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Inpatient Rehabilitation Performance of Patients with Paraneoplastic Cerebellar Degeneration

Jack B. Fu, MD, Vishwa S. Raj, MD¹, Arash Asher, MD², Jay Lee, PhD³, Ying Guo, MD, Benedict S. Konzen, MD, and Eduardo Bruera, MD

Department of Palliative Care and Rehabilitation Medicine The University of Texas MD Anderson Cancer Center 1515 Holcombe Blvd., Unit 1414 Houston, Texas 77030

¹ Department of Physical Medicine & Rehabilitation, Carolinas Health System

² Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center

³ Department of Educational Psychology, University of Houston

Abstract

Objective—To evaluate the functional improvement of rehabilitation inpatients with paraneoplastic cerebellar degeneration.

Design—Retrospective Review

Setting—Three tertiary referral based hospitals.

Interventions—Medical records were retrospectively analyzed for demographic, laboratory, medical and functional data.

Main Outcome Measure—Functional Independence Measure (FIM)

Participants—Cancer rehabilitation inpatients admitted to three different cancer centers with a diagnosis of paraneoplastic cerebellar degeneration (n=7).

Results—All 7 patients were white females. Median age was 62. Primary cancers included ovarian carcinoma (2), small cell lung cancer (2), uterine carcinoma (2), and invasive ductal breast carcinoma. Mean admission total FIM score was 61.0 (SD=23.97). Mean discharge total FIM score was 73.6 (SD=29.35). The mean change in total FIM score was 12.6 ($p=.0018$). The mean length of rehabilitation stay was 17.1 days. The mean total FIM efficiency was 0.73. 5/7 (71%)

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Correspondence: All correspondence and requests for reprints should be addressed to: Jack Fu, M.D., Department of Palliative Care and Rehabilitation Medicine, Unit 1414, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030; Tel: 713-792-6085; Fax: 713-792-6092; jfu@mdanderson.org..

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Disclosures:

This study will be presented at the 2014 American Academy of Physical Medical & Rehabilitation Annual Assembly as a poster presentation in November 2014. We certify that no party having a direct interest in the results of the research supporting this article has or will confer a benefit on us or on any organization with which we are associated AND, if applicable, we certify that all financial and material support for this research (e.g., NIH or NHS grants) and work are clearly identified in the title page of the manuscript.

patients were discharged home. 1/7 (14%) was discharged to a nursing home. 1/7 (14%) transferred to the primary acute care service.

Conclusions—This is the first study to demonstrate the functional performance of a group of rehabilitation inpatients with paraneoplastic cerebellar degeneration. Despite the poor neurologic prognosis associated with this syndrome, these patients made significant functional improvements on inpatient rehabilitation. When appropriate, inpatient rehabilitation should be considered. Further studies with larger sample sizes are needed.

Keywords

Paraneoplastic; Cerebellar; Degeneration; Inpatient; Rehabilitation

INTRODUCTION

Although rare, paraneoplastic cerebellar degeneration (PCD) is one of the most common paraneoplastic syndromes and is most often associated with lung, lymphoma, gynecologic, and breast cancer. However, it has been estimated that only 1 in 10,000 patients with cancer develop a paraneoplastic syndrome.¹ PCD is only a portion of this small population. The disease is characterized by a rapid and severe onset of cerebellar symptoms (ataxia, dysarthria, dizziness, tremors). High titers of antibodies that react with cerebellar Purkinje cells can be found.²

Unfortunately, effective treatments for PCD are limited and the prognosis for neurologic recovery is quite poor.³ The current published literature regarding PCD inpatient rehabilitation consists of 3 case reports.^{4,5,6} This is the first study to analyze the functional performance of a group of rehabilitation inpatients with PCD.

METHODS

Subjects

A retrospective review of medical records at 3 tertiary referral based American hospitals, revealed 7 patients who had been admitted to inpatient rehabilitation with a diagnosis of paraneoplastic cerebellar degeneration from 8/27/1997 through 4/29/2013.

Procedure

Approval for this study was obtained from the 3 respective institutional review boards (IRB). A waiver of informed consent was granted by the IRB's in compliance with federal and institutional guidelines. Data was shared based upon a materials transfer agreement. Information was collected by experienced clinicians from medical records. Data obtained included demographic, laboratory, medical and functional data. Demographic information included age, date of death, sex, race, and insurance type. Laboratory information including white blood cell, platelet, albumin, prealbumin, and creatinine at time of transfer to inpatient rehabilitation. Medical information included primary cancer, results of a paraneoplastic antibody panel, treatment received for PCD, time since PCD and cancer treatment, time since PCD and cancer diagnosis, and length of acute care stay prior to rehabilitation transfer. Functional information included Functional Independence Measure scores at both admission

and discharge to rehabilitation, length of stay on rehabilitation, discharge disposition, and type of therapy after discharge.

Because of the small sample size and the distribution of the patient's FIM scores, a *t*-distribution analysis was performed on total FIM and FIM subscores (ADL, mobility, and cognition). For each subscore the standard error for 95% of samples and 95% confidence intervals were calculated. A one-tailed test for improved subscores was performed.

RESULTS

The mean age was 62 (Range 47-86). Demographic and PCD characteristics are listed in Table 1. All of the patients were admitted to inpatient rehabilitation due to ataxia and incoordination.

Two of the patients were admitted directly from home to inpatient rehabilitation. Excluding the direct admissions from home to inpatient rehabilitation (2/7), the mean length of acute care hospital stay prior to rehabilitation transfer was 13.6 days (SD =7.3). The mean days from original cancer diagnosis to inpatient rehabilitation admission was 252 (SD=206). The mean days from PCD diagnosis to inpatient rehabilitation admission was 68 (SD=74). Excluding alive patients (2/7) as of 3/12/2014, the mean days from rehabilitation admission until death was 418 (SD=532). One patient received chemotherapy (carboplatin) while on inpatient rehabilitation. Out of the remaining patients, the mean days from last chemotherapy to rehabilitation admission was 82 (SD=78). Three patients received PCD treatment (1 patient received IVIG and 2 others received IV steroids) while on inpatient rehabilitation. Out of the remaining patients, the mean days from last PCD treatment to inpatient rehabilitation admission was 47.5 (SD=67).

Mean laboratory values (mean, SD) for white blood cell (5.7, 2.4), platelet (199.4, 57.2), prealbumin (25.5, 2.7), albumin (3.4, 0.5), and creatinine (0.8, 0.4) were within or nearly within clinically accepted limits.

One patient did return to the primary acute care service due to a syncopal episode. The patient was on inpatient rehabilitation for only 8 days (the shortest out of the group), had the lowest admission total FIM score, and showed no improvement in functional scores.

The mean inpatient rehabilitation length of stay was 17.1 days. The mean total FIM efficiency was 0.7. The mean FIM efficiency subscores were 0.2, 0.3, and 0.2 for ADL, mobility, and cognition respectively. The mean total FIM change from admission to discharge was 12.6 ($p=0.0018$). The average FIM score per item was a 3 (moderate assistance) at admission and a 4 (minimal assist) at discharge. None of our patients were ambulating independently at rehabilitation admission (FIM range was 1-3). Only 1/7 patient was walking without physical assistance at discharge (supervision). Occupational therapists addressed hand coordination and activities of daily living. Speech therapists performed memory training, articulation, and breathing exercises. Physical therapists addressed gait, balance, transfers, core strengthening, family training and assistive devices. Out of the 5 patients discharged home, 3 received home health therapy and 2 received outpatient therapies. Functional data and the results of the analysis are listed in Table 2.

A scatterplot with best fit line of total admission FIM scores and total FIM efficiency is shown in Figure 1. Patients with a lower admission FIM score tended to have a lower total FIM efficiency. Those with a higher admission FIM score tended to have a higher total FIM efficiency. A linear fit graphic is displayed ($R^2=0.596$).

DISCUSSION

While there have been 3 prior published individual case reports of PCD rehabilitation inpatients, this is the first study to look at a group of patients. Those reports demonstrated modest to substantial functional improvement.^{4,5,6} The results of this study confirm the results of the prior case reports. This information would be useful for rehabilitation professionals because of the complex nature of PCD patients which can include neurologic, musculoskeletal, and deconditioning issues.

Many oncologists do not recognize the potential benefit of rehabilitation and under-refer patients to physiatry.⁷ Besides its rarity, this also likely contributes to its infrequent occurrence in acute inpatient rehabilitation units.

Demographically, all of our patients were female. Given that gynecologic cancers and breast cancer (5/7 of our group of patients) are among the most common primary cancers associated with this condition, a predominance of females might be expected. Our patients received a diverse set of PCD treatments. There are no evidence based treatment strategies for PCD and thus most treatment is speculative.³

It has been reported that only 34% of PCD patients are ambulatory when the syndrome reaches its plateau.⁸ Therefore, many PCD patients likely have functional deficits that could be addressed through inpatient rehabilitation. The poor neurologic prognosis of PCD has also been well documented in the literature.⁸ Knowing this prognosis, one could argue that acute inpatient rehabilitation would be ineffective for these patients. However, the patients in our study were able to make statistically significant functional improvements in all FIM subscores and total FIM. Due to the retrospective nature of our study, we were unable to determine which improvements were due to recovery versus compensation. However, we suspect that the majority of the improvements were compensatory in nature. Nevertheless, the improved function can impact independence, quality of life and expedite discharge.

A rate of return to the primary acute care service of 8%-11% and transfer to a sub-acute rehabilitation of 3-7% has been reported in patients with brain tumors. Our PCD rehabilitation inpatients had total FIM efficiencies that were near what has been reported for primary brain mostly cerebral brain tumor patients (between 0.72 and 1.9).^{9, 10}

Limitations

The low number of patients in this study is a weakness. The rarity of the syndrome makes it difficult to amass a large numbers of patients.

The degree of ataxia was not quantified in this patient population and could be related to function. Future studies will also likely need to be multi-centered. Our study is limited to acute inpatient rehabilitation. Evaluating all PCD patients from initial diagnosis would shed

light on referral patterns. Documenting which improvements were compensatory versus recovery would be useful.

CONCLUSION

Despite the poor neurologic prognosis associated with paraneoplastic cerebellar degeneration, these patients can make significant functional improvements on inpatient rehabilitation. When appropriate, the results of this study strongly suggest that inpatient rehabilitation for PCD should be considered.

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Abbreviations

PCD	Paraneoplastic Cerebellar Degeneration
FIM	Functional Independence Measure
IRB	Institutional Review Board
ADL	Activities of Daily Living
R²	Coefficient of Determination

REFERENCES

1. Darnell RB, Posner JB. Paraneoplastic syndromes affecting the nervous system. *Semin Oncol*. 2006; 33:270–98. [PubMed: 16769417]
2. Posner, JB. Neurologic complications of cancer. F.A. Davis; Philadelphia: 1995.
3. Greenlee JE. Treatment of paraneoplastic cerebellar degeneration. *Curr Treat Options Neurol*. Apr; 2013 15(2):185–200. [PubMed: 23315179]
4. Liu S, Tunkel R, Lachmann E, Nagler W. Paraneoplastic Cerebellar Degeneration as the First Evidence of Cancer: A Case Report. *Arch Phys Med Rehabil*. 2000; 81:834–836. [PubMed: 10857534]
5. Sliwa J, Thatcher S, Jet J. Paraneoplastic Subacute Cerebellar Degeneration: Functional Improvement and the Role of Rehabilitation. *Arch Phys Med Rehabil*. 1994; 75:355–357. [PubMed: 8129592]
6. Perlmutter E, Gregory P. Rehabilitation Treatment Options for a Patient with Paraneoplastic Cerebellar Degeneration. *Am J Phys Med Rehabil*. 2003; 82:158–162. [PubMed: 12544763]
7. Cheville AL. Cancer rehabilitation. *Semin Oncol*. 2005; 32:219–224. [PubMed: 15815968]
8. Shams'ili S, Grefkens J, de Leeuw B, van den Bent M, Hooijkaas H, van der Holt B, Vecht C, Sillevs Smitt P. Paraneoplastic cerebellar degeneration associated with antineuronal antibodies: analysis of 50 patients. *Brain*. Jun; 2003 126(Pt 6):1409–18. [PubMed: 12764061]
9. Fu JB, Parsons HA, Shin KY, Guo Y, Konzen BS, Yadav RR, Smith DW. Comparison of functional outcomes in low- and high-grade astrocytoma rehabilitation inpatients. *Am J Phys Med Rehabil*. Mar. 2010; 89(3):205–12. [PubMed: 20068429]
10. Raj VS, Groves C, Kim H, Bomberger C, Norton JH. Variations in Functional Outcome Stratified by Discharge Disposition and Oncological Treatment Groups After Acute Inpatient Rehabilitation for Brain Tumor Patients. *The Open Rehabilitation Journal*. 2012; 5:41–47.

- 3 tertiary referral based hospitals pool their rehabilitation inpatients with paraneoplastic cerebellar degeneration to achieve a n=7.
- We examined the functional improvement of these rehabilitation inpatients.
- A statistically significant improvement in all functional independence measure (FIM) subscores and total FIM were achieved.
- Patients with a low admission FIM tended to have a lower FIM efficiency.

FIM=Functional Independence Measure, R^2 =Coefficient of Determination

Figure 1.

Scatterplot of Total Admission FIM vs. Total FIM Efficiency

Table 1

Demographic & Medical Data (n=7)

Race	Number (Percent)
White	7 (100)
Sex	
Female	7 (100)
Marital Status	
Married	5 (71)
Divorced	1 (14)
Widowed	1 (14)
Insurance Type	
Private Insurance	3 (43)
Medicare	3 (43)
Medicaid	1 (14)
Primary Cancer Type	
Endometrial Adenocarcinoma	2 (29)
Ovarian Serous Carcinoma	2 (29)
Small Cell Lung Carcinoma	2 (29)
Breast Invasive Ductal Carcinoma	1 (14)
Paraneoplastic Antibodies	
GAD 65	1 (14)
Hu	1 (14)
Yo	1 (14)
Purkinje Cell Type 1	1 (14)
Purkinje Cell Type 1 + Yo	1 (14)
Purkinje Cell Type 1 + Calcium Channel	1 (14)
None Found	1 (14)
Treatments Received for PCD	
IVIG alone	2 (29)
IVIG + Steroids	2 (29)
IVIG + Plasmapheresis	1 (14)
Carboplatin & Taxol	1 (14)
Plasmapheresis + Steroids	1 (14)
Discharge Disposition	
Home	5 (71)
Nursing Home	1 (14)
Return to the Primary Acute Care Service	1 (14)

GAD=glutamic acid decarboxylase; PCD= Paraneoplastic Cerebellar Degeneration; IVIG=Intravenous Immunoglobulin

Table 2*t*-Distribution Analysis of FIM Subscore Changes

FIM ADL	Admission	Discharge	Change
Median	23	26	5
Mean	20.57	24.71	4.14
Standard Deviation	9.27	10.35	2.79
Standard Error	3.50	3.91	1.05
One tailed test for improvement	$p=0.0039$		
FIM Mobility			
Median	11	16	5
Mean	10.42	15.14	4.71
Standard Deviation	4.15	8.29	5.08
Standard Error	1.57	8.29	5.08
One tailed test for improvement	$p=0.0249$		
FIM Cognition			
Median	25	29	1
Mean	22.14	25.28	3.14
Standard Deviation	10.82	9.65	4.18
Standard Error	4.09	3.64	1.58
One tailed test for improvement	$p=0.0469$		
FIM Total			
Median	72	80	13
Mean	61	73.57	12.57
Standard Deviation	23.97	29.35	7.20
Standard Error	9.06	11.09	2.72
One tailed test for improvement	$p=0.0018$		

FIM=Functional Independence Measure; ADL=Activities of Daily Living