atelier Euro-Méditerranée
des pathologies neuromusculaires
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orientation diagnostique devant une neuronopathie sensitive

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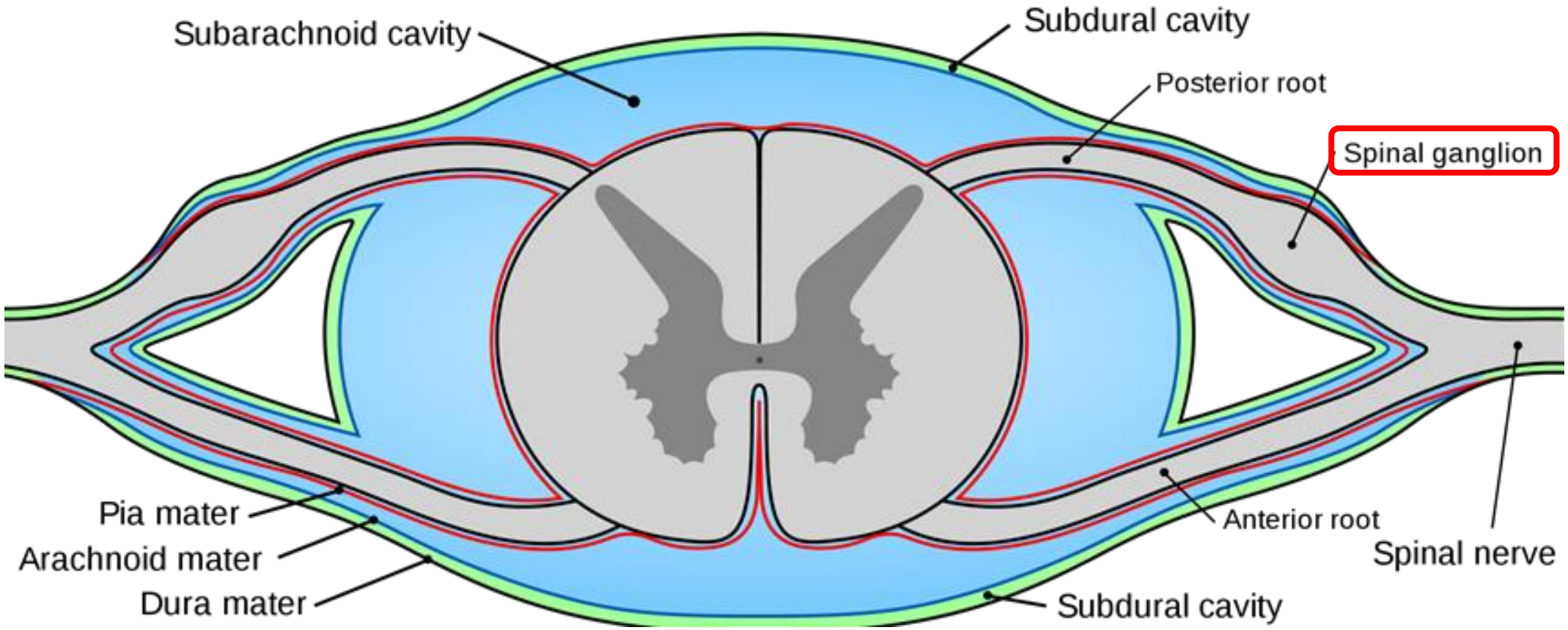
les neuronopathies sensitives

- **une entité neurologique spécifique**
  - atteinte sensitive pure, non longueur-dépendante, ROT altérés
  - conduit souvent à une perte d’ambulation
  - étiologies spécifiques

physiologie & physiopathologie


Subarachnoid cavity
Subdural cavity
Posterior root
Spinal ganglion
Pia mater
Arachnoid mater
Dura mater
Anterior root
Spinal nerve
Subdural cavity

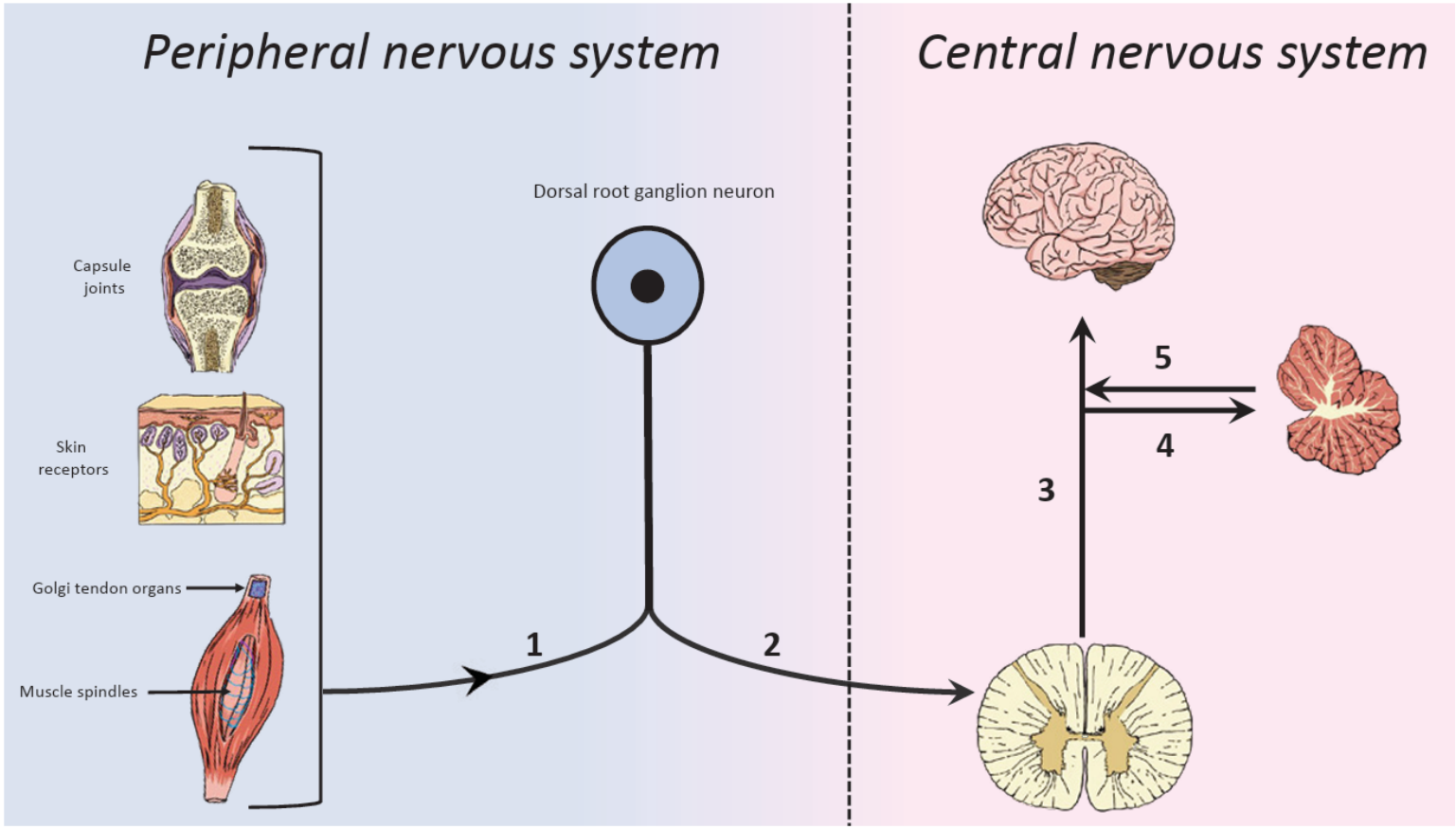


Figure 1 The DRG, a bridge between peripheral and CNS. (1) DRG peripheral process (large and small sensory fibres). (2) DRG central process (throughout posterior root). (3) Dorsal column medial lemniscus. (4) Spinocerebellar tracts. (5) Cerebellar efferent pathways, including cerebellothalamic tract. CNSs, central nervous systems; DRG, dorsal root ganglion

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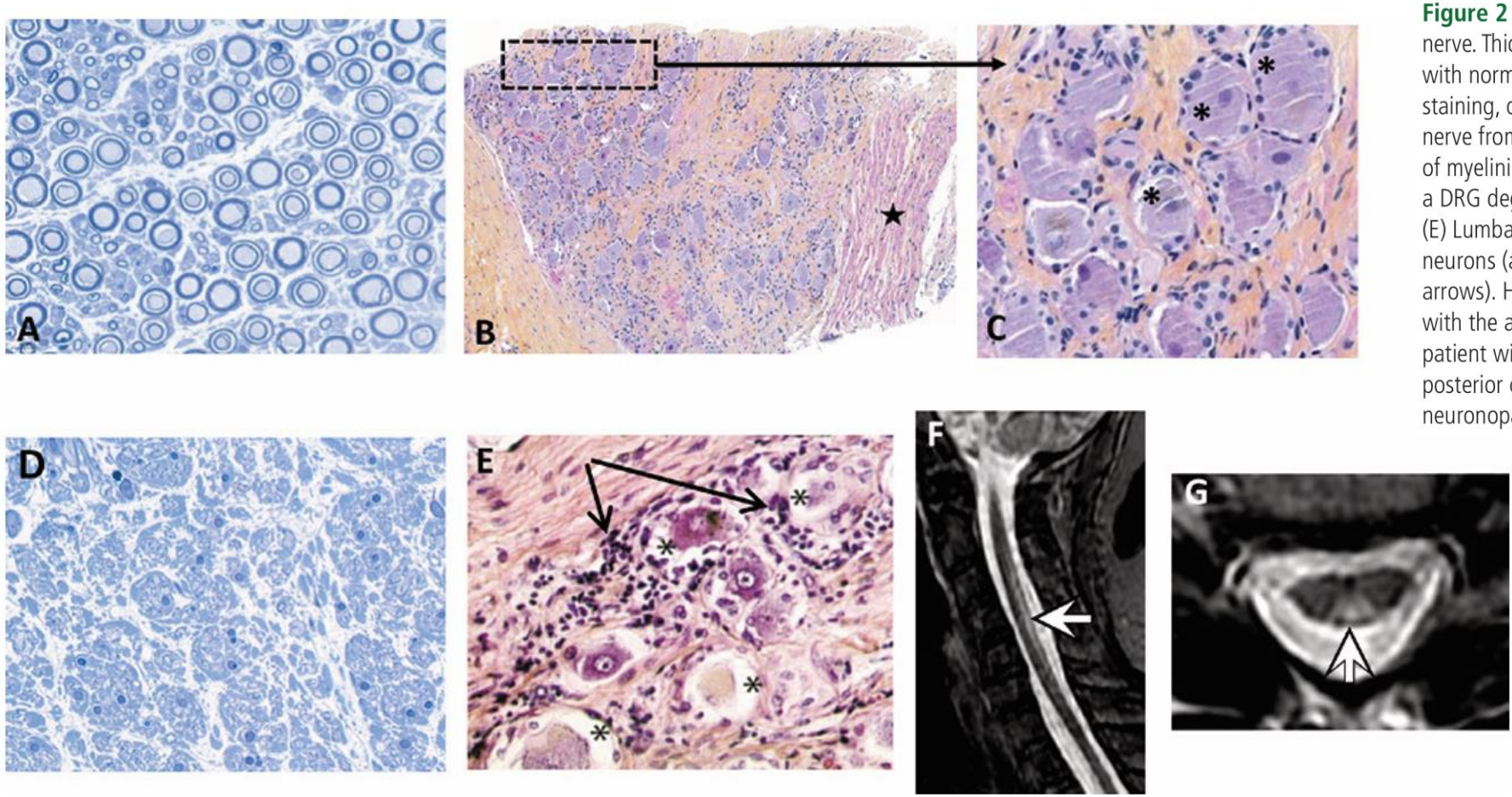

Figure 2 Pathology of normal and degenerating DRG. (A) Normal fibular nerve. Thionin blue staining, original magnification ×40. (B, C) Normal DRG with normal DRG cells (asterisk) and posterior root (black star). H&E saffron staining, original magnification ×10 (B) and ×40 (C). (D) Fibular sensory nerve from a patient with SN of autoimmune origin, showing severe loss of myelinic and amyelinic fibres without signs of regeneration, typical of a DRG degeneration. Thionin blue staining, original magnification ×40. (E) Lumbar DRG from a patient with anti-Hu SN, showing degenerating neurons (asterisks) and massive mononuclear cell infiltration (black arrows). H&E saffron staining, original magnification ×40. Reproduced with the authorisation of Kuntzer *et al*.[1] (F, G) Spinal cord MRI from a patient with autoimmune SN showing high signal intensity of the spinal posterior column (white arrow). DRG, dorsal root ganglion; SN, sensory neuronopathy.

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quelques caractéristiques du ganglion sensitif postérieur

- **une vascularisation dense & des capillaires fenêtrés**
  - réseau capillaire dense: région anatomique fortement vascularisée
  - capillaires perméables aux toxiques & aux anticorps
- **les neurones en T: de très grandes cellules avec des besoins énergétiques importants**
  - longueur axones souvent > 1 mètre
  - grande sensibilité aux carences énergétiques: mitochondrie, vitamines

Les ataxies sensitives par atteinte des voies proprioceptives conscientes.

Ataxie statique
- Mauvaise perception du sol
- Peu d'oscillations autour de la position d'équilibre. Pas de danse des tendons
- Chute brutale immédiate non latéralisée lors de la fermeture des yeux (signe de Romberg proprioceptif)

Ataxie locomotrice
- Démarche talonnante : le malade lance brusquement la jambe et pose le pied par le talon (il « ne sait plus » où se situe son pied dans l'espace par rapport au sol)

Marche proprioceptive
- Aggravation des troubles de la marche à l'occlusion des yeux et dans l'obscurité

Ataxie cinétique
- Oscillations avec rattrapage lors du maintien des attitudes
- Brusquerie du geste volontaire lors des épreuves doigt-nez, talon-genou ; mauvaise direction du geste compensée par des manœuvres de rattrapage (sous contrôle de la vue)
- Aggravation de la dysmétrie lors de la fermeture des yeux.
- La « main instable ataxique » est pseudo athétosique : les doigts sont animés de mouvements reptatoires, aggravés par l'occlusion des yeux, mais disparaissant ou très atténués lorsque la main repose sur un plan (qui supprime la pesanteur)

neuronopathies sensitives: critères diagnostics

CRITERES

Table 1 SN clinical and EDX criteria[14]

	Points
A. Ataxia in the lower or upper limbs at onset or full development.	+3.1
B. Asymmetrical distribution of sensory loss at onset or full development.	+1.7
C. Sensory loss not restricted to the lower limbs at full development.	+2.0
D. At least 1 SNAP absent or 3 SNAPs <30% of the LLN in the upper limbs, not explained by entrapment neuropathy.	+2.8
E. Less than two nerves with abnormal motor NCS in the lower limbs.	+3.1

A. SN is considered 'possible' if score >6.5 in a patient with a clinically pure sensory neuropathy.

B. SN is considered 'probable' if score >6.5 and if:

1. The initial workup does not show biological abnormalities or electroneuromyography findings excluding SN.
2. The patient has one of the following disorders: onconeural antibodies, a cancer within 5 years, cisplatin treatment, SS.
3. Or MRI shows abnormal hyperintense signal in the posterior column of the spinal cord.

C. SN is considered 'definite' if DRG degeneration is pathologically demonstrated (although DRG biopsy is not recommended).

Reproduced from Camdessanché *et al*[14] with permission of authors.
DRG, dorsal root ganglia; EDX, electrodiagnostic; LLN, lower limit of normal; NCS, nerve conduction study; SN, sensory neuronopathy; SNAP, sensory nerve action potential; SS, Sjögren's syndrome.

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neuronopathies sensitives acquises

ganglionopathies sensitives acquises

Type of SN	Onset	Cause	Other features
Paraneoplastic	Subacute	Small cell-lung cancer +++ Lung adenocarcinoma, prostate small cell carcinoma, gynaecological cancer, Hodgkin lymphoma	Cerebellar syndrome, motor involvement; anti Hu, anti-CV2/CRMP5 or antiamphiphysin Ab, CSF abnormalities (raised protein content, pleocytosis and OCBs)
Immune-mediated	Acute or subacute	Sjögren syndrome	Sicca syndrome; Anti SSA/SSB Ab, lymphocytic sialadenitis on salivary gland biopsy
		Anti-FGFR3 associated SN	Chronic course, symmetric involvement; anti-FGFR3 Ab
		Chronic ataxic neuropathy associated with antidisialosyl Ab	Ophthalmoplegia; antidisialosyl Ab, monoclonal gammopathy, cold agglutinins
		Autoimmune hepatitis, lupus, primary biliary cholangitis, coeliac disease	ANA, LAC, APL Ab, antimitochondrial Ab, anti-LKM Ab, antitransglutaminase and antiendomysium Ab
Toxic	Subacute	Platinum salts	None
		Vitamin B_6 intoxication	None
Nutritional	Acute or subacute	Vitamin B_{12} deficiency	Glossitis, pyramidal syndrome, impaired cognition; MB anaemia. Low serum vitamin B_{12}, high concentration of MMA and HC
	Chronic	Vitamin E deficiency	Head tremor. Low serum vitamin E.
Infectious	Acute or subacute	HIV, HTLV-1, mycoplasma, Zika, Rickettsia conorii	Specific serological testing

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ganglionopathies acquises

- **la plus fréquente**: sels de platine

- **quelques repères pratiques**

  - **homme, fumeur, > 50 ans: pensez paranéoplasique!**
  - **femme, < 50 ans: pensez GSS!**
  - **toujours penser à la carence en vitamine B12!**

Brain Commun. 2023 Sep 21;5(5):fcad247. doi: 10.1093/braincomms/fcad247. eCollection 2023.

Revisiting anti-Hu paraneoplastic autoimmunity: phenotypic characterization and cancer diagnosis

Macarena Villagrán-García [1 2], Antonio Farina [1 2 3], Sergio Muñiz-Castrillo [1 4], Valentin Wucher [1 2], Maroua Dhairi [1], Noémie Timestit [1 5], Nicolás Lundahl Ciano-Petersen [1 6], Alberto Vogrig [1 7 8], Géraldine Picard [1], Marie Benaiteau [1], Dimitri Psimaras [9 10], Ani Valentinova Petrova [11], Tifanie Alberto [12], Jérôme Aupy [13 14], Marine Giry [9 10], Véronique Rogemond [1 2], Virginie Desestret [1], Bastien Joubert [1 2], Jérôme Honnorat [1 2]

Abstract

Anti-Hu are the most frequent antibodies in paraneoplastic neurological syndromes, mainly associated with an often limited stage small cell lung cancer. The clinical presentation is pleomorphic, frequently multifocal. Although the predominant phenotypes are well characterized, how different neurological syndromes associate is unclear. Likewise, no specific study assessed the performance of new-generation CT and PET scanners for cancer screening in these patients. Herein, we aimed to describe the clinical pattern and cancer screening in a retrospective cohort of 466 patients with anti-Hu autoimmunity from the French Reference Centre on Paraneoplastic Neurological Syndromes registry. Clinical presentation, cancer screening and diagnosis were analysed. Among the 466 patients, 220 (54%) had multifocal neurological involvement. A hierarchical cluster analysis grouped the patients into (i) mainly limbic encephalitis, (ii) predominantly peripheral neuropathy and (iii) broad involvement of the nervous system (mixed group). Compared with limbic encephalitis and mixed groups, patients in the neuropathy group more frequently had a chronic onset of symptoms (29 versus 13 and 17%), elevated CSF proteins (83 versus 47 and 67%) and died from cancer progression (67 versus 15 and 28%; all $P < 0.05$). No significant difference in overall survival was observed between groups. Dysautonomia and brainstem signs were associated with a higher risk of death from the neurological cause; cancer diagnosis was the main predictor of all-cause death, especially when diagnosed within 2 years from clinical onset (all $P < 0.05$). Three hundred and forty-nine (75%) patients had cancer: in 295 (84%) neurological symptoms preceded tumour diagnosis, being lung cancer in 262 (89%), thereof small cell lung cancer in 227 (87%). First CT scan revealed lung cancer in 205/241 (85%), and PET scan shortened the interval to diagnosis when the initial CT scan was negative [7 months (1-66) in 27 patients versus 14 months (2-45) in 6; $P < 0.001$]. Although cancer diagnosis mostly occurred within 2 years from clinical onset, 13/295 (4%) patients exceeded that threshold. Conversely, 33 patients (7%) were 'cancer-free' after 2 years of follow-up. However, 13/33 (39%) had initial suspicious imaging findings that spontaneously regressed. In conclusion, although anti-Hu autoimmunity clinical presentation is mostly multifocal, we observed patients with a predominant limbic syndrome or isolated sensory neuropathy. Early implementation of PET scan shortens the interval to cancer diagnosis, which was the strongest predictor of death, especially if diagnosed ≤2 years from clinical onset. As cancer was diagnosed >2 years after clinical onset in few patients, screening should be extended up to 5 years. In addition, tumour regression was suspected in a substantial proportion of 'cancer-free' patients.

Anti-**FGFR3** antibody epitopes are functional sites and correlate with the neuropathy pattern.

Tholance Y, Antoine JC, Mohr L, Jung M, Reynaud-Federspiel E, Ferraud K, Camdessanché JP, Moritz CP.

J Neuroimmunol. 2021 Dec 15;361:577757. doi: 10.1016/j.jneuroim.2021.577757. Epub 2021 Oct 30.

PMID: 34768040

The aim of this study was to identify the epitope(s) of **anti**-**FGFR3** autoantibodies and potential epitope-dependent clinical subtypes. Using SPOT methodology, five specific candidate epitopes, three in the juxtamembrane domain (JMD) and two in the tyrosine kinase doma ...

What is the pattern of the neuropathy associated with **anti**-**FGFR3** antibodies?

Tholance Y, Moritz CP, Camdessanché JP, Antoine JC.

Eur J Neurol. 2020 Oct;27(10):e58. doi: 10.1111/ene.14376. Epub 2020 Jul 1.

PMID: 32498117 No abstract available.

Clinical characterisation of sensory neuropathy with **anti**-**FGFR3** autoantibodies.

Tholance Y, Moritz CP, Rosier C, Ferraud K, Lassablière F, Reynaud-Federspiel E, França MC Jr, Martinez ARM, Camdessanché JP, Antoine JC; anti-FGFR3 antibody Study Group.

J Neurol Neurosurg Psychiatry. 2020 Jan;91(1):49-57. doi: 10.1136/jnnp-2019-321849. Epub 2019 Nov 5.

PMID: 31690697

Detailed clinical and paraclinical data were collected for each **anti**-**FGFR3**-positive patient and as control for **anti**-**FGFR3**-negative patients from the same centres ('center-matched'). ...CONCLUSIONS: **Anti**-**FGFR3** antibodies occur in a subgrou ...

Anti–AGO1 Antibodies Identify a Subset of Autoimmune Sensory Neuronopathy

Christian P Moritz [1], Yannick Tholance [2], Pierre-Baptiste Vallayer [2], Le-Duy Do [2], Sergio Muñiz-Castrillo [2], Veronique Rogemond [2], Karine Ferraud [2], Coralie La Marca [2], Jerome Honnorat [2], Martin Killian [2], Stéphane Paul [2], Jean-Philippe Camdessanché [2], Jean-Christophe G Antoine [2]

Affiliations + expand

PMID: 37072227 PMCID: PMC10112859 DOI: 10.1212/NXI.0000000000200105

Abstract

Background and objectives: Autoantibodies (Abs) improve diagnosis and treatment decisions of idiopathic neurologic disorders. Recently, we identified Abs against Argonaute (AGO) proteins as potential autoimmunity biomarkers in neurologic disorders. In this study, we aim to reveal (1) the frequency of AGO1 Abs in sensory neuronopathy (SNN), (2) titers and IgG subclasses, and (3) their clinical pattern including response to treatment.

Methods: This retrospective multicentric case/control study screened 132 patients with SNN, 301 with non-SNN neuropathies, 274 with autoimmune diseases (AIDs), and 116 healthy controls (HCs) for AGO1 Abs through ELISA. Seropositive cases were also tested for IgG subclasses, titers, and conformation specificity.

Results: AGO1 Abs occurred in 44 patients, comprising significantly more of those with SNN (17/132 [12.9%]) than those with non-SNN neuropathies (11/301 [3.7%]; $p = 0.001$), those with AIDs (16/274 [5.8%]; $p = 0.02$), or HCs (0/116; $p < 0.0001$). Ab titers ranged from 1:100 to 1:100,000. IgG subclass was mainly IgG1, and 11/17 AGO1 Ab-positive SNN (65%) had a conformational epitope. AGO1 Ab-positive SNN was more severe than AGO1 Ab-negative SNN (e.g., SNN score: 12.2 vs 11.0, $p = 0.004$), and they more frequently and more efficiently responded to immunomodulatory treatments than AGO1 Ab-negative SNN (7/13 [54%] vs 6/37 [16%], $p = 0.02$). Regarding the type of treatments more precisely, this significant difference was confirmed for the use of IV immunoglobulins (IVIg) but not for steroids or second-line treatments. Multivariate logistic regression adjusted for potential confounders showed that AGO1 Ab positivity was the only predictor of response to treatment (OR 4.93, 1.10-22.24 95% CI, $p = 0.03$).

Discussion: Although AGO Abs are not specific for SNN, based on our retrospective data, they may identify a subset of cases with SNN with more severe features and a possibly better response to IVIg. The significance of AGO1 Abs in clinical practice needs to be explored on a larger series.

CASE REPORT

Regressive pyridoxine-induced sensory neuronopathy in a patient with homocystinuria

Andoni Echaniz-Laguna,[1] Rachel Mourot-Cottet,[2] Esther Noel,[2] Jean-Baptiste Chanson[1]

Learning points

- Pyridoxine (vitamin B6) is an essential vitamin playing a crucial role in amino acid metabolism.
- Pyridoxine is used for the treatment of isoniazid side-effects, pyridoxine-dependent epilepsy and cystathionine beta-synthase deficiency (homocystinuria).
- Physicians should be aware that vitamin B6 hypervitaminosis is neurotoxic.
- Pyridoxine uptake above 50 mg/day may provoke a progressive sensory neuronopathy with ataxia and impaired sensation in the extremities.
- Pyridoxine-linked neuropathy may be reversible, even after prolonged ingestion of vitamin B6 for more than 20 years.

neuronopathies sensitives génétiques

ganglionopathies sensitives génétiques

Cause	Onset	Mode of inheritance	Other features
Mitochondrial disorders	Chronic	Autosomal recessive (mainly *POLG* gene mutations) Maternal inheritance (mtDNA mutations)	Ophthalmoplegia, ptosis, hearing loss, cognitive/psychiatric symptoms, muscle weakness, diabetes, cardiomyopathy, epilepsy
FRDA	Chronic	Autosomal recessive	Cerebellar syndrome, pyramidal syndrome, skeletal deformities, cardiomyopathy
AVED	Chronic	Autosomal recessive	Cerebellar syndrome, pyramidal syndrome, skeletal deformities, head tremor, dystonia, retinitis pigmentosa
CANVAS	Chronic	Autosomal recessive	Cerebellar ataxia, vestibular areflexia, chronic cough
Abetalipoproteinaemia	Chronic	Autosomal recessive	Childhood-onset, chronic diarrhoea, failure to thrive, retinitis pigmentosa
PCARP syndrome	Chronic	Autosomal recessive	Retinitis pigmentosa
FXTAS	Chronic	X-linked	Cerebellar ataxia, intentional tremor
SCA 1, 2, 3, 4, 7	Chronic	Autosomal dominant	Cerebellar syndrome, visual loss, dystonia, Parkinsonism, pyramidal syndrome
RNF170 gene mutation	Chronic	Autosomal dominant	Vestibular areflexia (CANVAS-like syndrome)

Fargeot, JNNP 2021

ganglionopathies héréditaires

- la plus fréquente:
  - ataxie de Friedreich (FRDA):
    - syndrome cérébelleux
    - syndrome pyramidal
    - pied creux
    - scoliose
    - cardiomyopathie

Delayed-onset Friedreich's ataxia revisited

Claire Lecocq [1], Perrine Charles [2], Jean-Philippe Azulay [3], Wassilios Meissner [4], Myriam Rai [5], Karine N'Guyen [3], Yann Péréon [6], Nelly Fabre [7], Elsa Robin [3], Sylvie Courtois [8], Lucie Guyant-Maréchal [9], Fabien Zagnoli [10], Gabrielle Rudolf [1], Mathilde Renaud [1], Mathieu Sévin-Allouet [11], Fabien Lesne [12], Nick Alaerts [5], Cyril Goizet [13], Patrick Calvas [14], Alexandre Eusebio [3], Claire Guissart [15], Pascal Derkinderen [11], Francois Tison [4], Alexis Brice [16], Michel Koenig [17], Massimo Pandolfo [18], Christine Tranchant [19], Alexandra Dürr [16], Mathieu Anheim [20]

Affiliations + expand

PMID: 26388117 DOI: 10.1002/mds.26382

Abstract

Background: Friedreich's ataxia usually occurs before the age of 25. Rare variants have been described, such as late-onset Friedreich's ataxia and very-late-onset Friedreich's ataxia, occurring after 25 and 40 years, respectively. We describe the clinical, functional, and molecular findings from a large series of late-onset Friedreich's ataxia and very-late-onset Friedreich's ataxia and compare them with typical-onset Friedreich's ataxia.

Methods: Phenotypic and genotypic comparison of 44 late-onset Friedreich's ataxia, 30 very late-onset Friedreich's ataxia, and 180 typical Friedreich's ataxia was undertaken.

Results: Delayed-onset Friedreich's ataxia (late-onset Friedreich's ataxia and very-late-onset Friedreich's ataxia) had less frequently dysarthria, abolished tendon reflexes, extensor plantar reflexes, weakness, amyotrophy, ganglionopathy, cerebellar atrophy, scoliosis, and cardiomyopathy than typical-onset Friedreich's ataxia, along with less severe functional disability and shorter GAA expansion on the smaller allele ($P < 0.001$). Delayed-onset Friedreich's ataxia had lower scale for the assessment and rating of ataxia and spinocerebellar degeneration functional scores and longer disease duration before wheelchair confinement ($P < 0.001$). Both GAA expansions were negatively correlated to age at disease onset ($P < 0.001$), but the smaller GAA expansion accounted for 62.9% of age at onset variation and the larger GAA expansion for 15.6%. In this comparative study of late-onset Friedreich's ataxia and very-late-onset Friedreich's ataxia, no differences between these phenotypes were demonstrated.

Conclusion: Typical- and delayed-onset Friedreich's ataxia are different and Friedreich's ataxia is heterogeneous. Late-onset Friedreich's ataxia and very-late-onset Friedreich's ataxia appear to belong to the same clinical and molecular continuum and should be considered together as "delayed-onset Friedreich's ataxia." As the most frequently inherited ataxia, Friedreich's ataxia should be considered facing compatible pictures, including atypical phenotypes (spastic ataxia, retained reflexes, lack of dysarthria, and lack of extraneurological signs), delayed disease onset (even after 60 years of age), and/or slow disease progression.

maladie de Friedreich tardive: attention aux LOFA & VLOFA!

- formes tardives (LOFA) > 25 ans
- formes très tardives (VLOFA) > 40 ans

autres ganglionopathies héréditaires

- maladies mitochondriales:
  - syndrome SANDO -gène *POLG*
  - autres gènes possibles, e.g. TWINKLE

- déficit en vitamine E (AVED):
  - cardiomyopathie
  - syndrome cérébelleux
  - rétinite pigmentaire

- le CANVAS

ganglionopathies mitochondriales –gène *POLG*

The wide *POLG*-related spectrum: An integrated view

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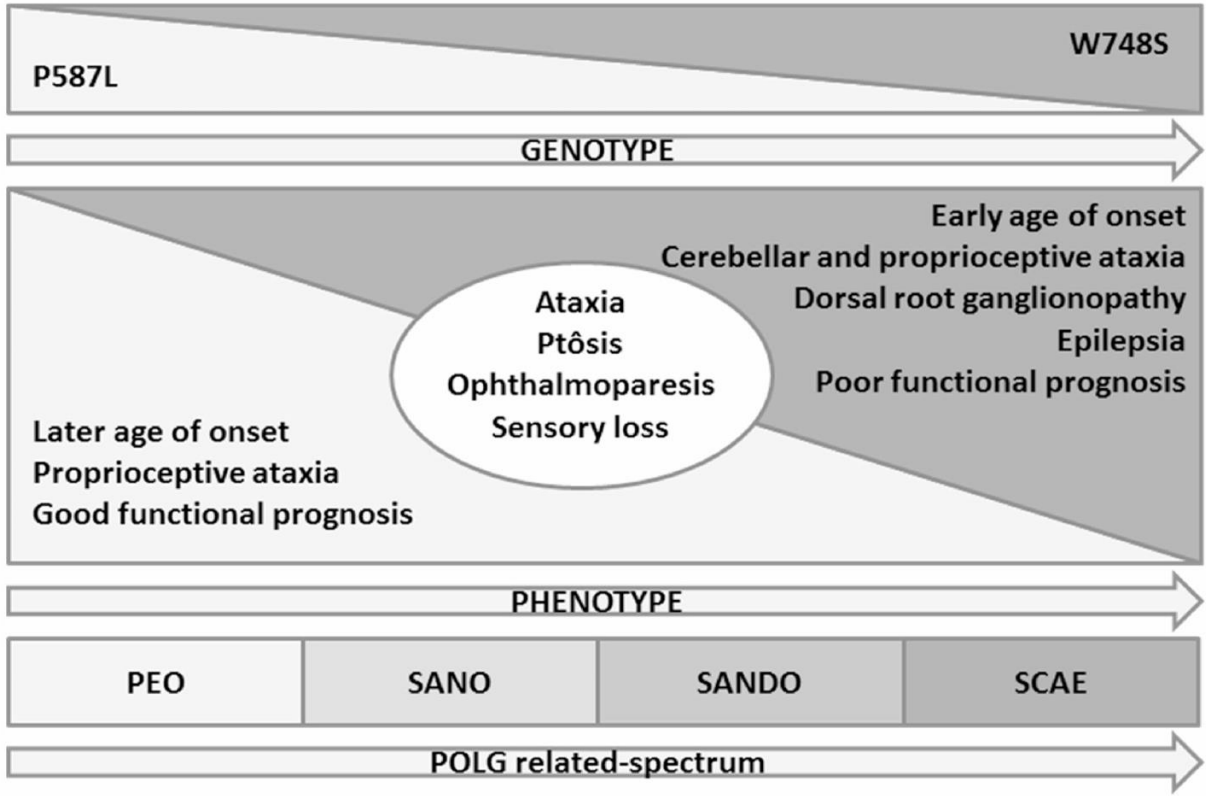


ganglionopathies mitochondriales –gène *TWINKLE*

Table 1 The clinical time course of five patients with the heterozygous R374W variation in the Twinkle protein

	Pto	Oph	Hear	Senso	Myo	Abnormal gait	Dysphagia	Dysphonia	Dementia
Patient BIII-7 (age 42)	+								
Patient BII-3 (age 62)	+	+	+	+	+				
Patient BII-1 (age 64)	+	+	+	+	+				
Patient AIII-5 (age 81)	+	+	+	+	+	+	+	+	+
Patient AIII-1 (age 82)	+	+	+	+	+	+	+	+	+

Age of patients is indicated in years

+ a symptom or a clinical sign is present, *Pto* ptosis, *Oph* ophthalmoplegia, *Hear* hearing loss, *Senso* sensory neuropathy, *Myo* myopathy

A novel variation in the Twinkle linker region causing late-onset dementia

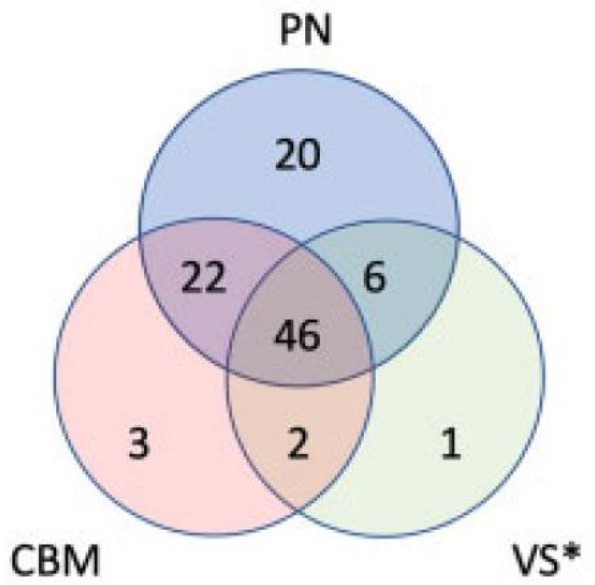
Andoni Echaniz-Laguna · Jean-Baptiste Chanson · Jean-Marie Wilhelm · François Sellal · Martine Mayençon · Michel Mohr · Christine Tranchant · Bénédicte Mousson de Camaret

le CANVAS

- *Cerebellar Ataxia with Neuropathy & Vestibular Areflexia Syndrome*
- autosomique récessif
- début après 50 ans: ataxie proprioceptive
- discrets signes vestibulaires et/ou cérébelleux
- premier signe clinique: toux chronique
- diagnostic: expansion intronique AAGGG gène *RFC1*

Biallelic *RFC1*-expansion in a French multicentric sporadic ataxia cohort

Solveig Montaut[1] · Nadège Diedhiou[2,3] · Pauline Fahrer[1] · Cécilia Marelli[4,5] · Benoit Lhermitte[6] · Laura Robelin[7,8] · Marie Claire Vincent[1] · Lucas Corti[11] · Guillaume Taieb[11] · Odile Gebus[1] · Gabrielle Rudolf[1,12] · Julien Tarabeux[13] · Nicolas Dondaine[13] · Matthieu Canuet[14] · Marilyne Almeras[15] · Mehdi Benkirane[9,10] · Lise Larrieu[9,10] · Jean-Baptiste Chanson[16] · Aleksandra Nadaj-Pakleza[16] · Andoni Echaniz-Laguna[17,18] · Cécile Cauquil[17] · Béatrice Lannes[7] · Jamel Chelly[12,13,19] · Mathieu Anheim[1,2,19] · Hélène Puccio[2,3] · Christine Tranchant[1,2,19]



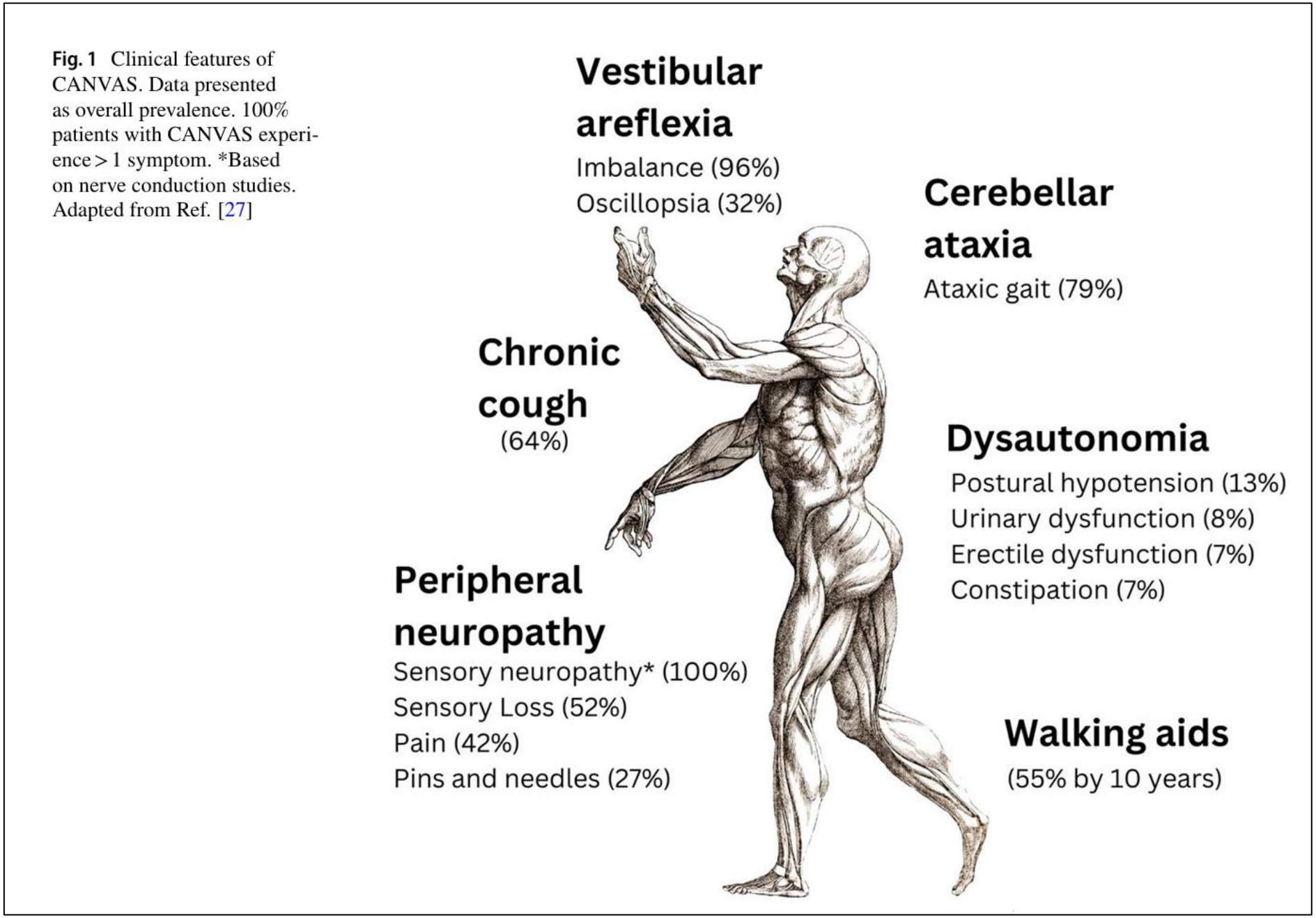


Fig. 1 Clinical features of CANVAS. Data presented as overall prevalence. 100% patients with CANVAS experience > 1 symptom. *Based on nerve conduction studies. Adapted from Ref. [27]

FXTAS: new insights and the need for revised diagnostic criteria

Emmanuelle Apartis [1], Anne Blancher, Wassilios G Meissner, Lucie Guyant-Maréchal, David Maltête, Thomas De Broucker, André-Pierre Legrand, Hichem Bouzenada, Hung Tran Thanh, Magali Sallansonnet-Froment, Adrien Wang, François Tison, Carole Roué-Jagot, Frédéric Sedel, Perrine Charles, Sandra Whalen, Delphine Héron, Stéphane Thobois, Alice Poisson, Gaetan Lesca, Anne-Marie Ouvrard-Hernandez, Valérie Fraix, Stephane Palfi, Marie-Odile Habert, Bertrand Gaymard, Jean-Claude Dussaule, Pierre Pollak, Marie Vidailhet, Alexandra Durr, Jean-Claude Barbot, Véronique Gourlet, Alexis Brice, Mathieu Anheim

Affiliations + expand

PMID: 23077007 DOI: 10.1212/WNL.0b013e318271f7ff

Abstract

Objective: Fragile X-associated tremor ataxia syndrome (FXTAS) is defined by FMR1 premutation, cerebellar ataxia, intentional tremor, and middle cerebellar peduncle (MCP) hyperintensities. We delineate the clinical, neurophysiologic, and morphologic characteristics of FXTAS.

Methods: Clinical, morphologic (brain MRI, (123)I-ioflupane SPECT), and neurophysiologic (tremor recording, nerve conduction studies) study in 22 patients with FXTAS, including 4 women.

Results: A total of 43% of patients had no family history of fragile X syndrome (FXS), which contrasts with previous FXTAS series. A total of 86% of patients had tremor and 81% peripheral neuropathy. We identified 3 electroclinical tremor patterns: essential-like (35%), cerebellar (29%), and parkinsonian (12%). Two electrophysiologic patterns evocative of non-length-dependent (56%) and length-dependent sensory neuropathy (25%) were identified. Corpus callosum splenium (CCS) hyperintensity was as frequent (68%) as MCP hyperintensities (64%). Sixty percent of patients had parkinsonism and 47% abnormal (123)I-ioflupane SPECT. Unified Parkinson's Disease Rating Scale motor score was correlated to abnormal (123)I-ioflupane SPECT ($p = 0.02$) and to CGG repeat number ($p = 0.0004$). Scale for the assessment and rating of ataxia correlated with dentate nuclei hyperintensities ($p = 0.03$) and CCS hyperintensity was a marker of severe disease progression ($p = 0.04$).

Conclusions: We recommend to include in the FXTAS testing guidelines both CCS hyperintensity and peripheral neuropathy and to consider them as new major radiologic and minor clinical criterion, respectively, for the diagnosis of FXTAS. FXTAS should also be considered in women or when tremor, MCP hyperintensities, or family history of FXS are lacking. Our study broadens the spectrum of tremor, peripheral neuropathy, and MRI abnormalities in FXTAS, hence revealing the need for revised criteria.

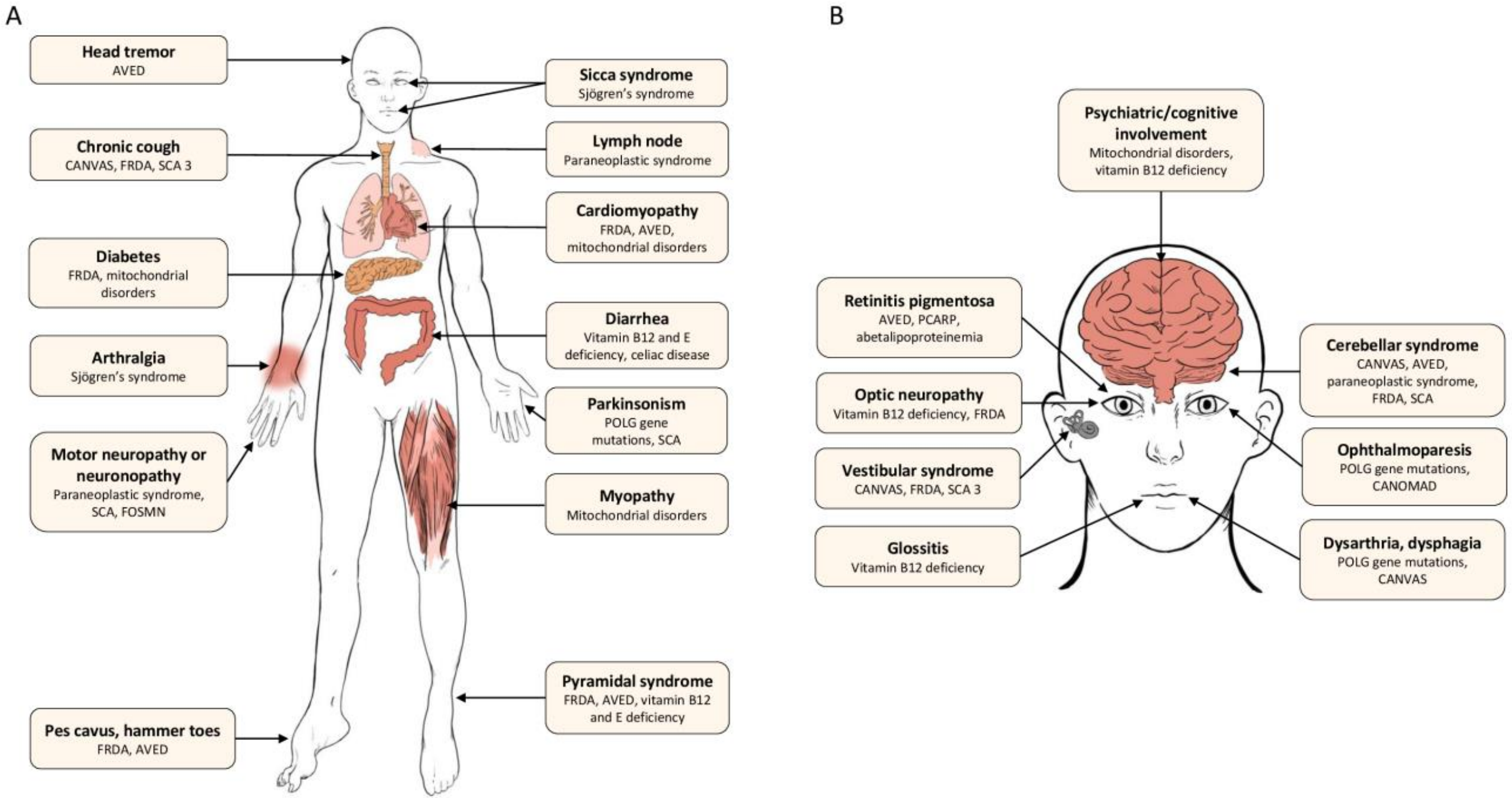
le FXTAS

- 81% des FXTAS ont une PN
- 56% de ces PN sont des ganglionopathies

ganglionopathies héréditaires « traitables »

- ataxie de Friedreich: omaveloxolone -SKYCLARYS
- déficit en vitamine E (AVED): vitamine E
- abétaliprotéinémie: supplémentation vitamines

neuronopathies sensitives: orientation diagnostique



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neuronopathies sensitives: prise en charge

Identifying a therapeutic window in acute and subacute inflammatory sensory neuronopathies

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A B S T R A C T

Background: Patients with inflammatory sensory neuronopathy (SNN) may benefit from immunomodulatory or immunosuppressant treatments if administered timely. Knowing the temporal profile of neuronal loss in dorsal root ganglia will help to ascertain whether a final diagnosis may be reached before the occurrence of irreversible neuronal injuries. Thus, we addressed the evolution of neuronal loss in SNN by using sensory nerve action potentials (SNAPs) as a surrogate marker of neuron degeneration.

Methods: Eighty-six patients with acute/subacute inflammatory SNN (paraneoplastic, associated with dysimmune diseases, or idiopathic) were retrospectively studied. The monthly SNAP reduction was determined and normalized with the lower limit of normal. Disability progression was expressed by the modified Rankin score and correlated with SNAP reduction.

Results: The monthly SNAP reduction was similar in the four limbs although the median nerve was less severely affected. The monthly SNAP reduction was very severe within the first two months of evolution, began to slow down after seven months, and stabilized after ten months. It was tightly correlated with disability progression. Kaplan–Meier analysis showed that the median time until matching the diagnostic criteria of SNN was 8.5 months. Within this period, 42% of nerves remained excitable.

Conclusions: Developing treatment aiming at the stabilization of SNN is possible within the first 8 months of evolution. An improvement of the disease is possible if patients are treated within two months, which needs an early referral to an expert center and ENMG testing of the radial and ulnar nerves, which are most sensitive to changes.

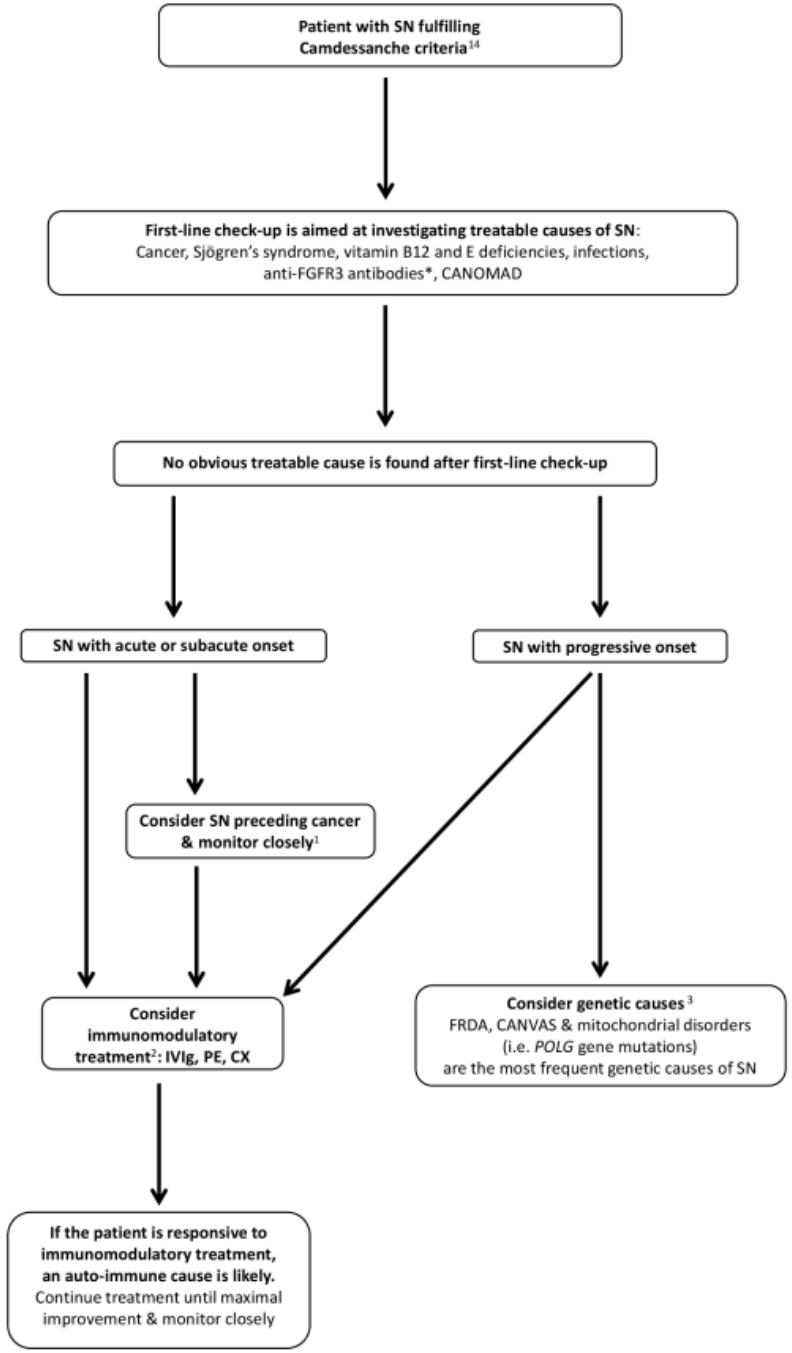

Figure 4 SN diagnostic algorithm. *anti-FGFR3 antibodies are not a cause of SN, but a possible marker of autoimmunity that may justify immunomodulatory treatment. [1]Especially if men >60 years, history of tobacco use, painful arm predominant SN, cerebellar and motor involvement, abnormal CSF analysis. [2]Especially if young women, associated autoimmune disease, monoclonal gammopathy, autoantibodies and abnormal CSF analysis. [3]Especially if progressive and pauci-symptomatic SN, family history, consanguinity, ophthalmoplegia, and so on. CANOMAD, chronic ataxic neuropathy, ophthalmoplegia, IgM paraprotein, cold agglutinins and disialosyl antibodies; CANVAS, cerebellar ataxia, neuropathy and vestibular areflexia syndrome; CSF, cerebrospinal fluid; CX, corticosteroids; FGFR3, fibroblast growth factor receptor 3; FRDA, Friedreich ataxia; IVIg, intravenous immunoglobulins; PE, plasma exchange; POLG, polymerase gamma disorder; SN, sensory neuronopathy.

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