Revista Eletrônica
Acervo Saúde
Electronic Journal Collection Health ISSN 2178-2091

Ataxia in patients with dystonic tremor

Ataxia em pacientes com tremor distônico

Ataxia en pacientes con temblor distónico

Joselin Valeska Martinez-Sobalvarro[1], Idonilton da Conceição Fernandes[1], Cleiber Marcio Flores[1], Josiane de Fatima Gaspari Dias[1], Marilis Dallarmi Miguel[1].

ABSTRACT

Objective: To gather available scientific evidence on ataxia in patients with dystonic tremor. **Methods:** This is an integrative review. The following databases were used: Medline (via PubMed), Embase and Web of Science. In addition, a secondary search was performed in the reference lists of the included studies and in the gray literature. The eligibility criteria were articles that described patients diagnosed with dystonic tremor and ataxia. **Results:** A total of 105 studies were identified, of which 18 studies were included. Twelve of the studies are case reports and six are case series, with a total sample of 27 patients. Dystonic tremor in the upper limbs was present in almost 80% of the patients, followed by dystonic tremor of the head (33.3%) and dystonic tremor of the neck and lower limbs (14.8%). Several types of ataxias were identified. **Final considerations:** Cerebellar ataxia is a neurological condition with clinical heterogeneity that can be identified concomitantly with dystonic tremor. Dystonic tremor may be the initial presenting symptom. Multiple genes are responsible for ataxia; however, additional observational studies are needed to establish an association between ataxia and dystonic tremor.

Keywords: Ataxia, Spinocerebellar ataxia, Dystonic tremor, Dystonia, Tremor.

RESUMO

Objetivo: Reunir evidências científicas disponíveis sobre ataxia em pacientes com tremor distônico. **Métodos:** Trata-se de uma revisão integrativa. Foram utilizadas as seguintes bases de dados: Medline (via PubMed), Embase e Web of Science. Além disso, foi realizada uma busca secundária na lista de referências dos estudos incluídos e na literatura cinzenta. Os critérios de elegibilidade foram artigos que descrevessem pacientes com diagnóstico de tremor distônico e ataxia. **Resultados:** Foram identificados 105 estudos, dos quais 18 estudos foram incluídos. Doze dos estudos são relatos de caso e seis são séries de casos, com uma amostra total de 27 pacientes. O tremor distônico em membros superiores esteve presente em quase 80% dos pacientes, seguido pelo tremor distônico de cabeça (33,3%) e tremor distônico de pescoço e membros inferiores (14,8%). Diversos tipos de ataxias foram identificados. **Considerações finais:** A ataxia cerebelar é uma condição neurológica com heterogeneidade clínica que pode ser identificada concomitantemente com o tremor distônico. O tremor distônico pode ser o sintoma inicial de apresentação. Vários genes são responsáveis pela ataxia; no entanto, estudos observacionais adicionais são necessários para estabelecer uma associação entre ataxia e tremor distônico.

Palavras-chave: Ataxia, Ataxia espinocerebelar, Tremor distônico, Distonia, Tremor.

[1] Universidade Federal do Paraná (UFPR), Curitiba - PR.

SUBMETIDO EM: 5/2025 | **ACEITO EM: 6/2025** | **PUBLICADO EM: 8/2025**

RESUMEN

Objetivo: Recopilar la evidencia científica disponible sobre la ataxia en pacientes con temblor distónico. **Métodos:** Se trata de una revisión integrativa. Se utilizaron las siguientes bases de datos: Medline (vía PubMed), Embase y Web of Science. Además, se realizó una búsqueda secundaria en la lista de referencias de los estudios incluidos y en la literatura gris. Los criterios de elegibilidad fueron artículos que describieran pacientes diagnosticados con temblor distónico y ataxia. **Resultados:** Se identificaron 105 estudios, de los cuales 18 fueron incluidos. Doce de los estudios son reportes de casos y seis son series de casos, con una muestra total de 27 pacientes. El temblor distónico en los miembros superiores estuvo presente en casi el 80% de los pacientes, seguido del temblor distónico de la cabeza (33,3%) y el temblor distónico del cuello y los miembros inferiores (14,8%). Se han identificado varios tipos de ataxias. **Consideraciones finales:** La ataxia cerebelosa es una condición neurológica con heterogeneidad clínica que puede identificarse concomitantemente con temblor distónico. El temblor distónico puede ser el síntoma de presentación inicial. Varios genes son responsables de la ataxia; Sin embargo, se necesitan estudios observacionales adicionales para establecer una asociación entre la ataxia y el temblor distónico.

Palabras clave: Ataxia, Ataxia espinocerebelosa, Temblor distónico, Distonía, Temblor.

INTRODUCTION

Ataxia is a clinical manifestation characterized by the incoordination of voluntary muscle movements (ASHIZAWA T and XIA G, 2016). Ataxia is considered an etiologically heterogeneous sign. It can be caused by vestibular alterations, sensory deficit of proprioception and cerebellar alterations (ASHIZAWA T and XIA G, 2016; PERLMAN S, 2007). Once cerebellar ataxia has been identified, it must be classified according to the clinical characteristics presented in the patient. It should be noted that there are several etiologies according to different classifications. Among the forms of presentation are transient, episodic, and progressive clinical ataxia (BATES C, et al., 2016).

Ataxia can have an acute, subacute, chronic, or sporadic onset (BATES C, et al., 2016). Acute onset ataxia can develop over hours to days, while subacute onset ataxia can develop over weeks to months, and finally, chronic onset ataxia can manifest over months to years (KUO SH, 2019; ASHIZAWA T and XIA G, 2016). On the other hand, there is another classification, which corresponds to the inheritance pattern of ataxia. Within the inheritance pattern are autosomal dominant, autosomal recessive, linked to the fragile X chromosome and ataxia due to mitochondrial mutation (KUO SH, 2019).

The signs and symptoms presented in ataxia are related to the lesions found in neuroimaging studies (ASHIZAWA T and XIA G, 2016). In this sense, lesions at the lateralized cerebellar level can cause ipsilateral symptoms and signs. Likewise, lesions in the cerebellar hemispheres can trigger appendicular ataxia (limbs) and, in the case of lesions in the cerebellar vermis, gait ataxia and truncal ataxia, respectively (ASHIZAWA T and XIA G, 2016). Among the signs presented in ataxia are, dysdiadochokinesia, tremor, dysmetria, dysarthria, and ocular disorders (ASHIZAWA T and XIA G, 2016). Ataxia may present concomitantly with other non-cerebellar characteristics, such as peripheral neuropathy, spasticity, parkinsonism, chorea, dystonia, tremor, ophthalmoplegia, intellectual deficit, among others, and some of these manifestations may even precede the onset of ataxia (VAN DE WARRENBURG BPC, et al., 2014).

In the case of dystonic tremor (DT), it is considered when the tremor occurs in a part of the body affected by dystonia (BHATIA KP, et al., 2018). The prevalence of tremor in dystonia varies widely, with ranges between 14% and almost 90% of the population presented in an article that included ten clinical studies dated from 1971 to 2013 (PANDEY S and SARMA N, 2016). Among patients with tremor and dystonia, kinetic and postural tremor were the predominant types of tremors (PANDEY S and SARMA N, 2016). Data presented in the study by Defazio G, et al. (2015) describe that action tremor was present in 47% to 55% of patients with dystonia. DT has variable and irregular amplitude and frequency (LENKA A and JANKOVIC J, 2021), with low-frequency peaks that can oscillate between 4 and 10 Hz, with an action amplitude greater than the resting amplitude and with greater frequency variability than in other types of tremors (SCHWINGENSCHUH P, et al., 2024; BOVE F, et al., 2018).

There are individuals who present both clinical conditions, ataxia, and DT concomitantly, but there is no information synthesized on these neurological conditions together. Therefore, it was considered necessary to prepare an integrative review that aims to narratively synthesize the studies that report ataxia and DT and describe the clinical characteristics presented in this population. Therefore, this review aims gather available scientific evidence on patients diagnosed with DT who present with ataxia.

METHODS

Prior to beginning to conduct the integrative review, a quick search for other possible reviews already published was carried out, to avoid duplication of studies on the same topic, and its absence was confirmed. Therefore, the proposal for this integrative review was developed.

An integrative review was conducted following the recommendations and methodological rigor structured in six steps (SOUZA MT de, et al., 2010; RUSSELL CL, 2005; WHITTEMORE R and KNAFL K, 2005), as well as the recommendations of the PRISMA statement (PAGE MJ, et al., 2021):

1. Delineation of the guiding question and identification of the problem.

To define the research question, the acronym PICo was used (STERN C, et al., 2014) as follows:

P: Patients diagnosed with dystonic tremor and ataxia.

I: What scientific evidence is available on the possible relationship between dystonic tremor and ataxia?

Co: What are the most prevalent characteristics in this population group with both concomitant conditions, which could relate these two neurological manifestations?

2. Search strategy.

To develop the search strategy, the search terms and controlled vocabulary were first defined using the MESH (Medical Subject Heading) descriptors via PubMed and Emtree via EMBASE. The Boolean operators "OR" and "AND" were also used to combine terms. A search strategy was developed for each of the databases used, as follows: Medline via PubMed, Embase and Web of Science (**Table 1**). In addition, an additional search was performed in the gray literature: medRxiv (“dystonic tremor” AND ataxia) and DANS Data Station Life Sciences through OpenGrey (“dystonic tremor” AND ataxia), as well as a manual search in the reference list of the included studies.

Table 1 – Search strategy.

Bases de dados	
MEDLINE via PubMed (28/11/2024)	"dystonic tremor"[All Fields] AND ("ataxia"[MeSH Terms] OR "Ataxias"[Title/Abstract] OR "Dyssynergia"[Title/Abstract] OR "Ataxy"[Title/Abstract] OR "Coordination Impairment"[Title/Abstract] OR "Appendicular Ataxia"[Title/Abstract] OR "Limb Ataxia"[Title/Abstract] OR "Motor Ataxia"[Title/Abstract] OR "Sensory Ataxia"[Title/Abstract] OR "Truncal Ataxia"[Title/Abstract] OR "Dyscoordination"[Title/Abstract] OR "Incoordination"[Title/Abstract] OR "Lack of Coordination"[Title/Abstract] OR "ataxia"[Title/Abstract])
Embase (28/11/2024)	1. 'dystonic tremor'/exp OR 'dystonic tremor' 2. 'ataxia'/exp OR 'ataxia' 3. Ataxias 4. 'dyssynergia'/exp OR 'dyssynergia' 5. Ataxy 6. ('coordination'/exp OR coordination) AND ('impairment'/exp OR impairment) 7. 'appendicular ataxia'/exp OR 'appendicular ataxia' 8. 'limb ataxia'/exp OR 'limb ataxia' 9. ('motor'/exp OR motor) AND ('ataxia'/exp OR ataxia) 10. 'sensory ataxia'/exp OR 'sensory ataxia' 11. 'truncal ataxia'/exp OR 'truncal ataxia' 12. Dyscoordination 13. 'incoordination'/exp OR 'incoordination' 14. lack AND of AND ('coordination'/exp OR coordination) 15. #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 16. #1 AND #15 = 60
Web of Science (28/11/2024)	(TS=("dystonic tremor")) AND TS=("ataxia" OR "ataxias" OR "Dyssynergia" OR "ataxia" OR "Coordination Impairment" OR "Appendicular Ataxia" OR "Limb Ataxia" OR "Motor Ataxia" OR "Sensory Ataxia" OR "Truncal Ataxia" OR "Dyscoordination" OR "Incoordination" OR "Lack of Coordination")

Source: Martinez-Sobalvarro JV, et al., 2025.

The eligibility criteria were: Articles describing patients diagnosed with dystonic tremor and ataxia who exhibited characteristics of both neurological conditions. No filters were used in the search, nor were there any limitations on publication date or language. Authors of incomplete papers or manuscript with incomplete information were contacted. Once the studies were identified in the databases, they were exported to the Rayyan platform (OUZZANI M, et al., 2016), and duplicates were removed.

3. Selection of studies

This stage of selecting the studies was carried out in two steps: reading the titles and summaries of the papers, carried out by two independent researchers (JVMS, ICF), who reached a consensus to determine which studies would advance to the next stage, and the second step, which consisted of reading the full text, also carried out by the two researchers independently and finally verified by one of the researchers (JVMS). Any disagreement was resolved through consensus. Therefore, all studies that met the eligibility criteria were included in this integrative review.

4. Data organization and evaluation

The following variables were extracted from the included studies: authors, year of publication, study design and type of publication, sample size, family history, clinical characteristics of dystonic tremor and ataxia, type of treatment used, neurological evaluation, types of examinations performed, and the conclusion of the study. This stage was conducted by two independent researchers (JVMS, ICF) and subsequently verified by one of them (JVMS).

5. Analysis and interpretation of the extracted data

A subjective analysis of the extracted data was performed in each of the included studies. This step was carried out by one of the researchers (JVMS).

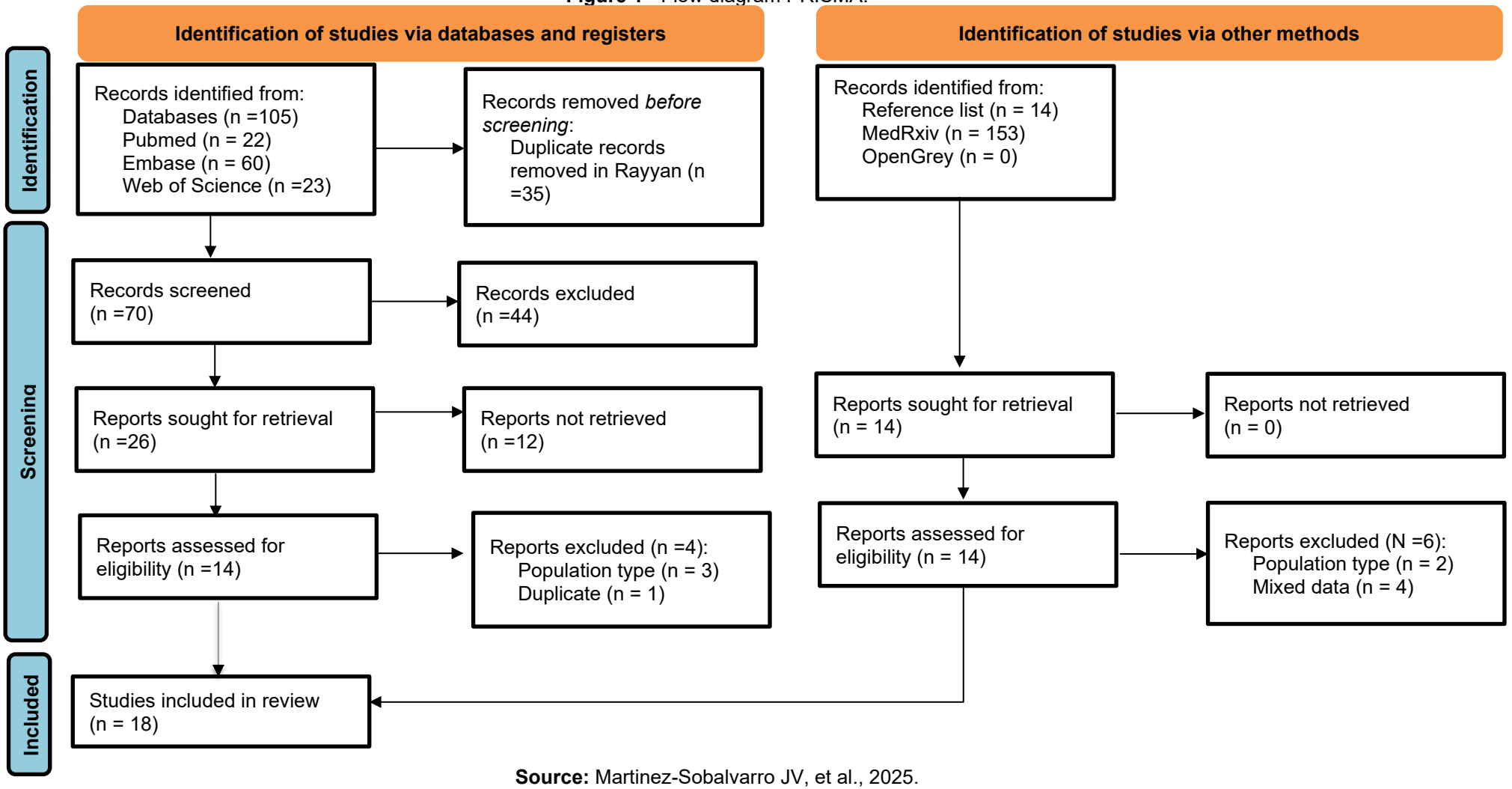
6. Presentation of the integrative review

This integrative review was presented narratively, using tables created in Microsoft Word to display the results in alphabetical order, and those studies that shared the diagnosis were ordered in sequence.

RESULTS

One hundred and five studies were found in the three databases, of which thirty-five were removed due to duplicate studies. Therefore, eighteen studies met the inclusion criteria for this integrative review (**Figure 1**). The characteristics of the included studies are presented in **Table 2**. The excluded studies and their reasons for exclusion are presented in **Table 3**.

Figure 1 - Flow diagram PRISMA.



Source: Martinez-Sobalvarro JV, et al., 2025.

Table 2 - Characteristics of the studies included.

Authors (year of publication)	Study design/ Publication type	Sample size	Family history	Tremor characteristics
Becker AE, et al. (2015)	Case report/ Conference Abstract	Two siblings, M, 14y; F, 11y	NR	M: generalized dystonia; F: CD, head DT, writer's cramp
Choquet K, et al. (2015)	Case series/ Short communication	Two-generation French Canadian family[g]; -Patient III:1: M, 31y	EA: Patients III:1, III:2, III:3; II:1	-Patient III:1: Paroxystic episodes of right UL DT
Freund HJ, et al. (2007)	Case report/ Article	F, 22y	Adopted (unknown)	UL, LL tremor; Head, chin, and trunk tremor; CD, hand dystonia.
Houghton DJ, et al. (2011)	Case report/ Conference Abstract	M, 34y	NR	Onset: 28y: head tremor, CD
Ganos C, et al. (2014)	Case report/ Article	F, 39y, Indian origin, 31y: postpartum right arm tremor; 36y: voice tremor with spasmodic dysphonia.	Father (59 y): head tremor; Paternal uncle: head and hands tremor.	Dystonia facial (eyebrows/ mouth), tongue, jaw, and head tremor, adductor dysphonia. UL tremor, hand dystonia.
Rossi J, et al. (2019)	Case report/ Article	F, 61y, Italian origin	Paternal aunt: died from an unspecified neurodegenerative disorder; 2 first-degree cousins: similar condition.	Onset 50y: First: adductor spasmodic dysphonia, then DT; -Head DT; UL tremor.
Keogh MJ, et al. (2015)	Case report/ Article	F 9y, Day 5: intermitent generalized seizures; 6 weeks: mixture of tonic seizures, intermitent focal seizures of left arm and right leg.	Consanguineous parents: (-)	7y: head nodding stereotypies; 9y: dystonic posturing of legs, UL DT.
Caballero Oteyza A, et al. (2014)	Case series/ Article	2 families[d], Germany origin; Patient 5: F, 42y.	5 members of same family.	-Patient 5: UL tremor, CD.
Dor T, et al. (2014)	Case series/ Article	2 families[f] II-1: M, NR, Moroccan origin	2 members of same family; Consanguineous parents: (+) cousins	II-1: tremor, CD.
Marchionni E, et al. (2019)	Case report/ Article	Fraternal twins 17y (F, M), Moroccan descendant.	Consanguineous parents: (+) first cousins	Primary school: writing difficulties and dysarthria; Adolescence: gait and speech worsened; M, 17y: UL DT; F, onset 12y: UL and neck DT.
Yücel-Yılmaz D, et al. (2018)	Case report/ Article	3 patients[e] M, 25y, Turkey origin	Consanguineous parents: (+); Brother: HSP	Onset: 3y: UL DT;

Authors (year of publication)	Study design/ Publication type	Sample size	Family history	Tremor characteristics
Oyama G, et al. (2014)	Case series/ Article	5** patients (2008-2011); -SCA2: Caucasian F, 41y, cuban descendant; -FXATAS: M, 72y; -NOS: M, 40y; -SCA17: Caucasian M, 37y; -SETX: M, 19y.	-NOS: NR; -SCA17: (-); -SETX: NR.	-NOS: Onset: 12y: head tremor, bilateral hand tremor, writer's cramp, LL dystonia; -SCA17: Onset:15y: generalized dystonia, UL tremor; Dystonia of face, shoulders, neck, and legs -SETX: Onset: 2y: UL tremor, head abnormal posture, myoclonus.
Riso V, et al. (2020)	Case report/ Letter to the editor	M, 41y, Italian origin	43 y, 39 y healthy sisters (-); Consanguineous parents: (-).	Onset: 30y; Generalized trunk and limbs axial DT
Sharawat IK, et al. (2021)	Case report/ Article	M, 16y, Indian origin	Consanguineous parents: (-)	UL DT
Fasano A, et al. (2017)	Case report/ Correspondence	M, 55y, Indian origin	Mother: ET	Onset: 20y: UL DT, voice tremor.
Camargo CHF, et al. (2021)	Case report/ Letter to Editor	M, 56y Brazilian, remote Italian descendant;	Mother: UL tremor; Paternal family history: NA	Onset: 51y: UL tremor, head tremor; hand dystonia.
Riso V, et al. (2021)	Case series/ Article	5 patients[h] Patient D (II-5): M, 7y, Italian origin	(-)	Onset: 1y: tremor, dysmetria; 7y: Hands dystonia.
Yahya V, et al. (2024)	Case series/ Article	Multigenerational north-east french family (6); Probands y, sex (II-2/ III-2/ III-3/ IV-1/ IV-2/ IV-3): (59, F/ 34, F/ 30, M/ 12, F/ 7, M/ 7, F).	Family history: 6 patients, Childhood-onset DT	Onset: Proband (II-2): 5y, Others 5 probands: 3y; (II-2/ III-2/ III-3/ IV-1/ IV-2/ IV-3) -Tremor head-neck: (+/-/+/-/-/-); -Tremor (R/L) UL: 6 patients; -Tremor LL (R/L): (+/-, +/+, -/-, -/-, -/-, -/-); -Dystonic posture neck: (-/+/+/-/-/-); -Dystonic posture (R/L) UL: 6 patients; -Dystonic posture LL (R/L): (+/-, -/-, +/+, -/-, +/-, -/-); -Writer´s cramp: 6 patients.

Source: Martinez-Sobalvarro JV, et al., 2025.
Legend: CD: Cervical dystonia; DT; Dystonic tremor; EA: Episodic ataxia; ET: Essential tremor; F: Female; FXATAS: Fragile X–associated tremor ataxia syndrome; HSP: Hereditary spastic paraplegia; LL: Lower limb; M: Male; NA: Non-available; NR: Not reported; NOS: Idiopathic ataxia/Ataxia not otherwise specified; SCA: spinocerebellar ataxia; SETX: Senataxin mutation; UL: Upper limb; Y:years; d: This study consisted of two families, one with five individuals and the other with two. Data were collected from only one member, as she had tremor and dystonia as an additional neurological sign; e: There are three patients, of which information was collected only from one patient who presented tremor and dystonia; f: This study included two families: a family of Palestinian origin with four members, and a Moroccan family with three members. Data were collected from only one individual (a Moroccan family) who presented signs of dystonia and tremor; g: This study presented three individuals, however, only data were collected from one patient who presented dystonia and tremor; h: This study included four families with five individuals. Data was collected from only one patient who presented with tremor and dystonia; **: Data were collected from only three patients with dystonic tremor and ataxia (NOS, SCA17, SETX) as this was the study population of interest.

Table 3 - Excluded studies and their reasons for exclusion.

Authors	Journal	Exclusion reason
Rinaldi D, et al. (2024)	Neurological sciences: official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology, 2024; 45(9):4589-92.	Type of population
Menéndez-González M, et al. (2014)	Frontiers in aging neuroscience, 2014; 6:56	Type of population
Riso V, et al. (2020)	Neurological sciences: official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology, 2020; 41(10):2989-91	Duplicate
Hooly P, et al. (2022)	Ceska a Slovenska Neurologie a Neurochirurgie, 2022; 85(2):163-7	Type of population
Choudhury S, et al. (2017)	Movement disorders clinical practice, 2017; 5(1):39-46	Mixed data
O'Hearn E, et al. (2001)	Neurology, 2001; 56(3):299-303	Mixed data
Bahl S, et al. (2005)	Annals of human genetics, 2005; 69(Pt 5):528-534	Mixed data
Holmes SE, et al. (2001)	Brain research bulletin, 2001; 56(3-4):397-403	Mixed data
Ganos C, et al. (2014)	Cerebellum, 2014; 13(1):89-96	Type of population
Chelban V, et al. (2018)	Movement disorders : official journal of the Movement Disorder Society, 2018; 33(7):1119-1129	Type of population

Source: Martinez-Sobalvarro JV, et al., 2025.

The publication years of the included articles range from 2007 to 2021, of which twelve are case reports (CAMARGO CHF, et al., 2021; SHARAWAT IK, et al., 2021; RISO V, et al., 2020; MARCHIONNI E, et al., 2019; ROSSI J, et al., 2019; YÜCEL-YILMAZ D, et al., 2018; FASANO A, et al., 2017; BECKER AE, et al., 2015; KEOGH MJ, et al., 2015; GANOS C, et al., 2014; HOUGHTON DJ, et al., 2011) and six are case series (YAHYA V, et al., 2024; RISO V, et al., 2021; CHOQUET K, et al., 2015; CABALLERO OTEYZA A, et al., 2014; DOR T, et al., 2014; OYAMA G, et al., 2014). Therefore, this integrative review consists of a sample size of twenty-seven patients, almost 60% male, with one study corresponding to a French multigenerational family of 6 individuals who presented with childhood-onset dystonic tremor (YAHYA V, et al., 2024). The other case series consisted of three individuals from a single family of French-Canadian origin, in which only data were collected from one patient who presented with tremor and dystonia (CHOQUET K, et al., 2015).

Among the other studies that also reported the origin or descent of the patients, three were of Italian origin (RISO V, et al., 2021, 2020; ROSSI J, et al., 2019), one Brazilian of Italian-remote descent (CAMARGO CHF, et al., 2021), three of Indian origin (SHARAWAT IK, et al., 2021; FASANO A, et al., 2017; GANOS C, et al., 2014), German (CABALLERO OTEYZA A, et al., 2014), Turkish (YÜCEL-YILMAZ D, et al., 2018), Moroccan (DOR T, et al., 2014) and Moroccan descent (MARCHIONNI E, et al., 2019), one of each, respectively. The remaining studies did not report this information (BECKER AE, et al., 2015; KEOGH MJ, et al., 2015; OYAMA G, et al., 2014; HOUGHTON DJ, et al., 2011; FREUND HJ, et al., 2007). Ninety-six percent of the patients were under 60 years of age at the time of publication of the study, of which ten individuals were still under 21 years of age (YAHYA V, et al., 2024; RISO V, et al., 2021; SHARAWAT IK, et al., 2021; MARCHIONNI E, et al., 2019; BECKER AE, et al., 2015; KEOGH MJ, et al., 2015;).

Regarding the family history reported in the studies, four patients were children of consanguineous parents, two of whom were diagnosed with Hereditary Spastic Paraplegia (HSP), with symptom onset at 7 and 10 years of age, respectively (YÜCEL-YILMAZ D, et al., 2018; DOR T, et al., 2014). These patients had parents who were carriers of the mutation (KIF1C gene) but were asymptomatic. The other study involved twin siblings carrying a homozygous variant in the same gene as the previous cases (MARCHIONNI E, et al., 2019). They were children of asymptomatic consanguineous parents, both also carriers of a heterozygous variant (MARCHIONNI E, et al., 2019). These twin patients were diagnosed with early-onset cerebellar ataxia.

Some parents and relatives also presented some type of tremor, from essential tremor to some unknown neurodegenerative disorder (CAMARGO CHF, et al., 2021; ROSSI J, et al., 2019; FASANO A, et al., 2017; GANOS C, et al., 2014). On the other hand, studies were identified that presented data from entire families (5 individuals) with clinical manifestations and diagnosed with Autosomal Dominant Episodic Ataxia (EA), from which information was collected only from one individual who reported tremor and dystonia (CHOQUET K, et al., 2015). Another study comprised both parents and three children with clinical manifestations, carriers of a mutation in the KIF1C gene, with a diagnosis of HSP type 58 (CABALLERO OTEYZA A, et al., 2014). Finally, a study of a French multigenerational family (six individuals) with a diagnosis of Spinocerebellar Ataxia (SCA) 21 (YAHYA V, et al., 2024).

Regarding the characteristics identified in DT, 77.7% of patients presented upper limbs DT, 33.3% head DT, 14.8% presented neck DT and the same number for tremor of the lower limbs, each one, respectively. In addition, eight individuals presented Writer's cramp (WC) (YAHYA V, et al., 2024; BECKER AE, et al., 2015; OYAMA G, et al., 2014), and both female patients diagnosed with SCA12 presented spasmodic dysphonia (ROSSI J, et al., 2019; GANOS C, et al., 2014) (**Table 1**).

In almost 70% of the studies, the type of treatment used was reported, from oral pharmacological treatment to the use of botulinum toxin (BoNT) with satisfactory results in three of the studies (YAHYA V, et al., 2024; GANOS C, et al., 2014; OYAMA G, et al., 2014; HOUGHTON DJ, et al., 2011). As well as the use of neurosurgical procedures, such as Deep Brain Stimulation (DBS), also with reliable results in three of the studies (FASANO A, et al., 2017; FREUND HJ, et al., 2007; OYAMA G, et al., 2014; RISO V, et al., 2020).

One of the main imaging methods reported was magnetic resonance imaging (MRI), performed in seventeen patients (16 brain, 1 cranial), of whom 70% had abnormal imaging results (**Table 4**). Furthermore, all patients underwent genetic analysis, identifying pathogenic variants with heterogeneous presentations of ataxia (**Table 5**). Except for the study by Houghton DJ, et al. (2011) in which the performance of genetic testing was not reported.

Table 4 - Assessments performed and types of treatments used.

Authors (year of publication)	Tests performed to evaluate DT	Other assessments	Image studies	Type of treatment (Good response:+) (Poor/negative response:-)
Becker AE, et al. (2015)	M: -Nerve conduction studies: N; F: NR	M: -Muscle biopsy: mild myopathic changes; F: NR	M: NR F: NR	NR
Choquet K, et al. (2015)	-Patient III:1: EMG: N	-Patient III:1: EEG: N	-Patient III:1: Brain MRI: N	Patient III:1: Acetazolamide: (-).
Freund HJ, et al. (2007)	NR	NR	NR	Clozapin: (-); Clonazepam: (-); Clobazam: (-); Primidone: (-); DBS subthalamic/ talamic: (++) tremor, ataxia.
Houghton DJ, et al. (2011)	NR	NR	-Brain MRI: cerebellar atrophy	Triheyphenidyl: (-); Baclofen: (-); Clonazepam: (-); Tizanidine: (-); Levetiracetam: (-); BoNT type A (150 total units): (+)
Ganos C, et al. (2014)	-EMG and accelerometry: 4-Hz tremor of her head and arms.	-Neuropsychiatric symptoms: (-)	-Cranial MRI: mild generalized volume loss.	BoNT: (+) partial head tremor and adductor dysphonia.
Rossi J, et al. (2019)	NR	-Cognitive: deterioration; -Depression: (+); - Neuropsychological test: executive and attentive function impairment, deficit of learning skills; - Acoustic and perceptual speech analysis: altered.	-Brain MRI: generalized cortical and milder subcortical atrophy.	Trihexyphenidyl (4 mg/day): (+) head and UL, spasmodic dysphonia.
Keogh MJ, et al. (2015)	NR	-One y: revealed global developmental delay; - Language, cognition severely impaired; -Lumbar puncture: N; -EEG: bilateral multifocal epileptiform activity; -Serum lactate, pyruvate, very long chain fatty acids, phenylalanine, white cell enzymes, alpha fetoprotein, vitamin E, acanthocytes, karyotype: N.	-CT head: N; -Brain MRI (4 months and 6y): N.	(4 months of age) Phenobarbitone: seizures (+).
Caballero Oteyza A, et al. (2014)	NR	Patient 5: -Cognition: N; -Nerve conduction studies: N; -EPs: VEP: N; AEP: N; MEP: UL/LL no potential (at age 34 prolonged CMCT); Tib SEP: increased latency cortical potential.	Patient 5: -Brain MRI: T2 hyperintensities (pre-/post central/ occipital white matter, pyramidal tract, superior cerebellar peduncles), mild vermian cerebellar and spinal atrophy.	NR
Dor T, et al. (2014)	NR	-Intellectual: N	NR	NR

Authors (year of publication)	Tests performed to evaluate DT	Other assessments	Image studies	Type of treatment (Good response:+) (Poor/negative response:-)
Marchionni E, et al. (2019)	-Polymyography: upper limbs tremor in both twins; F: DT of neck (frequency of 5.5 Hz), without myoclonus. -Nerve conduction: N.	-Test WAIS-IV: M/F: VCI: 84/83; POI: 72/84; WMI: 68/80; PSI: 55/66.	-Brain MRI: hypomyelinating leukoencephalopathy. -DaTscan: N.	NR
Yücel-Yılmaz D, et al. (2018)	-EMG: N.	-Cognitive: N; -Vitamin B12: N; -Homocysteine: increased; -Lysosomal enzymes, urine mucopolysaccharides and oligosaccharides, ceruloplasmin, copper in serum, 24 h collected urine, peroxisomal panel, biotinidase, urine and blood amino acids, urine organic acids, carnitine-acylcarnitine profile: N; -BAEP: bilateral prolonged central latencies; -VEP: bilateral prolonged P1 latencies; -EEG: N; -Muscle biopsy: mild fiber size variabilitiy with scattered atrophic fibers.	-Brain MRI: Cerebral hemispheres (perirolandic area brain stem) and upper cervical spinal atrophy, bilateral symmetrical pyramidal tract involvement, focal cerebral white matter lesions.	Primidone: (-); Propranolol: (-); Vitamin B12: (+) mild Clonazepam: NR
Oyama G, et al. (2014)	-NOS: NR -SCA17: NR -SETX: NR	-NOS: NR -SCA17: NR -SETX: EEG, EKG: N.	-NOS: NR -SCA17: NR -SETX: Brain MRI: N.	-NOS: Clonazepam, propranolol: (+) minor; Levodopa (-). Left Vim DBS: tremor: (+); ataxia (-). -SCA17: Levodopa, baclofen, trihexyphenidyl, BoNT: (-). [a]Bilateral Gpi DBS: UL DT (+); LL dystonia, gait (-). -SETX: Primidone, valproic acid, clonazepam, acetazolamide, buspirone, levodopa, levetiracetam (-); Propranolol 30 mg, gabapentin 1200 mg: (+) tremor; Bilateral Gpi DBS: DT, myoclonus (+), gait (-)
Riso V, et al. (2020)	NR	-Neurophysiological studies: N; -Cognitive test: mild impairment of executive functions.	-Brain MRI: moderate vermian atrophy and iron accumulation in globus pallidus areas detected by SWAN sequences; -CT scan: N; -Brain SPET, DaTscan, assessment of copper and iron metabolism: N.	Gpi DBS: (+) tremor.

Authors (year of publication)	Tests performed to evaluate DT	Other assessments	Image studies	Type of treatment (Good response:+) (Poor/negative response:-)
Sharawat IK, et al. (2021)	-Nerve conduction: N.	-IQ: 68; -Tandem mass spectrometry, urinary organic acid profile, serum prolactin, serum α-fetoprotein: N; -IG levels, blood, and cerebrospinal fluid lactate levels, serum vitamin E levels: N. -Ophthalmological assessment: N.	-Brain MRI: bilateral cerebellar hemispheric and midline cerebellar atrophy;	Trihexyphenidyl, levodopa/carbidopa, vitamin E: (-).
Fasano A, et al. (2017)	NR	NR	-Brain MRI: cerebellar atrophy	Propranolol (-); Primidone (-); Gabapentin (-); Trihexyphenidyl (-); Topiramate (-); Levodopa (-); Right Vim DBS (-).
Camargo CHF, et al. (2021)	NR	-Cognitive: N.	-Brain MRI: cerebellar atrophy	NR
Riso V, et al. (2021)	NR	-PMD: (+); -Cognitive: N; -Behaviour disorder: (+).	-Brain MRI: delayed myelination.	NR
Yahya V, et al. (2024)	NE	-Cognitive behavioral: (II-2/ III-2/ III-3/ IV-1/ IV-2/ IV-3) -PMD: (-/-/+/-/+/-); -ASD: (-/-/+/-/+/-); -Sleep disorder: (RLS/-/ Enuresis/ Insomnia/ OSAS, enuresis/-); -Executive dysfunction: (+/+/-/-/-/-); -Attention deficit: (+/+/+/ADHD/ -/ADHD); -Language impairment: (-/-/+/+/+/+); -MoCA score: (29/30; 29/30; NA; NA; NA; NA).	Proband (II2): -Brain CT (37y): N; Probands II2/ III2/ III3/ IV1/ IV2/ IV3: -Brain MRI: Mild cerebellar vermis atrophy/ N / ventricle enlargement/ NA/ NA/ NA); -DAT-SPECT: (NA/ N/ NA/ NA/ NA/ NA).	*

Source: Martinez-Sobalvarro JV, et al., 2025.

Legend: ADHD: Attention deficit hyperactivity disorder; AEP: Auditory evoked potentials; ASD: Autism spectrum disorder; BAEP: Brainstem evoked potentials; DBS: Deep brain stimulation; BoNT: botulinum toxin; CMCT: Central motor conduction time; CT: Computed tomography; DaTscan: dopamine transporter scan; DAT-SPECT, dopamine transporter single photon emission computed tomography; DT: Dystonic tremor; EEG: electroencephalogram; EKG: Electrocardiogram; EMG: electromyography; EPs: Evoked potentials; F: Female; Gpi: Globus pallidus internus; IG: Immunoglobulin; IQ: Intelligence Quotient; LL: Lower limb; M: Male; MEP: Motor evoked potentials; MoCA: Montreal Cognitive Assessment; MRI: Magnetic resonance imaging; N: Normal; NA: Non-available; NOS: Idiopathic ataxia/Ataxia not otherwise specified; NR: Not reported; OSAS: Obstructive sleep apnea syndrome; PMD: Psychomotor delay; POI: perceptual organization index; PSI: processing speed index; RLS; Restless legs syndrome; SCA: spinocerebellar ataxia; SETX: Senataxin mutation; SPET: single photon emission computed tomography; Tib SEP: Tibial sensory evoked potentials; UL: Upper limb; VCI: verbal comprehension index; VEP: Visual evoked potentials; Vim: Ventral intermediate nucleus; WAIS-IV: Wechsler Adult Intelligence Scale-Fourth Edition; WMI: working memory index; y: years; *: Response (+) (II-2/ III-2/ III-3/ IV-1/ IV-2/ IV-3): (Propranolol, ethanol, rotigotine/ Propranolol, ethanol, topiramate/ Botulinum toxin, trihexyphenidyl (not tolerated)/ Melatonin/ NA/ NA) Response (-) (II-2/ III-2/ III-3/ IV-1/ IV-2/ IV-3): (Primidone/ Levodopa, rotigotine, trihexyphenidyl, botulinum toxin/NA/ NA/ NA/ NA).

Table 5 - Characteristics of ataxia and study conclusion.

Authors (year of publication)	Ataxia characteristics	Neurological assessment	Tests performed to evaluate ataxia	Study conclusion
Becker AE, et al. (2015)	AVED	M: -Weakness: (+); -Reflexes: diminished; -Sensation: N; -Gait: unsteady; -Dysmetria limb: (+); -Dysdiadochokinesia: (+); F: NR	Heterozygous frameshift mutations in TTPA (c. 161_164del, c. 487delT)	Dystonia may be the presenting feature of AVED and should be considered in the differential diagnosis of progressive dystonia, particularly when combined with even subtle peripheral motor or sensory deficits.
Choquet K, et al. (2015)	Patient III:1: Onset: 26y: incoordination, unsteady gait; Progressive permanent cerebellar ataxia. Autosomal dominant EA	Patient III:1: -OE: horizontal nystagmus; -Hypotonia: UL, LL; -Dysarthria: (+); -Dysmetria: (+); -Dysdiadochokinesis: (+)	Patient III:1: CACNA1A, KCNA1: (-); -WES: Patients III:1: heterozygous 1-base pair insertion in FGF14 in (chr13:102527628_102527629insT; c.211_212insA), (p.I71NfsX27). -Father II:1, maternal aunts, and uncle II:3, II:4, II:5: (-)	The first French Canadian family affected with EA carrying a mutation in FGF14, which further expands the phenotypic spectrum of SCA27.
Freund HJ, et al. (2007)	SCA2 Onset: 15y: gait disturbances, ataxia	-OE: saccadic eye pursuit, gaze nystagmus, end grade gaze paralysis to all sides; -Dysmetria: (+); -Dysarthria: (+); -Dysphagia: (+).	-Expanded SCA2 allele with pure (CAG)49 and a normal SCA2 (CAG)22 allele.	In addition to the efficacy of DBS on cerebellar tremor, the results illustrate a remarkable improvement of the patient's general condition and independence.
Houghton DJ, et al. (2011)	SCA5 Onset: 28y: gait unsteadiness	-Dysarthria: (+); -Ataxia: truncal and appendicular	NR	Contrary to previously published reports, patients with SCA5 may develop CD and DT as part of the phenotype.
Ganos C, et al. (2014)	38 y: Late-onset cerebellar ataxia/ SCA12	-OE: N; -Pyramidal weakness: (-); -Sensory abnormality or bradykinesia: (-); -Heel-to-shin test: (-); -Stance and gait tandem: N	-CAG repeat length in PPP2R2B gene, a pathological repeats expansion (52/11 repeats).	Dystonic symptoms may predominate the clinical picture in SCA12, even during early stages, and could affect the upper limbs, neck, face, and voice. Possible syndromic association between SCA12 and DT.
Rossi J, et al. (2019)	SCA12	-Finger-to-nose test: dysmetria; -Hyperreflexia: (+); -Stance and gait: instability, wide-based stance; -Tandem gait: impossibility to perform.	- SCA1, SCA2, SCA3, SCA6: (-); - CAG repeat length in the PPP2R2B gene, heterozygosity for expanded allele with 61 CAG repeats.	Spasmodic dysphonia can be a presenting symptom of SCA12.

Authors (year of publication)	Ataxia characteristics	Neurological assessment	Tests performed to evaluate ataxia	Study conclusion
Keogh MJ, et al. (2015)	6y: ataxia	-Extrapyramidal syndrome: fine resting tremor, cogwheel rigidity, hypomimia); -Hyperreflexia: (+); -Upgoing plantar bilateral: (+)	- SCAs 1,2,3,6,7, 17, Friedreich's ataxia, MECP2, DRPLA, POLG, CDKL5, ataxia telangiectasia, oculomotor apraxia type 1 and 2: (-); -Mitochondrial biochemical: profound defect of respiratory chain complex I activity; - Muscle mitochondrial DNA levels: N; -WES: heterozygous missense mutation in exon 6 of the STXBP1 gene (c.416C>T, p.P139L)	STXBP1 should be considered a nuclear gene causing impaired mitochondrial function and secondary mitochondrial impairment may contribute to disease progression in patients with STXBP1 mutations.
Caballero Oteyza A, et al. (2014)	SPG58, Cerebellar ataxia, UL>LL ataxia; -Onset, Patient 5: 18y; -Severity SPRS, Patient 5: 27	Patient 5: UL: -Spasticity: (+); -Reflexes: increased; -Weakness: (-); -Amyotrophy: (-); LL: -Spasticity: (+) severe; -Reflexes: increased; -Weakness: (+); -Amyotrophy: (-); -Extensor plantar sign: (+); -OE: cerebellar (saccadic pursuit, gaze evoked nystagmus, dysmetric saccades); -Dysarthria: (+); -Vibration sense: lower limb distal reduced; -Urinary symptoms: (-).	WES: -Patient 5: KIF1C gene Gly102Ala/Pro176Leu	SPG58 exemplifies the diagnostic and counseling challenge rare hereditary diseases with phenotypic variability that impedes pattern recognition strategies for diagnosis, a phenotype overlapping with other disorders (hereditary ataxias and spastic paraplegias), and a mode of inheritance that blurs the lines between traditional mendelian inheritance patterns.
Dor T, et al. (2014)	HSP Onset: 7y	-Spasticity: (-); -Reflexes: decreased; -Babinski sign: (+); -Ankle clonus: (-); -Dysarthria: NAD -Dysmetria: (+) -Head titubation: (+); -Nystagmus: (-); -Gait: ataxic; -Sphincter disturbances: (-); -Deep sensory loss: (-).	WES: Patient II-1, Brother symptomatic, father asymptomatic KIF1C gene, c.505C>T, p.R169W	The KIF1C mutation is associated with a HSP subtype (SPAX2/SAX2) that combines spastic paraplegia and weakness with cerebellar dysfunction.

Authors (year of publication)	Ataxia characteristics	Neurological assessment	Tests performed to evaluate ataxia	Study conclusion
Marchionni E, et al. (2019)	Early-onset cerebellar ataxia; M, 17y: cerebellar ataxia, SARA 12/40; F, onset 12y: cerebellar ataxia, SARA 10/40	M: -Hyperreflexia: (+); -Babinski sign: (+); -Vibration sense: reduced; -OE: saccadic pursuit with dysmetric saccades, bilateral ptosis. F: -Vibration sense: reduced; -Pyramidal sign (-); -OE: saccadic pursuit with dysmetric saccades.	WES: homozygous variant in KIF1C in both twins (NM_006612.5:c.1019+1dup) -Both parents were heterozygous carriers of the variant.	Biallelic KIF1C variants can cause a predominant movement disorder characterized by cerebellar ataxia and DT.
Yücel-Yılmaz D, et al. (2018)	HSP Onset: 10y: mild ataxia and wide based gait.	-Hyperreflexia: (+); -Extensor flexor: (+); -Spasticity: (+); -Babinski sign; (+); -Ataxia: truncal; -OE: nystagmus; -Dysarthria: (+); -Dysmetria: (+); -Titubation: (+); -Extrapyramidal signs: dystonia; -Sphincter disturbance: (-).	WES: KIF1C gene, homozygous variant c.463C>T(p.R155*) in exon 7; -Heterozygous variant in healthy brother and parents.	Patients with KIF1C mutations may present with cerebellar signs and pyramidal findings may emerge later, therefore complicated HSP should be considered in the differential diagnosis of unidentified cases with cerebellar dysfunction.
Oyama G, et al. (2014)	-NOS: ataxia, and gait instability. -SCA17: Onset (12y): gait difficulty. -SETX: ataxia.	NOS: -Proprioception: poor; -Vibratory sense: poor; -Hyporeflexia (+); -Ankle jerks: (-); -Babinski sign: (+). SCA17: -Dysarthria: (+); -Dysmetria: (+); -Gait ataxia: severe; -OE: N; -Stance ataxia: (+); -Appendicular ataxia: (+). -SETX: -OE: limited horizontal gaze in both directions, horizontal saccades slow; -Oculocephalics: N; -Nystagmus: (-); -Finger to-nose test: dysmetria; -Heel-to-shin test: dysmetria; -Gait: wide based.	-NOS: SCAs1, 2, 3, 6, 7, 8, 10, DRPLA: (-); -SCA17: DYT1, SCAs 1, 2, 3, 6, 7, 8, 10, DRPLA: (-); Expanded allele of 43 repeats, and a normal allele of 32 CAA/CAG repeats in TATA-binding protein gene; -SETX: SCA1, 2, 3, 6, 7, 8, 10, Wilson's disease, Niemann–Pick disease: (-); Amino acid change: codon 992 (lysine to arginine) on SETX gene: senataxin-associated myoclonus, dystonia, and tremor syndrome.	DBS may be an option to treat tremor, including DT in patients with underlying ataxia; however, gait and other symptoms may be worsened.

Authors (year of publication)	Ataxia characteristics	Neurological assessment	Tests performed to evaluate ataxia	Study conclusion
Riso V, et al. (2020)	Late-onset, sporadic progressive cerebellar ataxia; SARA 26 SCA14	-Gait and standing: severe imbalance.	-NGS: PRKCG, (p.Gln127Pro) (ENST00000263431) missense variant c.380A>C; -SCA1-2-3-6-7-12-17, DPRLA, FXTAS, FA: (-); -NGS healthy sisters (43y, 39y): (-).	This report expands the mutational spectrum of PRKCG gene, underlines the recurrence of axial tremor as diagnostic key element of SCA14 subtype.
Sharawat IK, et al. (2021)	Onset: 9y: gait instability, incoordination; SCA35	-Dysmetria: (+); -Dysarthria: (+); -Dysdiadochokinesia: (+); -Finger-nose test: (+); -Heel-knee test: (+); -Hypereflexia: (+); -Appendicular and axial ataxia: (+) -OE: horizontal gaze nystagmus, oculomotor apraxia with saccadic pursuits.	- Antibody against GAD65, TG: (-); -WES: missense variant c.1876G>A (p.V626M) in TGM6 gene. Parents, one healthy M sibling: (-) variant.	In patients with SCA like presentation with the probable autosomal dominant transmission, extrapyramidal features, spasmodic torticollis, impaired proprioception, or myoclonus, TGM6 mutation should be clinically suspected.
Fasano A, et al. (2017)	SCA35	-Hypereflexia: (+); -Babinski sign: (+); -Dysmetria: (+); -Dysarthria: (+); -OE: nystagmus: (-); -Position sense: N; -Rigidity, hypokinesia: (-); -Gait: mild imbalance.	-Heterozygous variant in TGM6 gene, c.288_290del (p.Leu97Aspfs*86).	Previous reports, and particularly our patient, prove that DT in the absence of clear cerebellar signs can be seen in SCA35 patients and be used as a clue to its diagnosis when cerebellar atrophy is found.
Camargo CHF, et al. (2021)	SCA21	-Ataxia: (+); -Dysarthria: (+); -Dysphagia: (+).	-WES: heterozygous missense pathogenic variant in the TMEM240 gene (p.Pro170Leu). Siblings, mother: WES (-)	SCA21 may also present a large genotypic/ phenotypic heterogeneity. Thus, it should be kept in mind in the differential diagnosis of familial ataxias and hyperkinetic movement disorders, with or without cognitive impairment.
Riso V, et al. (2021)	SCA21 Onset: 1y: truncal ataxia	-Gait ataxia: (+); -Appendicular ataxia: (+); -Dysarthria: (-); -Hyperkinetics signs: (+); -OE: opsoclonus.	WES: TMEM240 gene missense mutation c.196G>A (p.Gly66Arg)	The phenotype of these novel SCA21 variants indicates that slowly progressive cerebellar ataxia, cognitive and psychiatric symptoms are the most typical clinical features associated with mutations in the TMEM240 gene.
Yahya V, et al. (2024)	SCA21 (II-2/ III-2/ III-3/ IV-1/ IV-2/ IV-3) -Limb ataxia: (+/+/+/-/-/-); -Gait ataxia: (+/+/-/-/-/+); -SARA: (6/ 7/ 11/ 4/ 4/ 6).	Proband (II-2): Rotigotine-responsive restless legs syndrome; -Dysarthria: III-3, IV-3; -Dysphagia: III-2, III-3, IV-3; -OE: Pursuit impairment: III-2/ Slow saccades: III-3/ Strabismus: IV-1, IV-3; -Bradykinesia: II-2, III-2, III-3; -Resting tremor: III-2.	Proband (II2): FXTAS (-); - 6 patients, WES: recurrent TMEM240 variant c.509C > T, (p.P170L) (transcript NM_001114748.2), heterozygous state.	DT can represent the core clinical feature of SCA21, even in absence of overt cerebelar ataxia. Therefore, TMEM240 pathogenic variants should be considered disease-causing in subjects displaying DT, variably associated with ataxia, parkinsonism, neurodevelopmental disorders, and cognitive impairment.

Source: Martinez-Sobalvarro JV, et al., 2025.
Legend: AVED: Ataxia with Vitamin E Deficiency; CD: Cervical Dystonia; CDKL5: Cyclin-dependent kinase-like 5; DBS: Deep brain stimulation; DRPLA: Dentatorubral-pallidoluysian atrophy; DT: Dystonic tremor; DYT1: Early-onset isolated dystonia; EA: Episodic ataxia; F: Female; HSP: Hereditary spastic paraplegia; LL: Lower limb; M: Male; MECP2: Methyl CpG binding protein 2; N: Normal; NOS: Idiopathic ataxia/Ataxia not otherwise specified; NR: Not reported; OE: Oculomotor examination; POLG: polymerase gamma; SARA: Scale for the Assessment and Rating of Ataxia; SCA: Spinocerebellar ataxia; SETX: Senataxin mutation; SPG58: Hereditary Spastic Paraplegia type 58; SPRS: Spastic Paraplegia Rating Scale; UL: Upper limb; WES: Whole exome sequencing; Y: years.

DISCUSSION

The identification of eighteen articles published since 2007 reinforces the growing interest in this condition. DT is a type of movement disorder that affects the same body region as dystonia (BHATIA KP, et al., 2018). In this type of patients, the placement of DBS implants is increasingly being used for individuals with tremor refractory to drug treatment. In this regard, one of the chosen targets is the thalamic or subthalamic region (FASANO A, et al., 2014). However, one of the main adverse effects observed after DBS has been gait disturbances and ataxia (TSUBOI T, et al., 2020).

One of the most widely studied types of ataxias has been cerebellar ataxia, in which there is a genetic component involved, as in autosomal dominant spinocerebellar ataxia (ADSA) (HARDING AE, 1982). According to Harding's classification, there are three types: I, II, III (HARDING AE, 1982). In this sense, fifteen of the 27 individuals that make up this integrative review are considered ACDA type I, which correspond to SCA type 2, 12, 14, 17, 21, 35 (YAHYA V, et al., 2024; CAMARGO CHF, et al., 2021; SHARAWAT IK, et al., 2021; RISO V, et al., 2021, 2020; ROSSI J, et al., 2019; FASANO A, et al., 2017; GANOS C, et al., 2014; OYAMA G, et al., 2014; FREUND HJ, et al., 2007). Likewise, a patient with SCA5, which according to Harding's classification, corresponds to ACDA type III (HARDING AE, 1982; HOUGHTON DJ, et al., 2011; SULLIVAN R, et al., 2019).

In one study describing the use of DBS, satisfactory benefits were reported for both tremor and dystonia in a patient diagnosed with SCA2 (FREUND HJ, et al., 2007). This is contrary to the literature, which reports the presence of ataxia as an adverse event (TSUBOI, T, et al., 2020). In that patient, some of the clinical manifestations presented were oculomotor (saccadic eye pursuit, gaze nystagmus), which is consistent with the literature addressed, in which this type of clinical manifestation stands out as the main characteristic (KUO SH, 2019; ASHIZAWA T and XIA G, 2016).

Some of the types of variants identified in this integrative review were the repeat expansion variants, two of the included studies identified a variant (CAG) in the PPP2R2B gene, corresponding to SCA12, in which both patients developed late-onset cerebellar ataxia, with a family history of tremor and unexplained neurodegenerative disorder, with pyramidal signs and normal stance and tandem gait (GANOS C, et al., 2014) and dysmetria and with gait instability, wide-based stance, impossibility to perform tandem gait (ROSSI J, et al., 2019). SCA12 is considered a relatively pure ataxia according to the International Parkinson and Movement Disorder Society Task Force (MARRAS C, et al., 2016). One of the patients with SCA12 is of Indian origin, which is consistent with the literature, which considers this type of ataxia common in India (BATES C, et al., 2016).

Another notable feature is the presence of adductor spasmodic dysphonia in both patients, which was even the initial neurological manifestation in the report by Rossi J, et al. (2019) (ROSSI J, et al., 2019). Therefore, SCA12 could be considered in cases with an autosomal dominant family history of symptoms of DT, spasmodic dysphonia, and ataxia. Even more in patients with initial presentation of spasmodic dysphonia, it becomes necessary to perform genetic tests.

The other patient with a repeat expansion (CAA/CAG) in the TATA-binding protein gene, diagnosed with SCA17, presented dysmetria, gait and stance ataxia, and mild appendicular ataxia without any psychiatric symptoms or cognitive deficit being reported in the study (OYAMA G, et al., 2014). These latter symptoms are considered among the clinical characteristics associated with SCA17 (SULLIVAN R, et al., 2019).

In this sense, another of the cerebellar ataxias that present cognitive impairment or mental retardation as a dominant characteristic is SCA21 (SULLIVAN R, et al., 2019; MARRAS C, et al., 2016). This characteristic was predominant in a multigenerational family group of six members, being more accentuated in three minor members (YAHYA V, et al., 2024). In the other studies that identified SCA21, one of the studies in a minor also presented behavioral disorder and psychomotor delay (RISO V, et al., 2021). Despite the recognition of cognitive deficit as a predominant characteristic in patients with SCA21, in Camargo's study CHF et al. (2021) the patient did not present this clinical characteristic (CAMARGO CHF, et al., 2021; MARRAS C, et al., 2016). As well as the type of tremor in the upper extremities suggesting essential tremor, which was later associated

with focal dystonia in this patient, broadens the phenotypic variability of SCA21 (CAMARGO CHF, et al., 2021). This makes it necessary to consider screening for this genetic variant (TMEM240 screening) in patients with DT, even without the onset of ataxia. This is a type of ataxia with broad phenotypic heterogeneity, presenting not only cognitive deficits but also Parkinsonism and tremor.

Other variants identified as missense were patients diagnosed with SCA14 and SCA35 (SHARAWAT IK, et al., 2021; RISO V, et al., 2020). Some of the prominent symptoms in patients with SCA14 according to the literature surveyed are pyramidal signs, dystonia, myoclonus, and parkinsonism (SULLIVAN R, et al., 2019; MARRAS C, et al., 2016). However, the patient with SCA14 only reported dystonia and tremor, and mild executive function deficits, without providing detailed characteristics of other symptoms that could fully agree with the literature (RISO V, et al., 2020).

In relation to the patient with SCA35, a missense variant c.1876G>A (p.V626M) was identified in the TGM6 gene, in which pyramidal and oculomotor signs, dysmetria, as well as appendicular and axial ataxia were observed (SHARAWAT IK, et al., 2021). In contrast, the other study that reported on a patient with SCA35 did not specify the type of mutation in the TGM6 gene (FASANO A, et al., 2017). That patient presented some pyramidal signs, which is in line with the published literature (MARRAS C, et al., 2016).

The other patients present genetic mutations that cause diverse phenotypic expression, as in the case of the patient with a mutation in the SETX gene who presented oculomotor alterations, dysmetria, hesitation when walking and ataxia, who finally received the diagnosis of senataxin-associated myoclonus, dystonia, and tremor syndrome (OYAMA G, et al., 2014). Other genetic variants identified were a heterozygous missense mutation in the STXBP1 gene, with a wide range of symptoms, from extrapyramidal syndrome, severe cognitive deficit, ataxia, and early onset of seizures, starting at 5 days of age (KEOGH MJ, et al., 2015).

On the other hand, there were three studies that presented the mutation in the KIF1C gene and were diagnosed with HSP (YÜCEL-YILMAZ D, et al., 2018; CABALLERO OTEYZA A, et al., 2014; DOR T, et al., 2014).

The diagnosis of ataxia requires the clinical experience of the examining professional and that, in repeated cases, it is a challenging task with specific diagnoses yet to be clarified. Indeed, there are individuals with evident manifestations of ataxia and DT who are classified as NOS, which occurred in the patient in the case series of Oyama G, et al. (2014), who underwent various genetic tests (SCAs1, 2, 3, 6, 7, 8, 10, dentatorubral-pallidoluysian atrophy) without any alterations (OYAMA G, et al., 2014).

Only one of the studies did not report the type of genetic mutation carried by the patient, however, he had a diagnosis of SCA5 (HOUGHTON DJ, et al., 2011). Among the clinical manifestations reported in this 34-year-old patient were head tremor, cervical dystonia, dysarthria, and truncal and appendicular ataxia, which is not in line with the reviewed literature, which generally reports age of onset as after 50 years of age (PERLMAN S, 2007).

On the other hand, in two patients, one diagnosed with SCA12 and the other with SCA21, dystonic symptoms predominated in early stages, even before the onset of ataxia (YAHYA V, et al., 2024; GANOS C, et al., 2014). This reinforces the importance of prolonged follow-up of patients with DT, as they may later manifest other types of neurological symptoms.

It is important to highlight that some patients presented episodic ataxic symptoms, which can last from a few hours to days, in which genetic testing will be necessary to rule out the main genes involved in this type of ataxia (CACNA1A, KCNA1) (SULLIVAN R, et al., 2019; MARRAS C, et al., 2016). However, in the case series included in this integrative review, the patients presented EA with a mutation in the FGF14 gene (CHOQUET K, et al., 2015). It should be noted that this mutation is present in patients with SCA27 (ASHIZAWA T and XIA G, 2016; MARRAS C, et al., 2016). Therefore, in patients with tremor and EA who do not present mutations in the CACNA1A, KCNA1 genes, it is necessary to consider mutations in the FGF14 gene.

Therefore, patients with ataxia may concomitantly present with DT with varied body distribution, from axial to appendicular and truncal, and which can involve both motor and sensory areas and a heterogeneous age of onset, which reinforces the level of complexity of these types of neurological conditions (ASHIZAWA T and XIA G, 2016).

This leads to the use of various pharmacological treatments and, in some cases, neurosurgical treatments, such as DBS. Therefore, it is necessary for the patient to be evaluated by a highly trained professional, and for neuroimaging studies to be used to rule out other pathologies, as well as genetic testing to identify associated variants and provide a more accurate diagnosis and appropriate treatment. Further studies are needed in this area to determine the relationship between DT and ataxia, using functional imaging and pathophysiological assessments.

CONCLUSION

Cerebellar ataxia is a neurological condition with clinical heterogeneity that can be identified concomitantly with DT. DT may be the initial presenting symptom. Several genes are responsible for ataxia; however, further observational studies are needed to establish an association between ataxia and dystonic tremor.

ACKNOWLEDGMENTS AND FUNDING

This work is being funded by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior- Brazil (CAPES)- Funding Code 001. The funder has no direct or indirect participation in the preparation and reporting of this Integrative Review.

REFERÊNCIAS

1. ASHIZAWA T, XIA G. Ataxia. CONTINUUM Lifelong Learning in Neurology, 2016; 22:1208–26.
2. BATES C, et al. Management of the ataxias towards best clinical practice. 3rd ed, 2016.
3. BECKER AE, et al. Atypical Presentation of Ataxia with Vitamin E Deficiency with Cervical and Upper Limb Dystonia in Two Siblings: 111. Annals Of Neurology, 2015; 78:S205.
4. BHATIA KP, et al. Consensus Statement on the classification of tremors. from the task force on tremor of the International Parkinson and Movement Disorder Society. Movement Disorders, 2018; 33(1):75–87.
5. BOVE F, et al. A role for accelerometry in the differential diagnosis of tremor syndromes. Functional neurology, 2018; 33(1):45–9.
6. CABALLERO OTEYZA A, et al. Motor protein mutations cause a new form of hereditary spastic paraplegia. Neurology 2014; 82(22):2007–16.
7. CAMARGO CHF, et al. Spinocerebellar ataxia type 21 (TMEM240) with tremor and dystonia. European Journal of Neurology, 2021; 28(8):e63–4.
8. CHOQUET K, et al. A novel frameshift mutation in FGF14 causes an autosomal dominant episodic ataxia. Neurogenetics, 2015; 16(3):233–6.
9. DEFAZIO G, et al. Is tremor in dystonia a phenotypic feature of dystonia? Neurology, 2015; 84(10):1053–9.
10. DOR T, et al. KIF1C mutations in two families with hereditary spastic paraparesis and cerebellar dysfunction. Journal of Medical Genetics, 2014; 51(2):137–42.
11. FASANO A, et al. The treatment of dystonic tremor: A systematic review. Journal of Neurology, Neurosurgery, and Psychiatry, 2014; 85(7):759–69.
12. FASANO A, et al. SCA 35 presenting as isolated treatment-resistant dystonic hand tremor. Parkinsonism & Related Disorders, 2017; 37:118–9.
13. FREUND HJ, et al. Subthalamic-thalamic DBS in a case with spinocerebellar ataxia type 2 and severe tremor- A unusual clinical benefit. Movement Disorders : official journal of the Movement Disorder Society, 2007; 22(5):732–5.
14. GANOS C, et al. Dystonic Tremor and Spasmodic Dysphonia in Spinocerebellar Ataxia Type 12. Movement Disorders Clinical Practice, 2014; 1(1):79–81.
15. HARDING AE. The clinical features and classification of the late onset autosomal dominant cerebellar ataxias. A study of 11 families, including descendants of the 'the Drew family of Walworth'. Brain, 1982; 105:1–28.

16. HOUGHTON DJ, et al. Botulinum toxin-responsive cervical dystonia in spinocerebellar ataxia type 5. Movement Disorders, 2011: S5–S5.
17. KEOGH MJ, et al. A novel de novo STXBP1 mutation is associated with mitochondrial complex I deficiency and late-onset juvenile-onset parkinsonism. Neurogenetics, 2015; 16(1):65–7.
18. KUO SH. Ataxia. CONTINUUM Lifelong Learning in Neurology, 2019; 25(4):1036–54.
19. LENKA A, JANKOVIC J. Tremor Syndromes: An Updated Review. Frontiers in Neurology, 2021; 12:684835.
20. MARCHIONNI E, et al. Kif1c variants are associated with hypomyelination, ataxia, tremor, and dystonia in fraternal twins. Tremor and Other Hyperkinetic Movements 2019; 9:10.7916/tohm.v0.641.
21. MARRAS C, et al. Nomenclature of genetic movement disorders: Recommendations of the international Parkinson and movement disorder society task force. Movement Disorders : official journal of the Movement Disorder Society, 2016; 31(4):436–57.
22. OUZZANI M, et al. Rayyan-a web and mobile app for systematic reviews. Systematic reviews, 2016; 5(1):210.
23. OYAMA G, et al. Deep brain stimulation for tremor associated with underlying ataxia syndromes: a case series and discussion of issues. Tremor and Other Hyperkinetic Movements, 2014; 4:228.
24. PAGE MJ, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ, 2021; 372:n71.
25. PANDEY S, SARMA N. Tremor in dystonia. Parkinsonism & Related Disorders, 2016; 29:3–9.
26. PERLMAN S. Evaluation and Management of Ataxic Disorders: An Overview for Physicians. Minneapolis, MN: National Ataxia Foundation, 2007.
27. RISO V, et al. A next generation sequencing-based analysis of a large cohort of ataxic patients refines the clinical spectrum associated with spinocerebellar ataxia 21. European Journal of Neurology, 2021; 28(8):2784–8.
28. RISO V, et al. NGS-based detection of a novel mutation in PRKCG (SCA14) in sporadic adult-onset ataxia plus dystonic tremor. Neurological Sciences: official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology, 2020; 41(10):2989–91.
29. ROSSI J, et al. Spasmodic dysphonia as a presenting symptom of spinocerebellar ataxia type 12. Neurogenetics 2019; 20(3):161–4.
30. RUSSELL CL. An overview of the integrative research review. Progress in Transplantation 2005; 15(1):8–13.
31. SCHWINGENSCHUH P, et al. Clinical neurophysiology for tremor: Common questions in clinical practice. Parkinsonism & Related Disorders, 2024; 130: 107196.
32. SHARAWAT IK, et al. Clinical Spectrum of TGM6-Related Movement Disorders: A New Report with a Pooled Analysis of 48 Patients. Journal of Neurosciences in Rural Practice, 2021; 12(4):656–65.
33. SOUZA MT de, et al. Integrative review: what is it? How to do it? Einstein (São Paulo), 2010; 8(1):102–6.
34. STERN C, et al. Developing the review question and inclusion criteria. American Journal of Nursing, 2014; 114(4):53–6.
35. SULLIVAN R, et al. Spinocerebellar ataxia: an update. Journal of Neurology, 2019; 266(2):533–44.
36. TSUBOI T, et al. Motor outcomes and adverse effects of deep brain stimulation for dystonic tremor: A systematic review. Parkinsonism & Related Disorders, 2020; 76:32–41.
37. VAN DE WARRENBURG BPC, et al. EFNS/ENS Consensus on the diagnosis and management of chronic ataxias in adulthood. European Journal of Neurology, 2014; 21(4):552–62.
38. WHITTEMORE R, KNAFL K. The integrative review: Updated methodology. Journal of Advanced Nursing, 2005; 52(5):546–53.
39. YAHYA V, et al. Dystonic Tremor as Main Clinical Manifestation of SCA21. Movement Disorders Clinical Practice, 2024; 11(11):1445-1450.
40. YÜCEL-YILMAZ D, et al. Clinical phenotype of hereditary spastic paraplegia due to KIF1C gene mutations across life span. Brain and Development, 2018; 40(6):458–64.