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WORD COUNT	3718	TIME SUBMITTED	27-APR-2022 05:14PM
		PAPER ID	85284830

Name of Journal: *World Journal of Clinical Cases*
Manuscript NO: 74640
Manuscript Type: CASE REPORT

Mills' syndrome is a unique entity of upper motor neuron disease with N-shaped progression: Three case reports

Zhang ZY *et al*. Three case reports of Mills' syndrome

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Abstract

BACKGROUND

Mills' syndrome is an extremely rare degenerative motor neuron disorder (MND) first described by Mills in 1900, but its nosological status is still not clear. We aimed to analyze the clinical features of Mills' syndrome.

CASE SUMMARY

Herein, we present three cases with similar features as those described in Mills' original paper and review the related literature. Our patients showed middle- and older-age onset, with only upper motor neuron symptoms evident throughout the course of the disease. Spastic hemiplegia began in the lower extremity with a unique progressive pattern.

CONCLUSION

We consider that Mills' syndrome is a unique entity of NMD with an N-shaped progression. Clinicians should maintain a high index of suspicion for the diagnosis of Mills' syndrome when the onset involves lower extremity paralysis without evidence of lower motor neuron or sensory involvement.

Key Words: Mills' syndrome; Motor neuron disease; Primary lateral sclerosis; Amyotrophic lateral sclerosis; N-shaped progression; Case report

Zhang ZY, Ouyang ZY, Zhao GH, Fang JJ. Mills' syndrome is a unique entity of upper motor neuron disease with N-shaped progression: Three case reports. *World J Clin Cases* 2022; In press

Core Tip: Mills' syndrome is an extremely rare degenerative motor neuron disorder, whose nosological status is currently uncertain. We report three cases with similar features as those described in Mills' original paper. All three patients had initial symptoms in one lower extremity that spread up to the homolateral upper limb, followed by the contralateral lower limb, and finally the contralateral upper limb. It is necessary to clarify the clinical features to receive more attention from clinicians.

INTRODUCTION

In 1900, Mills[1] described eight cases of progressive hemiplegia that begins in the extremity of the lower limb and ascends to the ipsilateral upper extremity without significant sensory impairment. Mills claimed that this disorder is a new form of degenerative disease characterized by a gradually progressive, unilateral ascending clinical syndrome of upper motor neuron-predominant hemiparesis. His description was based on clinical examination only, and different disorders such as multiple sclerosis, syphilis, parkinsonism, and amyotrophic lateral sclerosis were not excluded. Analysis of the post-mortem findings of a patient from one of his original case series who had been symptomatic for 8 years showed unilateral degeneration of the crossed and uncrossed pyramidal tracts at the level of spinal cord and brainstem, but no Betz cell degeneration in the motor cortex and no attrition of anterior horn cells[2]. The advances in the diagnostic laboratory, electromyography (EMG), and neuroimaging tests confirmed the picture of progressive unilateral ascending weakness associated

with pyramidal tract impairment of Mills' syndrome. In the recent two decades, only about 50 additional cases have been reported in the literature[3,4], and mostly as single case reports. Owing to the lack of pathological examination, most of the cases did not allow reliable differential diagnosis; one progressed to frontotemporal dementia[5] and also developed an extrapyramidal syndrome[6]. Although the syndrome currently has an uncertain nosological status, some authors consider it as a lateralized variant of primary lateral sclerosis (PLS)[4,7], while others refer to it purely as a clinical term including different disorders[8,9]. The progression of the disease and the natural course of the reported cases suggest a different pathophysiologic basis for neuronal death. Here, we report three cases that have similar features as the ones described in Mills' original paper to shed light on the clinical characteristics of Mills' syndrome.

CASE PRESENTATION

Imaging examinations

Case 1: Brain magnetic resonance imaging (MRI) showed isolated atrophy of the right occipital lobe. No remarkable findings were observed with the cervical and thoracic vertebrae on either MRI or EMG.

Case 2: No decrement was noted in repetitive nerve stimulation. Brain MRI showed mild periventricular ischemic changes, but cervical spine MRI was normal. Positron-emission tomography (PET) scan was essentially normal.

Case 2: Brain MRI was normal, and cervical spinal MRI showed mild non-compressive degeneration of C5/6 and C6/7 disks. EMG was performed again, the results showed minor chronic denervation in the left dorsal interosseous, left sternocleidomastoid muscle, and thoracic paraspinal muscles. No evidence of lower motor neuron involvement or polyneuropatic impairment was found. We performed MR diffusion tensor imaging to study the brain white matter connections, but the findings were normal.

Physical examination

Case 1: Physical examination revealed left hemiparesis with spastic hypertonia and hyperreflexia, particularly in the left lower limb. Muscle power in the left lower limb was graded 3/5 based on the Medical Research Council (MRC) scale. Babinski sign was negative. Superficial and proprioceptive sensations were normal, and cranial nerve functions were unimpaired.

Case 2: Neurological examination revealed mild weakness in the right-sided limbs (MRC grade 4) with hypermyotonia; tendon reflexes were pathologically brisk in all limbs, particularly on the right side. Right foot clonus was noted and right Babinski's and Hoffmann's signs were positive. Sensory examination including pain sensation, position sensation, and vibration sensation was unremarkable. Cranial nerve functions were unimpaired, and coordination and vision were normal.

Case 3: Neurological examination revealed left-side hemiparesis with hyperreflexia, hypertonia, and ankle clonus. Muscle power was graded 4/5 in the left upper limb and 1/5 in the left lower limb. Babinski's and Hoffmann's signs were negative, and amyotrophy was not detected. The right limbs, cranial nerves, superficial and proprioceptive sensation, and cerebellar functions were normal.

Personal and family history

Family history of genetic disease was all negative in three cases.

History of past illness

Case 1: Her personal and social history was unremarkable.

Case 2: Her personal and social history was unremarkable.

Case 3: His personal history was unremarkable, except for paroxysmal atrial fibrillation.

History of present illness

Case 1: The symptoms developed slowly and remained unnoticed by the patient attention until 1 year ago when she felt weakness on her left leg that affected her

walking. She did not notice any muscle twitching. Furthermore, altered cognitive function, language and swallowing problems, sensory disturbance, or sphincter dysfunction were noted.

Case 2: The onset was described as "heaviness" in her right leg when running, and progressively difficult walking with tripping and stumbling. She experienced weakness that ascended to her right upper limb 2 mo before presentation. She also noticed that her handwriting worsened, and she was unable to raise her right arm above her head. She denied any abnormal sensation or altered perception, any language problem, bulbar symptom, or bowel or bladder incontinence. Madopar was prescribed because the diagnosis of the outpatient doctor was Parkinson's disease.

Case 3: Evaluations included multiple brain, spine, and lower limb MRI; abdominal computed tomography (CT); cerebrospinal fluid (CSF) examination; EMG and visual, auditory, and somatosensory evoked potentials; all tests showed negative results. The patient was discharged without treatment but continued to be followed-up. Sixteen months after he noticed weakness in his left lower extremity, he experienced weakness in his left arm. The paresis became increasingly evident, and the symptoms progressed from difficulty in walking to dependence on a wheeled walker.

Chief complaints

Case 1: A 68-year-old woman was admitted to our outpatient clinic with chief complains of stiffness in her left lower extremity for about 3 years.

Case 2: A 72-year-old woman presented with a half year history of slow progressive right-sided hemiparesis.

Case 3: A 55-year-old man was admitted to the hospital with complaints of the weakness in his left lower extremity for 7 mo.

Laboratory examinations

Case 1: The results of routine laboratory tests including blood routine examination, biochemical and immunoserologic indices, tumor markers, thyroid function test,

vitamin B_{12} Level, serological tests for syphilis and human immunodeficiency virus (HIV), and CSF examination were negative.

Case 2: Blood tests for paraneoplastic autoantibodies, serum B_{12}, copper, HIV, and syphilis showed negative results. Nerve conduction study was normal, and somatosensory evoked potentials were unremarkable.

Case 3: Routine blood, creatine kinase, autoantibodies, and HIV and syphilis screening were normal. CSF test with isoimmune electrofocusing was negative.

FINAL DIAGNOSIS

The final diagnosis was motor neuron disorder (MND) with the three patients.

TREATMENT

Case 1: No special treatment of the patient.

Case 2: By consensus, baclofen and riluzole were prescribed upon discharge.

Case 3: The patient was discharged without treatment but continued to be followed-up.

OUTCOME AND FOLLOW-UP

Case 1: The patient underwent 28 mo of follow-up, and she developed slow progressive spastic hemiplegia without sensory disturbance. The stiffness gradually spread to the left upper extremity and mildly affected her housework activities. She progressed to using a cane outside the home 4.5 years after the first symptom manifested. She felt slight stiffness on her right lower limb, but no bulbar symptoms were observed at the last follow-up visit.

Case 2: Over the subsequent months, the stiffness and weakness in her right limb gradually aggravated. She noted stiffness in her left leg 6 mo later, and she became wheelchair-bound. Sixteen months into her disease course, she noted her left hand become clumsy and her daily living abilities were limited. Eighteen months into her

course, she developed mild pseudobulbar symptoms and occasional choking when eating. She died from respiratory failure 32 mo after the initial onset of symptoms.

Case 3: The patient's symptoms progressed sharply during the course of the follow-up: the right lower limb was affected within 19 mo of his disease onset, and the right upper limb was affected 24 mo after onset. After 28 mo of the first symptoms onset, the patient developed severe bulbar dysfunction including dysarthria and dysphagia. He died from respiratory failure 44 mo after the onset of symptoms. Throughout his course, he had no marked fasciculations or muscle atrophy.

DISCUSSION

The clinical picture presented by our three patients (details shown in Table 1) showed several primary distinctive features: (1) Onset at middle- and old-age; (2) only upper motor neuron findings were evident throughout the course of their disease; (3) could affect bilateral limbs in advanced stages, but strictly began in one lower extremity and spread to the homolateral upper limb, followed by the contralateral lower limb, and finally the contralateral upper limb, which we refer to as N-shaped progression; and (4) extremely asymmetric and the lower extremity is much more severely affected that the upper limb, even in the late stages of the disease. Features supporting its classification fall within the spectrum of MND, and evolution to both amyotrophic lateral sclerosis (ALS) and PLS has been described[4]. We propose that Mills' syndrome can be considered a unique entity of MND, because there is some heterogeneity in the progression, including its N-shaped progressive manner. It should be emphasized that few published cases that did not have onset in the in the lower limb or did not show descending progressive hemiplegia[9,10] did not strictly meet the criteria of Mills' syndrome.

In light of the present situation, these cases were well differentially diagnosed with ALS. The clinical hallmarks of ALS are clear, there are definitive electrophysiological criteria called EI Escorial Criteria that requires evidence of both upper and lower MND. The symptoms usually spread and progress within a segment and from one segment to

the other (cranial, cervical, thoracic, and lumbosacral)[11]. Obviously, our patients did not meet these diagnostic criteria for ALS, given the absence of lower motor neuron signs in the clinical and electrophysiological examination.

Some authors have illustrated the associated clinical and radiologic asymmetry and absence of LMN involvement, supporting a hemiparetic variant of PLS[12]. PLS is a progressive upper MND without the clinical signs of lower motor neuron involvement, wherein the patterns of progression most commonly spread from side to side and from region to region that commonly start symmetrically in the lower extremities and evolve to spastic tetraparesis, ultimately with bulbar involvement[13]. Zhai *et al*[14] conducted a study to identify the subsets of PLS patients with common clinical, physiological, and anatomical features; they termed PLS as ascending, multifocal, or sporadic paraparesis owing to its pattern of symptom progression. Ascending progression was noted in patients with one limb onset and progression from one side to the other occurring first, followed by ascending progression[15]. Therefore, we speculate that the pattern of symptom progression is one of the key features to distinguish Mills' syndrome from PLS. Maragakis *et al*[7] reported five cases that have features consistent with the original clinical description by Mills. The researchers claimed that these cases should be classified as hemiparetic PLS rather than a distinct clinical entity. However, two patients described in this paper had onset in the upper extremity, without the tell-tale N-shaped progression pattern. The different sequences of clinical manifestations presumably reflect the different nosology with PLS. Moreover, through Pringle's diagnostic criteria, PLS shows benign clinical prognosis, slow rate of progression, and average symptom duration ranging from 7.2-14.5 years[16]. Distinct from that, the duration from the onset of symptoms to death was < 4 years in patient 3, whereas the bulbar symptoms involved rapidly in patient 2. The prognosis of our cases was not so benign (Table 2). A recent 18F-fluorodeoxyglucose PET study[17] found significant hypometabolism in motor and premotor areas contralateral to the limb weakness in Mills' syndrome patients, which is more limited than that of ALS and PLS

patients. Taken together, Mills' syndrome is better to be considered a unique nosological entity of the MND spectrum rather than a variant of PLS.

Another dominant view about Mills' syndrome is that it is purely a clinical description that can have secondary etiologies. The cases reported in the literature related to Mills' syndrome included different disorders such as multiple sclerosis, syphilis, and unilateral cerebral atrophy[8]. Mirian *et al*[3] described a 63-year-old woman diagnosed with Mills' syndrome progressing to corticobasal syndrome. Turner *et al*[13] used 11C-(R)-PK11195 PET scanning *in vivo* to explore the cortical lesion in cases of upper MND. In this study, two patients had clinical features similar to Mills' syndrome: one demonstrated marked focal increase in the binding of (11)C-(R)-PK11195 in the superior frontal region contralateral to the affected limbs; by contrast, the other patient showed no focal areas of increased binding in the cerebral cortex. The second patient however had a high cervical cord lesion and was presumed to have extra cerebral inflammatory disease. The authors summarized that Mills' syndrome is a purely clinical description that should be reserved for patients with a progressive spastic hemiparesis for which no other explanation can be found. The lack of evidence of secondary etiology in our three patients enables us to propose that the degeneration may be idiopathic. However, given that neither pathological examination nor autopsy was conducted, we failed to conclude whether Mills' syndrome is a clinical diagnosis that includes complex disorders.

In our first case, MRI of the brain showed atrophy of the right occipital lobe, while the spinal cord was normal, and no other alternative etiologies seemed plausible after serological tests and cerebrospinal fluid screening. Previous imaging studies have demonstrated that cerebral atrophy is widespread in ALS, involving the grey matter, white matter, and motor and extra-motor regions[18]. Recently, a study using deformation-based morphometry analysis showed significant bilateral atrophy in the motor cortex and corticospinal tract and ventricular enlargement, along with significant longitudinal atrophy in the precentral gyrus, frontal, and parietal white matter[19]. To

our knowledge, no previous morphometric study of MND has mentioned occipital lobe atrophy, and we believe that this change is not related to this syndrome.

Phosphorylated transactive response DNA-binding protein 43kDa (pTDP-43) aggregates in the cytoplasm of motor neurons and neuroglia in the brain are one of the pathological hallmarks of ALS[20]. Correlation analysis showed that the severity of pTDP-43 pathology in the white matter was linearly associated to that in the overlying grey matter. In addition, the severity of pTDP-43 pathology and neuronal loss correlated closely with grey and white matter oligodendrocyte involvement. Sainouchi *et al*[21] reported the clinicopathological features of two autopsy cases of hemiplegic-type ALS and discussed the possible pathomechanism; their results revealed that in the upper motor neuron (UMN) system, there was heavier pTDP-43 accumulation in the motor areas controlling the clinically predominant limb. Bäumer *et al*[22] reported a 72-year-old patient with co-occurrence of aphasia and progressive right hemiparesis. Postmortem examination revealed striking left hemisphere atrophy within primary motor cortex, accompanied by neuronal loss, gliosis, and TDP-43-positive neuronal and glial cytoplasmic inclusions. However, with respect to axonal propagation, pTDP-43 oligomers would have primarily spread along the unilateral corticospinal tract[23]. The N-shaped progression pattern in Mills' syndrome is considered an orderly and sequential process in the UMN system, and such contiguous lesion spread in Mills' syndrome may further support the above-mentioned TDP-43 propagation hypothesis. Additional studies are needed to further understand the commonalities and differences from other neurodegenerative diseases and elucidate its underlying physiopathology.

A proper diagnosis can hardly be provided at the early stage of disease for cases when weakness emerges unilaterally in one limb. In the second patient of our report, Parkinson's disease was initially considered. Thus, understanding the N-shaped progression pattern of Mills' syndrome is particularly important to improve the clinician's ability to identify these patients early in their disease course and to provide patients with adequate counselling.

CONCLUSION

Mills' syndrome should be conceptualized as a unique nosological entity of upper NMD spectrum, with typical onset in one lower extremity which eventually spreads with an N-shaped progression pattern. Clinicians should maintain a high index of suspicion for the diagnosis of Mills' syndrome when the onset is restricted to one lower extremity paralysis without evidence of lower motor neuron involvement or sensory impairment. However, whether Mills' syndrome is a clinical diagnosis that includes complex disorders remains unclear. Further studies should extensively look into this matter to gain a better understanding of the natural history and underlying pathogenic mechanisms.

REFERENCES

1 **CK M**. A case of unilateral progressive ascending paralysis, probably representing a new form of degenerative disease. *J Nerv Ment Dis* 1900; **27**: 195-200 [DOI: 10.1097/00005053-190004000-00002]

2 **Mills CK**, Spiller WG. A case of progressively developing hemiplegia later becoming triplegia resulting from primary degeneration of the pyramidal tracts. *J Nerv Ment Dis* 1903; **30**: 385-397

3 **Mirian A**, Romsa J, Jenkins ME, Budhram A. Mills' Syndrome (Ascending Spastic Hemiparesis) Progressing to Corticobasal Syndrome. *Can J Neurol Sci* 2021; **48**: 852-853 [PMID: 33472710 DOI: 10.1017/cjn.2021.9]

4 **Algahtani H**, Shirah B, Algahtani S, Attar A, Abuzinadah AR. Mills' syndrome: Reporting the disease course with a monthly intravenous immunoglobulin program. *J Neuroimmunol* 2021; **355**: 577562 [PMID: 33813319 DOI: 10.1016/j.jneuroim.2021.577562]

5 **Doran M**, Enevoldson TP, Ghadiali EJ, Larner AJ. Mills syndrome with dementia: broadening the phenotype of FTD/MND. *J Neurol* 2005; **252**: 846-847 [PMID: 15834648 DOI: 10.1007/s00415-005-0755-6]

6 **Turner MR**, Gerhard A, Al-Chalabi A, Shaw CE, Hughes RA, Banati RB, Brooks DJ, Leigh PN. Mills' and other isolated upper motor neurone syndromes: *in vivo* study with

11C-(R)-PK11195 PET. *J Neurol Neurosurg Psychiatry* 2005; **76**: 871-874 [PMID: 15897516 DOI: 10.1136/jnnp.2004.047902]

7 **Maragakis NJ**, Holland NR, Corse AM. Hemiparetic Primary Lateral Sclerosis: Revisiting Mills Syndrome. *Case Rep Neurol* 2015; **7**: 191-195 [PMID: 26500542 DOI: 10.1159/000440713]

8 **Jaiser SR**, Mitra D, Williams TL, Baker MR. Mills' syndrome revisited. *J Neurol* 2019; **266**: 667-679 [PMID: 30631918 DOI: 10.1007/s00415-019-09186-3]

9 **Wang SP**, Xu FC, Chen XW. Mills' syndrome: progressive hemiplegia with atrophy of unilateral cerebral peduncle and pontine base. *Neurol Sci* 2015; **36**: 1487-1489 [PMID: 25681213 DOI: 10.1007/s10072-015-2106-4]

10 **Van Laere K**, Wilms G, Van Damme P. Neurological picture. FDG-PET findings in three cases of Mills' syndrome. *J Neurol Neurosurg Psychiatry* 2016; **87**: 222-223 [PMID: 25922081 DOI: 10.1136/jnnp-2014-309952]

11 **Brooks BR**, Miller RG, Swash M, Munsat TL; World Federation of Neurology Research Group on Motor Neuron Diseases. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. *Amyotroph Lateral Scler Other Motor Neuron Disord* 2000; **1**: 293-299 [PMID: 11464847 DOI: 10.1080/146608200300079536]

12 **Huynh W**, Tu S, Mahoney CJ, Schwartz R, Kiernan MC. Mills Syndrome: Clinical and Radiologic Asymmetry. *Neurology* 2021; **96**: 677-678 [PMID: 33593860 DOI: 10.1212/WNL.0000000000011710]

13 **Turner MR**, Barohn RJ, Corcia P, Fink JK, Harms MB, Kiernan MC, Ravits J, Silani V, Simmons Z, Statland J, van den Berg LH; Delegates of the 2nd International PLS Conference, Mitsumoto H. Primary lateral sclerosis: consensus diagnostic criteria. *J Neurol Neurosurg Psychiatry* 2020; **91**: 373-377 [PMID: 32029539 DOI: 10.1136/jnnp-2019-322541]

14 **Zhai P**, Pagan F, Statland J, Butman JA, Floeter MK. Primary lateral sclerosis: A heterogeneous disorder composed of different subtypes? *Neurology* 2003; **60**: 1258-1265 [PMID: 12707427 DOI: 10.1212/01.wnl.0000058900.02672.d2]

15 **Statland JM**, Barohn RJ, Dimachkie MM, Floeter MK, Mitsumoto H. Primary Lateral Sclerosis. *Neurol Clin* 2015; **33**: 749-760 [PMID: 26515619 DOI: 10.1016/j.ncl.2015.07.007]

16 **Pringle CE**, Hudson AJ, Munoz DG, Kiernan JA, Brown WF, Ebers GC. Primary lateral sclerosis. Clinical features, neuropathology and diagnostic criteria. *Brain* 1992; **115 (Pt 2)**: 495-520 [PMID: 1606479 DOI: 10.1093/brain/115.2.495]

17 **Scialò C**, Morbelli S, Girtler N, Mandich P, Mancardi GL, Caponnetto C, Nobili F. Bilateral motor and premotor cortex hypometabolism in a case of Mills syndrome. *Amyotroph Lateral Scler Frontotemporal Degener* 2015; **16**: 414-417 [PMID: 25967545 DOI: 10.3109/21678421.2015.1026828]

18 **Agosta F**, Spinelli EG, Filippi M. Neuroimaging in amyotrophic lateral sclerosis: current and emerging uses. *Expert Rev Neurother* 2018; **18**: 395-406 [PMID: 29630421 DOI: 10.1080/14737175.2018.1463160]

19 **Dadar M**, Manera AL, Zinman L, Korngut L, Genge A, Graham SJ, Frayne R, Collins DL, Kalra S. Cerebral atrophy in amyotrophic lateral sclerosis parallels the pathological distribution of TDP43. *Brain Commun* 2020; **2**: fcaa061 [PMID: 33543125 DOI: 10.1093/braincomms/fcaa061]

20 **Riva N**, Gentile F, Cerri F, Gallia F, Podini P, Dina G, Falzone YM, Fazio R, Lunetta C, Calvo A, Logroscino G, Lauria G, Corbo M, Iannaccone S, Chiò A, Lazzerini A, Nobile-Orazio E, Filippi M, Quattrini A. Phosphorylated TDP-43 aggregates in peripheral motor nerves of patients with amyotrophic lateral sclerosis. *Brain* 2022; **145**: 276-284 [PMID: 35076694 DOI: 10.1093/brain/awab285]

21 **Sainouchi M**, Tanaka H, Shimizu H, Mashima T, Fukushima T, Hatano Y, Ishihara T, Makino K, Onodera O, Kakita A. Hemiplegic-type ALS: clinicopathological features of two autopsied patients. *J Neurol Neurosurg Psychiatry* 2021; **92**: 1014-1016 [PMID: 33883200 DOI: 10.1136/jnnp-2021-326257]

22 **Bäumer D**, Butterworth R, Menke RA, Talbot K, Hofer M, Turner MR. Progressive hemiparesis (Mills syndrome) with aphasia in amyotrophic lateral sclerosis. *Neurology* 2014; **82**: 457-458 [PMID: 24363135 DOI: 10.1212/WNL.0000000000000090]

23 **Fatima M**, Tan R, Halliday GM, Kril JJ. Spread of pathology in amyotrophic lateral sclerosis: assessment of phosphorylated TDP-43 along axonal pathways. *Acta Neuropathol Commun* 2015; **3**: 47 [PMID: 26216351 DOI: 10.1186/s40478-015-0226-y]

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