Evaluating CNS Lesions in HIV Patients: A Radiologic/Pathologic Review

A thesis submitted to the University of Arizona College of Medicine – Phoenix in partial fulfillment of the requirements for the degree of Doctor of Medicine

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Abstract

**Background and Significance.** HIV/AIDS is a commonly encountered disease process in many cities and medical centers throughout the world. Approximately 35 million people live with HIV/AIDS worldwide, many of whom develop pathology of the central nervous system (CNS). Many HIV/AIDS patients undergo substantial morbidity and mortality with the development of CNS abnormalities including toxoplasmosis encephalitis (TE), progressive multifocal leukoencephalopathy (PML), primary central nervous system lymphoma (PCNSL), and other opportunistic infections. Especially in these immunocompromised patients, early accurate diagnosis can affect patient management, which is vital to patient survival. **Research Question.** We hypothesized that fellowship-trained neuroradiologists are more accurate than general radiologists in the diagnosis of HIV related CNS lesions. **Methods.** Following institutional IRB approval, we retrospectively analyzed patients with known HIV infection who underwent radiologic imaging and subsequent biopsy of an identified neuropathologic lesion(s) at Maricopa Medical Center between January 2007 and January 2015. Diagnostic scan reports were analyzed to determine whether or not the correct diagnosis was provided in the impression, and rates of correct diagnosis were compared between fellowship trained neuroradiologists and a general radiologists. **Results.** Thirty-three patients received neurologic imaging with MRI for a pathologically proven HIV/AIDS related illness with 78 total lesions identified. The correct diagnosis was mentioned in 79% (15/19) of cases read by a neuroradiologist, but only 43% (6/14) of cases read by a general radiologist. Overall, the correct diagnosis was mentioned in the initial impression in 21 of 33 (64%) cases. Chi-squared analysis showed a statistically significant relationship in the number of mentioned correct diagnoses by neuroradiologists versus general radiologists (p=0.033). **Conclusions.** Our study suggests that the availability and utilization of specialty fellowship trained staff in radiology is an essential part of accurate early diagnosis. Taking an active role in the work up and diagnosis of specialized disease processes is essential for successful and comprehensive care, especially in our local community where HIV/AIDS support and treatment is on the cutting-edge.
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Introduction/Significance

Background of the research Question
Approximately 35 million people live with HIV/AIDS worldwide, many of whom develop pathology of the central nervous system (CNS). A basic understanding of each pathologic process is crucial to completely evaluate and diagnose a CNS lesion in our study population. Below is a review of each disease endemic to the AIDS population, including a review of typical imaging characteristics.

Toxoplasmosis Encephalitis:
TE infection is caused by the intracellular protozoan Toxoplasma gondii. The host is primarily affected through the mechanism of latent reactivation, especially among the immunocompromised. Toxoplasmosis is the most common opportunistic CNS infection in HIV/AIDS patients, occurring in up to 30-40% of patients. In fact, up to two-thirds of all brain masses in HIV/AIDS patients are caused by toxoplasmosis. Even in immunocompetent individuals, subclinical infections may be seen in up to 15-70% of the population. Patients typically present with headache, confusion, fever and focal neurological deficits. At time of diagnosis, mean age is 35.7 years old with mean survival of 28 months. Eighty percent respond to the six month treatment regimen of pyrimethamine, sulfadiazine and leucovorin. Steroids are also given if there are signs of critically elevated intracranial pressure or clinical deterioration. Lifelong treatment may be necessary for latent toxoplasmosis.

There are two forms of toxoplasmosis: acute and latent. Acute illness is caused by rupture of cysts which contain free tachyzoites. In the latent form, encysted bradyzoites remain in tissues until the host becomes immunocompromised. Because our study specifically addresses the HIV/AIDS population, only the acute illness will be considered. Three distinct parenchymal zones appear on histology in the acute necrotizing phase of the infection; a central avascular zone with coagulative necrosis; an intermediate zone with engorged blood vessels, tachyzoites
and an inflammatory reaction; and a peripheral zone containing encysted organisms (bradyzoites) with fewer vascular abnormalities.\textsuperscript{12}

On CT, the classic appearance is a single or multiple, rim enhancing or nodular enhancing ill-defined hypodense lesion(s) with surrounding edema. On MR, there is variable imaging presentation, likely due to pathologic features at differing stages of toxoplasmosis infection. Most commonly, single or multiple ill-defined T1/T2 hypointense lesions that demonstrate surrounding T2 hyperintense vasogenic edema are seen. Necrotizing encephalitis is generally T2 hyperintense, while organizing abscesses are T2 hypo-/isointense.\textsuperscript{11} Occasionally the lesions can demonstrate T1 hyperintense signal, thought to be due to coagulative necrosis/proteins.

The “target” sign has been discussed in the literature, although this is seen in less than 30% of cases.\textsuperscript{14} On T1W imaging with contrast (C+) the target sign has been described as a concentric or eccentric enhancing core with an intermediate hypointense zone and peripherally enhancing hyperintense outer zone.\textsuperscript{16} Occasionally, T1W C+ images will only demonstrate an iso-/hypointense lesion that rim enhances.\textsuperscript{9} ON FLAIR/T2 imaging, the presentation is a hypointense core, intermediate hyperintense zone and peripheral hypointensity.\textsuperscript{9} Other target signs have also been described: a central hypointense zone with peripheral isointensity on a T1W unenhanced MR, as well as a three layer target sign by this same author.\textsuperscript{15}

Diffusion weighted imaging is variable. Usually the center of an abscess is iso-/hypointense compared to adjacent white matter. The wall may be iso-/hyperintense. The necrotic centers have increased diffusion restriction.\textsuperscript{12} Perfusion-weighted imaging reveals hypovascularity. Rim and nodular enhancement, or less commonly punctate enhancement, is seen after the administration of intravenous contrast.

The most common locations of toxoplasmosis are the basal ganglia, thalamus, cerebellum, and corticomedullary junction. Lesions are multiple the majority of the time, but may also be solitary.
Figure 1: Examples of TE on CT and MRI. Mass occupying lesions with ring enhancement and “target sign” on MRI and hypodensity on CT.
Primary CNS Lymphoma:
PCNSL, most of which is diffuse large B-cell lymphoma, makes up between 1-15% of all central nervous system tumors.\textsuperscript{1-3} There is a strong association with HIV/AIDS, with an estimated 2-6% of all HIV/AIDS patients developing primary CNS lymphoma at some point. There is a male:female predominance of 2:1. The typical clinical presentation includes focal neurological deficits, seizures and impaired higher cortical function. Mean survival in HIV/AIDS patients is 36 months, with a mean age at onset of 39 years. Among the immunocompromised, prognosis is worse with multiple lesions, periventricular or meningeal involvement and age greater than 60. Treatment includes chemotherapy with or without radiation, steroids to decrease peritumoral edema, and surgical resection if tumor is low grade.

Due to PCNSL hypercellularity, high nuclear/cytoplasmic ratio, and predilection for the periventricular and superficial regions, imaging has a characteristic appearance.\textsuperscript{1-5} On CT, PCNSL is classically a central hemispheric isodense to hyperdense enhancing lesion which can cross midline. A negative CT exam, however, cannot exclude the presence of PCNSL.\textsuperscript{6}

On MR, lesions are iso-/hypointense on unenhanced T1WI and iso-/hyperintense on unenhanced T2WI (hypointense when compared to gray matter). Less commonly, hemorrhage/necrosis may cause heterogeneity of the lesion. If calcium is present, T2* GRE sequences may have areas of “blooming,” which is usually seen after therapy. FLAIR demonstrates iso-/hypointense signal. DWI may show restricted diffusion due to hypercellularity. ADC sequences have been used to differentiate PCNSL from other etiologies.\textsuperscript{7} T1WI C+ demonstrates peripheral enhancement with central necrosis or homogeneous enhancement 75% of the time.\textsuperscript{1}

Approximately two-thirds of lesions are supratentorial, most commonly the frontal, temporal and parietal lobes. The deep gray nuclei are affected 10% of the time. Five to ten percent of lesions cross midline. Lesions cluster around ventricles and the gray-white junction and frequently abut or extend along ependymal surfaces. Leptomeningeal spread is present in 30-
40% of cases. PCNSL may present as a solitary mass or multiple lesions and may be circumscribed or infiltrative.
Figure 2: Examples of PCNSL on CT and MRI. Periventricular lesions with mass effect and peripheral contrast enhancement on MRI.
TE v PCNSL:
As both primary CNS lymphoma and toxoplasmosis can appear as single or multiple ring enhancing lesions on CT and MRI, a common practice of management is to treat empirically with anti-toxoplasmosis therapy and perform follow up imaging to assess response. If the lesion has interval decrease in size and if the patient clinically improves, it is presumed that the lesions are toxoplasmosis. If not, then PCNSL is presumed to be the diagnosis. There are two fundamental problems with this approach. First, there is a decrease in size and number of the majority of toxoplasmosis lesions about 10 days after the start of anti-toxoplasmosis therapy with mean resolution time of 2-4 weeks. However, some lesions may take up to 6 months to resolve. In fact, encysted bradyzoites may never disappear, as therapy does not affect them.14 Second is the issue with drug toxicity. Rates of toxicity range from 38-71% with side effects in 62% of patients.9 Because of these problems, other imaging can be utilized to help differentiate between the two, thus helping the patient avoid an unnecessary biopsy. Although many clinical and laboratory tests have been used to differentiate between these two entities, only the radiologic differences will be discussed here.

It is important to note that although each of these imaging tests may be a useful aid in definitive diagnosis, each has its own shortcomings and time has shown that none have proven conclusive. Perfusion studies have shown an increase in cerebral blood volume (CBV) in patients with PCNSL, thought to be secondary to the increased blood supply of a neoplastic process, although areas of necrosis may demonstrate decreased CBV. In contrast, CBV is decreased in both the toxoplasmosis lesions and the surrounding edema.37

Multiple studies have been performed using apparent diffusion coefficients (ADC) to differentiate toxoplasmosis and PCNSL. Camacho et al. found that ADC ratios were 1.63 +/- 0.41 (mean +/- SD) (range, 1.04–2.26) in the 13 toxoplasmosis lesions and 1.14 +/- 0.25 (range, 0.84–1.52) in the 8 lymphoma lesions. With this data, they concluded that ADC ratios of >1.6 were only seen in toxoplasmosis and not in PCNSL (seen in 7 of their 13 patients with
toxoplasmosis). They also wrote that ratios of 1-1.6 were inconclusive, as there was overlap between the two.\(^7\)

SPECT with thallium-201 has been used to aid in distinguishing between toxoplasmosis and PCNSL. Thallium biologically acts like potassium and is taken into cells via the Na+/K+ ATPase pump. It has been shown that PCNSL uptakes thallium at a rate greater than toxoplasmosis.\(^38\) Miller et al. concluded that high uptake values (>2.9) could only represent lymphoma.\(^39\) However, some PCNSL lesions had uptake values between 1.5 and 2.1 and could not be distinguished from toxoplasmosis.\(^39\)

Using PET/CT, PCNSL has been shown to be more metabolically active than toxoplasmosis.\(^40\) Pierce et al was able to distinguish PCNSL from non-lymphoma in 17 of 18 cases.\(^41\) The problem is that other lesions seen in AIDS patients, such as progressive multifocal leukoencephalopathy, may be metabolically active and mimic PCNSL.\(^40\) MR proton spectroscopy has very mixed results, with some studies showing that toxoplasmosis and CNS lymphoma have distinct metabolite profiles, while other studies show that they do not.\(^7\)

Although there is not a single definitive imaging modality which allows for distinction between PCNSL and toxoplasmosis, imaging improvements and methods are continually being developed to allow for more definitive imaging diagnoses.

**Progressive Multifocal Leukoencephalopathy:**

PML is an often fatal subacute demyelinating disease caused by the reactivation of the *JC polyomavirus* infecting oligodendrocytes. There are three phases to a PML infection. The first is the primary, typically asymptomatic infection with JC virus, which is thought to be spread via respiratory or fecal-oral transmission. The second phase is the latent phase of the virus within the human host. The third phase is reactivation and dissemination into the brain.\(^18\) This symptomatic third phase is seen primarily in immunocompromised individuals, with a spike in prevalence during the AIDS epidemic, with 5% of AIDS patients developing PML at some point\(^17\)
and 85% of all PML cases being diagnosed in AIDS patients. It is estimated that up to 70% of the population has the latent form of *JC polyomavirus* that would only become clinically significant if the host becomes immunocompromised. Clinical presentation includes weakness, speech disturbances, limb incoordination, cognitive deficits, and visual impairment. Historically, prognosis was dismal, with a one year survival at around 10%, and mean survival being four to eight months. With the use of HAART therapy, the one year survival has climbed to 50%. However, not all patients show improvement with therapy. Although symptoms and survival are improved with restitution of the immune system using differing therapies, there is still no definitive cure for PML.

PML is a demyelinating disease, so white matter is predominantly affected. A typical appearance is multiple demyelinating lesions in a bilateral asymmetric distribution that may become confluent. Single lesions in a unilateral distribution may less commonly be seen. Sixty-eight percent of patients also have cortical atrophy, the majority being mild. There is involvement of the subcortical “U” fibers, which are myelin tracts at the gray-white junction that connect cortex to cortex. The gray matter may also rarely be involved. Typically no mass effect or enhancement is present, but both may rarely be seen. One author found that mass effect correlated with decreased survival. However, this finding is infrequently seen and considered to be of no true significance. In rare instances faint peripheral or patchy enhancement may be seen, which may represent active disease or response to therapy.

On CT there is hypodense subcortical and periventricular white matter involvement without mass effect. MR demonstrates T1 hypointensity and T2/FLAIR hyperintensity in a subcortical and periventricular distribution which involves the subcortical “U” fibers, resulting in a scalloped appearance. As mentioned above, mass effect and enhancement are rare. Diffusion weighted imaging may elucidate areas of active disease, which can be demonstrated by the following two examples: newer lesions exhibit slight diffusion restriction and older lesions do not show any diffusion restriction. In addition, some PML lesions only demonstrate diffusion restriction along the rim of the lesion, which is the site of active disease.
Most PML has supratentorial involvement seen classically in the parietal, frontal and occipital white matter. Periventricular and subcortical white matter are affected in 95.5% and 82.2% of cases respectively.\textsuperscript{21} Lobar involvement may extend into the corpus callosum. Rarely, isolated callosal involvement can be seen.\textsuperscript{23}
Figure 3: Examples of PML on CT and MRI. Asymmetric demyelinating lesions without mass effect or contrast enhancement.
Cryptococcus:
Cryptococcal infection, or cryptococcosis, is caused by the encapsulated yeast-like fungus *Cryptococcus neoformans* which is normally found in soil contaminated with bird feces, particularly that of pigeons. This infection is acquired through inhalation and spreads through hematogenous dissemination to the CNS. Cryptococcosis is the most common CNS fungal infection in patients with AIDS. Any immunocompromised patient is at increased risk for cryptococcal infection, but up to 30% of patients with cryptococcosis are actually immunocompetent. The most common clinical presentation is headache. Other symptoms include seizures, blurred vision, or findings related to increased high intracranial pressure secondary to hydrocephalus, which is common. Males are more commonly infected than females. Treatment is anti-fungal medication.

Cryptococcal infection can present three distinct ways on imaging: meningitis, pseudocyst formation and cryptococcomas. One study showed that the overwhelming presentation of cryptococcosis is meningitis, being found in 9/10 patients who presented. If meningeal involvement extends intracranially, a cryptococcoma may result. A cryptococcoma is a chronic granuloma composed of lymphocytes, macrophages and giant cells. Additionally, if cryptococcal organisms extend into the perivascular spaces, gelatinous pseudocysts may form. Each of these presentations will appear different on imaging and thus will be discussed separately.

Meningitis and hydrocephalus are the most common clinical presentations, although both are nonspecific for cryptococcus. A CT of the head will often appear normal. In the initial stages, the majority of patients will have leptomeningeal enhancement with or without adjacent white matter vasogenic edema on MRI. This is a finding seen in meningitis from other causes as well. Imaging may also demonstrate a normal appearing MRI due to inability of the immune system to mount a response.
If the cryptococcus organism spreads intracranially, there can be formation of a cryptococcoma. On MR these are usually lobulated T1 hypo-/isointense and T2 hyperintense lesions that may demonstrate either no enhancement or rim enhancement if the host’s immune system is functioning sufficiently to mount a response. These appear most commonly in the basal ganglia. They also may be found on the ependyma of the choroid plexus.\(^{30}\) Most cryptococcomas do not show diffusion restriction, which may assist in distinguishing them from pyogenic abscesses.\(^{12}\)

With perivascular space spread of the Cryptococcus organism, there may be gelatinous pseudocyst formation, most commonly in a bilateral symmetrical distribution. These lesions present as well-circumscribed round or oval lesions that are hypodense on CT and typically follow CSF intensity on MR. However, they may be T1 hyperintense depending on the level of proteinaceous material contained therein.\(^{29}\) These lesions do not typically enhance. The most common locations are the midbrain and basal ganglia.

Cryptococcal infection may present in the spinal cord as well, although this is uncommon. Imaging shows T2 hyperintense signal within the cord, with or without enhancement.\(^{29}\)
Figure 4: Examples of Cryptococcosis seen on CT and MRI. Innumerable lesions with mass effect, edema, and contrast enhancement.
Coccidioides:

The dimorphic fungus *Coccidioides immitis* may cause the systemic infection coccidioidomycosis. This fungus is endemic to the southwestern United States and northern Mexico and infects humans through inhalation of an endospore. There are estimated to be 100,000 new cases in the United States annually. Spread from inhalation to the disseminated form will occur in 4-5% of patients and up to 30% in AIDS patients. CNS involvement, which has the highest mortality rate, is seen in one-third to one-half of patients who present with disseminated disease.

Clinical presentation varies according to which organ system is involved. CNS symptoms are most commonly secondary to meningitis or hydrocephalus. Prognosis is related to the extent of infection. Both the rapidity with which treatment is initiated and the correct choice of treatment options affect prognosis. Mean survival time was only 4 months in untreated patients compared to 21 months in those treated with amphotericin B.

There is an array of radiologic presentations in CNS coccidioidomycosis including meningitis or ependymitis, hydrocephalus, vasculitis, granulomas, white matter disease and spinal arachnoiditis. On MR, meningitis presents with intense, diffuse leptomeningeal enhancement in up to 91% of patients. It typically affects the basal cisterns, sylvian fissures and pericallosal regions. Hydrocephalus is seen in 68-93% of cases, with 67% of these requiring CSF shunting. Vascular involvement is seen in about 40% of patients, typically as diffuse arteritis. Ischemia presents commonly, with an estimated 35-58% prevalence, seen on MR as T2 hyperintensity and diffusion restriction. Granulomas are uncommon, and may be seen as focal areas of white matter or deep gray matter enhancement. White matter findings are focal or diffuse, typically in a periventricular pattern and may be secondary to abscess, drug toxicity or edema from hydrocephalus.
Arachnoiditis is nonspecific and presents the same as in other etiologies. In a study of 23 patients with MR brain abnormalities, 86% also had concomitant spinal abnormalities, 74% of which had spinal leptomeningeal enhancement.32
Figure 5: Examples of Coccidiomycosis seen on CT and MRI. Nonspecific enhancement on CT and MR. Abnormal enhancement of meninges in basal cisterns showing Coccidioidomycosis meningitis.
Significance and rationale for research question

HIV/AIDS is a commonly encountered infectious disease process throughout the world. Fortunately, for patients in Arizona, specialized diagnosis and treatment facilities are available for state of the art diagnosis and treatment. Given the immunocompromised status of patients, early diagnosis can affect patient management, which is vital to patient survival.\(^4\) For appropriate patient outcomes, knowing rates of accurate early diagnosis is important.

Hypothesis/Research question

We hypothesized that fellowship-trained neuroradiologists would mention the correct diagnosis more often than general radiologists in their initial impression of imaging studies showing HIV related CNS lesions.

Goals for the Study

In this study, we hope to demonstrate that the availability and utilization of specialty fellowship trained staff in radiology is an essential part of accurate early diagnosis of HIV related CNS lesions.
**Research Materials and Methods**

Following institutional IRB approval, all MRI neuroradiology imaging performed at Maricopa Integrated Health System in Phoenix, Arizona between January 2007 and December 2014 was screened in order to identify positive pathology in a known or subsequently diagnosed patient with HIV/AIDS. Radiologic reports were analyzed to determine whether or not the correct diagnosis was provided in the impression. The gold standard for correct diagnosis was the final pathology report of the biopsy specimen. Images of CNS pathology were reviewed to evaluate for “classic” imaging characteristics which included: mass effect, edema, location, margins, enhancement, enhancement pattern, T1 signal intensity, diffusion/ADC characteristics, and single or multiple foci. Finally, rates of correct diagnosis were compared between exams interpreted by fellowship trained neuroradiologists and general radiologists.
Results

During the duration of the study, 33 patients received neurologic imaging with MRI for a pathologically proven HIV/AIDS related illness, with 78 total lesions identified. Overall, the correct diagnosis was mentioned in the impression in 21 of 33 (64%) cases, while it was not mentioned in 12 of the 33 (36%) cases. Nineteen patients had their studies interpreted by a fellowship trained neuroradiologist while 14 did not. The fellowship trained neuroradiologist mentioned the correct diagnosis in the impression in 15 of the 19 (79%) cases while the correct diagnosis was not mentioned in 4 of the 19 (21%) cases. The remaining 14 patient cases were interpreted by a general radiologist who mentioned the correct diagnosis in 6 of 14 (43%) cases and did not mention the correct diagnosis in 8 of the 14 (57%) cases.

Chi-squared analysis showed a statistically significant relationship in the number of mentioned correct diagnoses by the neuroradiologist versus general radiologist (p=0.033).

Results Toxoplasmosis:
A total of seven patients (16 total lesions) were found with pathology proven toxoplasmosis. Five patients demonstrated mass effect, 7 patients had edema and 5 patients had at least one lesion in a classic location. Ten lesions were circumscribed while 6 were ill-defined. Seven showed enhancement: 8 lesions showing peripheral nodular enhancement, 3 complete homogeneous enhancement, 2 peripheral and central nodular enhancement, and 3 showing patchy enhancement. Ten lesions were T1 hyperintense while 6 lesions were T1 hypointense/isointense. Seven lesions showed peripheral nodular diffusion restriction, 4 had complete diffusion restriction and 5 lesions had no diffusion restriction. Two patients had multiple lesions and 5 had single lesions.

Two examinations were interpreted by fellowship trained neuroradiologists. One listed toxoplasmosis as a primary consideration and one listed it as a secondary diagnosis. Five examinations were interpreted by general radiologists, two of which mentioned TE as a primary
diagnosis. Two did not mention toxoplasmosis. One only described findings without giving a diagnosis.

Neuroradiologists suggested toxoplasmosis as the primary diagnosis 50% of the time and as a secondary diagnosis 50% of the time. Toxoplasmosis was mentioned in the differential in 100% of neuroradiologist’s impressions. The general radiologists listed toxoplasmosis as primary diagnosis 40% of the time. Toxoplasmosis was not listed in the differential diagnosis 40% of the time. Twenty percent of general radiologists did not mention any diagnosis, only describing findings.

Results PCNSL:
In the seven patients (23 total lesions) which had pathology proven PCNSL, 6 patients demonstrated mass effect, 7 patients had edema, and 6 patients had lesions in classic locations. Thirteen lesions were circumscribed, while 10 were ill-defined. Seven showed enhancement: 14 lesions demonstrated peripheral nodular enhancement, 7 had complete homogeneous enhancement and 2 had patchy enhancement. Sixteen lesions were T1 hypointense, and 5 were T1 isointense. Fifteen lesions showed peripheral nodular diffusion restriction, 7 had complete diffusion restriction and 1 lesion had no diffusion restriction. Five patients had multiple lesions and 2 had single lesions.

Five examinations were interpreted by fellowship trained neuroradiologists, three of whom listed PCNSL as a primary consideration. Two interpretations by neuroradiologists did not mention PCNSL in the differential diagnosis. Two examinations were interpreted by general radiologists, and both mentioned lymphoma in their diagnosis, one as less likely and the other as “abscess versus multifocal neoplasm, possibly lymphoma.”

Neuroradiologists suggested PCNSL as the primary diagnosis 60% of the time. PCNSL was not mentioned in the differential diagnosis in 40% of the impressions. No general radiologists listed PCNSL as primary, but all mentioned the possibility as a secondary diagnosis.
**Results PML:**
In the five patients (7 total lesions) which had pathology proven PML, zero patients demonstrated mass effect, 5 patients had edema, and 5 patients had at least one lesion in a classic location. The seven lesions were all ill-defined with 1 demonstrating patchy/nodular enhancement. All seven lesions were T1 isointense. Two lesions showed peripheral diffusion restriction, and 5 lesions had no diffusion restriction. Two patients had multiple lesions and 3 had single lesions.

Three examinations were interpreted by fellowship trained neuroradiologists, all of whom listed PML as a primary consideration. Two examinations were interpreted by general radiologists with only one mentioning PML as a primary diagnosis.

Neuroradiologists suggested PML as the primary diagnosis 100% of the time. The general radiologists listed PML as primary in 50% of cases, and none mentioned the possibility as a secondary diagnosis. PML was not listed as a differential diagnosis 50% of the time.

**Results Cryptococcus**
In the two patients (innumerable lesions) which had pathology proven cryptococcus, one patient demonstrated mass effect, both patients had edema and both patients had at least one lesion in a classic location. All lesions were ill-defined with 2 showing enhancement, both demonstrating a peripheral nodular enhancement pattern. All lesions were T1 hypointense/isointense. Zero lesions had diffusion restriction. Both patients had multiple lesions.

One examination was interpreted by a fellowship trained neuroradiologist, who listed infection as a primary consideration, with cryptococcus included. One examination was interpreted by a general radiologist; cryptococcus was not listed as a primary diagnosis, although infection was mentioned.
The neuroradiologists suggested cryptococcus as the primary diagnosis 100% of the time. The general radiologist did not list cryptococcus as primary, but infection was listed in the impression.

Results Coccidioides:
In the seven patients (23 total lesions) with pathology proven Coccidioides, one patient demonstrated mass effect, 7 patients had edema and 6 patients had at least one lesion in a classic location. Two lesions were circumscribed while 21 were ill-defined. Nineteen lesions showed enhancement: 6 lesions showing peripheral nodular enhancement, 9 demonstrating complete enhancement, and 4 showing patchy enhancement. Five patients had leptomeningeal enhancement. Three lesions were T1 hyperintense while the remainder were T1 hypointense/isointense. Three had nodular peripheral diffusion restriction thought to be secondary to ischemia. One patient had multiple lesions, and 6 had single lesions.

Five examinations were interpreted by a fellowship trained neuroradiologist, four of which listed coccidioides as a primary consideration. One did not mention coccidioides as a consideration, which was in an atypical location. Two examinations were interpreted by general radiologists, none of whom mentioned coccidioides as a primary diagnosis.

Neuroradiologists suggested coccidioides as the primary diagnosis 80% of the time, while coccidioides was not mentioned in the differential on 20% of impressions. None of the exams interpreted by general radiologists listed coccidioides as primary or specifically within the differential diagnosis.
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<td>General Radiologist: <strong>6/14</strong></td>
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Table 1: Results table of correct initial diagnoses. Numerator = correct diagnosis noted in initial report; Denominator = number of patients interpreted by this type of radiologist
Figure 6: Results showing rates of correct diagnoses by neuroradiologist and non-neuroradiologist.
**Discussion**

The correct diagnosis was mentioned in 64% of cases overall and there was a significant difference in the accuracy of reporting the correct diagnosis between fellowship trained neuroradiologists and those without specialized neuroradiologic training (79% versus 43%). This suggests that the availability and utilization of specialty fellowship trained staff in radiology is an essential part of accurate early diagnosis to ensure the most appropriate intervention and therefore maximize patient survival.

A limitation of this study was the small sample size of HIV/AIDS patients. Increasing the number of patients would increase the power of the study and allow for analysis of accuracy based on classic presentation versus atypical presentation. Another limitation was the small number of interpreting radiologists. Radiologists arise from diverse backgrounds, varied stages of experience and different levels of expertise. With a larger number of interpreting radiologists the differential diagnosis would be more accurate, as incorrect interpretations would be minimized, and a greater knowledge pool would be contributing to the diagnoses.

Additional factors contributing to the results of the study include the study location. The study was performed in a single center in Arizona. Thus, diseases endemic to the southwestern United States were over represented compared to true national epidemiology. For example, Coccidioides represented 7 of our 33 patients, which would not be the case in other populations throughout the United States or internationally.

The wide prevalence of HIV/AIDS in the United States population makes diagnostic imaging a vital and crucial part of the care process of these patients. With so many patients regularly presenting to the health care system, taking an active role in the workup and diagnosis of these specialized disease processes is essential for successful and comprehensive care, especially in our local community where HIV/AIDS support and treatment is on the cutting-edge.
**Future Directions**

Additional studies should be performed with a focus on increasing geographic diversity, patient sample size, and number of interpreting radiologists. These future studies could also include comparisons to other modalities such as CT, MRI perfusion, ADC values, MR spectroscopy, etc.
Conclusions

This study showed that neuroradiologists mentioned the correct diagnosis of HIV related CNS lesions more often than general radiologists. There was a statistically significant relationship in the number of mentioned correct diagnoses by the neuroradiologists versus general radiologists. This suggests that the availability and utilization of specialty fellowship trained staff in radiology is an essential part of accurate early diagnosis. Taking an active role in the work up and diagnosis of specialized disease processes is essential for successful and comprehensive care, especially in our local community where HIV/AIDS support and treatment is on the cutting-edge.
References


