RESEARCH

Pneumocystis jirovecii Pneumonia in Neurologic Disorders

Is Prophylaxis Necessary?

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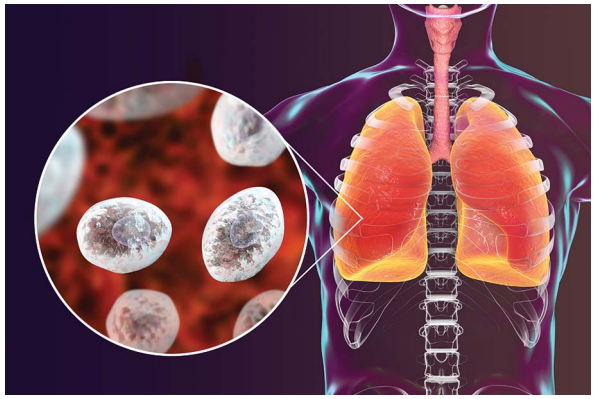
Abstract

Background

The incidence of *Pneumocystis jirovecii* pneumonia (PJP) in patients with underlying neurologic conditions is not well established, and the necessity of PJP prophylaxis for immunocompromised patients with neurologic disorders is uncertain.

Methods

Single-center retrospective analysis of non-HIV PJP patients at a tertiary referral center from 2007 to 2016 to determine the incidence of PJP in patients with primary neurologic disorders.



Results

The study included 142 patients with PJP without HIV. Twenty patients had primary neurologic diagnoses, and 122 had non-neurologic conditions. Associated neurologic diagnoses included brain malignancies (N = 14), myasthenia gravis (MG) (N = 2), myopathy (N = 2), neuromyelitis optica (NMO) (N = 1), and CNS vasculitis (N = 1). Estimated incidences of PJP were 0.7% for patients with NMO and 0.3% for patients with MG for the 10-year study period, whereas 4.6% of patients with NMO and 3.8% of patients with MG were placed on PJP prophylaxis. A survey of 24 neurologists who prescribe immunotherapy or chemotherapy confirmed an infrequent occurrence of PJP in their practice. Malignancy or parenchymal organ failure was present in 90% of neurologic patients with PJP, and coexisting infections occurred in 45%.

Conclusions

The overall incidence of PJP in patients with non-neoplastic neurologic disorders is exceedingly low, raising doubt about the value of routine PJP prophylaxis in neurologic patients outside neuro-oncology. PJP infection occurs frequently in patients with malignancy or parenchymal organ failure, indicating that overall health status may serve as a predisposing factor for PJP.

Pneumocystis jirovecii pneumonia (PJP) is an opportunistic infection caused by a ubiquitous fungus, *Pneumocystis jirovecii*, formerly known as *Pneumocystis carinii*.[1] PJP is well known to affect patients infected with HIV and increasingly reported in immunocompromised patients such as solid organ and hematologic transplant recipients, patients on chemotherapy, or patients receiving immunotherapy for inflammatory/autoimmune conditions.[1,2] PJP has been described in patients with a variety of CNS and peripheral nervous system (PNS) disorders,[3–8] and its occurrence has led to the proposal that neurologists should consider prescribing PJP prophylaxis in selected patients.[9] However, the true incidence of PJP in patients with underlying neurologic conditions is not well

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established, and there has been no risk-benefit assessment for PJP prophylactic regimen in neurologic disorders. Thus, the necessity of PJP prophylaxis for patients with neurologic conditions is uncertain.

The aims of the current study are the following: (1) to determine the overall incidence of PJP in primary neurologic patients at a single tertiary center during a 10-year period, (2) to identify the relationship between PJP and premorbid use of immunosuppressive medications, concomitant conditions including parenchymal organ failure, malignancy, or coexisting infections, (3) to compare patient characteristics and outcomes from PJP seen in primary neurologic disorders with non-neurologic non-HIV conditions; and (4) to describe the current practice pattern of neurologists at a single center in regard to routine PJP prophylaxis.

Methods

Patients and Clinical Data

A retrospective chart review was performed on patients with PJP who were admitted to our institution from 2007 to 2016. Patients were identified by using *International Classification of Diseases, 9th and 10th Revision* codes for PJP in a search of our institutional electronic medical record. The diagnosis of PJP was established based on the identification of organisms through bronchoalveolar lavage material, transbronchial biopsy or open lung biopsy using Gomori methenamine silver staining, or PCR analysis. Patients were excluded from this study if they had suspected but unconfirmed PJP, historical colonization with PJP, or HIV infection. Identified patients with PJP were classified as having primary neurologic diagnoses or non-neurologic diagnoses, based on the primary condition for which they had received immunotherapy/chemotherapy or the most immunocompromised condition if not on immunosuppressive/chemotherapeutic agents.

Clinical data obtained included the following: demographics, underlying disorders, premorbid corticosteroid dosage or immunosuppressive/chemotherapeutic regimen, use of PJP prophylaxis, PJP diagnostic method, associated infection, organ failure during hospitalization, white blood cell count, and absolute lymphocyte count at the time of PJP diagnosis. Results were presented as mean values and SDs for continuous variables and as percentages for categorical variables. Data analysis was conducted using χ^2 tests for comparisons between groups and the Student *t* test for comparing mean values. *p* Value <0.05 was considered as statistically significant.

PJP Prophylaxis Provider Survey

A 10-item questionnaire was constructed to assess the current clinical practice of neurologists (neuromuscular specialists, neuroimmunologists, and neuro-oncologists) at our institution with regard to PJP prophylaxis (see appendix e-1 for survey questions, links.lww.com/CPJ/A191). Questions addressed providers' overall opinion of PJP prophylaxis for patients without HIV, frequency of a provider applying PJP prophylaxis, and number of patients with PJP a provider encountered previously.

Standard Protocol Approvals, Registrations, and Patient Consents

The study was approved by the Institutional Review Board at Cleveland Clinic.

Data Availability

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

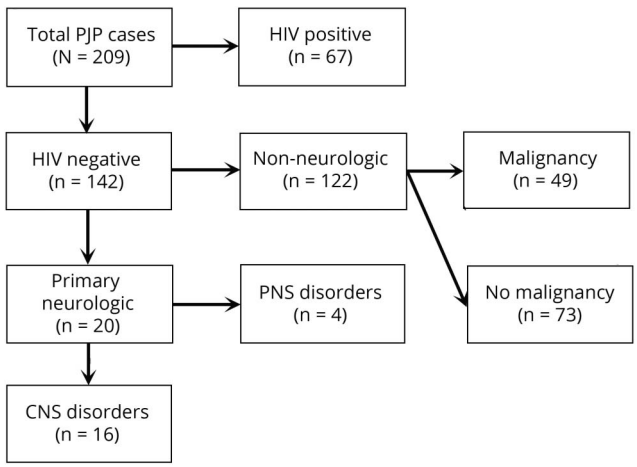
Results

Neurologic Disorders Associated With PJP

A total of 209 patients with PJP were treated at our institution between 2007 and 2016 (figure). Sixty-seven patients were excluded due to confirmed HIV infection. Of the 142 patients without HIV, 131 (92%) patients were evaluated and treated by an infectious disease specialist during hospitalization. Among the 142 patients, 122 were found to have primary non-neurologic diagnoses. The remaining 20 patients carried primary neurologic diagnoses. Sixteen (80%) patients had CNS disorders, including 14 (70%) patients with brain malignancies (6 primary brain and 8 metastatic malignancy), 1 patient each of neuromyelitis optica (NMO) and CNS vasculitis. The remaining 4 (20%) patients had PNS disorders, including 2 patients with myasthenia gravis (MG), 1 with polymyositis, and 1 with coexisting myopathy with idiopathic pulmonary fibrosis (IPF). Both patients with MG were found to have active malignancies, making a total of 16 (80%) neurologic patients having solid organ or hematologic cancer. The mean interval duration between neurologic diagnosis and PJP occurrence was 25.2 months (range: 0.5–164 months).

Corticosteroids were the most commonly used immunosuppressive agent in patients with PJP with neurologic disorders, with dexamethasone used in 9 patients and prednisone in 7

Figure Flow Diagram of Patients With PJP Based on Underlying Diagnoses



PJP = *Pneumocystis jirovecii* pneumonia; PNS = peripheral nervous system.

Table 1 List of 20 Patients With Primary Neurologic Diagnoses

Patient	Age, y/sex	Neurologic or oncologic diagnoses	Preexisting organ failure	Corticosteroid duration, mo	Corticosteroid dose before PJP diagnosis	Chemo/corticosteroid-sparing agent	Concurrent infections
1	48/M	GBM	RF (PE)	4	DXM 10 mg/d	NA	CMV
2	82/M	GBM	Renal, CHF, and RF (asthma)	0.3	DXM 16 mg/d	NA	*Aspergillus* and *Enterobacter*
3	50/M	GBM	Renal	2	DXM 12 mg/d	Bevacizumab and CTX	CMV
4	26/M	Oligodendroglioma	None	4	DXM 12 mg/d	Etoposide	None
5	79/M	PCNSL	None	NA	NA	AZA	None
6	42/M	PCNSL	RF (PE)	4	DXM 16 mg/d	RTX, MTX, ARA-C, and temozolomide	None
7	42/F	NSCLC mets	RF (lung mets)	19	DXM 4 mg/d	Crizotinib	None
8	29/M	Osteosarcoma mets	None	NA	NA	Pazopanib	*Klebsiella*
9	69/F	NSCLC mets	None	6	DXM 16 mg/d	NA	MSSA
10	68/M	RCC mets	RF (lung mets and COPD) and CHF	2	DXM 12 mg/d	Everolimus	None
11	58/F	ALL and CNS involvement	None	NA	NA	MTX and dasatinib	Rhinovirus
12	86/M	DLBCL mets	RF (PHTN)	3	DXM 8 mg/d	NA	None
13	23/M	CML and CNS involvement	None	4	Pred 60 mg/30 mg alternating	Ponatinib	INFL-A
14	46/M	AML and CNS involvement	Renal	NA	NA	Mitoxantrone, ARA-C, etoposide, and IT MTX	None
15	74/M	MG, CLL, and prostate cancer	RF (IPF)	36	Pred 10 mg/d	NA	CMV
16	83/F	MG and bladder cancer	RF	5	Pred 40 mg/d	NA	*Candida albicans*
17	58/M	Myopathy	RF (IPF)	1	Pred 40 mg/d	NA	CMV
18	29/F	NMO	CHF	4	Pred 40 mg/d	AZA and leflunomide	None
19	63/F	PM	None	84	Pred 30 mg/d	NA	None
20	75/M	CNS vasculitis	None	3	Pred 60 mg/d	MMF	None

Abbreviations: ALL = acute lymphocytic leukemia; AML = acute myelogenous leukemia; ARA-C = cytarabine; AZA = azathioprine; CHF = congestive heart failure; CLL = chronic lymphocytic leukemia; CML = chronic myelogenous leukemia; CMV = cytomegalovirus; COPD = chronic obstructive pulmonary disease; CTX = cyclophosphamide; DLBCL = diffuse large B-cell lymphoma; DXM = dexamethasone; GBM = glioblastoma; INFL-A = influenza A; IPF = idiopathic pulmonary fibrosis; IT = intrathecal; Mets = metastasis; MG = myasthenia gravis; MMF = mycophenolate mofetil; MSSA = methicillin-sensitive *Staphylococcus aureus*; MTX = methotrexate; NMO = neuromyelitis optica; NSCLC = non–small-cell lung cancer; PCNSL = primary CNS lymphoma; PE = pulmonary embolism; PHTN = pulmonary hypertension; PJP = *Pneumocystis jirovecii* pneumonia; PM = polymyositis; Pred = prednisone; RCC = renal cell carcinoma; RF = respiratory failure; RTX = rituximab.

(table 1). Prednisone daily dosage equivalent was ≥20 mg in 15 (75%) patients and <20 mg in 1 (5%). Four patients were on chemotherapeutic or corticosteroid-sparing agents without corticosteroid usage before their PJP diagnosis. The median duration of immunosuppressant/chemotherapy usage before PJP diagnosis was 4 months (range: 0.3–84 months).

Twelve of 20 (60%) neurologic patients experienced parenchymal organ failure including 9 (45%) respiratory, 4 (20%) renal, and 3 (15%) cardiac failure before diagnosis of PJP. The following pulmonary disorders were encountered: lung metastases (N = 2), current pulmonary embolism (N = 2), IPF (N = 2), chronic obstructive lung disease (N = 1), pulmonary hypertension (N = 1), and asthma (N = 1). Malignancy or organ failure was present in a total of 18 (90%) neurologic patients. Concomitant infections were detected in 9 (45%) patients, including 4 with CMV viremia (table 1).

During the study period, a total of 151 patients with NMO and 651 patients with MG received evaluation and treatment at our institution. Among them, 7 (4.6%) patients with NMO and 31 (4.8%) patients with MG were placed on *Pneumocystis jiroveci*

pneumonia (PCP) prophylaxis. The estimated incidences of PJP in our clinic population were 0.7% per 10-year study period for patients with NMO and 0.3% per 10-year study period for patients with MG. Among the 20 neurologic patients with PJP, only 1 patient with PJP (patient 5 in table 1) was placed on prophylaxis.

A Comparison of Neurologic and Non-Neurologic Disorders Associated With PJP

Table 2 lists non-neurologic diagnoses that are associated with PJP infection. Hematologic malignancies were the most common, followed by a variety of rheumatologic and gastrointestinal inflammatory diseases, solid organ tumors, and organ transplantation. Altogether, 24 patients with PJP had underlying rheumatologic disorders. Table 3 lists a comparison of selected clinical and laboratory features for neurologic and non-neurologic patients with PJP. Patients in the neurologic group received more corticosteroids, as demonstrated by a higher percentage of patients who received prednisone dosage equivalent of ≥20 mg per day for ≥1 month ($p = 0.01$). No significant differences were observed between the neurologic and the non-neurologic groups in age, sex, usage of other immunosuppressive/chemotherapeutic agents, incidences of concomitant infection, organ failure, malignancy, mortality rate, percentage of patients with lymphopenia, and mean absolute lymphocyte count at the time of PJP diagnosis.

PJP Prophylaxis Survey

To further explore reasons for the observed low incidence of PJP in patients with neurologic disorders, we conducted a survey among neurologists who frequently prescribe immunotherapy or chemotherapy at our institution (appendix e-1, links.lww.com/CPJ/A191). The survey was sent to 28 eligible providers, and 24 providers responded, including 12 neuroimmunologists treating CNS inflammatory and demyelinating disorders, 10 neuromuscular specialists, and 2 neuro-oncologists. The average duration of practice was 15.5 (range: 1–40) years. Thirteen (54%) providers believed that PJP prophylaxis should be prescribed for patients on immunotherapy/chemotherapy; however, only 5 (21%) providers indicated a routine usage of PJP prophylaxis. Based on provider self-reporting, approximately 1%–10% (range: 0%–60%) of patients treated with immunotherapy or chemotherapy were eligible for PJP prophylaxis, and approximately 11%–20% (range: 0%–60%) of eligible patients received PJP prophylaxis. Fifteen (63%) providers reported having never encountered PJP among patients of their own or their colleagues of the same subspecialty. When focusing on the last 10 years, 2 (8.3%) providers reported that their own patients (a total of 2 patients) developed PJP, and 4 (16.7%) providers reported having encountered patients with PJP under the care of their colleagues of the same subspecialty.

Table 2 List of Non-Neurologic Underlying Diseases in Association With PJP (N = 122)

Underlying condition	No. of patients (%)
Hematologic disorder	57 (46.7)
Lymphoma	30 (24.6)
Leukemia and myeloma	27 (22.1)
Solid organ tumor	17 (13.9)
Organ transplant	9 (7.4)
Inflammatory condition	29 (23.8)
Granulomatosis with polyangiitis	5 (4.1)
Rheumatoid arthritis	5 (4.1)
Microscopic polyangiitis	4 (3.3)
Other inflammatory disorder[a]	15 (12.3)
Miscellaneous disorders[b]	10 (8.2)

[a] Idiopathic pulmonary fibrosis, inflammatory bowel disease, Henoch-Schonlein purpura, antineutrophil cytoplasmic antibody vasculitis, autoimmune hepatitis, psoriatic arthritis, polymyalgia rheumatica, systemic lupus erythematosus, Sjogren, and poorly differentiated connective tissue disease.
[b] Warts, hypogammaglobulinemia, infections, and myelokathexis syndrome, liver cirrhosis, idiopathic cellular and humoral immunodeficiency, common variable immunodeficiency, asthma, antiglomerular basement membrane glomerulonephritis, and chronic obstructive pulmonary disease.

Discussion

Patients with HIV infection and low CD4 count have a high risk for PJP. Other risk factors include hematologic or solid organ malignancies, stem cell and solid organ transplantation, and use of corticosteroids and chemotherapeutic or immunosuppressive agents. The underlying conditions found in our studies are similar to previous publications.[1,5,10,11] In view of the high risk for PJP, guidelines were published for PJP prophylaxis in HIV-positive patients with low CD4 count, hematologic and solid organ malignancies, and stem cell and solid organ transplant recipients.[12–15]

The first choice for PJP prophylaxis is often trimethoprim-sulfamethoxazole (TMP-SMX). Use of this low-cost medication results in >90% reduction in the occurrence of PJP.[16] However, PJP prophylaxis has its own risks, including side effects, development of antibiotic resistance, and potentially serious drug interactions with certain medications such as methotrexate.[1,17] The rate of adverse reactions to TMP-SMX in the non-HIV population was estimated to be approximately 15%, whereas that of severe adverse reactions may reach 3%.[16] Two meta-analyses concluded that the benefit of PJP prophylaxis outweighs the risk only when the PJP infection risk exceeds 3.5% and 6.2%, respectively.[16,18]

Our study suggests that the overall occurrence of PJP in primary neurologic diagnoses is low, excluding patients with neurologic or non-neurologic malignancy. The low incidences of PJP in our group during the 10-year study period (0.7% in NMO and 0.3% in MG) are unlikely a result of widespread PJP prophylaxis as <5% of patients with NMO and MG encountered in our institution were placed on PJP

Table 3 Comparison of Neurologic and Non-Neurologic Patients With PJP

Characteristics	Non-neurologic	Neurologic	*p* Value (95% CI)
Total patient number	122	20	
Male, n (%)	68 (55.7)	14 (70.0)	0.23 (−0.09 to 0.38)
Age, y, mean ± SD	60.6 ± 167	56.5 ± 20.4	0.33 (−4.13 to 12.29)
On baseline PJP prophylaxis, n (%)	19 (15.6)	1 (5)	0.21 (−0.27 to 0.06)
Immunosuppressive/chemotherapeutic regimen, n (%)			
Corticosteroid alone	49 (40.2)	8 (40)	0.99 (−0.23 to 0.23)
Other immunosuppressants/ chemotherapy alone	31 (25.4)	4 (20)	0.60 (−0.26 to 0.15)
Corticosteroids + other immunosuppressants/chemotherapy	23 (18.9)	8 (40)	0.04 (0.02 to 0.41)
Corticosteroid dosage (prednisone equivalent), n (%)			
<20 mg daily or <1 mo	26 (21.3)	2 (10)	0.25 (−0.30 to 0.78)
≥20 mg daily for ≥1 mo	46 (37.8)	14 (70)	0.01 (0.09 to 0.55)
Concomitant organ failure, n (%)	56 (45.9)	12 (60)	0.24 (−0.10 to 0.38)
Malignancy, n (%)	73 (59.8)	16 (80)	0.08 (−0.03 to 0.43)
Deaths, n (%)	54 (44.3)	8 (40)	0.72 (−0.28 to 0.20)
Lymphopenia, n (%)	28 (22.9)	5 (25)	0.84 (−0.18 to 0.22)
Absolute lymphocyte count, k/μL, mean ± SD[a]	0.81 ± 1.34	0.61 ± 0.57[b]	0.54 (−0.80 to 0.40)

Abbreviations: CI = confidence interval; PJP = *Pneumocystis jirovecii* pneumonia.
[a] Normal values between 1.45 and 7.50 k/μL.
[b] Result excludes 1 patient with chronic lymphocytic leukemia and significantly elevated lymphocyte count.

prophylaxis during the same study period. It was difficult for us to capture the total number of patients with inflammatory myopathy accurately; thus, the incidence of PJP in this population was not calculated. However, as only 2 patients with PJP with myopathy were encountered, it can be speculated that the incidence of PJP in inflammatory myopathy should have been low as well.

The infrequent occurrence of PJP in neurologic disorders outside neuro-oncology and the rarity of PJP prophylaxis in patients with NMO and MG corroborate with our survey results. Our survey focused on the main group of neurologists who prescribe immunotherapy or chemotherapy. Results indicated that by self-reporting, approximately 80% of relevant neurology providers at our institution do not routinely institute PJP prophylaxis, and less than 20% of eligible neurologic patients were placed on PJP prophylaxis. In addition, most providers never encountered PJP in neurologic patients treated by themselves or their colleagues over a long duration.

Our observation of low PJP incidence in patients with neurologic disorders is consistent with several previous analyses. For example, no neurologic diagnosis associated with PJP was encountered in 3 large series, except for patients with CNS malignancy.[1,10,11] In another series of 116 consecutive patients with PJP, only 1 patient with neurologic disorder (demyelinating polyneuropathy) outside CNS malignancy was listed.[5] Finally, in a recent study of various opportunistic infections in neuromuscular patients receiving immunosuppression, no PJP was observed.[19] Much of the warning for neurologists to consider PJP prophylaxis arose from isolated reports of various nononcologic neurologic patients developing PJP.[4,7,8]

In our series, most patients with PJP with primary neurologic disorders had underlying brain or other solid organ/ hematologic malignancy, which was previously known to be associated with an increased risk of PJP.[2,5,12,20] Primary and metastatic brain malignancies are both risk factors for the development of PJP, with varying incidences reported of 0.3%–6%.[3,6,21–24] Therefore, PJP prophylaxis could still be considered for this subgroup of patients, especially when they are treated with immunotherapy or chemotherapy.

Similarities between neurology and rheumatology practices contribute to the advocacy for PJP prophylaxis in neurologic

disorders.[9] Although similar immunotherapies—azathioprine, methotrexate, mycophenolate mofetil, and corticosteroids—may be used, rheumatologic disorders may be associated with a higher incidence of PJP when compared with neurologic disorders. For example, in a series of 116 consecutive patients with PJP, only 1 patient with neurologic disorders but 21 patients with connective tissue disorders were found with PJP.[5] In our series, we have encountered a total of 6 patients with PJP with neurologic disorders excluding brain malignancy and 24 patients with PJP with rheumatologic disorder, suggesting a possibly higher incidence in the latter group. Rheumatologic disorders such as granulomatosis with polyangiitis (GPA), polyarteritis nodosa, or systemic lupus erythematosus (SLE) may cause more parenchymal organ damage than neurologic disorders such as MG or NMO. Interstitial pulmonary fibrosis, as a risk factor for PJP, is often seen in patients with polymyositis/dermatomyositis.[1,11,25] These factors likely contribute to the estimated incidence of 2–3% in all rheumatologic patients.[26–29] Although there are no evidence-based guidelines for PJP prophylaxis in rheumatologic disorders receiving immunosuppressive therapy, there have been published recommendations that PJP prophylaxis should be considered in patients with GPA undergoing induction therapy and patients with SLE, polymyositis/dermatomyositis, and vasculitis who are receiving high-dose corticosteroids and have lymphopenia or low CD4 count.[30]

Corticosteroid usage has been viewed as the most common predisposition factor for developing PJP. In 2 large series, it was observed that 90% of patients with PJP were receiving corticosteroids.[5,31] The threshold corticosteroid dose rendering a patient to increased risk of PJP remains unknown. In a study of 142 mostly oncology and transplant patients, the median duration of corticosteroid treatment was 2 months, at a maximum daily dose equivalent to 40 mg of prednisone.[20] This led to the practice that PJP prophylaxis being given to immunosuppressed patients who received corticosteroid therapy for a duration of ≥4 weeks and at an equivalent prednisone dose of ≥20 mg daily.[20] One subsequent study on patients with rheumatologic disorders confirmed that 86% of patients with PJP were receiving ≥20 mg prednisone daily at the time of PJP diagnosis.[29] The American Thoracic Society advised practitioners to consider prophylaxis when prednisone dose exceeds 20 mg per day for longer than 1 month, but acknowledged that this is not evidence based.[14]

However, PJP can occur with lower prednisone doses or no corticosteroid usage at all.[5] In the group of neurologic patients with PJP in our series, 70% of patients received prednisone equivalent dose of ≥20 mg per day for longer than 1 month, but the percentage of similar patients dropped to 37.8% in the non-neurologic group. Such a group difference could reflect the more frequent usage of corticosteroids in neuro-oncology patients. Nearly 40% of non-neurologic patients in our series were not on corticosteroids at the time of PJP diagnosis (table 3). The presence of multiple coexisting risk factors (corticosteroid usage, immunosuppressive/chemotherapeutic treatment, and malignancy) may limit the ability to separate PJP risk attributable to steroid dose from other factors. Implementations of recommendations based on prednisone dosage and duration alone would inevitably include many patients with limited risk for PJP, and more specific determination of PJP risk is needed.

In animal models, rats treated with corticosteroid injection developed PJP due to reactivation of latent infection.[32] It was observed that low protein diet and poor nutrition status enhanced the immunosuppressive property of corticosteroids in these rats, making them more prone for PCP infection.[32] Similarly, other coexisting conditions may render patients at low-dose corticosteroids to high risk for PJP. Baseline lymphopenia has been recognized as a risk factor for PJP in patients with rheumatologic disorders receiving prolonged corticosteroids.[33] A high prevalence of parenchymal organ failure was previously observed in patients with PJP.[29,34,35] Previously existing pulmonary diseases such as COPD, interstitial lung disease, chronic inflammation, and lung damage may contribute to the onset of PJP.[29] In our neurologic patients with PJP, 60% had preexisting parenchymal organ dysfunction (pulmonary dysfunction being the most frequent) and 90% had either malignancy or organ failure. The frequent presence of organ failure and malignancy and the use of immunosuppressive or chemotherapeutic agent usage may argue that PJP simply develops in sick patients due to a reactivation of latent infection. This notion seems to be supported by the high incidence of coexisting infections in patients with PJP.[5,10]

Our retrospective analysis has limitations and possible selection bias. We do not use a control group of patients who were at risk but did not develop PJP. Such a comparison could be very helpful in elucidating underlying mechanisms and risk factors for PJP occurrence. Nevertheless, we have shown that PJP is rare in neurologic patients treated with immunosuppressive agents despite the infrequent usage of PJP prophylaxis. Our data raise questions about the risks vs benefits of a general recommendation for PJP prophylaxis in neurologic patients simply due to being on immunosuppression. Patients with coexisting malignancy and/or parenchymal organ failure appear more vulnerable to PJP, but further study is needed to better characterize the risk of PJP in subgroups of neurologic patients.

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Disclosure

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TAKE-HOME POINTS

- Other than brain malignancy, neurologic disorders are rarely associated with PJP.
- Routine PJP prophylaxis in neurologic patients treated with immunosuppressive or chemotherapeutic agents may not be necessary.
- Patient's overall health status should be taken into consideration when administering PJP prophylaxis for patients with neurologic disorders.
- Neurologic patients with coexisting solid organ or hematologic malignancies or parenchymal organ failure appear to be more vulnerable to PJP.

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Appendix Authors

Name	Location	Contribution
Tiffany Pike-Lee, MD	Cleveland Clinic, OH	Statistical analysis, acquisition and analysis of data, and writing of the manuscript
Sana Syed, DO	Cleveland Clinic, OH	Acquisition of data
Mary Alissa Willis, MD	University of Mississippi Medical Center, Jackson	Study concept and design and critical revision of the manuscript
Yuebing Li, MD, PhD	Cleveland Clinic, OH	Statistical analysis, study concept and design, acquisition and analysis of data, writing of the manuscript, and critical revision of the manuscript

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