (63%) and gait imbalance (37%) and eight patients (72%) showed symptoms and signs of autonomic disease. All but one patient complained of coughing episodes of unknown cause.

Swallowing study data of the patients are shown in Table 2. When patients were asked if they had to make any dietary changes to avoid swallowing difficulties, seven patients (45%) reported having made some eating adjustments and two (18%) used thickeners regularly. 3 patients (27%) reported an increase in average intake time of more than 40 min.

The mean EAT-10 score of our patients was 8.73 (±6.41 standard deviation) (range 1–24). 9 patients (82%) presented an EAT-10 score ≥ 3, indicating an abnormal subjective perception of dysphagia. The average SWAL-QOL score was 80 (± 10.44 standard deviation) (range 61.9–98.3). The average value of the MDADI questionnaire was 79.6 (± 15.7 standard deviation) (range 51.94–100). A correlation between this QoL questionnaires was found ($p = 0.002$). We also found a correlation between the EAT-10 questionnaire results and those from the MDADI ($p = 0.009$), although the correlation was not found between EAT-10 and SWAL-QoL results.

After analyzing the objective swallowing study by V-VST and FEES, we found that in the analysis of the clinical signs of impaired effectiveness of swallow, only 2/11 patients (18%) presented failure in the lip seal with escapes. In only 1/11 patients (9%) oral residues were found, whereas some degree of pharyngeal residue was found in all 11 cases (100%). Conversely, fractional swallowing was found in 10/11 patients (91%). To define the grade of effectiveness impairment we carried out the summation of this alterations, stablishing that only 1/11 (9%) patients presented a mild grade of swallowing impairment, 1/11 (9%) a severe grade and the remaining 9/11 (82%) a moderate grade of swallowing impairment.

In the study of the clinical signs of impaired safety of swallow, we observed coughing after the ingest in 3/11 patients (27%) and voice changes in 7/11 (64%). We found clinical signs of penetration in 3/11 patients (27%) and of aspirations in 2/11 (18%). No decreases in the oxygen saturation were found in any patient during the study. In the same way, to establish the grade of safety impairment we carried out the summation of the alterations, stablishing that 6/11 patients (54%) presented a mild grade of impairment, 2/11 (18%) presented a severe grade. No moderate degree of impairment was found in our patients. 3/11 patients (27%) did not present any safety alteration. In these two patients who presented aspirations, a decreased sensitivity of the laryngeal structures was found, being the biggest decrease the one in case 8, which showed no sensitivity at all. No statistically significant correlations were found between the scores in the QoL tests and the degree of effectiveness or

Table 2 Summary of swallowing study data

Case	EAT-10	SWALL-QoL	MDADI	ILS	OR	PR	FS	Effectiveness impairment	Cought	VC	DESAT	PEN	AS	Safety impairment
1	8	61.93	51.94	−	−	+	+	Moderate	+	+	−	+	+	Severe
2	10	73.86	71.25	+	−	+	+	Moderate	−	+	−	−	−	Mild
3	5	81.82	91.67	−	−	+	+	Moderate	−	+	−	−	−	Mild
4	8	86.93	77.92	−	−	+	+	Moderate	−	+	−	−	−	Mild
5	6	85.80	92.36	−	−	+	+	Moderate	−	+	−	−	−	Mild
6	1	98.30	100	−	−	+	+	Moderate	−	+	−	−	−	Mild
7	11	80.11	75.97	−	−	+	+	Moderate	−	-	−	−	−	None
8	14	66.48	72.15	+	+	+	+	Severe	+	+	−	+	+	Severe
9	1	90.34	95.83	−	−	+	+	Moderate	−	−	−	−	−	None
10	8	78.41	88.54	−	−	+	−	Mild	−	−	−	−	−	None
11	24	76.14	57.71	−	−	+	+	Moderate	+	−	−	+	−	Mild

ILS incompentet labial seal, *OR* oral residue, *PR* pharyngeal residue, *FS* fractionated swallowing, *VC* voice changes, *DESAT* oxygen desaturation, *PEN* penetration, *AS* aspiration

safety impairment. A correlation was found between the degree of effectiveness impairment and the degree of safety impairment. ($p = 0.024$).

As reflected in Table 3, in all patients (100%), the safest and most effective volume was the smallest administered (5 ml). It was observed that an increase in volume has a negative impact on the safety and efficiency of swallowing, that is, the higher the volume, the greater the swallowing disorder. In one of the patients, alterations with 10 and 20 ml volumes were not taken into account, since when detecting alterations in safety with the 5 ml volume, the test was stopped. The safest consistency tested was the nectar, as being the less associated with swallowing events and being the liquid the less safe. The most effective consistency was the liquid one, being the less effective the pudding.

The evolution time of the disease was defined as the time after diagnosis of the first component of the triad and quantified in months. The average time of evolution was 60 months with a range from 12 to 156 months. No correlation was found between the time of evolution of the disease and the findings in FEES and V-VST nor with the final scores of the QoL questionnaires.

Regarding the follow-up in terms of life-threatening situations, one patient presented two episodes of severe aspirative pneumonia.

Discussion

CANVAS is a neurodegenerative multisystem disease with an increasing diagnosis and recognition, but currently severely underdiagnosed. The finding of a pathognomonic genetic alteration associated with this syndrome means that the diagnosis of these patients has been modified. While previously the diagnosis was made in those patients who had the characteristic clinical triad, currently the diagnosis is genetic and previously unstudied symptoms may be present. To our knowledge, this is the first study that explores the presence of oropharyngeal dysphagia in CANVAS.

Oropharyngeal dysphagia is an under-diagnosed and poorly managed disorder in neurodegenerative patients. The initial diagnosis is made frequently when patients present an episode of aspiration pneumonia [18]. Oropharyngeal dysphagia impedes food consumption and may lead to weight loss, malnutrition and dehydration, and more drastically it may cause life-threatening aspiration with increased morbidity and mortality [9].

Common symptoms of oropharyngeal dysphagia are coughing and choking, complaints of food sticking to the throat, drooling, prolonged mealtimes and unexplained weight loss. Moreover, oropharyngeal dysphagia is known to have lasting psychosocial impacts on QoL [14].

Identifying dysphagia in the early stages of a progressive neurological disorder can assist in implementing preventative measures, reduce the risk of complications, and assist in achieving optimal health and QoL outcomes [18]. The assessment tools used for screening are questionnaires and, for patients that fail screening, further assessment is required. Currently, FEES is considered as the gold standard to assess oropharyngeal dysphagia [19].

In our analysis, the 82% of the patients presented an abnormal EAT-10 score, reflecting an abnormal swallowing experience in these patients. After applying the QoL questionnaires, no correlation was found between the EAT-10 and the SWAL-QoL scores, but it was found between the EAT-10 and MDADI and between both QoL questionnaires. This data suggests that EAT-10 works as a useful screening test to predict the results in the QoL questionnaires.

Table 3 Effectiveness and safety in the different consistencies and volumes. Central tendency data

	Liquid		Nectar		Honey		Pudding		5 ml		10 ml		20 ml	
	Average	Mode	Average	Mode	Average	Mode	Average	Mode	Average	Mode	Average	Mode	Average	Mode
Effectiveness alteration	0.46	0 (7/11)	0.77	1 (8/11)	1.62	2 (5/11)	1.92	2 (10/11)	0.77	0 (6/11)	1.17	1 (6/11)	2.08	2 (9/11)
Safety alteration	0.46	0 (11/11)	0.15	0 (11/11)	0.31	0 (11/11)	0.31	0 (11/11)	0.23	0 (11/13)	0.0	0 (11/11)	0.58	0 (8/11)
Total	0.92	0 (6/11)	0.92	1 (6/11)	1.94	2 (5/11)	2.23	2 (9/11)	1	1 (6/11)	1.17	1 (6/11)	2.67	2 (6/12)

() In parentheses, the number of cases that make up the mode over the total

FEES has great sensitivity, specificity and predictive values, and it can be used with patients from different age groups and settings and takes about 10–15 min to conduct. In addition to assessing the motor activity of the effectors, FEES allows to test sensation as well, being this one of the most important advantages of this tool compared to fluoroscopy [20]. As limitations, FEES shows events prior to and after the pharyngeal stage of swallowing, but does not show most of the ongoing movement during the pharyngeal swallow, including hyoid motion, airway closure at the entrance, tongue base to pharyngeal wall contact, the majority of laryngeal elevation, and cricopharyngeal opening. In contrast, videofluoroscopy visualizes all of those events, but does not visualize movements of the vocal folds, arytenoid, and some portions of the airway entrance [21].

After the FEES and V-VST analysis, all 11 patients presented some degree of swallow effectiveness impairment, being the most common alteration the presence of pharyngeal residue, which was found in 100% of cases. Most of patients presented between two or three alterations, being classified as a moderated grade of effectiveness impairment. In the same way, voice changes were the most common safety alterations found (64% of patients). Most patients presented one alteration, being classified as a mild grade of safety impairment. 3/11 patients did not present any safety alterations.

The safest and more effectiveness volume during swallowing was evaluated, being the smallest volume the best tolerated. Likewise, the consistency was evaluated being the liquid consistency the best tolerated but associated with greater safety impairment. The higher the volume and lesser the consistency, greater the disorder. These findings are similar to those described by Mamolar et al. [22] in patients with Parkinson´s disease.

The fact that no statistically significant correlations were found between the scores in the QoL tests and the degree of effectiveness or safety impairment, supports the theory that QoL questionnaires fail to predict the objective degree of swallowing impairment in patients affected by neurological diseases. The deteriorated proprioception and the diminished sensory due to disease´s progression, could decrease the subjective complaints regarding their impaired swallowing. A correlation was found between the degree of effectiveness impairment and the degree of safety impairment, the worst the effectiveness of swallowing, the greater the risk of aspiration and penetration.

Szmulewicz et al. [10] reported that most CANVAS patients suffering from dysphagia responded to indirect strategies (behavioral techniques such as the chin-tuck position) needing to make changes in food consistency in very few of them. In our sample, after the study, only 1/11 patient (9%) did not need any recommendation about food consistency or volume modifications to improve their swallowing

mechanisms. 9/11 (82%) required some degree of modification and in 1/11 patients (case 8), the FEES study revealed aspiration and penetration in all volumes and consistencies, so we recommended to avoid oral intake and the realization of a percutaneous gastrostomy, which the patient rejected. These data are noteworthy in relation to the infrequent prestudy dietary modification in our patients reflecting that most of CANVAS patients are not aware of the magnitude of their swallowing problems and do not take action to prevent them, findings also shown by other patients with neurodegenerative diseases [22]. Despite the fact that CANVAS patients usually manifest some clinical degree of dysphagia, as reflected in the screening tests, they are not aware of the severity of their problem and they do not take the adequate measures to deal with the situation.

Conclusion

1. Despite the recent discovery of genetic diagnosis, CANVAS remains a severely underestimated and underdiagnosed condition.
2. The prevalence of swallowing disorders in CANVAS population is higher than expected and is essential to suspect it to focus on it properly. The screening test EAT-10, detected abnormal subjective perception of dysphagia in more than 80% of studied CANVAS patients. In the same line, instrumental assessment reflected an effectiveness impairment in all patients and safety alterations in most of them.
3. Despite finding a correlation between the results of QoL tests, this is not shown between then and the FEES and V-VST. To properly evaluate the patients swallowing status, objective instrumental procedures must be conducted, because it cannot be extrapolated from the QoL tests.
4. Most patients could be benefited from assessment and some degree of modification in food consistency and volume.

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Availability of data and material Authors declare that all data and materials are available for review.

Code availability Statistical analyses were performed using IBM SPSS statistics software version 22 for MacOS.

Compliance with ethical standards

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. The project was approved by the Research Ethics Committee of Principado de Asturias (2020.169).

Consent to participate Written informed consent was obtained from patients who participated in this study.

Consent for publication Publication consent was obtained from the patients who participated in this study.

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