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# Audit of computed tomography brain findings in HIV-infected patients with space occupying infective lesions at a regional level hospital in KwaZulu-Natal

**Somasundram Pillay[1,2] and Kaveer Ramchandre[3]**

**Abstract**

**Background:** With the increased prevalence of HIV pandemic, more focus is placed on pathology involving the central nervous system secondary to HIV infection. Medical computerised tomography scans have become an integral investigation at a regional hospital level.

**Objective:** To provide a description of central nervous system space occupying infective lesion found within this cohort of patients.

**Setting:** Edendale Hospital, Pietermaritzburg, KwaZulu-Natal.

**Methods:** This was a retrospective study in which the charts of all HIV-infected medical patients with findings of a space occupying infective lesion on computerised tomography brain seen for the time period 1 January 2015 up to and including 31 December 2015 were analysed. A total of 110 patient files were evaluated.

**Results:** Most patients were in the third to fourth decade of life with mean cluster of differentiation 4 of 125 cells/mm$^3$. A differential comprising toxoplasmosis or tuberculoma (80.9%) was the leading aetiology described. Most frequent clinical features in these patients included seizures (41.8%), confusion or altered mental state (38.2%), headaches (33.6%), hemiparesis (48.2%) and cranial nerve abnormality (22.7%). The most common central nervous system sites involved were, in order of decreasing prevalence was parietal, basal ganglia, frontal cortex (31.8% vs 31.8% vs 26.4%, respectively). Early initiation of co-trimoxazole and anti-tuberculosis treatment yielded better outcomes compared to the group who received delayed or no treatment with p-values (Pearson's $\chi^2$) of 0.0002 and $<0.0001$, respectively.

**Conclusion:** Computerised tomography scans to detect space-occupying infective lesion of the brain are invaluable for rapid diagnosis and to reduce morbidity and mortality.

**Keywords**

Infectious diseases, neurology, radiology, space-occupying infective lesions, HIV infected, computerised tomography brain findings, cerebral toxoplasmosis, cerebral tuberculoma

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## Introduction

Current estimates indicate that HIV/AIDS (Acquired Immunodeficiency Syndrome) affects 12.7% of the general population of South Africa.[1] HIV is a multisystem disease that complicates with various types of opportunistic infections (OIs) often because of immunodeficiency. The prevalence of pathology involving the central nervous system (CNS) has become increasingly important since OIs have accounted for the bulk of HIV-induced CNS pathology.[2] These OIs occur more commonly in patients who have cluster of differentiation

[1]Department of Internal Medicine, Edendale Hospital, Pietermaritzburg, South Africa
[2]School of Clinical Medicine, College of Health Sciences, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa
[3]Rondebosch Medical Centre, Cape Town, South Africa

**Corresponding author:**
Somasundram Pillay, School of Clinical Medicine, College of Health Sciences, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, PO Box 22, Seadoone Amanzimtoti KwaZulu-Natal, Durban 4126, South Africa.
Email: drspillay@iafrica.com

4 (CD4) counts <200 cells/μL.[3] Neurological complications are sometimes the first and may occasionally be the only manifestation of AIDS. CNS complications may also be the cause of sudden or unexpected death. Many HIV patients that did not present with neurological complications sometimes have CNS lesions found on post mortem, thus highlighting that HIV-associated CNS pathology is widespread and often undetected.[4]

The spectrum of space-occupying infective lesion (SOIL) associated with HIV infection ranges from toxoplasmosis, tuberculomata to brain abscesses. Toxoplasmosis has been demonstrated as being the most common SOIL in HIV-infected patients.[5] It has been shown to occur in 3%–10% of patients with AIDS in the United States and in up to 50% of the patients in Europe and Africa.[3] Bhigjee[6] has described that in KwaZulu-Natal (KZN), a province in South Africa which is the epicentre for the HIV pandemic, neurological complications in HIV-infected patients ranges from intracranial mass lesions, bacterial and fungal meningitis, acute disseminated encephalomyelitis, spinal cord disorders and peripheral nerve dysfunction. Toxoplasmosis was the most common SOIL found in their study which was successfully treated with co-trimoxazole. Other important aetiologies include multiple bacterial abscesses and tuberculomata while primary CNS lymphoma was rare.[6]

These HIV-infected patients with SOIL usually present to primary healthcare level and are often problematic to treat at this level either due to staff or resource constraints. These patients often present as diagnostic dilemmas to the clinical staff at these institutions. This results in a delay in initiation of appropriate therapy in these patients. The use of computerised tomography (CT) scanning of the brain is one such example of limited resources. CT scanning is also a costly investigation with limited availability. Neurological imaging of the CNS has become a very important tool for achieving a diagnosis as it allows us to differentiate between the different aetiologies. Some findings may include intracranial mass lesions, white matter disease, meningo-encephalitis, vascular complications and hydrocephalus.[2]

The characteristic feature of CNS toxoplasmosis on CT scans and magnetic resonance imaging (MRI) is the asymmetrical target sign; however, although MRI is more sensitive, availability is much more limited to this expensive radiological investigation.[7] With toxoplasmosis, CT scans of the brain may indicate single or multiple nodular lesions. Imaging following administration of intravenous contrast shows thin walled cavitating lesions with ring enhancement. Oedema of surrounding white matter is also a common finding. Toxoplasmosis has a tendency to involve the basal ganglia. Other sites may include the grey–white matter junction, cerebellum, brainstem and spinal cord. Following medical treatment, the appearance of haemorrhage and calcification might be visualised on brain CT scanning. Concomitant cerebral atrophy seen in some patients may be due to direct cellular damage by the HIV virus.[8] When atrophy is a prominent finding, it usually indicates a poor prognosis.[9] Traditionally, it has been a problem to diagnose and treat these patients who present with features of space-occupying lesions. A specific diagnosis cannot often be made and hence patients are treated with polypharmacy to offer empirical cover for most of the differential diagnoses. Since toxoplasmosis is one of the most common OI, empirical treatment is often started if imaging is highly suggestive while the patient is being investigated.[10]

Findings on CT imaging for brain abscesses are characterised by a thin, uniform ring, which is thinner on the medial border, and with a smoother outer margin; satellite lesions are often present. The enhancing ring lesions caused by pyogenic brain abscesses are commonly located at the grey–white matter junction.[3]

For tuberculoma, features include hypo- or isodense lesions with ring enhancement and irregular outline. Intracranial tuberculoma can occur with or without tuberculous meningitis. Numerous small tuberculomas are common in patients with miliary pulmonary tuberculosis. The diameter of these enhancing lesions usually ranges from 1 mm to 5 cm. Tuberculomas frequently show varied types of enhancement, including irregular shapes, ring-like shapes, open rings and lobular patterns. Target-like lesions are common.[3]

CT scan together with MRI is not regarded only as tools to differentiate AIDS-related CNS disease but also to help clinicians to prognosticate the patient.[11] Although other investigations such as molecular and serological are available, they are also costly, time-consuming and often unavailable at most public healthcare facilities. CT brain findings of all adult medical patients have been analysed from Edendale Hospital medical wards, out-patient referrals and the emergency department.

This study has highlighted the importance of CT scan imaging of the brain with regard to providing a rapid differential diagnosis of SOIL in the brain. Secondary outcomes correlated the CT findings of infective space-occupying lesions with the various clinical and biochemical variables.

## Methods

This was a retrospective study in which the charts of all HIV-infected medical patients seen during the period 1 January 2015 up to and including 31 December 2015 with findings of a SOIL on CT brain were analysed.

The following were used as the inclusion criteria for this study:

HIV-infected patients;

Radiological finding of space-occupying lesion most likely infective in nature;

Period between 1 January 2015 and 31 December 2015.

Exclusion criteria used:

HIV-uninfected patients.

**Table 1.** Demographic data of all patients.

| | Toxoplasmosis/ tuberculoma | Brain abscess | Toxoplasmosis | Tuberculoma |
|---|---|---|---|---|
| Number of females | 45 | 4 | 3 | 1 |
| Number of males | 44 | 11 | 0 | 2 |
| Total number of patients | 89 | 15 | 3 | 3 |
| Mean age (years) | 38 ± 12.7 | 44.7 ± 20.7 | 42.7 ± 6.7 | 40 ± 6.6 |
| Number of patients on anti-retroviral therapy (ART) | 13 | 0 | 0 | 0 |
| Mean CD4 (cells/mm$^3$) | 112.1 ± 153.9 | 235.3 ± 301.6 | 94 ± 8.5 | 187.5 ± 53 |

CD4: cluster of differentiation 4.

**Table 2.** Signs and symptoms found in patients with SOIL.

| | Toxoplasmosis/ tuberculoma | Brain abscess | Toxoplasmosis | Tuberculoma | n |
|---|---|---|---|---|---|
| Seizures | 40 | 4 | 1 | 1 | 46 |
| Confusion/altered mental state (AMS) | 36 | 5 | 1 | 0 | 42 |
| Headaches | 29 | 6 | 1 | 1 | 37 |
| Hemiparesis | 42 | 9 | 2 | 0 | 53 |
| Hemiplegia | 3 | 0 | 0 | 0 | 3 |
| Cranial nerve abnormality | 22 | 1 | 1 | 1 | 25 |
| Neck stiffness | 15 | 5 | 0 | 1 | 21 |
| Aphasia | 9 | 1 | 0 | 0 | 10 |
| Vomiting | 6 | 2 | 0 | 0 | 8 |
| Dysarthria | 7 | 0 | 0 | 0 | 7 |
| Drowsiness | 6 | 0 | 0 | 0 | 6 |
| Fever | 5 | 1 | 0 | 0 | 6 |
| Ataxia | 1 | 0 | 0 | 0 | 1 |

SOIL: space-occupying infective lesion.

A total of 110 patient files were evaluated based on the above inclusion and exclusion criteria. This study was conducted at Edendale hospital, a regional hospital situated in Pietermaritzburg, KwaZulu-Natal, South Africa. Ethics approval for this retrospective study was obtained from University of KwaZulu-Natal's Biomedical Research and Ethics Committee (BREC) – BE 311/16.

Data were obtained from CT scan reports as well as from in- and out-patient medical records. CT scan reports of all patients were retrieved from the radiology department. Personalised information such as the names and date of birth was kept confidential by password protected files on computer.

Data obtained from these patient files were further subdivided according to differential diagnoses made on CT brain findings. These subgroups included patients with

Brain abscesses;

Toxoplasmosis;

Tuberculomas;

A category that combined toxoplasmosis and tuberculomas.

Data obtained for variables in demographic, clinical, radiologic, laboratory and patient outcomes were entered onto a flow sheet and were thereafter captured onto a Word Excel® spreadsheet. Means (± standard deviation (SD)) are presented for continuous variables and frequencies (%) are presented for categorical variables. Chi-square tests and t-tests are used to compare groups. Continuous variables are tested for normality and if normal, t-tests are used and if not normal, non-parametric tests are used. A p of $<0.05$ was considered significant. All analyses were performed using (SAS Institute, Cary, NC) SAS version 9.3.

## Results

Table 1 highlights the demographic variables of patients with SOIL. The mean age of patients was in the third or fourth decade of life while the mean CD4 count is in keeping with what is already known globally which is that OIs that cause SOIL occur in patients with low CD4 counts.

Tables 2 and 3 highlight the most common to least common clinical findings. It demonstrates that confusion or altered mental state as well as headaches is a symptom that

**Table 3.** Comparisons of clinical features.

| Factors | n (%) | p-value (Pearson's $\chi^2$) |
|---|---|---|
| Right hemiparesis versus confusion/AMS | 35.4 versus 64.6 | 0.0050 |
| Right hemiparesis versus headaches | 38.3 versus 61.7 | 0.0341 |
| Cranial nerve palsy versus confusion/AMS | 62.7 versus 37.3 | 0.0128 |

AMS: altered mental state.

**Table 4.** Radiological features and complications of SOIL on CT scan.

| | Toxoplasmosis / tuberculomas | Brain abscess | Toxoplasmosis | Tuberculomas | n |
|---|---|---|---|---|---|
| Ring enhancing | 76 | 13 | 2 | 3 | 94 |
| Multiple lesions | 51 | 3 | 2 | 2 | 58 |
| Single lesion | 38 | 12 | 1 | 1 | 52 |
| Mass lesion/effect | 30 | 7 | 0 | 2 | 39 |
| Increased intracranial pressure | 18 | 4 | 0 | 3 | 25 |
| Impending herniation | 2 | 2 | 0 | 1 | 5 |

SOIL: space-occupying infective lesion; CT: computed tomography.

should not be underestimated when compared to other traditionally thought of common symptoms such as seizures, hemiparesis and cranial nerve abnormalities.

Table 4 highlights that the majority of patients (n = 103; 93.6%) had a contrasted CT scan. Ring enhancement is a common feature for diagnosis of both toxoplasmosis and tuberculomas. This is possibly the major reason for the combined group of toxoplasmosis and tuberculomas containing the most patients.

Table 5 illustrates that the parietal, basal ganglia and frontal regions were the most common sites within the CNS to be affected. Single lesion affecting a region and multiple lesions affecting more than one region are both represented.

Table 6 details the therapeutic options that were used to treat these SOILs. Since most patients had a differential of either toxoplasmosis or tuberculoma, they had been treated with multiple drugs that include co-trimoxazole and anti-tuberculosis (TB) drugs. Corticosteroid therapy was also commonly used. The preferred anti-epileptic drug used was sodium valproate.

Table 7 illustrates that most patients had a good outcome since many had been discharged. However, with very little information regarding follow-up, the final outcome of patients diagnosed with infective space-occupying lesions is unknown.

## Discussion

One hundred and ten HIV-infected patients with a mean CD4 count of $125.3 \pm 164.5$ cells/mm$^3$ were evaluated in this study. The majority (88.18%) of these patients were not on anti-retroviral therapy. Most of the affected patients were in the third to fourth decade of life.

Toxoplasmosis has been demonstrated as being the most common SOIL in HIV-infected patients.[5] It has been shown to occur in 3%–10% of patients with AIDS in the United States and in up to 50% of the patients in Europe and Africa.[3] Bhigjee[6] has described that in KZN, a province in South Africa which is the epicentre for the HIV pandemic, neurological complications in HIV-infected patients ranges from intracranial mass lesions, bacterial and fungal meningitis, acute disseminated encephalomyelitis, spinal cord disorders and peripheral nerve dysfunction. Toxoplasmosis was the most common SOIL found in their study which was successfully treated with co-trimoxazole. Ring enhancement was a key feature used for detecting SOIL in our study. This feature was utilised by the radiologist for the diagnosis of both toxoplasmosis and tuberculomas in this study. This resulted in difficulty in distinguishing one lesion from the other and was therefore the most plausible reason that the category comprising combined toxoplasmosis and tuberculomas having the most number of patients.

Ermak et al.[12] showed that in Russia, cerebral toxoplasmosis was the leading cause of neurologic disease in patients with end-stage HIV infection with 34.7% cases involving the brain. Ferrer et al.[13] illustrated in their study conducted in Spain that encephalic toxoplasmosis involved 44% of the total number of patients with 80% of these patients having a CD4 count of $<100$ cells/mm$^3$. The most frequent clinical presentation in their study was focal neurological signs (80.9%), headache (53.3%) and fever (42.4%). They found that the most common findings on CT scan were hypodense lesions (92%) and ring enhancement (68.9%). The majority of patients in their study had a hemispheric location for their CNS lesions. There is limited such data documented for Africa.[6] When reviewing clinical findings in this study, the most common features were

**Table 5.** Location of lesions within the CNS.

| | Toxoplasmosis/ tuberculomas | Brain abscess | n |
|---|---|---|---|
| Parietal | 30 | 5 | 35 |
| Basal ganglia | 30 | 5 | 35 |
| Frontal | 25 | 4 | 29 |
| Temporal | 7 | 1 | 8 |
| Cerebellar | 6 | 0 | 6 |
| Occipital | 4 | 0 | 4 |
| Mid-brain | 3 | 0 | 3 |
| Pons | 2 | 0 | 2 |
| Medulla oblongata | 0 | 0 | 0 |

CNS: central nervous system.

**Table 6.** Therapy initiated or was currently used for patients who presented with neuro-clinical features suggestive of a SOIL.

| | Toxoplasmosis/ tuberculomas | Brain abscess | Toxoplasmosis | Tuberculomas | n |
|---|---|---|---|---|---|
| Anti-TB drugs | 77 | 5 | 3 | 3 | 88 |
| Co-trimoxazole | 67 | 2 | 3 | 2 | 74 |
| Dexamethasone | 59 | 1 | 3 | 1 | 64 |
| Prednisone | 50 | 1 | 3 | 1 | 55 |
| Sodium valproate | 36 | 2 | 1 | 0 | 39 |
| Ceftriaxone | 15 | 9 | 0 | 0 | 24 |
| Anti-retroviral drugs | 13 | 0 | 0 | 0 | 13 |
| Phenytoin | 1 | 2 | 0 | 0 | 3 |

SOIL: space-occupying infective lesion; TB: tuberculosis.

**Table 7.** Outcomes.

| | Toxoplasmosis/ tuberculoma | Brain abscess | Toxoplasmosis | Tuberculomas | n |
|---|---|---|---|---|---|
| Discharged home | 72 | 13 | 3 | 3 | 91 |
| Sent to base hospital/step down facility | 8 | 1 | 0 | 0 | 9 |
| Deaths in the wards | 9 | 0 | 0 | 0 | 9 |
| Transferred to neurosurgery | 0 | 1 | 0 | 0 | 1 |

TB: tuberculosis.
Outcome of groups that received early therapy of co-trimoxazole (65%) compared to the group that had delayed or no co-trimoxazole (0%) yielded fewer deaths with p-value of 0.0002 (Pearson's $\chi^2$).
Similar findings were documented for the group that received early therapy of anti-TB drugs (79%) compared to the group with delayed or no anti-TB drugs (0%) with p-value of $<0.0001$ (Pearson's $\chi^2$).

seizures, confusion or altered mental state, headaches and neurological deficits that include cranial nerve abnormalities and hemiparesis. Although seizures and neurological deficits are considered serious clinical findings, headaches and confusion or altered mental state in an HIV-infected patient should also alert the clinician about the possibility of a SOIL and should not be taken lightly.

Although SOIL can affect any part of the CNS, this study showed that they have an affinity to involve the parietal, basal ganglia and frontal regions of the brain. Because most patients had a differential of either toxoplasmosis or tuberculoma, they were treated with multiple drugs that include co-trimoxazole and anti-TB drugs. Steroids such as dexamethasone and prednisone were also commonly used. The preferred anti-epileptic drug used was sodium valproate. The patients whom had demised had a delay in initiating treatment or was not on any co-trimoxazole nor anti-TB drugs. This was significant when compared to patients who received co-trimoxazole and anti-TB drugs with p-values of 0.0002 and $<0.0001$, respectively.

Most patients had a good outcome since only 9 of the 110 patients analysed had demised. However, with very little

information regarding follow-up including no information on repeat CT scans after follow-up, the final outcome of patients diagnosed with infective space-occupying lesions is unknown. The study emphasises that although CT scans are limited and costly investigation, its use for detecting SOIL in the brain is invaluable; hence, it is recommended that government should be investing more towards improving the availability of this investigation.

*Limitations of the study* included not finding all the patient files. At least 15 files were not found when compared to the CT reports in the radiology database. Radiological reporting was dependent on the expertise of the radiologist and hence, the differential diagnosis generated. Serology was not ordered as part of the investigation in majority of the cases which may have been used to differentiate the group that comprised cerebral toxoplasmosis and tuberculomas. The above limitations are often inherent within retrospective studies.

## Conclusion

HIV infection with its complications places a huge burden on countries globally. This is increasingly important in developing world countries with their inherent resource limitations. Access to CT scanning is an essential if we are to diagnose and treat these HIV-related complications appropriately. This study provides an audit of CT scans of HIV-infected patients with SOILs and can serve as a baseline for future prospective studies.

### Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Ethical approval

Ethical approval for this study was obtained from University of KwaZulu-Natal Biomedical Research Ethics Committee BREC BE311/16.

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### Informed consent

This was a retrospective chart review study and therefore no informed consent was required. The University of KwaZulu-Natal Biomedical Review and Ethics Committee (BREC) does not require written informed consents for retrospective chart review studies in South Africa.

### ORCID iD

Somasundram Pillay https://orcid.org/0000-0002-5604-645X

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