Opinion and Special Articles:

An interdisciplinary neuroinfectious diseases clinic to improve patient care and training

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Neuroinfectious diseases is an emerging subspecialty of neurology.¹ We are seeing an increasingly immunocompromised patient population due to advances in transplant medicine and novel treatments for autoimmune disorders and cancer. This growing group of high-risk patients, in combination with a rise in international travel, has expanded the quantity and spectrum of infections of the nervous system. Substantial progress in molecular diagnostic testing has resulted in greater awareness of pathogens able to cause neurologic infections. While neurologic opportunistic infections in HIV-infected individuals are often deadly complications, a new set of challenges has arisen in HIV-infected individuals with well-controlled disease.

The socioeconomic burden of neuroinfectious diseases is enormous. Patients often require lengthy hospitalizations, extensive diagnostic evaluations, long-term antimicrobial therapy, and prolonged rehabilitation.² As such, the care of neuroinfectious diseases requires collaboration among various areas of expertise, including neurology, infectious diseases, HIV medicine, and microbiology. Clinicians with experience and training in neuroinfectious diseases possess a unique perspective, distinct set of skills, and specialized fund of knowledge to provide high-quality care for these patients. This unique skill set and fund of knowledge represent a knowledge gap among practicing neurologists that should be an important focus of current residency training.

As a joint effort between the Department of Neurology and Division of Infectious Diseases at the University of California, San Francisco (UCSF), we recently created an interdisciplinary neuroinfectious diseases clinic serving the local and surrounding communities with a focus on the care of individuals with infections of the nervous system and neurologic complications of HIV. We describe our efforts to develop a one-of-a-kind clinical and training experience in order to provide expert care and to fill this knowledge gap among practicing neurologists.

CLINIC STRUCTURE AND PATIENT POPULATION The neuroinfectious diseases clinic was established within the general infectious diseases outpatient clinic in July 2012 by a neurologist with infectious diseases subspecialty training (F.C.C.). This neuroinfectious diseases faculty member is directly embedded in the infectious diseases clinic. Between July 2012 and March 2014, we saw 44 new consultations in our monthly clinic. Referrals were accepted if they had an established infection of the nervous system, if there was a high degree of suspicion for an infection, or if they were HIV-infected with a neurologic chief complaint. The mean age of the patients was 47.6 years (SD 15.2 years) and ranged from 20 to 79 years. Fourteen (32%) of the 44 new patients were women and 18 (41%) were of nonwhite race/ethnicity. Twenty-one (48%) patients were HIV-infected. Of the 23 non-HIV-infected patients, 7 were immunocompromised (3 due to malignancy, 1 from chronic corticosteroid use, 1 from treatment for multiple sclerosis, 1 due to a renal transplant, and 1 from diabetes mellitus). Six patients were immigrants and 3 were returning travelers.

REFERRAL PATTERNS Referrals originated from the infectious diseases consult team for patients seen in the hospital who required outpatient follow-up, the neurology or neurosurgery inpatient service, HIV primary care clinics, and general neurology or other neurology subspecialty clinics (e.g., neuro-oncology, multiple sclerosis clinic). Ten patients were referred by outside physicians. Most patients were seen within 1 month of referral, and the majority of patients (more than 80%) were followed over multiple visits.

PATIENT CASE MIX A wide range of diagnoses was seen in the clinic (table). Among immunocompetent patients, diagnoses included pyogenic brain infections and fungal and viral meningitis. Neurocysticercosis was the most common diagnosis in immigrants and returning travelers. For non-HIV-infected immunocompromised

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Table	Diagnoses seen in a neuroinfectious diseases clinic
Immunocompetent patients	
Diagnoses	
Bacterial	
	Pyogenic brain abscess with associated seizures
	Pyogenic bacterial meningitis with associated strokes
	Neurosyphilis
Fungal	
	Coccidioidal meningitis (2)
	<i>Sporothrix</i> meningitis
	<i>Histoplasma</i> meningitis
	Subacute meningitis, presumed fungal
Viral	
	HSV-2 meningitis
	VZV meningitis
	West Nile virus
Parasitic	
	Neurocysticercosis (4)
Miscellaneous	
	Chronic meningoencephalitis, unknown etiology
	Neuropathy, rule out infectious cause
Immunocompromised (non-HIV) patients	
Diagnoses	
Bacterial	
	<i>Nocardia</i> brain abscess (2)
	Pyogenic bacterial meningitis
Viral	
	EBV encephalitis
	PML
Fungal	
	<i>Sporothrix</i> meningitis
Unknown	
	Chronic meningoencephalitis, unknown etiology
HIV-infected patients	
Diagnoses	
Infectious	
	PML/PML IRIS (2)
	Cryptococcal meningitis/IRIS (2)
	CNS toxoplasmosis with associated seizure
	HIV CNS escape
	Neurosyphilis (2)
Noninfectious	
	Myelopathy
	Myopathy + cognitive impairment
	Cognitive impairment (3)
	Seizure (2)

Continued

Table	Continued
	Neuropathy (2)
	Migraine/headache (3)
	Chronic meningitis with cranial nerve deficits

Abbreviations: EBV = Epstein-Barr virus; HSV = herpes simplex virus; IRIS = immune reconstitution inflammatory syndrome; PML = progressive multifocal leukoencephalopathy; VZV = varicella-zoster virus.

patients, diagnoses included *Nocardia* brain abscesses and Epstein-Barr virus encephalitis. Of the 21 HIV-infected individuals, 10 (48%) had incompletely controlled HIV and were primarily seen for HIV-associated neurologic infections, including progressive multifocal leukoencephalopathy and CNS toxoplasmosis. Of those whose HIV viral load was suppressed, frequent neurologic complaints included headache, seizure, and cognitive impairment.

For half of the new patients seen in the clinic, a definitive diagnosis was already established at the time of referral, while the remainder presented without a known diagnosis. Nearly half (48%) of patients were actively treated with antimicrobial therapy as part of an outpatient management plan, while 30% received only symptomatic management (e.g., pain control, seizure management). A small subset of patients was referred for a specific diagnostic or prognostic question (e.g., lumbar puncture to rule out neurosyphilis or neurologic prognosis following viral encephalitis) that did not require long-term follow-up.

TRAINEE INVOLVEMENT Neurology trainees have been incorporated into the clinic and independently see new consultations (2–3 per clinic) and discuss cases with the attending, in addition to observing follow-up visits. Fellows in the UCSF HIV Neurology Research Training Program also have the option to rotate through the clinic as part of their clinical training. Visiting international residents and medical students participate largely in an observatory role.

The resident experience in the clinic is one component of a neuroinfectious diseases elective designed to provide UCSF residents with broad exposure to the diagnosis and management of infections of the nervous system and neurologic complications of HIV. In addition to rotating in the neuroinfectious diseases clinic, residents are able to spend time on the inpatient consult infectious disease teams, in an outpatient tuberculosis clinic, in an HIV-associated cognitive impairment clinic, and in an HIV urgent care clinic. Similar clinical experiences are available to fellows in the HIV Neurology Research Training Program who are interested in more rigorous clinical

training. HIV Neurology fellows supervise residents at a county hospital, where neuroinfectious diseases are a common diagnosis, and also lecture on neuroinfectious diseases topics in the residency core curriculum. These fellows are involved in longitudinal research projects in which interested residents can also participate as either an elective experience or as part of a broader flexible residency project.

As part of the neuroinfectious diseases elective, residents are expected to independently evaluate patients and synthesize and interpret clinical data, while working closely with an attending physician from various disciplines, including infectious diseases, HIV medicine, and neurology. Residents also gain experience in communicating and maintaining a professional and productive working relationship with health care providers in non-neurologic fields and in interdisciplinary settings. In addition to clinical teaching and feedback, dedicated didactics include small group lectures, one-on-one case-based teaching with an attending physician in neuroinfectious diseases, microbiology plate rounds, and grand rounds in infectious diseases and HIV. Each rotating resident is exposed to a set curriculum of topics that are complemented by direct patient contact.

DISCUSSION The neuroinfectious diseases clinic at UCSF, a joint effort between neurology and infectious diseases, delivers subspecialty outpatient care to patients with infections of the nervous system and HIV-infected individuals with neurologic disease. Interdisciplinary neuroinfectious diseases clinics, even in major academic medical centers, are rare. Services provided by neuroinfectious diseases clinicians through this type of clinic include management of antimicrobial therapy, symptomatic and supportive treatment of neurologic sequelae of infections, and prognostication after debilitating infections of the CNS. Strengths of the clinic include harnessing and developing expertise in a unique and emerging field of neurology, offering prompt access to subspecialty care, and affording an unmatched training opportunity for medical students, residents, and fellows with the goal of filling the knowledge gap in neuroinfectious diseases among neurologists.

We care for a broad array of diagnoses in the clinic, ranging from CNS infections in immunocompromised hosts to more common neurologic complaints in HIV-infected individuals. While new diagnoses are made in clinic, a substantial proportion of patients present to the clinic with a known diagnosis. In our experience, a primary service of the clinic is to provide longitudinal outpatient management of established, often immensely complicated neurologic infections and associated sequelae. Indeed, neuroinfectious

diseases clinicians are one of many examples of the movement of neurologists toward a paradigm where they are actively engaged in the longitudinal treatment and prevention of neurologic disease.

The wide range of pathology and diverse patient population seen in the clinic result in a unique learning opportunity for neurology trainees in neuroinfectious diseases. Overall, the educational goals for trainees rotating through the neuroinfectious diseases clinic and elective, adapted from the American Academy of Neurology neuroinfectious diseases subspecialty training core curriculum,¹ are to (1) formulate a differential diagnosis, including potential causative pathogens, for common neurologic infectious syndromes (i.e., meningitis, encephalitis, brain abscess) in the immunocompetent and immunocompromised host; (2) devise a systematic approach to common neurologic sequelae (e.g., seizures, headache, cognitive impairment) of infections, including HIV; (3) develop a working knowledge of the utility and validity of various laboratory tests in the serum and CSF when a CNS infection is suspected; (4) recognize the role of specific imaging techniques, including restricted diffusion and postcontrast sequences, in distinguishing between infections and other processes; and (5) understand the principles of antimicrobial therapy, including antibiotic selection and frequently encountered drug–drug interactions and enhanced toxicities with combinations of antimicrobials and medications regularly used to treat neurologic disease (e.g., antiepileptic drugs, neuropathic pain agents). Simple metrics are used to gauge progress toward meeting these educational goals through one-on-one discussions of patients and didactic cases as well as during lectures. Administration of a neuroinfectious diseases pretest and post-test may also help in the future to quantify the knowledge obtained from rotating in the clinic.

Establishing an interdisciplinary neuroinfectious diseases clinic at UCSF has successfully allowed neurology and infectious diseases groups to partner together to provide a clinical service to patients and to fill a knowledge gap in neuroinfectious diseases and HIV neurology among practicing neurologists. This clinic may serve as an example of interdisciplinary collaboration in neurology that benefits patients and trainees alike in complex systems of care that increasingly require this type of partnership to deliver high-quality care.

AUTHOR CONTRIBUTIONS

Dr. Chow participated in the study concept and design, performed the data analysis and interpretation, and drafted the manuscript. Dr. Schwartz participated in the study concept and design and provided critical revisions to the article. Dr. Josephson participated in the study concept and design, supervised the study, and provided critical revisions to the article.

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DISCLOSURE

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