Marie hereditary cerebellar ataxia: recalling a classic eponym fallen into disuse

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ABSTRACT

Introduction. The term hereditary ataxia was introduced by Nikolaus Friedreich to designate a clinical-pathological description of a new form of early-onset familial ataxia, described in papers published between 1863 and 1877. This designation was soon replaced by the eponym Friedreich ataxia, leaving vacant the term hereditary ataxia. In 1893, Pierre Marie proposed that the term hereditary ataxia be reintroduced, adding the epithet cerebellar; many authors, particularly French-speaking researchers, replaced this designation with the eponym Marie ataxia.

Objective. To clarify the nosology of Marie ataxia, addressing the question as to whether or not continued use of the term is warranted.

Development. The original descriptions of Friedreich ataxia and Marie ataxia are reviewed in depth. Friedreich gave a magnificent description of a disease, which quite rightly carries his name. Marie based his proposal not on his own clinical-pathological studies, but on four previous reports by other authors. Essential features differentiating it from Friedreich ataxia were older age of onset and preservation of tendon reflexes. By 1893, two autopsy studies had revealed predominant cerebellar changes; because of this, Pierre Marie introduced the term hereditary cerebellar ataxia. Over the following four decades, eight additional studies showed that main lesions affected the spinal cord, involving the columns of Clarke, the anterior spinocerebellar tracts, and to a lesser degree the posterior spinocerebellar tracts and posterior columns. With no appropriate justification, Marie and his pupils proposed that ventral spinocerebellar tract degeneration was a distinctive feature of cerebellar hereditary ataxia. The notion of Marie ataxia received well-founded criticisms.

Conclusion. There is no justification to continue using the eponym Marie ataxia.

KEYWORDS

Cerebello-olivary atrophy, Friedreich ataxia, hereditary ataxia, hereditary cerebellar ataxia, International Classification of Diseases (ICD), Marie ataxia, olivopontocerebellar atrophy, OMIM, spinocerebellar degeneration

Introduction

The basic clinical-pathological hallmark of familial ataxias and paraplegias was outlined in the early 20th century; meanwhile, a series of cases not conforming to those so far described was appearing in the literature.[1-3] Ladame,[4] in a review of 165 cases of the so-called Friedreich ataxia (FA) from published reports, found that many were "incomplete, doubtful, or absolutely atypical to Friedreich." Under these circumstances, in 1893, Pierre Marie[5] drew attention to four families in which the clinical and pathological picture differed from those described by Friedreich: age of onset was older, tendon reflexes were increased, ophthalmoplegia or visual loss were present, and neither kyphoscoliosis nor foot deformity was observed.[6-9] By that time, two

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autopsies had shown pathological features restricted to the cerebellum.[6,7] Since the term hereditary ataxia had been left "vacant" after the acceptance of the eponym FA, Pierre Marie proposed that term be applied to families with normoreflexia or hyperreflexia, adding the epithet "cérébelleuse" on the basis of pathological findings from the two mentioned autopsy studies. This proposal was the starting point of a heated discussion over the last century, whose understanding obliges us to review the original descriptions of FA and Marie ataxia. The aim of this historical paper is to revise the evolution over time of the concepts of "hereditary cerebellar ataxia."

Material and methods

We reviewed the series of five papers published by Nikolaus Friedreich (1825-1882; Figure 1) between 1863 and 1877, in which he developed the concept of hereditary ataxia.[10-14]

Likewise, we reviewed the four families upon which Pierre Marie (1853-1940; Figure 1) based the concept of hereditary cerebellar ataxia.[5-9] Furthermore, we scrutinised additional pathological studies performed in members of these pedigrees, which were reported after the seminal paper by Pierre Marie in 1893.[15-21]

Finally, we call attention to two opposing lines of thought on the nosology of Marie ataxia: *i)* the view that it represents a distinct clinical-pathological entity; and *ii)* the argument that neither the clinical nor the pathological experience justifies its retention as a descriptive title of any form of disease.

Results

Friedreich ataxia

Between 1863 and 1877, Nikolaus Friedreich described a distinctive syndrome in nine patients (seven male and two female) belonging to five sibships.[10-14] The age of onset was near puberty. The established clinical picture consisted of progressive gait and limb ataxia and dysarthria. Other symptoms and signs appearing over the course of the disease included nystagmus, areflexia (cases II, VI, VII, and IX, examined after 1875), sensory loss, muscle weakness, scoliosis, diabetes and tachycardia. Autopsy studies of four patients showed a uniform pathological picture consisting of degeneration of the posterior funiculi, posterior spinal roots, columns of Clarke, and spinal lateral funiculi. As Friedreich's papers do not contain illustrations, Figures 2 and 3 show histological lesions to the spinal cord, spinal roots, posterior root ganglion, and sural nerve. Furthermore, Friedreich described cardiomyopathy in three cases. The proposal that the disorder he reported was a distinct entity, called hereditary ataxia, was initially met with considerable opposition. In 1868, Charcot suggested that Friedreich's patients actually presented multiple sclerosis.[4] In 1876, Friedreich[13] wrote:

> It is incomprehensible that anyone can still speak of disseminated sclerosis when I have provided the results of three detailed studies. I am pleased to know that some French pathologists (Bourdon and Topinard) have recognised my cases as examples of authentic non-complicated ataxia […] and I hope that Charcot, in the vast field of observation which he commands, will sooner or later find a case analogous to those I have described.

Ironically, Charcot recognised hereditary ataxia two years after Friedreich's death, which occurred in 1882.[4,22] Subsequent papers have demonstrated that FA may feature a loss of Purkinje cells with gliosis in cerebellar vermis[23] and degeneration of dentate nucleus.[24]

Thus, Nikolaus Friedreich not only introduced the concept of hereditary ataxia, but he was also the first author to precisely describe a clinical-pathological study of a form of spinocerebellar degeneration. Because of this, Brousse's proposal that the term Friedreich ataxia be applied to hereditary ataxia was soon universally accepted.[4]

Marie hereditary cerebellar ataxia

In this section, we will analyse the four pedigrees[6-9] that Pierre Marie used to propose the term hereditary cerebellar ataxia, thus filling the gap left by the recognition of Friedreich ataxia.[5] At the time of Pierre Marie publication, in 1893, just two autopsy studies were available that suggested a predominantly cerebellar pathology.[6,7] Let us summarise the clinical and pathological features of these four pedigrees, including pathological data from patients who died subsequently to Pierre Marie's description.

— Fraser's pedigree. In 1880, Fraser[7] reported the case of a brother and sister presenting similar semiology. There was no history of neurological disorders in their parents or grandparents. In the male patient, onset of symptoms with gait ataxia began at three years of age. Examination at age 30 revealed severe static and appendicular ataxia,

Figure 1. The protagonists of this story: Nikolaus Friedreich on the left (source: UB Graphische Sammlung. Universitätsbibliothek Heidelberg) and Pierre Marie on the right (source: photograph by Eugène Pirou, Biu Santé Portrait Collection).

right convergent strabismus, dysarthria, and optic atrophy. No dementia, paresis, sensory deficit, or nystagmus was observed. The patient died at the age of 33 years. The pathological findings are summarised in Table 1. Macroscopic examination showed reduced cerebellar volume. The histological study was limited to cerebellum and spinal cord. There was a marked reduction of Purkinje cells in the cerebellar cortex (estimated at about half of the normal amount). The cerebellar white matter and spinocerebellar fascicles were normal, though this "normality" should be viewed with great caution, as Weigert staining was not yet available.[16] According to Holmes,[25] this pedigree should be classified under cortical cerebellar atrophies. Figure 4 illustrates a case of cortical cerebellar atrophy from our files.

— Nonne's pedigree. In 1891 and 1905, Nonne reported the cases of 3 brothers with a similar clinical picture characterised by cerebellar ataxia and vision loss; their parents and four other siblings were unaffected.[6,15] Symptom onset with gait ataxia occurred at the ages of 10, 14, and 24 years, respectively. In the advanced stage of the disease, patients presented static and appendicular ataxia, dysarthria, nystagmus, moderate cognitive decline, vision loss with contraction of the visual fields and optic atrophy, and reduction of vertical and horizontal ocular movements. Sensitivity and tendon reflexes were preserved. Two autopsy studies, 30 and 43 years after clinical onset, demonstrated reduced cerebellar volume. In the histological study, lesions were restricted to degeneration of the optic nerves and anterior spinal roots.

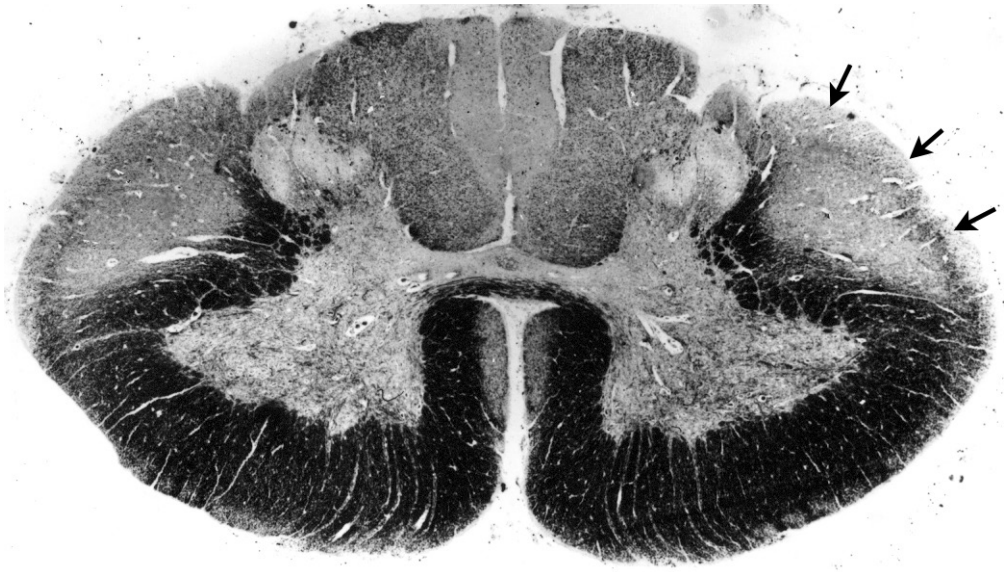

Figure 2. Thoracic spinal cord from a patient with Friedreich ataxia, displaying the classical phenotype studied by the authors. The myelin stain reveals pallor of the dorsal columns, the lateral corticospinal tracts, the anterior corticospinal tracts and the dorsal spinocerebellar tracts (arrows). Note that fasciculi graciles are more demyelinated than fasciculi cuneati, this finding indicating that posterior column degeneration is length-dependent. Klüver-Barrera method. Reproduced from Berciano et al.[2,3]

With such histopathological data, the classification of this disorder remains uncertain, though Holmes[25] tentatively included it under syndromes with congenital smallness of the central nervous system.

— Sanger Brown's pedigree. In 1892, Sanger Brown[9] reported a pedigree with 22 patients over four generations suffering from a homogeneous clinical picture comprising progressive cerebellar ataxia, vision loss, and spasticity. Age of onset ranged between 11 and 45 years, and disease duration from two to 27 years. Over the next decade, three autopsies were performed,[16,17] showing reduced volume of the cerebellum and brainstem. The histological findings are summarised in Table 1; lesions mainly affected the columns of Clarke and dorsal spinocerebellar tracts (Flechsig tracts); changes in other neural systems, including the griseum pontis, inferior olivary nuclei, and cerebellum, were inconstant and of a lesser degree.

— Klippel and Durante's pedigree. Also in 1892, these authors described a family in which three out of five siblings, their mother, and a maternal aunt presented a homogeneous clinical picture characterised by progressive cerebellar ataxia.[8] Later, Crouzon and Mathieu expanded the pedigree, adding a new affected member from the third generation.[26] Symptom onset occurred between 26 and 37 years of age. The established clinical picture included static and appendicular cerebellar ataxia, nystagmus, hyperreflexia, hypoesthesia, impassive face, and fasciculations, and amyotrophy in late stages of the disease. Although Klippel and Durante mentioned the presence of Argyll Robertson pupils and contraction of visual fields, these clinical signs were not corroborated by Londe.[27] The results of four autopsy studies are summarised in Table 1. The main lesions involved the spinal cord, including the columns of Clarke, spinocerebellar tracts (particularly the anterior tracts), anterior grey matter, and spinal roots; posterior columns were also constantly involved, but to a lesser degree. Changes to the olivo-ponto-cerebellar system were partial and inconstant. In the patient Chass., Guillain et al.[21] describe severe degeneration of cerebellar dentate nuclei, and mild changes in the locus niger. Intriguingly, Thomas and Roux[19] highlighted the need to expand of

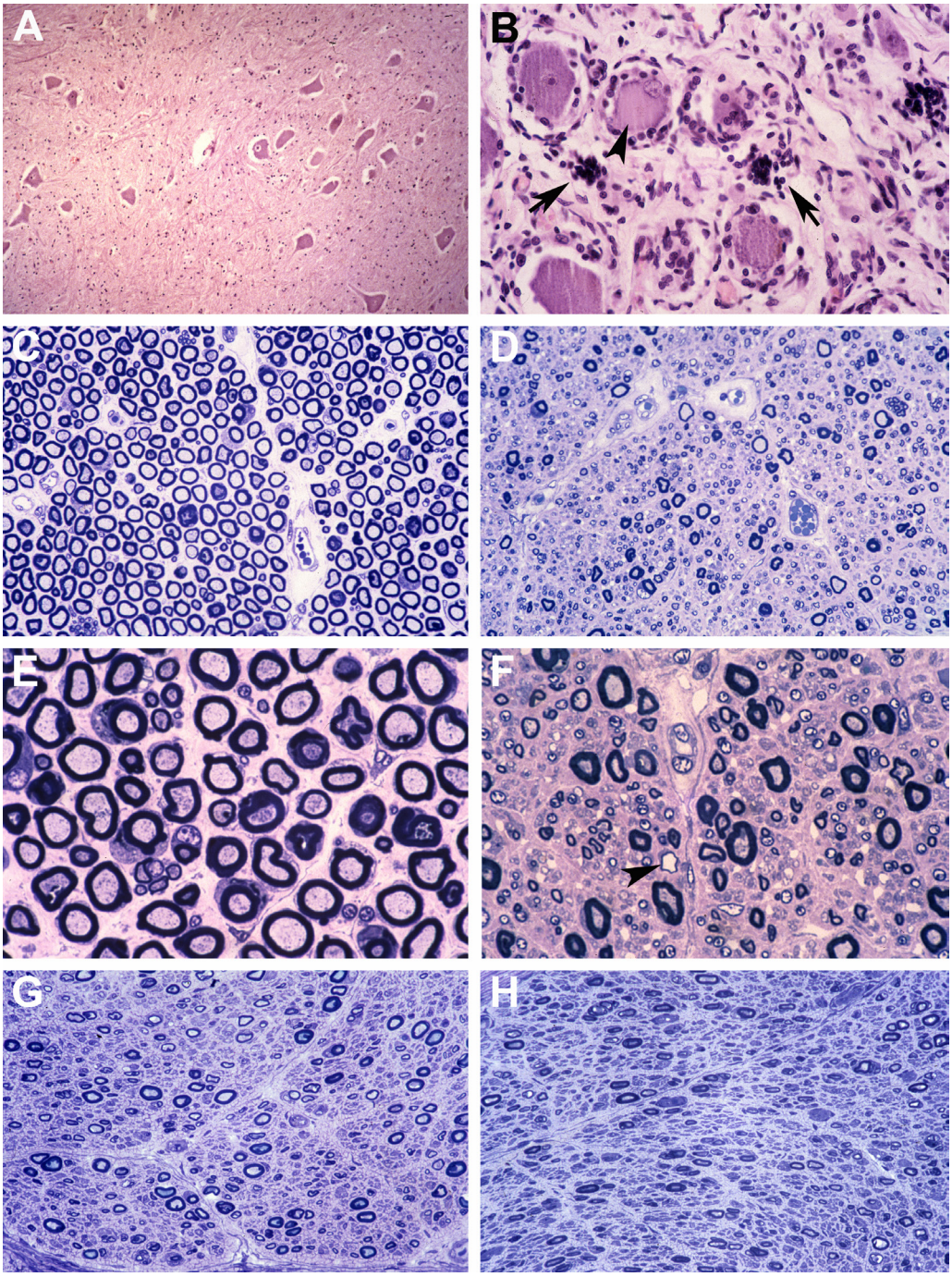

Figure 3. Spinal and peripheral nerve lesions in the same patient as the previous figure. A) Neurons in the anterior horn of the spinal cord at the L5 level are preserved (haematoxylin and eosin stain). B) L5 spinal ganglion showing loss of nerve cells with presence of Nageotte nodules (arrows) and proliferation of capsule cells; note also central chromatolysis in one of remaining nerve cells (arrowhead) (haematoxylin and eosin stain). Semithin sections of L5 ventral (C) and dorsal (D) roots showing a normal population of myelinated fibres in the ventral root and a marked reduction in the dorsal root (Toluidine blue stain). At higher magnification, note the preservation of myelinated fibres in the L5 ventral root (E), whereas the L5 dorsal root (F) presents a near-complete loss of larger myelinated fibres; note also the presence of remyelinated fibres (F, arrowhead) (Toluidine blue stain). G) Semithin transverse section of the sural nerve at the mid-calf level, showing marked loss of myelinated fibres, particularly larger fibres (Toluidine blue stain). H) Semithin transverse section of the sural nerve at the ankle, showing massive loss of large myelinated fibres (Toluidine blue stain). This proximal-to-distal gradient in the loss of myelinated fibres supports the notion of a dying-back process, with degeneration of the peripheral sensory axons slowly progressing from the distal portion of the fibre toward its cell body. Reproduced from Berciano et al.[2,3]

Table 1. Marie hereditary cerebellar ataxia: original neuropathological findings.

		Spinal cord						Brainstem – cerebellum					
Case No.	Author (reference)	Posterior columns	Fleschig tracts	Gowers tracts	Pyramidal tracts	Gray anterior horns	Clarke columns	Inferior olivary nuclei	Middle cerebellar peduncles	Griseum pontis	Cerebellar cortex	Cerebellar white matter	Other lesions
1	Fraser[7]	–	–	–	–	–	–	NM	NM	NM	++	NM	
2	Nonne[6], case A. Stub	–	–	–	–	–	–	–	–	NM	–	–	Ventral and dorsal spinal roots (+)
2a	Nonne[15], case F. Stub	–	–	–	–	–	–	–	–	NM	–	–	Optic nerve (++); ventral and dorsal spinal roots (+)
3	Meyer[16], case VI	+	+++	+	+	–	+++	+	NM	NM	+	–	
3a	Barker[17], case XVIII	+	+++	+	–	+	+++	+	–	–	–	–	Ventral and dorsal spinal roots (+) Cerebellar dentate nuclei (++)
3b	Barker[17], case XX	+/–	+++	+	–	–	+++	–	–	–	–	–	Fastigi (++) and dentate (++) nuclei
4	Switalski[18], case François H	++	+++	++	+	+++	+++	–	+	–	–	+	Ventral and dorsal spinal roots (+); optic nerve (++)
4a	Thomas and Roux[19], case Amelie H	+	++	+++	–	+	+++	–	+	–	–	–	Ventral and dorsal spinal roots (+)
4b	Rydel[20], case Louis H	++	+++	+++	–	+++	+++	++	+	NM	+	NM	Ventral spinal roots (+++)
4c	Guillain et al.[21], case Chass	+	+	+++	–	+++	NM	–	+/–	–	+	+	Dentate nuclei and superior cerebellar peduncles (+++); substantia nigra (+)

Cases 3 to 3a belong to the Sanger Brown pedigree[9] and cases 4 to 4c to the Klippel and Durante[8] pedigree.

(+++) = severe lesion; (++) = moderate lesion; (+) = mild lesion; (+/–) = doubtful lesion; (–) = no lesion detectable; (NM) = not mentioned.

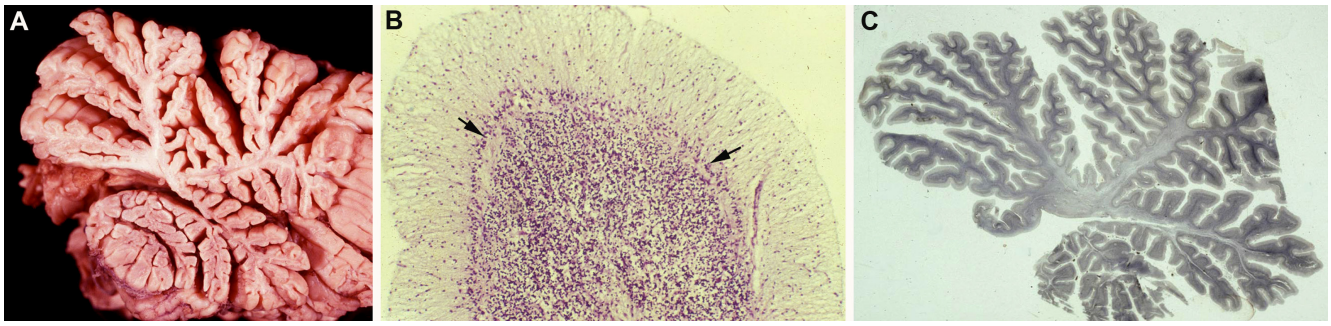

Figure 4. Pathological findings in an unpublished case of idiopathic late-onset cerebellar ataxia studied by the authors, who exhibited "pure" cerebellar semiology. A) Midsagittal section of the cerebellum showing severe atrophy of the vermis. B) A transverse section through a cerebellar folium showing complete loss of Purkinje cells with proliferation of Bergmann glia (arrows) (haematoxylin and eosin stain). C) Midsagittal section of the cerebellum showing extensive demyelination predominating in central segments of the album, a pattern characteristic of efferent pathway degeneration (cerebellofugal atrophy) (Naoumenko-Feigin method). Histological study performed by Prof José Ramón Ricoy.

the concept of hereditary cerebellar ataxia to include syndromes involving the spinocerebellar tracts.

Subsequent evolution of the concept of Marie ataxia

The notion of hereditary cerebellar ataxia presents numerous issues. Let us briefly comment on these.

After learning that the pathological background of hereditary cerebellar ataxia also included spinal cord changes, Pierre Marie himself and his students[28,29] proposed that the characteristic lesion was selective involvement of spinal fascicles anterior to the transverse commissure, namely with the anterior spinocerebellar tracts (Gowers tracts) presenting greater degeneration than the posterior tracts (Flechsig and corticospinal tracts, and posterior columns), which characteristically present degeneration in FA (Figure 2). Pierre Marie and Foix[28] wrote that "Le fait important est que cette dégénéresence associée à celle du fasceau de Gowers parait assez special à l'hérédo-ataxie cérébelleuse" ("The important fact is that this degeneration of the Gowers tracts seems to be quite particular to hereditary cerebellar ataxia"). This proposal has a blatant contradiction, given that the columns of Clarke, where the Flechsig tracts originate, were severely involved in the pedigrees published by Sanger Brown and by Klippel and Durante (Table 1). Be that as it may, the notion of predominant Gowers tract degeneration as a characteristic manifestation in Marie ataxia persisted in the French literature.[30-33] To complicate matters further, in a clinical-pathological study on olivo-ponto-cerebellar atrophy (OPCA), Hassin[34] asserted that Marie ataxia and familial OPCA were one and the same entity.

The most critical remarks on the nosology of Marie ataxia were made by Holmes[25] in 1907, when both OPCA and cerebellar-olivary degeneration had already been identified.[35,36] Holmes considered that the majority of cases of progressive cerebellar disease belonged to the class of OPCA, and more rarely to cerebello-olivary atrophy, thus outlining the pathological classification of ataxias; concerning Marie ataxia, he wrote:

> […] A convenient pigeon-hole in which to group together cases of obscure nature with some symptoms in common, and it may have been of service in drawing attention to such cases till it was possible to clarify them accurately; but neither clinical nor pathological experience justifies its retention as a descriptive title of a form of disease.

Indeed, Holmes' view prevailed when Greenfield[37] proposed a pathological classification of the ataxias, where he distinguished three main groups: *i) predominantly spinal forms* (FA and hereditary spastic paraplegia); *ii) spinocerebellar forms* (Menzel type of hereditary ataxia);

Figure 5. Professor Anita Harding (1952-1995) giving her keynote speech on "Hereditary ataxias" at the IX Spanish Congress of Neurology, which took place in Santander (May 26-29, 1993).

and *iii) predominantly cerebellar forms* (Holmes type of hereditary ataxia, OPCA, and dentatorubral atrophy).

More recently, Uchihara et al.[38] reviewed the clinical and pathological findings from an unpublished case from the Salpêtrière Hospital (Raymond Escourolle Laboratory of Neuropathology), belonging to the Klippel and Durante pedigree (*Haudebourg* family; autopsy number 1541; October 15, 1943). Clinical features included heredity compatible with autosomal dominant inheritance, spasticity, increased tendon reflexes, mask-like face, visual impairment, nuclear ophthalmoparesis, and exophthalmos, in addition to progressive cerebellar ataxia. Pathological lesions affected the spinal cord (anterior and posterior spinocerebellar tracts, columns of Clarke, anterior horns, and posterior columns), cerebellar dentate nuclei, griseum pontis, pallidum, oculomotor nuclei, and substantia nigra. The cerebellar cortex, inferior olivary nuclei, and lateral corticospinal tracts were preserved; interestingly, the authors also reviewed the pathological material from the patients Amélie H.[19] and François H.,[18] confirming that the inferior olivary nuclei were preserved (see Table 1). These histological features are characteristic of spinopontine atrophy, which is the typical pathological background in SCA3/Machado-Joseph disease.[1] It is worth noting that the clinico-pathological dissociation observed between florid pyramidal signs and preserved lateral corticospinal tracts had already been reported in familial OPCA.[39]

Discussion

In this historical review, we analysed the evolution and meaning of the term hereditary ataxia. In this sense, the series of five papers reported between 1863 and 1877 by Nikolaus Friedreich[10-14] represents one of the greatest milestones in the history of neurology. Friedreich not only introduced the concept of hereditary ataxia, but also reported a novel, well-defined clinical-pathological entity of early-onset progressive familial ataxia. Because of this, the proposal made shortly thereafter that the eponym Friedreich ataxia be used to refer to hereditary ataxia was universally accepted.[4] The nosology of FA was updated by Anita Harding (Figure 5), who proposed a set of diagnostic criteria, including autosomal recessive transmission, onset before 25 years of age, and tendon areflexia.[22,40] With the advent of modern genetics, the molecular basis of the disease was established, with the identification of a homozygous unstable GAA repeat expansion in the first intron of the *frataxin* gene on chromosome 9.[41] Subsequently, the clinical spectrum was considerably expanded, given that about one-quarter of the patients, despite being homozygous for the mutation, presented atypical FA, with older age at presentation or intact tendon reflexes.[42]

In his seminal paper, Pierre Marie aimed to distinguish FA from other familial ataxias exhibiting features differentiating them from that disorder, particularly later age of onset and preservation of tendon reflexes.[5] Marie based his proposal not on his personal experience, but rather on four pedigrees reported by other authors.[6-9] Retrospectively, Marie's paper has a number of shortcomings: *i)* the papers analysed had reported patients belonging to

families with autosomal dominant transmission (Sanger Brown's and Klippel and Durante's pedigrees) or recessive inheritance (Fraser's and Nonne's pedigrees probably fit in well here); *ii)* there is a mixture of patients with early-onset and late-onset symptoms, whose clinical semiology was far from uniform; and *iii)* the proposal of a pathological disorder of the cerebellum as the hallmark of hereditary ataxia was based on two autopsy studies available by 1893, one of which presented no evidence of microscopic cerebellar changes.[6,7] Under these circumstances, it is understandable that Gordon Holmes[25,43] so harshly critiqued Marie's proposal, advocating OPCA and cerebello-olivary atrophy as the only well-identified pathological patterns of hereditary cerebellar ataxia.

Seven autopsy studies performed in cases from the Sanger Brown and the Klippel and Durante pedigrees, between 1897 and 1904, revealed the relevance of spinal cord lesions, particularly those involving the columns of Clarke and spinocerebellar tracts (Table 1). These spinal pathological findings were confirmed by Pierre Marie himself and by his students[28,29] in four autopsy studies of hereditary cerebellar ataxia, in which the maximal lesions predominately affected the columns of Clarke and ventral spinocerebellar tracts (Gowers tracts), with lesser involvement of the posterior columns and dorsal spinocerebellar tracts (Flechsig tracts; Figure 6). French authors argued that, conversely to FA, in which lesions predominately affect posterior tracts (posterior columns, lateral corticospinal tracts, and Flechsig tracts), hereditary cerebellar ataxia may be a syndrome with more severe lesions in the Gowers tracts. Nevertheless, a subsequent well-documented histopathological study by Uchihara et al.,[38] analysing a case from Klippel and Durante's pedigree, showed similar changes in the ventral and dorsal spinocerebellar tracts. Furthermore, involvement of the columns of Clarke implies dysfunction of the dorsal spinocerebellar tracts, with or without patent demyelination. In short, we may interpret that the presence of predominant lesions in the Gowers tract as a distinctive feature of Marie ataxia is a flawed conception.[28,29] In any case, spinal lesions, particularly those involving the posterior columns, occur in almost two-thirds of cases of familial OPCA[1,39]; this finding does not support the notion that the pathological background of hereditary cerebellar ataxia affects spinal structures anterior to the transverse commissure of the grey matter.

Since the early 20th century, the International Classification of Diseases (ICD; CIE in Spanish), promoted by the World Health Organization, has been used in most hospital organisations. In the mid-1960s, the ICD-8 was operative for disease classification in Spain; in that classification, sub-paragraph 332.1 was devoted to "Hereditary cerebellar ataxia," that is to Marie ataxia. At the time, Spanish neurology was strongly influenced by French neurology, and particularly by the famous "Encyclopédie medico-chirurgical," in which Recondo[30] lent his support to the original description of "hérédoataxie cérébelleuse" by Pierre Marie. During the 13th World Congress of Neurology (Hamburg, 1985), Dr Bruce S. Schoenberg brought together a panel of ataxia experts chaired by Dr Anita Harding, with participation of one of the authors of the present review (J.B.); the objective was to prepare an updated paragraph of the Ataxia section (334.0-334.9) for the ICD-9. After a highly charged discussion with a French colleague, who was in favour of maintaining a subsection on Marie ataxia, the panel proposed to adopt the clinical/genetic classification of ataxias,[22,44] omitting any reference to hereditary cerebellar ataxia; this proposal came into effect in the

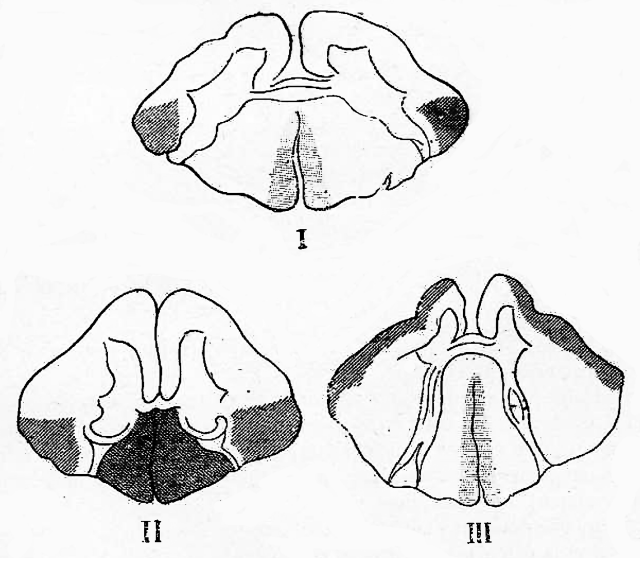

Figure 6. Diagrams of spinal cord lesions in hereditary spastic paraplegia (I), Friedreich ataxia (II), and hereditary cerebellar ataxia (III), as illustrated by Foix and Trétiakoff.[29] Note that lesions are posterior to the transverse commissure of the grey matter in Friedreich ataxia, and anterior this commissure in hereditary cerebellar ataxia (for details, see text).

ICD-10-CM (first edition published in 2016; available at https://www.cdc.gov/nchs/data/icd/icd10cm/2016/ICD-10CM_FY2016_Full_PDF.ZIP). It is worth noting that in the ICD-9-CM (January 2014, 9th revision, available at https://www.cdc.gov/nchs/icd/icd9cm.htm), subsection 334.2, devoted to "Primary cerebellar degeneration," still included both Marie ataxia and Sanger Brown ataxia. In any case, even the ICD-10 does not comply with the clinico-genetic classification of the ataxia, and therefore will require an extensive revision, including the following modifications (for a recent review, see reference by Witek et al[45]): *i)* there should be a subsection devoted to congenital ataxia; *ii)* regarding FA, there are more variants than FA with preserved tendon reflexes (eg, late-onset FA); *iii)* in other early-onset cerebellar ataxias, it would be better to mention the expanding group of autosomal recessive cerebellar ataxias (ARCA), which includes DNA repair-deficiency disorders; *iv)* there should be a specific subsection for autosomal dominant cerebellar ataxia or SCA; *v*) in the same way, there should be subsections devoted to episodic ataxias, mitochondrial ataxia and X-linked ataxia; *vi)* there should be at least three subsections for hereditary spastic paraplegia, according to inheritance pattern (autosomal dominant, autosomal recessive, and X-linked); *vii)* there should be a subsection devoted to idiopathic late-onset cerebellar ataxia different from multiple system atrophy of cerebellar type; and *viii)* given that inherited neurological disorders are in constant flux, it may be interesting to add a recommendation to consult the OMIM catalogue (Online Mendelian Inheritance in Man; accessible at https://www.omim.org/), which is periodically updated.

Conclusions

Starting from four previously reported ataxia pedigrees studied by others, in 1893 Pierre Marie proposed that the eponym hereditary ataxia be used for families with late onset and normoreflexia or hyperreflexia, adding the epithet "cerebellar" on the basis of the first two autopsies reported by the time. Subsequent pathological studies demonstrated that the main changes were localised both in the spinal cord and in cerebellar structures; furthermore, based upon their own autopsy studies, Pierre Marie himself and his students suggested that the disease may be correlated with predominant degeneration of the anterior spinocerebellar tracts, a misconception bearing in mind the systematic coexistence of severe atrophy of the columns of Clarke that can also account for ataxia. There is no longer any justification to continue using the eponym Marie ataxia.

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Conflicts of interest

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