

Gait Apraxia in Multiple Sclerosis

Nuhad E. Abou Zeid, Brian G. Weinshenker, B. Mark Keegan

ABSTRACT: Background: Gait apraxia is a gait disorder not attributable to motor, cerebellar, or sensory dysfunction. Gait impairment is common in Multiple Sclerosis (MS), but is mostly attributed to spasticity and ataxia. Impairment ratings scales are designed accordingly and do not separately evaluate apraxia. **Objective:** To describe 15 patients with gait apraxia resulting from MS as their major functional impairment. **Methods:** The Mayo Clinic database (1994-2007) was searched for the terms MS and gait apraxia. Inclusion criteria: Definite MS, significant gait apraxia. Exclusion criteria: alternative disorder causing apraxia, predominantly spastic/ataxic gait disorder. **Results:** 9 (60%) of the patients were women, and 12 (80%) had a progressive MS course. Gait apraxia was evident at a median of 8 years (range 0-34) following MS onset. Median EDSS at recognition of gait apraxia was 6.5 (range 5-8). Cognitive dysfunction was present in 11 (73%) and neurogenic bladder dysfunction in 14 (93%). The commonest MRI findings were confluent periventricular T2 lesions, T1 hypointensity and generalized cerebral atrophy with symmetrical ex vacuo ventricular enlargement. **Conclusion:** Gait apraxia can cause significant functional impairment in MS patients, and may be underrecognized. The natural course of the neurological deficit in such patients is unknown, and may differ from that of MS patients with other ambulatory disabilities.

RÉSUMÉ: Démarche apraxique dans la sclérose en plaques. Contexte : La démarche apraxique est un trouble de la démarche qui n'est pas attribuable à une dysfonction motrice, cérébelleuse ou sensitive. Une altération de la démarche est fréquente dans la SP, mais elle est la plupart du temps imputée à la spasticité et à l'ataxie. Les échelles d'appréciation de l'altération de la démarche sont conçues en ce sens et n'évaluent pas séparément l'apraxie. **Objectif :** Le but de l'étude était de décrire 15 patients qui présentaient une démarche apraxique due à la SP et dont c'était l'atteinte fonctionnelle la plus importante. **Méthodes :** Nous avons effectué une recherche dans la base de données de la clinique Mayo (1994-2007) en utilisant les termes SP et démarche apraxique. Les critères d'inclusion étaient les suivants : SP établie, démarche apraxique importante. Les critères d'exclusion étaient les suivants : apraxie causée par un autre problème de santé, trouble de la démarche à prédominance spastique/ataxique. **Résultats :** Neuf des patients (60%) étaient des femmes et 12 (80%) présentaient une SP progressive. La démarche apraxique était devenue évidente après un intervalle médian de 8 ans (écart de 0 à 34) du début de la SP. Le score médian à l'EDSS au moment de l'observation de la démarche apraxique était de 6,5 (écart de 5 à 8). Une dysfonction cognitive était présente chez 11 (73%) et une dysfonction vésicale neurogène chez 14 (93%). L'observation la plus fréquente à l'IRM était des lésions T2 périventriculaires confluentes, une hypointensité T1 et une atrophie cérébrale généralisée avec agrandissement ventriculaire symétrique ex vacuo. **Conclusion :** La démarche apraxique peut occasionner une détérioration fonctionnelle significative chez les patients atteints de SP et peut être sous identifiée. L'évolution naturelle du déficit neurologique chez ces patients est inconnue et pourrait être différente de celle de patients atteints de SP qui présentent d'autres difficultés ambulatoires.

Can. J. Neurol. Sci. 2009; 36: 562-565

Gait ignition failure or gait "apraxia" is a gait impairment characterized by impairment in integration of essential gait processes with intact motor, sensory and cerebellar functions required for ambulation. Affected patients experience difficulty with initiation, hesitation, and freezing of gait, especially on turns. Gait apraxia is often associated with cognitive dysfunction, emotional lability, bladder dysfunction, frontal lobe behavioral abnormalities, and frontal release signs.¹

Higher level gait impairment is usually due to lesions affecting the corticobasal-thalamocortical loop, and could be due to altered communication between the basal ganglia and the supplementary motor cortex.^{2,3} Gait apraxia is frequently associated with cerebrovascular disease with multiple subcortical infarcts, basal ganglia infarcts, or severe leukoariosis.³ Other etiologies for gait apraxia include normal pressure hydrocephalus, neurodegenerative disorders, such as Parkinson's disease, Alzheimer disease, and corticobasal

degeneration, and frontal lobe-confined lesions such as hemorrhage or neoplasm.^{1,3,4}

Gait impairment is a common and disabling symptom of Multiple Sclerosis (MS). Weakness due to corticospinal dysfunction and ataxia, either cerebellar or sensory, are the major contributors to MS-related gait impairment.

Gait apraxia is under-appreciated in MS patients. Scales that assess global impairment in MS patients, such as the expanded disability status scale (EDSS)⁵ are designed to rate impaired gait

From the Department of Neurology, Mayo Clinic, Rochester, Minnesota, USA.

RECEIVED FEBRUARY 26, 2009. FINAL REVISIONS SUBMITTED APRIL 23, 2009.

Correspondence to: B. Mark Keegan, Neurology, Mayo Clinic College of Medicine, 200 First Street SW, Rochester, Minnesota, 55905, USA.

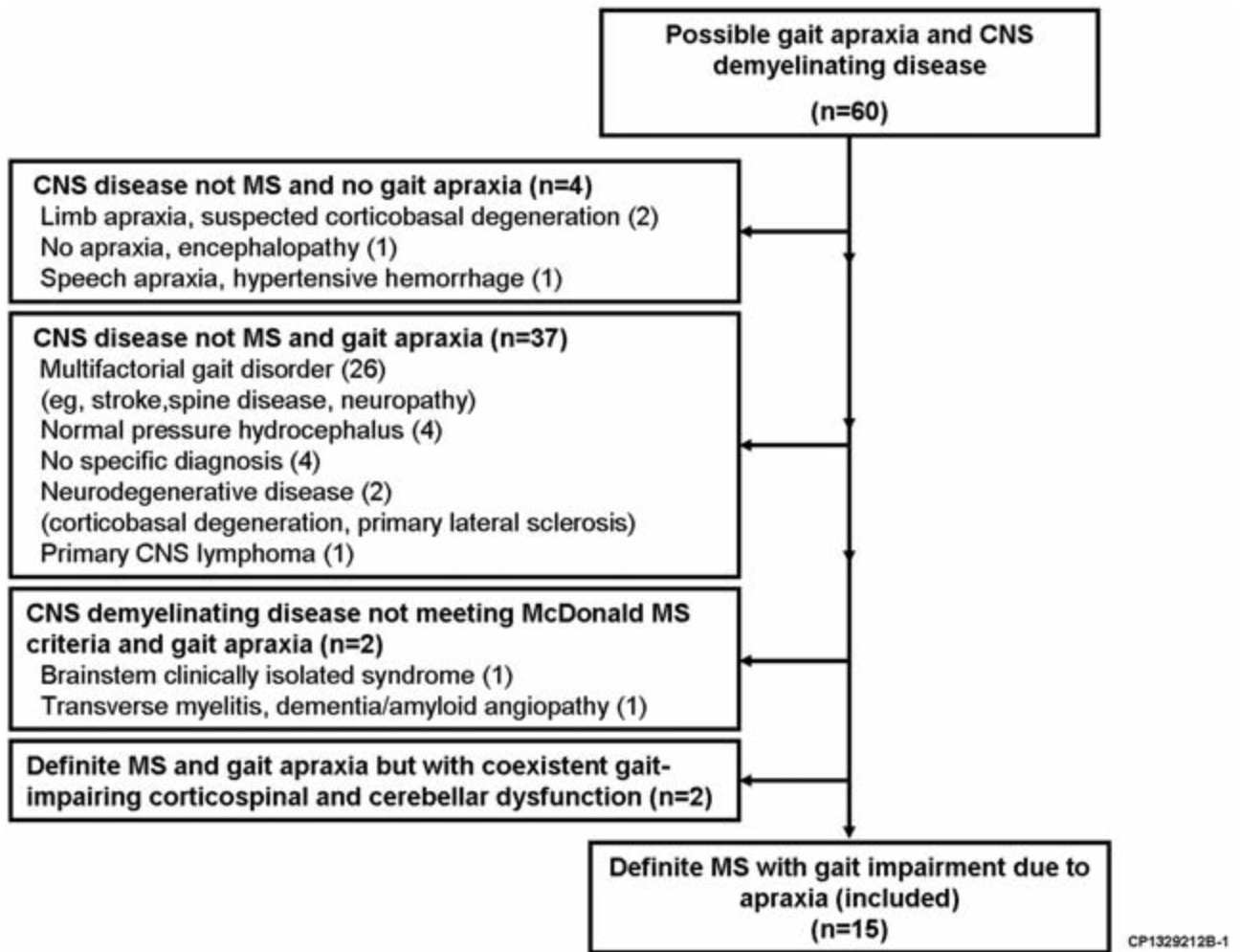


Figure: Flow diagram demonstrates clinical characteristics and alternative diagnoses of excluded patients. CNS=central nervous system

related to corticospinal, sensory or cerebellar dysfunction, and do not separately evaluate gait apraxia. We describe 15 patients with frontal gait disorder and severe gait ignition failure or gait “apraxia” due to MS.

METHODS

This is a retrospective study approved by the Mayo Clinic Institutional Review Board (IRB# 08-001805). Inclusion criteria for this study were: Definite MS (revised McDonald criteria)⁶, and gait apraxia as a predominant MS-related disability. Exclusion criteria were comorbid disorders that are associated with gait apraxia (e.g. normal pressure hydrocephalus, significant cerebral infarction) and presence of MS-related significant confounding functional system disorders that might otherwise explain gait dysfunction (e.g. corticospinal tract, sensory or cerebellar dysfunction).

The Mayo Clinic (Rochester MN) patient database (1994–2007) was searched for diagnostic codes for central nervous system demyelinating disease combined with gait apraxia code. In addition the demyelinating disease codes were combined with gait disturbance codes and then a search was performed for the word “apraxia” to identify patients assigned only the gait disturbance code rather than the gait apraxia code. This search identified 60 patients and, of these, 15 met our study criteria (Figure).

We reviewed the Mayo medical record for patient demographics, clinical course, coexisting medical conditions and medications. We reviewed detailed neurologic examinations performed by MS specialists. In addition, given the comorbidities associated with gait apraxia in other patients, we examined the records for the presence of bowel/bladder dysfunction and cognitive dysfunction. Cognitive status was

evaluated by the Kokmen short test of mental status.^{7,8} We evaluated patients' disability through their estimated expanded disability status scale.⁵ We reviewed MS-targeted and symptomatic therapies used by these patients and their association with progression of gait apraxia.

Brain and spinal cord MRIs were examined and documented for presence and extent of MS related T2 lesion burden and location, T1 hypointensity, cerebral atrophy, and ventricular dilatation. Cerebrospinal fluid (CSF) results were examined in particular for elevations in immunoglobulin G index and unique CSF oligoclonal bands.

RESULTS

Patient Demographics and Clinical Course

Our cohort consisted of nine women and six men, three of whom consented to videotaping of their gait (video). Their median age at MS onset was 40 years (range 21-64), and age at gait apraxia onset was 50 years (range 30-68). The median MS disease duration when gait apraxia was recognized as an impairing deficit was eight years (range 0-34). The clinical course of MS was secondary progressive in seven (47%) patients, primary progressive in five (33%) patients, and relapsing remitting in three (20%). Median EDSS at the time of gait apraxia diagnosis was 6.5 (range 5-8).

A history of smoking was present in 9 (60%) patients. Other medical comorbidities included: hypertension [3], hyperlipidemia [2], diabetes mellitus [1], basal ganglia lacunar infarction clinically and radiologically [1].

Cognitive dysfunction was present in 11 (73 %) patients; it was mild (Kokmen short test of mental status score >30)(7) in 3, moderate (score 20-30) in 5, and severe (score <20) in 3. Four patients underwent formal neuropsychiatric evaluations which revealed predominant impairment in attention, multitasking and rapid decision making with relative preservation of language and visuo-perceptual abilities, suggesting subcortical cognitive dysfunction. Of patients with cognitive dysfunction, four had a frontal lobe behavioral disorder characterized by bradyphrenia, impaired judgment and problem solving skills, social withdrawal, motor apraxia, perseveration, or bilateral grasp reflex.

Bladder dysfunction occurred in 14 (93%) patients, and was mild (frequency, urgency and rare incontinence) in three, moderate (frequent incontinence) in four, and severe (persistent incontinence) in seven. Three patients (20%) had accompanying bowel incontinence.

Neuroimaging and CSF analysis

All patients had confluent periventricular T2 signal abnormality on brain MRI. Diffuse atrophy was present in 13 (87%) patients. Ventricular enlargement was present in 10 (66%) patients and was commensurate with the degree of cerebral atrophy, without evidence of elevated transependymal CSF flow. Focal T1 hypointensity (black holes) was present in 12 of 13 (92%) cases where T1 weighted images were available. Multiple sclerosis plaques were present in the brainstem in 11 (73%) patients, and in the spinal cord in five of six (83%) patients who had available spinal cord MRI. No demyelinating lesions were seen in the basal ganglia, but one patient had a single small lacunar infarct.

Cerebrospinal fluid was available in ten patients, of whom eight (80%) had CSF abnormalities of IgG synthesis (elevated oligoclonal bands in five and elevated IgG index in six).

THERAPY

Multiple sclerosis therapies were used in seven (47%) patients but no significant improvement in the gait apraxia was noted. Treatments used include: interferon β 1-a [6], interferon β 1-b [4], glatiramer acetate [2], azathioprine [1], mitoxantrone [1], monthly intravenous corticosteroids [1], and cyclophosphamide [1]. One patient was treated with levodopa/carbidopa without significant improvement in gait apraxia.

DISCUSSION

Gait apraxia may cause significant impairment in MS patients without significant corticospinal tract, sensory or cerebellar dysfunction. Although poorly recognized, the presence of gait apraxia without arm apraxia is perhaps not surprising given that MS plaques tend to be bilateral, periventricular and progressive, and may preferentially damage the leg fibers as they sweep around the ventricles in a similar fashion to what occurs in hydrocephalus, which is a known cause of gait apraxia.⁹ Under recognition of gait apraxia may result from the masking of this important clinical feature by coexistent cerebellar, corticospinal, or dorsal column impairment in unselected MS patients all of which contribute more to gait impairment and the presence of which invalidates a diagnosis of pure "gait apraxia". The natural course of gait apraxia in MS is unknown, and these patients may follow a different course than patients with standard impairments; hence their behavior in terms of standard impairment scales such as the EDSS that are used to evaluate outcome of clinical trials may differ from non-apraxic MS patients.

Gait apraxia is uncommonly described in prior MS literature. One prior case series of twelve MS patients with cognitive impairment described nine as having gait apraxia with seven "moderate" and two "severe" cases.¹⁰ The patients described had a lower EDSS (median 3.5) and were more likely to have a relapsing clinical course than in our cases, however the two patients with severe gait apraxia had a progressive disease course and higher EDSS and are therefore likely more comparable to our cases.

Pharmacologic treatment for gait apraxia is not well established and has been studied mostly in the setting of gait ignition failure occurring as a symptom of Parkinson's disease. Dopaminergic medications have shown some mild benefit in postural adjustment for gait initiation in Parkinson's patients. Patients with gait initiation failure due to Parkinson's plus syndromes such as progressive supranuclear palsy, corticobasal syndrome or even normal pressure hydrocephalus, occasionally respond to dopaminergic medications.¹¹ Ventriculoperitoneal shunting of CSF is the primary therapy for gait apraxia due to normal pressure hydrocephalus.¹² Physical therapy with gait assessment and retraining, and the provision of adequate assistive devices is important in maximizing function and improving safety in patients with higher level gait disorders.^{13,14}

Early identification of gait apraxia in MS patients may lead to important interventions to improve gait safety. In addition, better

understanding of gait apraxia as an etiology of gait impairment in MS patients will help design better tools for evaluation of MS-related disability.

REFERENCES

1. Zadikoff C, Lang AE. Apraxia in movement disorders. *Brain*. 2005;128:1480-97.
2. Nadeau SE. Gait apraxia: further clues to localization. *Eur Neurol*. 2007;58:142-5.
3. Liston R, Mickelborough J, Bene J, Tallis R. A new classification of higher level gait disorders in patients with cerebral multi-infarct states. *Age Ageing*. 2003;32:252-8.
4. Elble RJ. Gait and dementia: moving beyond the notion of gait apraxia. *J Neural Transm*. 2007;114:1253-8.
5. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*. 1983;33:1444-52.
6. Polman CH, Reingold SC, Edan G, Filippi M, Hartung HP, Kappos L, et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria". *Ann Neurol*. 2005;58:840-6.
7. Kokmen E, Naessens JM, Offord KP. A short test of mental status: description and preliminary results. *Mayo Clin Proc*. 1987;62:281-8.
8. Kokmen E, Smith GE, Petersen RC, Tangalos E, Ivnik RC. The short test of mental status. Correlations with standardized psychometric testing. *Arch Neurol*. 1991;48:725-8.
9. Yakovlev PI. Paraplegia of Hydrocephalus. (A clinical Note and Interpretation). *Am J Mental Defic*. 1947;51:571-6.
10. Franklin GM, Nelson LM, Filley CM, Heaton RK. Cognitive loss in multiple sclerosis. Case reports and review of the literature. *Arch Neurol*. 1989;46:162-7.
11. Rascol O, Fabre N, Brefel-Courbon C, Montastruc JL. The pharmacologic treatment of gait ignition failure. *Adv Neurol*. 2001;87:255-64.
12. Bradley WG, Jr., Whittemore AR, Kortman KE, Watanabe AS, Homyak M, Teresi LM, et al. Marked cerebrospinal fluid void: indicator of successful shunt in patients with suspected normal-pressure hydrocephalus. *Radiology*. 1991;178:459-66.
13. Liston R, Mickelborough J, Harris B, Hann AW, Tallis RC. Conventional physiotherapy and treadmill re-training for higher-level gait disorders in cerebrovascular disease. *Age Ageing*. 2000;29:311-18.
14. Rubino FA. Gait disorders. *Neurologist*. 2002;8:254-62.