Inpatient vs Outpatient Evaluation of Suspected Paraneoplastic Cerebellar Degeneration

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Abstract

Objective

To determine the differences in outcomes of adult patients with ataxia initially evaluated for paraneoplastic cerebellar degeneration (PCD) as inpatients or outpatients.

Methods

In this retrospective cohort analysis, diagnosis, workup, and functional outcomes based on the change in the modified Rankin Scale (mRS) score were compared between patients with ataxia who underwent workup for PCD initially as inpatients vs outpatients between March 2011 and June 2018 at Rush University Medical Center.
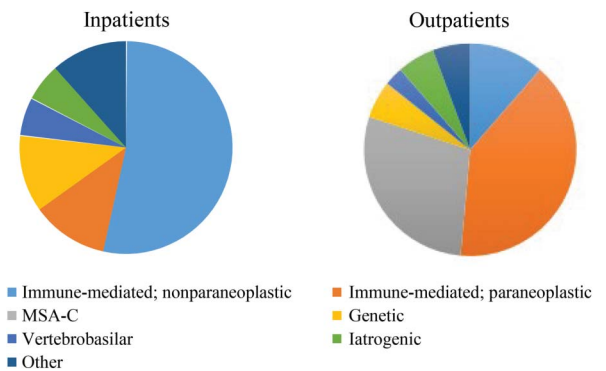
Results

There were 78 patients included in the analysis; 59% were women, and the average age at symptom onset was 57 ± 19.5 years. Nineteen patients (24.3%) underwent evaluation as inpatients and 59 (75.6%) as outpatients. Admitted patients were more likely to receive immunotherapy (73.7% vs 20.3%, $p < 0.0001$) and received it faster than outpatients (0.40 months for inpatients, interquartile range [IQR] 0.03–1 months, vs 6.6 months for outpatients, IQR 2–11.7 months; $p = 0.01$). A greater percentage of inpatients improved based on the mRS score compared with those who underwent evaluation as outpatients (52.63% vs 22.81%, $p = 0.01$).

Conclusions

More patients improved from baseline in the inpatient cohort.

Classification of Evidence

This study provides Class III evidence that for patients undergoing initial evaluation for PCD, patients undergoing inpatient evaluation have better outcomes compared with those undergoing outpatient evaluation.

Inpatients / Outpatients

Immune-mediated; nonparaneoplastic
MSA-C
Vertebrobasilar
Other
Immune-mediated; paraneoplastic
Genetic
Iatrogenic

MORE ONLINE

→ **Class of Evidence**
Criteria for rating therapeutic and diagnostic studies
NPub.org/coe

> Navigating the evaluation of ataxia can be challenging as the number of possible diagnostic tests continues to expand as new genetic and autoimmune biomarkers are discovered.

Paraneoplastic cerebellar degeneration (PCD) is rare. Paraneoplastic neurologic syndromes affect 1% of patients with cancer overall, but the prevalence may be as high as 10% of patients with certain malignancies, such as lymphoma.[1] However, neurologists routinely consider PCD as part of their differential diagnosis for subacute ataxia in adults, which progresses over weeks to months.[2,3] Although this diagnosis may signify underlying malignancy, once diagnosed, it opens the possibility for additional treatment options. Navigating the evaluation of ataxia can be challenging as the number of possible diagnostic tests continues to expand as new genetic and autoimmune biomarkers are discovered.

Immune-mediated cerebellar ataxia (IMCA) includes PCD and other etiologies, such as MS, anti–GAD65 antibody–associated cerebellar ataxia, or postinfectious cerebellitis.[4] Identification and treatment of the underlying malignancy is essential in patients with PCD, and these patients may warrant concomitant immunotherapy.[5,6] Patients with nonparaneoplastic IMCA, such as anti–GAD65 antibody–associated cerebellar ataxia, have been shown to respond better to immunotherapy than patients with paraneoplastic IMCA.[7] There is a limited timeframe during which the treatment of patients with IMCA can restore function, and thus, timely diagnosis is crucial.[5] A growing body of evidence suggests that time is cerebellum and that earlier treatment of IMCA confers a better chance of recovery.[4,7–9]

When clinicians consider PCD as an etiology of ataxia, there is little evidence to guide whether patients should undergo inpatient or outpatient evaluation. Patients with PCD often present with relatively acute onset of balance deficits that may be associated with other debilitating features such as nausea, diplopia, dysphagia, and, at times, cognitive impairment.[10] Providers must consider numerous factors in making a decision to admit patients for expedited evaluation, including the patient's disease severity, socioeconomic background, autonomy, safety, and potential outcomes. This study aims to assess the outcomes of patients with ataxia who underwent evaluation for PCD and to compare the outcomes of those who had their initial consultation and workup completed as inpatients vs outpatients. The hypothesis was that admitted patients with PCD would experience greater improvement in functional outcomes based on the change in the modified Rankin Scale (mRS) score.

Methods

Primary Research Question and Classification of Evidence

Do patients with suspected PCD who are admitted for initial workup experience a greater functional outcome compared with patients who undergo initial workup as an outpatient? This retrospective cohort analysis provides Class III evidence because of the retrospective observational design with baseline confounding.

Setting

This study is a retrospective cohort analysis, reviewing the electronic medical records of all patients older than 18 years with a diagnosis of ataxia who underwent evaluation for PCD at Rush University Medical Center (RUMC), Chicago, IL, between March 2011 and June 2018. RUMC is a tertiary medical center that evaluates patients with ataxia in outpatient general neurology clinics, subspecialty clinics, and as inpatients.

Definitions

Ataxia was defined by motor dysfunction including documented imbalance, impaired coordination, limb and body tremor, dysarthria, and/or oculomotor abnormalities on examination.[11] A probable or definitive diagnosis of PCD was determined clinically and was confirmed based on the diagnostic criteria outlined by Graus et al.[10] A probable or definitive diagnosis of the etiology of the ataxia from all causes was determined by the patient's clinician, and subcategory designation was assigned by consensus of 3 investigators (N.W., D.H., and M.A.).[6,7,12] For patients who had an identifiable etiology of ataxia, the diagnostic etiologies were categorized as immune mediated, with subgroup classification as paraneoplastic or nonparaneoplastic (such as cerebellitis, GAD65-associated ataxia, or multiple sclerosis); vascular; multiple system atrophy; genetic (confirmed by genetic testing); or other etiology (such as prion disease) (figure e-3, links.lww.com/NXI/A263). Acute time course was defined as the onset progressing over minutes to days, subacute lasting days to weeks, and chronic as progressing over months to years. The presence of antibodies was determined using standardized indirect, immunofluorescence tissue-based or cell-binding assays, such as the Mayo paraneoplastic or autoimmune encephalopathy panel, which were ordered at the time of clinical encounter. These panels collectively tested for antineuronal nuclear antibody type 1 (ANNA-1 or anti-Hu); antineuronal nuclear antibody type 2 (ANNA-2 or anti-Ri); antineuronal nuclear antibody type 3 (ANNA-3); antiglial and/or neuronal nuclear antibody type 1 (AGNA-1); Purkinje cell cytoplasmic (PCA type 1, 2, and Tr); striational (striated muscle); voltage-gated calcium channel (VGCC); collapsin response-mediator protein 5 (CRMP-5); acetylcholine receptor; amphiphysin; voltage-gated potassium channel; NMDA receptor; leucine-rich glioma

Table 1 Baseline Characteristics

	Inpatient (n = 19)	Outpatient (n = 59)	p Value
Age at onset, years, mean (SD)	54.4 (16.7)	57.9 (15.1)	0.39
Time from symptom to presentation (mo), median (IQR)	4.0 (1–10)	18.0 (6–58)	0.0005
Women, n (%)	13 (68.4%)	33 (55.9%)	0.34
Race, ethnicity n (%)[a]			0.62
African American	3 (15.8%)	10 (17.2%)	
Asian	0	1 (1.7%)	
White, Hispanic	3 (15.8%)	5 (8.6%)	
White, Non-Hispanic	12 (63.2%)	41 (70.7%)	
Middle Eastern	1 (5.3%)	1 (1.7%)	
Missing	0	1	
Baseline severity (mRS score), median (IQR)	4 (2–4)	2 (1–3)	0.0005
Baseline severity (AS), n (%)			0.0005
Wheelchair dependent (5)	9 (47.4%)	4 (6.8%)	
Walks with walker (4)	2 (10.5%)	15 (25.4%)	
Walks with cane (3)	0	2 (3.4%)	
Abnormal gait, but walks without aid (2)	6 (31.5%)	36 (61.0%)	
Normal gait (1)	2 (10.5%)	2 (3.4%)	
Preexisting autoimmune condition, n (%)	8 (42.1%)	13 (22.0%)	0.09
Active or remote tobacco smoking, n (%)	7 (36.8%)	30 (50.9%)	0.29
Clinical features at presentation			
Seizure, n (%)	3 (15.8%)	2 (3.4%)	0.09
Behavioral change, n (%)	2 (10.5%)	2 (3.4%)	0.25
Encephalopathy, n (%)	8 (42.1%)	7 (11.9%)	0.007
Weakness, n (%)	4 (21.1%)	11 (18.6%)	1
Weight loss, n (%)	8 (42.1%)	16 (27.1%)	0.22
Tremor, n (%)	2 (10.5%)	5 (8.5%)	1
Dystonia, n (%)	1 (5.3%)	3 (5.1%)	1
LOC, n (%)	0	1 (1.7%)	1
Pain, n (%)	4 (21.1%)	8 (13.6%)	0.47
Dysarthria/dysphagia, n (%)	3 (15.8%)	18 (30.5%)	0.21
Vertigo, n (%)	5 (26.3%)	17 (28.8%)	0.83
Diplopia, n (%)	3 (15.8%)	6 (10.2%)	0.68
Numbness, n (%)	1 (5.3%)	12 (20.3%)	0.17
CC: ataxia, n (%)	15 (78.0%)	54 (91.5%)	0.21
Time course, n (%)			0.01
Less than 4 weeks	7 (36.8%)	8 (13.6%)	
4 weeks–6 months	5 (26.3%)	9 (15.3%)	
6 months–1 year	2 (10.5%)	7 (11.9%)	

Continued

Table 1 Baseline Characteristics *(continued)*

	Inpatient (n = 19)	Outpatient (n = 59)	*p* Value
Acute or subacute on chronic	4 (21.1%)	10 (17.0%)	
Chronic	1 (5.3%)	25 (42.4%)	

Abbreviations: AS = ambulatory status; CC = chief complaint; IQR = interquartile range; LOC = loss of consciousness; mRS = modified Rankin Scale.
This describes the demographics, presenting features, and the time course of the illness of the patients.
a There was 1 missing variable point in the outpatient cohort.

inactivated 1 (LGI1); contactin-associated protein 2 receptor (CASPR2); glutamic acid decarboxylase (GAD65); and gamma-aminobutyric acid receptor (GABABR) antibodies. Immunologic therapy was defined as receiving an immunosuppressant or immunomodulatory medication, such as steroids, IV immunoglobulin (IVIG), rituximab, cyclophosphamide, and azathioprine.[4] Oncologic therapy was defined as receiving a therapy, radiation, or surgery to treat an underlying malignancy. Symptomatic therapy of cerebellar motor dysfunction was defined as treatment for ataxia with medications such as riluzole, 4-aminopyridine, buspirone, amantadine, varenicline, and others as outlined by Zesiewicz et al.[11] Follow-up time was defined as the last appointment within the study period with documentation of examination and functional status.

Patients

To identify all relevant patients, electronic medical records were searched for patients diagnosed with ataxia based on *ICD-10* codes (R 27.0 and G 11.9) who also underwent testing for serum and/or CSF neuronal and glial antibody testing ordered for suspected PCD at RUMC. Patients were excluded from the analysis if they did not have an examination documenting ataxia in their medical records. Demographic data including age, sex, race/ethnicity, clinical features at presentation, and baseline severity of illness defined by the mRS score were recorded. The time between symptom onset, presentation, diagnosis, and treatment were recorded. Collected data were stored in a deidentified manner in a password-protected database. Based on documentation in the medical records, the principal investigator (N.W.) divided patients into 2 cohorts: those who underwent initial evaluation as an inpatient and those who underwent evaluation in an outpatient clinical setting.

The primary outcome assessed was the change in the mRS score from baseline to follow-up (dichotomized as improved or worsened/stayed the same). The mRS score for each patient was determined by review of the records by a movement disorders trained neurologist (M.A.), who was blinded to patients' group designation and visit chronology (e.g., if the visit was a baseline or follow-up visit) to minimize bias. The mRS score was designed to measure disability following stroke, but has been used in many retrospective studies assessing the outcomes of patients with PCD.[7,13,14]

Secondary outcomes included change in ambulatory status, as outlined by Jones et al. , which is a descriptive 5-point scale

rating patients from having a normal gait (1) to being wheelchair dependent or bedbound (5).[7] In regard to diagnostic evaluation, the frequency of physician ordering, test completion, and the results of the following diagnostic tests were analyzed: neuronal and glial autoantibody testing, MRI of the brain, MRI of the spine, lumbar puncture, CT of the chest, CT of the abdomen, CT of the pelvis, and PET-CT. Other secondary outcomes included type of therapy received and the timing between symptom onset, presentation, diagnosis, and treatments. Treatments analyzed included immunologic therapy, oncologic therapy, and symptomatic therapies.

Statistical Analysis

Baseline demographic, clinical, diagnostic, and outcomes of those who underwent initial workup as inpatient vs outpatient were compared using a *t*-test or Mann-Whitney *U* test to assess differences in continuous variables and a χ^2 test or Fisher exact test to assess differences between categorical variables. Missing data were excluded from the analysis. A *p* value <0.05 was considered statistically significant. Data were analyzed between November 2018 and March 2019. All statistical analyses were performed using SAS version 9.4 (Cary, NC).

Standard Protocol Approvals, Registrations, and Patients Consents

The research protocol was approved by Rush University Hospital IRB (17080806-IRB01).

Data Availability

Anonymized data not published within this article will be made available by request from any qualified investigator with IRB approval.

Results

Baseline Characteristics

Of the 81 patients identified, 78 patients met the inclusion criteria for ataxia based on physical examination in the medical records and were included in the analysis: 19 patients (24.4%) underwent initial evaluation for ataxia as an inpatient, and 59 (75.6%) underwent workup as an outpatient (figure e-1, links. lww.com/NXI/A263). Three patients were excluded for not having documentation of ataxia on physical examination in the medical records. Two of the 59 patients were lost to follow-up

in the outpatient cohort, but available data were included in the statistical analysis.

There was no difference between age, sex, and race between the 2 groups (table 1). The majority of the patients evaluated were women (59.0%). Admitted patients were more likely to be clinically severe, encephalopathic, present to care sooner after symptoms developed, and have a more acute time course (table 1). The mRS score of patients who underwent workup for ataxia as an inpatient had higher (worse) mRS scores on presentation than those who underwent workup as an outpatient (median mRS score 4, interquartile range [IQR] 2–4 vs median mRS score 2, IQR 1–3; $p = 0.0005$). Patients who were admitted for initial evaluation were also more severe based on ambulatory status at the time of presentation. For example, 47.4% of the patients evaluated as inpatients were wheelchair dependent compared with 6.8% of the patients evaluated as outpatients ($p = 0.0005$). Admitted patients presented sooner after their symptoms started (median 4.0 months, IQR 1–10 months, vs median 18.0 months, IQR 6–58 months). Admitted patients had a more rapid time course than patients who were evaluated as outpatients (table 1). Also, admitted patients were more likely to present with encephalopathy in addition to ataxia compared with the outpatient cohort (42.1% vs 11.9%, $p = 0.007$).

Diagnostic Evaluation
Patients evaluated as inpatients were more likely to undergo a lumbar puncture (84.2% vs 39.0%, $p = 0.0006$), CT of the chest (94.7% vs 62.7%, $p = 0.01$), and CT of the abdomen/pelvis (84.2% vs 59.3%, $p = 0.047$) than those evaluated initially as outpatients (table 2). Nearly all patients had an MRI of the brain (89.5% of patients evaluated as inpatients vs 94.9% of patients evaluated as outpatients, $p = 0.59$), and cerebellar atrophy was seen in a minority of these patients (25.0% of inpatients vs 30.2% of outpatient cohort, $p = 0.76$). An elevated serum neuronal or glial autoantibody titer was present in 16/71 (22.5%) of all of the patients who completed the serum paraneoplastic panel and autoimmune encephalopathy panels. The most common abnormally elevated antibody was P/Q type VGCC antibody in the patients who were eventually diagnosed with PCD (figure e-2, links.lww.com/NXI/A263 and table e-1, links.lww.com/NXI/A264). GAD65 antibody was the second most common abnormally elevated antibody overall, but was not elevated in any patients diagnosed with PCD in this cohort.

Diagnostic Outcomes and Etiologies
Patients who were admitted for initial workup were more likely to receive a diagnosis for their ataxia compared with outpatients (89.5% vs 57.6%; $p = 0.01$), and those who received a diagnosis received it faster after presentation than those who underwent outpatient workup (median 0.16 months, IQR 0.03–0.83 months vs median 2.0 months, IQR 0.4–7.1 months; $p = 0.03$; Tables 3 and 4). Follow-up times between those evaluated as an inpatient or outpatient were similar (median follow-up 14 months [IQR 5–40.5 months] vs 17 months [IQR 5–37 months], $p = 0.96$; table 4). In both

This study showed that for patients with ataxia with suspected paraneoplastic syndrome, inpatient admission to the hospital was associated with improved outcomes.

inpatients and outpatients alike, only a minority of the patients was ultimately diagnosed with PCD (2/17 [10.5%] of the inpatients vs 12 [20.3%] of the outpatients; $p = 0.5$; table 3). Of the patients who received a definitive or probable diagnosis for their ataxia, the most common diagnosis made in the inpatient cohort was nonparaneoplastic IMCA 9/17 (52.9%), and the most common diagnosis in the outpatient cohort was PCD 12/34 (35.3%; table 3). No patients were diagnosed with a neurodegenerative disease in the inpatient cohort, but in the outpatient cohort, 11/59 (18.6%) of patients were diagnosed with multiple systems atrophy, with predominant cerebellar ataxia.

Treatment Outcomes
Patients who underwent inpatient workup were more likely to receive immunotherapy than outpatients (73.6% vs 20.3%; $p < 0.0001$; table 3). In addition, of the patients who received immunotherapy, those who underwent inpatient workup received treatment in a shorter time frame from presentation than outpatients (median of 0.4 months, IQR 0.03–1 months vs 6.6 months, IQR 2–11.7 months; $p = 0.01$, table 4). Steroids were the most commonly prescribed immunosuppressant, followed by IVIG and plasma exchange. Patients evaluated as an inpatient or outpatient received similar rates of oncologic (21.1% vs 20.3%, $p = 1.0$) and symptomatic therapy (47.4% vs 49.2%, $p = 0.89$).

Functional Outcomes
A greater proportion of patients who were admitted for workup of ataxia improved, based on the mRS score, compared with those who underwent evaluation as an outpatient (52.6% vs 22.8%, $p = 0.01$, table 5). Of the patients who were treated with immunotherapy, the median change in the mRS score improved in the inpatient cohort and worsened in the outpatient cohort (-0.5 [IQR -1 to 1] vs 0.5 [0–2.5], $p = 0.04$).

Discussion

This study showed that for patients with ataxia with suspected paraneoplastic syndrome, inpatient admission to the hospital was associated with improved outcomes. Patients admitted for evaluation of ataxia with suspected PCD were more likely to receive a diagnosis in an expedited fashion. Likewise, they were more likely to receive immunotherapy

Table 2 Diagnostic Evaluations of Patients With Suspected Paraneoplastic Cerebellar Degeneration

Completed investigations	Inpatient (n = 19), n (%)	Outpatient (n = 59), n (%)	*p* Value
CT of the chest			
Ordered	18 (94.7%)	37 (62.7%)	0.01
Completed when ordered	17 (94.4%)	30 (81.1%)	0.25
Abnormality	8 (47.1%)	9 (30.0%)	0.24
CT of the abdomen/pelvis			
Ordered	16 (84.2%)	35 (59.3%)	0.047
Completed when ordered	15 (93.8%)	32 (91.4%)	1
Abnormality	3 (20.0%)	15 (46.9%)	0.08
PET scan			
Ordered	7 (36.8%)	11 (18.6%)	0.12
Completed when ordered	5 (71.4%)	9 (81.8%)	1
Abnormality	1 (20.0%)	7 (77.8%)	0.09
MRI of the brain			
Ordered	17 (89.5%)	56 (94.9%)	0.59
Completed when ordered	16 (94.1%)	53 (94.6%)	1
Abnormality	10 (62.5%)	43 (81.1%)	0.18
Cerebellar atrophy	4 (25.0%)	16 (30.2%)	0.76
Lumbar puncture			
Ordered	16 (84.2%)	23 (39.0%)	0.0006
Completed when ordered	16 (100.0%)	20 (87.0%)	0.26
Elevated WBC ≥8	3 (18.8%)	5 (25.0%)	0.71
Elevated prot ≥50	6 (37.5%)	7 (35.0%)	0.88
OCBs ordered	10	8	
≥4 OCBs	2 (20.0%)	4 (50.0%)	0.32
Neuronal antibodies ordered	3	6	
Elevated neuronal antibody titer	0	1 (16.7%)	1
Neuronal autoantibody panel			
Ordered	19 (100%)	58 (98.3%)	1
Completed when ordered	18 (94.7%)	53 (91.4%)	1
Elevated titer	3 (15.8%)	13 (24.5%)	0.53
GAD65 antibody			
Ordered	9 (47.4%)	30 (50.9%)	0.79
Completed when ordered	9 (100.0%)	28 (93.3%)	1
Elevated titer	4 (44.4%)	1 (3.6%)	0.01

Abbreviations: GAD65 = glutamate decarboxylase 65; OCB = oligoclonal band; PCD = paraneoplastic cerebellar degeneration; Prot = protein; WBC = white blood count.
This describes the diagnostic workup that was ordered and then completed on patients with suspected PCD.

Table 3 Diagnostic and Therapeutic Outcomes of Patients

Variable	Inpatient (n = 19)	Outpatient (n = 59)	p Value
Immunotherapy, n (%)	14 (73.6%)	12 (20.3%)	<0.0001
IVIG	8 (61.5%)	10 (83.3%)	0.38
Steroids (IV)	12 (92.3%)	9 (75%)	0.32
Steroids (PO)	6 (46.1%)	5 (41.7%)	0.82
Rituximab	2 (15.4%)	0	0.48
Cyclophosphamide	2 (15.4%)	3 (25%)	0.64
PLEX	6 (46.2%)	1 (8.3%)	0.07
Azathioprine	3 (23.1%)	1 (8.3%)	0.59
Oncologic treatment, n (%)	4 (21.1%)	12 (20.3%)	1
Symptomatic therapy, n (%)	9 (47.4%)	29 (49.2%)	0.89
Definitive or probable diagnostic etiology of ataxia, all causes, n (%)	17 (89.5%)	34 (57.6%)	0.01
Definitive or probable diagnostic etiology of ataxia, paraneoplastic, n (%)	2 (10.5%)	12 (20.3%)	0.5
Diagnostic etiology of those with a diagnosis, n (%)	N = 17	N = 34	
Immune mediated	2 (11.8%)	12 (35.3%)	0.002
Paraneoplastic immune mediated	9 (52.9%)	4 (11.8%)	
Nonparaneoplastic			
MSA-C	0	11 (32.4%)	
Genetic	2 (11.8%)	2 (5.9%)	
Vertebrobasilar insufficiency	1 (5.9%)	1 (2.9%)	
Iatrogenic	1 (5.9%)	2 (5.9%)	
Other	2 (11.8%)	2 (5.9%)	

Abbreviations: IVIG = IV immunoglobulin; MSA-C = multiple system atrophy, cerebellar variant; PO = oral; PLEX = plasma exchange.
This table describes the treatments administered to patients and the diagnostic etiologies given to patients who received a diagnosis for their ataxia. Of note, all genetic diagnoses were confirmed with genetic testing.

Table 4 Timing (Months) From Symptom Onset and Presentation to Diagnosis and Treatment

Variable	Inpatient (n = 19)[a]	Outpatient (n = 59)[a]	p Value
Follow-up time (months)	14 (5–40.5)	17 (5–37)	0.96
Time from symptom to immunotherapy	5.8 (1.5–9)	18 (8.6–50.75)	0.003
Time from presentation to immunotherapy	0.4 (0.03–1)	6.6 (2–11.7)	0.01
Time from symptom to diagnosis	5.3 (1.7–8.5)	23.7 (7.5–56.5)	0.0005
Time from presentation to diagnosis	0.16 (0.03–0.83)	2.0 (0.4–7.1)	0.03
Time from symptom to presentation	4 (1–10)	18 (6–58)	0.0005

[a] All statistics are median (interquartile range). The time to immunotherapy and diagnosis only includes those patients who received immunotherapy and a diagnosis, respectively. There were 2 patients who were lost during follow-up in the outpatient cohort.

Table 5 Functional Outcomes of All Patients

Variable	Inpatient (n = 19)	Outpatient (n = 59)	*p* Value
mRS score at follow-up, median (IQR)	3 (2 to 4)	2 (1–3)	0.12
mRS score at follow-up, n (%)			0.32
0	1 (5.3%)	3 (5.3%)	
1	1 (5.3%)	16 (28.1%)	
2	4 (21.1%)	11 (19.3%)	
3	7 (36.8%)	13 (22.8%)	
4	3 (15.8%)	9 (15.8%)	
5	2 (10.5%)	2 (3.5%)	
6	1 (5.3%)	3 (5.3%)	
Change in the mRS score, median (IQR)	−1 (−1 to 1)	0 (0–1)	0.08
Change in the mRS score,	10 (52.6%)	13 (22.8%)	0.01
Improved n (%)			
Change in the mRS score of those treated with immunotherapy; median (IQR)	−0.5 (−1 to 1)	0.5 (0–2.5)	0.04
Change in the mRS score of those treated with immunotherapy; improved, n (%)	7 (50%)	1 (8.3%)	0.04
Change in the mRS score, stayed the same or worse, n (%)	9 (47.4%)	44 (77.2%)	
Ambulatory status at follow-up, median (IQR)	4 (2 to 5)	4 (2–4)	0.39
Ambulatory status at follow-up, n (%)			0.79
1	1 (5.3%)	7 (12.3%)	
2	4 (21.1%)	16 (28.1%)	
3	3 (15.8%)	4 (7.0%)	
4	5 (26.3%)	16 (28.1%)	
5	5 (26.3%)	11 (19.3%)	
6	1 (5.3%)	3 (5.3%)	
Change in ambulatory status, median (IQR)	0 (−1 to 1)	0 (0–1)	0.21
Change in ambulatory status, improved, n (%)	6 (31.6%)	10 (17.5%)	0.21
Change in ambulatory status, stayed the same or worse, n (%)	13 (68.4%)	47 (82.5%)	

Abbreviations: AS = ambulatory status; IQR = interquartile range; mRS = modified Rankin Scale.
This describes the functional outcomes of patients based on the change in the mRS score and ambulatory status in those who were evaluated initially as inpatients verses outpatients.

and to receive it faster. Patients who were admitted for initial evaluation in this study received immunotherapy over 15 times faster than the outpatients. It has been shown that the delay of treatment affects the outcome of patients, particularly those with immune-mediated neurologic diseases.[5]

Although there are potential benefits to an inpatient admission, almost all of the patients in this study had outpatient follow-up. For those who do not have a malignancy identified during hospitalization, these patients may need additional testing after discharge.[7] It is important to note that there are a number of diagnostic tests that can be helpful in identifying occult malignancy, such as mammogram or PET-CT, but these tests may be challenging to obtain as inpatients in the United States.[15] Collaboration between inpatient and outpatient providers is important to facilitate ongoing care and treatment between settings. Although there are benefits to expedited inpatient evaluation and treatment noted in this study, the cost-effectiveness of this approach remains unknown. More work is needed to refine the diagnostic approach to more quickly diagnose and treat patients with suspected PCD.

Similar to previous assessments of paraneoplastic disorders, which largely rely on retrospective analyses, the limitations in

this study arise from using medical record chart abstraction to identify the clinical presentation and outcomes.[16] Because of limitations in abstracting information from the records, details of whether patients were offered inpatient admission and declined were not available. There were differences between the patient cohorts both at baseline and throughout their workup, introducing both selection and ascertainment biases. Those who were admitted presented earlier in their disease course and were more severe at presentation. The diagnostic workup differed, with inpatients undergoing more lumbar punctures and CT scans of the chest, abdomen, and pelvis. The ultimate etiology of the ataxia differed between the cohorts as well. PCD was more commonly diagnosed as an outpatient. Nonparaneoplastic immune-mediated ataxia, which is more amenable to treatment, was a more common diagnosis in the inpatient cohort. Given the nature of this study as pilot data, no correction was performed for multiple analyses. More research is needed to delineate which subgroup of patients with ataxia with suspected PCD would benefit most from inpatient admission. The generalizability of this study may also be limited due to the geographic and practice-based variation of treatment of neurologic paraneoplastic syndromes and other immune-mediated neurologic disorders.[17]

Patients admitted for the evaluation of a suspected PCD received a diagnosis and immunotherapy faster than their outpatient counterparts did. Despite the limitations, this study provides evidence supporting the use of initial expedited inpatient evaluation and treatment of patients with ataxia with a suspected paraneoplastic syndrome, particularly those who are severely functionally affected. Further research is needed to identify a systematic approach to the evaluation and treatment of patients with ataxia.

Study Funding

TAKE-HOME POINTS

→ Inpatient admission in patients with ataxia with suspected PCD was associated with improved outcome.

→ Patients admitted for evaluation of paraneoplastic cerebellar degeneration were more likely to receive a diagnosis and to receive a diagnosis faster than those evaluated initially as outpatients.

→ Patients admitted for evaluation of paraneoplastic cerebellar degeneration were more likely to receive immunotherapy and receive immunotherapy faster than those evaluated initially as outpatients.

Disclosure

Publication History

Appendix Authors

Name	Location	Contribution
Natalie Witek, MD, MS	Rush University, Chicago, IL	Designed and conceptualized the study; major role in acquisition of data; analyzed the data; interpreted the data; and drafted the manuscript for intellectual content
Mitra Afshari, MD, MPH	Rush University, Chicago, IL	Interpreted the data; analyzed the data; and revised the manuscript for intellectual content
Yuanqing Liu, MS	Rush University, Chicago, IL	Analyzed the data; performed statistical analysis; revised the manuscript for intellectual content; and interpreted the data
Bichun Ouyang, PhD	Rush University, Chicago, IL	Analyzed the data; performed statistical analysis; revised the manuscript for intellectual content; and interpreted the data
Deborah Hall, MD, PhD	Rush University, Chicago, IL	Designed and conceptualized the study; interpreted the data; and revised the manuscript for intellectual content

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