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Managing Advanced Progressive Supranuclear Palsy and Corticobasal Degeneration in a Palliative Care Unit: Admission Triggers and Outcomes

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Abstract

Background: Progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) are characterized by rapid deterioration and a fatal outcome. **Objectives:** Admission triggers, treatment efficacy, and care patterns. **Methods:** Retrospective analysis of patients with PSP/CBD admitted to an inpatient specialized palliative care service. **Results:** In 38 patients, there were 63 admissions for swallowing difficulties, falls, pain, impaired communication, cognitive/mood disturbances, respiratory symptoms, and infection. Mean length of stay was 11.6 days. Treatment response was variable. In 68%, of admission episodes there was stabilization or improvement, 75% were discharged home. In case of readmission, the mean interval has been 9.7 months. Time since diagnosis and admission triggers were not associated with outcome or death. **Conclusion:** Patients showed high symptom load contrasting with discharge rates and subsequent health care utilization. Brief multidisciplinary interventions might be helpful to preserve autonomy.

Keywords

progressive supranuclear palsy, corticobasal degeneration, palliative care, symptom management, late phase, health care utilization

Introduction

Only recently it has been recognized that patients with Parkinson's disease (PD) and atypical Parkinsonian disorders like progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and multiple systems atrophy (MSA) benefit from specialized palliative care,[1] a well-established approach for patients with other disabling and progressive neurologic conditions such as amyotrophic lateral sclerosis. In the absence of effective disease-modifying pharmacologic management, the therapeutic goal is to alleviate symptom burden, to preserve patient autonomy as long as possible, and to provide high quality end-of-life (EoL) care.

Atypical Parkinsonian disorders present with PD-like symptoms but do not or only transiently respond to dopaminergic drug regimens. Although there is some reduction in life expectancy in patients with PD,[2,3] patients diagnosed with atypical Parkinsonian disorders face a more rapid disease progression and a poorer prognosis with a median overall survival of 3 to 6 years after diagnosis.[4,5] Patients with PSP present with a gradually worsening coordination of gait, speech, and swallowing, complicated by pain, respiratory, and neuropsychiatric symptoms; median survival after onset of symptoms is 5.8 years,[6-9] while early onset dysphagia, cognitive impairment, old age, and time to disability seem to predict poor survival.[10] Patients with CBD have similar clinical features—nonfluent aphasia, frontal dementia, limb dystonia, and postural instability[11]—and considered a spectrum of diseases rather than a distinct entity by some authors since investigations often lack neuropathologic confirmation.[8] Both conditions share the common etiology of a pathological misfolding of the tau protein.

As these conditions are rare with an age-adjusted PSP prevalence of 6.4 per 100 000 (95% confidence interval 2.3-10.6)[12] and an unknown prevalence for CBD in Europe, patients with PSP and CBD are usually seen at highly specialized

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neurology outpatient clinics. However, there is little published information on health care utilization by these patients as disease progresses toward its final stage. Usually they die at home or in general hospitals.[13] In most cases, bronchopneumonia, aspiration pneumonia, or falls with severe injuries will precipitate the dying process. Because reimbursement is sometimes linked to a life expectancy shorter than the observed 15 to 24 months from the onset of swallowing difficulties in patients with PSP and CBD,[4] hospice programmes may be reluctant to enroll these patients. Initiation of palliative and hospice care is frequently delayed by lacking awareness and structural barriers, while at the same time health status and autonomy of these patients are deteriorating rapidly and family caregivers experience a growing need for multidisciplinary support.

Therefore, to obtain basic information on this cohort's utilization of health care resources and the role of inpatient palliative care services in particular, the authors focused on palliative care unit (PCU) referrals and retrospectively evaluated admission triggers, overall efficacy of symptom management, and the patterns of subsequent care.

Patients and Methods

Patients were regularly seen at the movement disorder outpatient clinic at the Department of Neurology, Klinikum Grosshadern, Ludwig-Maximilians University Munich (April 2006-December 2012). If in high demand for inpatient care, they were admitted by the neurology team in charge (GN or SL) to the institution's PCU which was run by an integrated palliative care/neurology team. In patients residing outside the Munich area, telephone contacts with the general practitioner, home care nurse, informal carer, or the patient herself/himself (if possible) facilitated a thorough preadmission assessment of the acute problems. The study was approved by the local institutional review board. Written informed consent was not required since it was a retrospective chart review.

For inclusion in the analysis, a clinical diagnosis of PSP or CBD had to be made before admission to the PCU. In several cases, magnetic resonance imaging and nuclear imaging had been performed since onset of the disease. Diagnosis was further confirmed upon admission by clinical examination and review of imaging data, which was conducted by board-certified movement disorder experts.

The authors retrospectively collected the following demographic data of all patients by systematically hand searching all discharge documents: age, sex, neurologic diagnosis, time since diagnosis, other conditions, and distance from the patient's residence to the PCU. Dates of admission and discharge, length of stay (LoS), time intervals between admissions, and the date of death in the PCU (if applicable) were recorded. The symptoms on admission were prospectively assessed by the standard assessment tools used in the PCU; however, symptoms were not quantified but recorded in a ''yes/no'' fashion. From the discharge documents, the following categories of features triggering admission were derived:

- swallowing difficulties included dysphagia, pseudohypersalivation, and frequent aspiration resulting from progressive bulbar involvement;
- gait instability/falls specifically referred to any impairment of posture and locomotion;
- spasticity/pain was defined as impairment of motility caused by pathological muscle tonus, possibly associated with musculoskeletal pain;
- impaired communication referred to any dysarthria or the need for a communication device;
- cognitive/mood disorders included personality changes, depression, hallucinations, and cognitive impairment;
- respiratory symptoms were defined as cough and dyspnea; and
- infection covered both pneumonias and urinary tract infections.

Each pharmacological and nonpharmacological intervention, regardless of its specific intention (disease modifying or symptom oriented), was recorded. Symptom control at discharge was documented, and for each symptom a response rate was calculated (admission episodes with improvement divided by all admission episodes with this symptom). In addition, the overall clinical meaningful outcome of each PCU admission was documented (general stabilization or improvement as opposed to deterioration). Finally, the setting of patient care after PCU discharge was documented as well as the health care structures involved in the subsequent management (home/home with nursing support/home with palliative care team $\pm$ nursing support/nursing home or rehabilitation facility).

Frequencies of the events were analyzed by descriptive statistics. To detect possible associations between patient variables (age, sex, distance from home to PCU, time since diagnosis, time interval between admissions, LoS, or presence of any of the symptoms) and outcome variables (stabilization/improvement vs deterioration and death during admission), the chi-square (χ^2) test (for dichotomous variables), and the Mann-Whitney U and Kruskal-Wallis tests (for continuous variables) were performed. To correct for multiple testing, the Bonferroni correction was applied when appropriate. Statistical significance was assumed at a P value of $<.05$. IBM SPSS version 20 was used for calculations.

Results

From April 2006 to December 2012, among a total of 649 PCU admissions, 38 (5.9%) patients with PSP or CBD were identified: 35 of these patients were clinically diagnosed with PSP and 3 with CBD.

Table 1 displays the demographic characteristics of this cohort. In short, patients were predominantly elderly individuals, all of a caucasian origin, and the female:male ratio was balanced. They had a cardiovascular comorbidity profile typically seen in this age-group (data not shown) and had long-standing PSP or CBD (mean time from first diagnosis to PCU admission: 4.5 years). The LoS value of ''0 days'' in 1 patient

Table 1. Patient Characteristics

Age, mean ± SD (range), years	68.6 ± 7.2 (51-86)
Sex: females/males, no.	18/20
Diagnosis: PSP/CBD, no.	35/3
Distance pt.'s home—PCU, mean ± SD (range), km	114 ± 173.2 (3-775)
LoS in the PCU, mean ± SD (range), days	11.6 ± 5.9 (0-34)
Patients with 1 admission, no.	20 (53%)
Patients with 2 admissions, no.	11 (29%)
Patients with 3 or more admissions, no.	7 (18%)
Time since diagnosis, mean ± SD (range), years	4.5 ± 2.9 (0.75-12)
Interval between readmissions, mean ± SD (range), months	9.7 ± 10.6 (0.25-40)

Abbreviations: CBD, corticobasal degeneration; LoS, length of stay; PCU, palliative care unit; PSP, progressive supranuclear palsy; SD, standard deviation.

resulted from death on the day of admission. Eighteen patients were admitted more than once to the PCU after a median time interval of 9.7 months; in total, there were 63 admissions in these 38 patients. All study participants were living at home or in a nursing facility at the time of PCU admission and were recruited from a large catchment area covering the whole of Germany.

Figure 1 shows the symptoms most frequently triggering admission to the PCU and the numbers of responses to treatment. Response to treatment ranged from 4 (11%) of the 37 patients who benefitted from approaches addressing swallowing difficulties up to 15 (52%) of the 29 who had an improvement in their spasticity and pain.

Presence of communication deficits was associated with gait instability/falls (χ^2 test, $P = .018$ after Bonferroni correction for multiple testing). Patients who presented with swallowing problems were less likely to have cognitive/mood disturbances ($P = .018$). However, no further symptom clustering could be observed. General stabilization or improvement was observed in 43 (68%) of the 63 admission episodes, deterioration or death in 15 (24%) of the 63, and for 5 (8%) of the 63 admission episodes outcome data were missing (Figure 2A). Symptoms triggering admission did not correlate with overall outcome or death during admission (χ^2 test, $P > .05$) after the Bonferroni correction; a trend toward stable or improved outcome in patients presenting with swallowing difficulties did not reach statistical significance ($P = .056$). Age, distance of residence to the PCU, time since diagnosis, LoS, and time intervals between admissions did not correlate with either overall outcome or death in the PCU (Mann-Whitney U test, $P > .05$) nor did sex (χ^2 test, $P > .05$). Place of subsequent care (Figure 2B) was not associated with presenting symptoms, sex (χ^2 test, $P > .05$), and the other patient variables (Kruskal-Wallis test, $P > .05$).

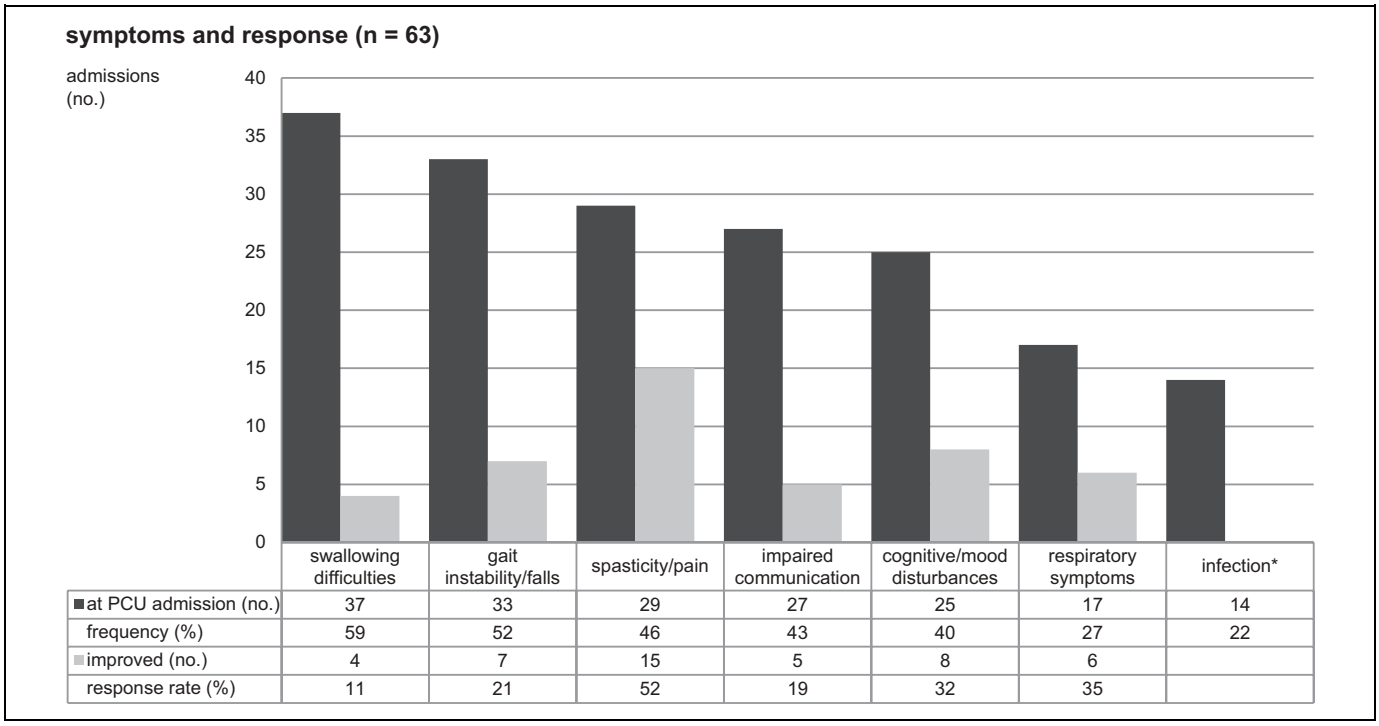
Table 2 specifies the most common therapeutic interventions (pharmacological and nonpharmacological) actually performed. In addition, physiotherapy, swallowing exercises, rehabilitation, nutritional counselling, and psychological support were provided to all patients if needed. The aim of any of these actions was palliation of symptoms and maintenance of patient autonomy.

Figure 2B shows the distribution of settings of care after discharge from the PCU. In 75% of admission episodes, patients were discharged home—without professional caregiver support at home (47%), with nursing support only (9%), or with a hospice or palliative care team ± nursing support (19%). Two discharges were made to a nursing home, one to a rehabilitation facility.

Discussion

In this retrospective patient chart-based survey on 63 PCU admissions in a cohort of 38 patients with PSP or CBD, the authors observed that (1) these patients had long-standing disease with a median time from diagnosis of 4 years and experienced death in the PCU in only 14% of cases, (2) they were referred across long distances of up to 775 km for highly specialized symptom management, indicating that symptom burden might not be well controlled by local support, (3) they presented with a variety of symptoms such as swallowing difficulties that were only partly amenable to interventions, with treatment responses ranging from 11% (swallowing difficulties) to 52% (spasticity and pain), (4) some of the agents used here may be unfamiliar to palliative care physicians (eg, anti-Parkinson drugs and botulinum toxin), (5) symptoms refractory to therapy were not associated with an adverse outcome at the time of discharge, (6) in 68% of admission episodes, there was stabilization or improvement in symptoms, and (7) in 75%, patients returned home after a brief inpatient period, the majority without specialist support, with an interval of several months between readmissions. Surprisingly, high symptom load seemed to contrast with low health care utilization after discharge.

It has been acknowledged by the UK National Health Service that "palliative care requirements of people with PD should be considered throughout all phases of the disease." (p. 24)[14] This applies also to patients with atypical Parkinsonian disorders. They experience early disability[15] but are usually diagnosed late in the course of their disease,[16] commonly present with symptoms such as dysarthria or dysphagia, which are associated with a survival of only 15 to 24 months,[17] suffer frequently from depression, which affects their subjective health status,[18] and have a higher risk of respiratory-related death than patients with PD.[13] A longitudinal UK study of 50 PD, 15 PSP, and 17 MSA patients having clinical characteristics similar to our cohort recently found a complex mix of poorly controlled symptoms, a high rate of deterioration at 1 year, and prediction of future symptoms by palliative problems.[19] According to a recent questionnaire survey involving 69 patients with PSP in Germany,[16] despite significant disabilities 87% of them were living at home with little or no support from professional caregivers, which is in line with the findings of this work. However, a Swedish study of 23 patients with PSP, CBD, or MSA revealed a high need for care by different



	swallowing difficulties	gait instability/falls	spasticity/pain	impaired communication	cognitive/mood disturbances	respiratory symptoms	infection*
at PCU admission (no.)	37	33	29	27	25	17	14
frequency (%)	59	52	46	43	40	27	22
improved (no.)	4	7	15	5	8	6	
response rate (%)	11	21	52	19	32	35	

Figure 1. Prevalence of symptoms at admission (black columns) and response (gray columns); * response of infections was not documented. PCU indicates palliative care unit.

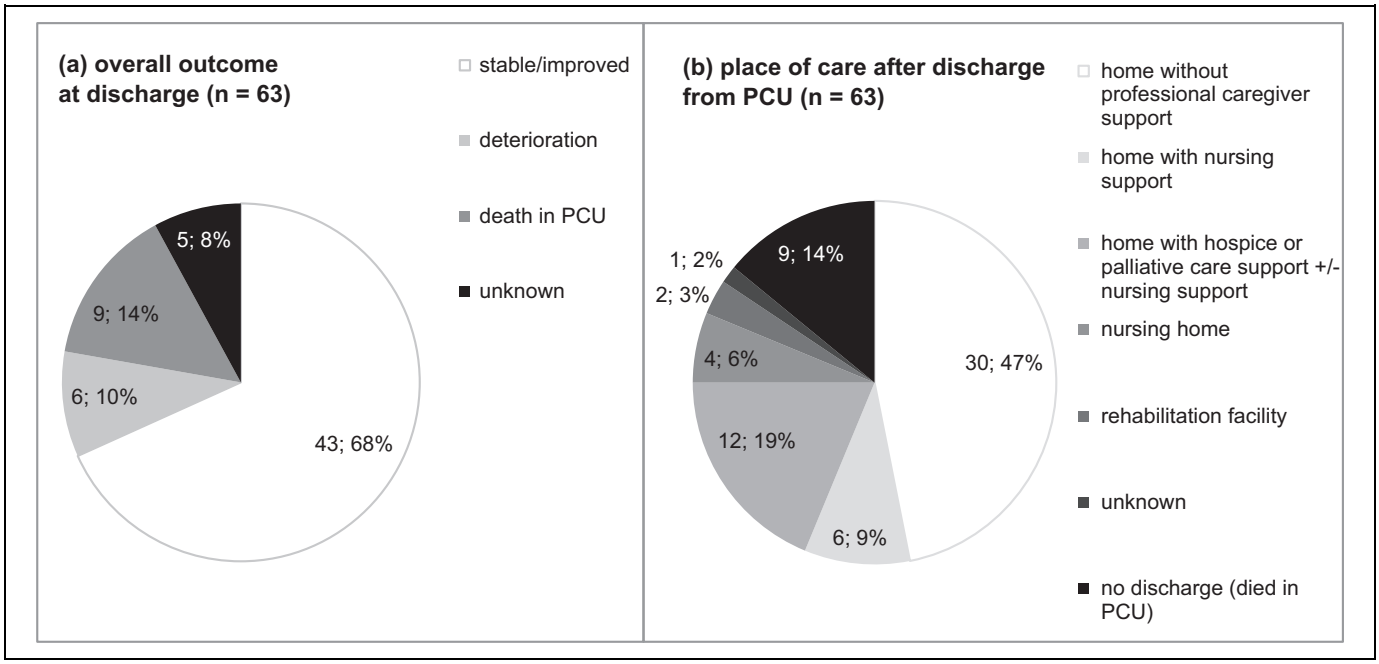


Figure 2. A, Outcome of all admission episodes as documented at discharge (no., %) and (B) place of outpatient care and professional home care after discharge (no., %). PCU indicates palliative care unit.

specialties including palliative care because of complex, disease-related symptom burden.[20] In the present study, although long time intervals suggested a chronic rather than a progressing, fatal condition, the symptoms that led to admission were incapacitating and required management at a facility with special expertise in both neurodegenerative diseases and palliative care. Even with this support, treatment response was very variable. Despite this narrow margin of benefit, in 68% of admission episodes, patients experienced stabilization or improvement after a brief inpatient stay, and in 75% they could

Table 2. Summary of therapeutic interventions

Treatment option	Specification	n	% of admissions (n = 63)
Anti-Parkinson drugs	L-Dopa, amantadine, rotigotin, bornaprin, rasagiline	27	43
Antidepressants, neuroleptics, and anticholinergics	Amitriptylin, mirtazapine, quetiapin, melperon, butylscopolamin	20	32
Opioids	Morphine, tilidin, tramadol, tapentadol	16	25
Treatment-related discussions	EoL discussion, decisions on artificial nutrition and hydration	15	24
Antibiotics	Broad-spectrum penicillins, chinolones, macrolides	15	24
Nonsteroidal anti-inflammatory drugs	Metamizol, diclofenac	12	19
Spasmolytic analgesics	Flupirtin maleate, baclofen	11	17
Benzodiazepines	Midazolam, lorazepam	10	16
Botulinum toxin	Local injection therapy	7	11
Invasive procedures	Urinary catheter, PEG insertion	6	10
Palliative sedation	Continuous midazolam or propofol infusion	2	3

Abbreviations: EoL, end of life; PEG, percutaneous endoscopic gastrostomy.

be discharged home. Thus, the role of the PCU for patients with PSP and CBD was to provide a multidisciplinary, short-term intervention with the aim to preserve and possibly restore long-term function. Only in a minority (14%) of admissions, EoL care was indicated.

Limitations are of methodological nature. First of all, the study design was retrospective. Although a prospective evaluation with validated instruments therefore could not be performed, this approach is in accordance with the purpose of the study to capture triggers for admission and not symptom severity. Second, correlations must be interpreted cautiously as absolute numbers were small and cases were not independent. Therefore, etiologic conclusions cannot be drawn from the data. Third, as data collection was cross-sectional by design and restricted to inpatient admissions only, there is no information about disease trajectories and the results do not reflect the different settings of care.

However, to the authors' knowledge, this is the first report on PSP or CBD patients' symptoms and conditions that triggered admission to a PCU. The main strength of this work is data collection in a pathophysiologically and clinically homogenous population. Availability of a highly specialized movement disorder service enabled the authors to recruit patients from a large catchment area and in any stage of disease progression. Thus, selection bias was minimized, and this sample is likely to provide a representative picture of the whole range of issues relating to advancing PSP or CBD disease. These data confirm results published by other groups that mostly enrolled only small PSP or CBD subgroups within larger study populations.[17,19,20]

Several unresolved issues arise from the results of this study. Regarding health care structures, gaps have been identified in this and other work. Therefore, the question why a high prevalence of symptoms goes along with low health care utilization has to be addressed by prospectively evaluating the role of professional and informal caregivers. Furthermore, from a drug researcher's point of view, hallmarks of PSP and CBD are absence of empirical evidence, variable treatment responses, and low disease prevalence. Carefully published case series (eg, on the response of spasticity/pain to opioids) will be a first step toward gathering experience in order to optimize symptom management, confirmed by clinical trials where appropriate.

This work documents specialist palliative care needs in a German population of patients with PSP and CBD admitted to a PCU indicating high burden both for the patients and their caregivers. The key challenge is to translate these findings of PCU utilization by patients with a rare condition and highly specialized needs into a clinical model of care for these and similar patient cohorts. Medical associations such as the European Society of Cardiology[21] and the American Society of Clinical Oncology[22] advocate integration of palliative care into their respective field by different approaches. However, both specialist neurology services and the 2-level generalist/specialty palliative care model proposed recently[23] may fail to provide adequate support to patients with PSP and CBD: fine-tuning of specific drug regimens alongside resource-consuming palliative interventions may be required while integrated neurology/palliative collaboration is not routinely established. "Third-level," multidisciplinary palliative care at selected centers may help to bridge this gap, to promote continuity of care, and to preserve long-term function and autonomy.

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Declaration of Conflicting Interests

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