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Impact of brain biopsy on management of nonneoplastic brain disease☆

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ABSTRACT

Introduction: Diagnostic yield of brain biopsy in neoplastic brain disease is high and its clinical impact is well established. In nonneoplastic brain disease with negative conventional investigation, decision to undergo invasive procedures is difficult due to its inherent risk and known lower diagnostic yield. Research question: What is the clinical impact of brain biopsy results on management of nonneoplastic brain disease ?

Material and methods: A multidisciplinary team retrospectively reviewed and included all nonneoplastic brain disease cases submitted to biopsy between 2009 and 2019, in a tertiary hospital in Lisbon. Baseline characteristics were registered, including immunosuppression status, diagnostic workup, and treatment prior to biopsy. Diagnostic yield, clinical impact and in-hospital complication rates were assessed.

Results: Sixty-four patients were included, 20 (31.3%) of them immunosuppressed (15 HIV + patients). Thirty-five (67.7%) were previously treated with steroids or antiinfectious agents, with higher percentage (93.3%) in the immunosuppressed group. Biopsy results were diagnostic in 46 (71.9%) cases. More frequent diagnosis was infectious in 20 (31.2%), neoplastic in 12 (18.8%) and inflammatory diseases in 8 (12.5%). Brain biopsy resulted on impact on patient's clinical management in 56 (87.5%), of which 37(57.8%) were submitted to treatment change. In-hospital complications were registered in 4 (6.6%) patients.

Discussion and conclusion: Brain biopsy had clinical impact, including a change in treatment, in most patients studied, and may be considered a useful diagnostic option in nonneoplastic brain disease. However, associated complication rate is not negligible, and previous thorough workup, patient selection and risk-benefit assessment are important.

1. Introduction

Brain biopsy (BB) has a critical role in the diagnosis of central nervous system (CNS) tumours (Livermore et al., 2014). However, its contribution in nonneoplastic CNS diseases (such as encephalitis, chronic meningitis and atypical space-occupying lesions) remains divisive.

In this set, studies have shown controversial results. In 2015, a meta-analysis showed low diagnostic success and clinical impact rates, although the initial hypothesis influenced these rates (Bai et al., 2015). However, recent small cohort studies (Noronha et al., 2019; Rice et al., 2011), showed higher rates, suggesting better patient selection. Also, in a 2016 meta-analysis including HIV + population with neurological disease, benefit of BB seemed to overcome risk (Lee et al., 2016), although most studies were pre-HAART (highly active antiretroviral therapy).

Recent evolution of imaging and laboratory testing may have increased diagnostic accuracy. Therefore, it is relevant to clarify whether brain biopsy is still a diagnostic tool to consider when facing nonneoplastic brain disease. The main goals of this study were to assess clinical impact and diagnostic success rates, and in-hospital complications of BB in patients with nonneoplastic brain disease, in which previous thorough

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workup could not establish an unequivocal diagnosis.

2. Material and methods

2.1. Methods

We performed a retrospective analysis of consecutive neuropathological reports of patients submitted to BB between January 2009 and November 2019 in a tertiary hospital centre. Protocol was approved by the hospital ethics commission. Electronic database search and manual exploration of physical files of all BB were made to reduce selection bias. Search was guided by the following keywords in the diagnostic hypothesis: "tuberculosis"/"tuberculoma", "toxoplasmosis", "cysticercosis", "parasite", "parasitosis", "meningitis", "demyelinating", "multiple sclerosis", "sarcoidosis, "vasculitis", "angiitis", "infectious"/"infection", "abscess", "angiopathy", "congophilic", "amyloid", "encephalitis" and "inflammatory". Clinical and ancillary tests data were collected from patients' electronic records.

2.2. Patient selection

Adult patients were included if the main diagnostic hypothesis was nonneoplastic brain disease after extensive non-invasive workup. Patients were excluded if primary goal of surgery was therapeutic, if the main diagnostic hypothesis was brain neoplasm (primary or metastatic), if electronic health records were insufficient or inaccessible or if previously submitted to a biopsy of the same brain lesion. Cases were retrospectively and independently reviewed by a multidisciplinary specialist team, to decide inclusion in the study. In case of disagreement between the neurologist and the neurosurgeon, the neuropathologist blind judgement was used as tiebreaker. Selection of cases was also blind to the final neuropathological result.

2.3. Outcome definitions

Diagnostic success was considered when the BB allowed a definitive or probable diagnosis. Data from microbiology studies and PCR (polymerase chain reaction) analysis in brain tissue were included for diagnosis. Unspecific inflammatory processes were considered nondiagnostic. Positive clinical impact was considered when the result changed clinical management, which means directly changing patient treatment, or leading to better workup orientation or better prognostic acuity definition. Medical or surgical morbidities after biopsy procedure were registered until the day of hospital discharge, regardless of being unequivocally procedure related. Classification of diagnostic success, clinical impact and in-hospital morbidities was done independently by the multidisciplinary team.

2.4. Statistical analysis

Outcomes were analysed in HIV positive and negative subgroups. Categorical variables are displayed as frequencies and percentages, and continuous variables are displayed as means and standard deviation or median and interquartile range, depending on the results of normality test. One-way ANOVA test was performed to compare means and Kruskal-Wallis non-parametric test was performed to compare medians between groups, as appropriate. Outcomes were compared between groups using Pearson Chi-square test (with Yates correction when necessary) for categorical variables, and t student test or Mann-Whitney *U* test for continuous variables as appropriate. Statistical significance was considered when $p < 0.05$. Statistical analysis was performed using SPSS Statistics® version 20.0.

3. Results

3.1. Selection of patients and baseline characteristics

Seventy-eight cases were selected, but 14 were excluded: neoplasm was the first hypothesis (n = 7), first surgery goal was treatment (n = 1), insufficient data (n = 5), and submission to previous BB (n = 1). Agreement about patient selection between neurologist and neurosurgeon was achieved in most cases (66; 84.6%).

Sixty-four patients were then included in the study. Five patients (7.8%) were treated with immunosuppressant drugs. Fifteen (23.4%) were HIV positive: 11 (73.3%) patients were treated with HAART at presentation and $CD4^+$ lymphocyte count was <200 cells/μL in 7 (53.3%). In 3 patients, HIV diagnosis was made during workup. Patients were divided in two subgroups, regarding their HIV status. Baseline characteristics and previous management are displayed in Table 1.

Most patients (34; 53.1%) were studied in the neurology and neurosurgery departments. Thirteen (20.3%) patients were studied in other hospitals and then transferred to our centre for the procedure. Most procedures (42; 65.6%) were performed between 2009 and 2013.

Brain CT scan and MRI were performed in all patients, except in 2 who had an absolute contraindication for MRI. Lesions with mass effect were present in 34 (53.1%) patients. Lumbar puncture was performed in 42 (85,7%) patients; in 7 the presence of a space-occupying lesion contraindicated the procedure; in 15 data was not available. Two patients with suspected vasculitis were submitted to digital subtraction angiogram, and one to CT angiogram.

Data about previous treatment was available for 51 patients (11 HIV+). Most patients, including all HIV+, received empirical treatment. Most frequent treatments in non-HIV+ patients were steroids (23; 42.5%), followed by antibiotics (9; 22.5%). In HIV+ patients, anti-toxoplasmosis (11; 72.7%) and anti-tuberculosis (5; 45.5%) treatments were the most frequent. In patients treated with steroids, the main goal was to treat brain lesion-related oedema.

3.2. Biopsy procedure

Time between first symptoms and BB was on average less than two months (Table 1). Median time between hospital admission for investigation and BB was significantly different depending on HIV status: 15.5

Table 1
Baseline characteristics and management of patients before biopsy, according to their HIV status.

	HIV- population	HIV + population	Total
Male patients (n, %)	30 (61.2)	10 (66.7)	40 (62.5)
Age (mean, SD)	54.3 (15.8)	44.7 (7.7)	52.0 (14.9)
Previous workup			
Brain CT scan (n, %)	49 (100.0)	15 (100.0)	64 (100.0)
Brain MRI (n, %)	47 (95.9)	15 (100.0)	62 (96.9)
Lumbar puncture (n, %)	30 (83.3)	12 (92.3)	42 (85.7)
Previous treatment			
Steroids (n, %)	17 (42.5)	4 (36.4)	21 (41.2)
Anti-toxoplasmosis (n, %)	0 (0)	8 (72.7)	8 (15.7)
Anti-tuberculosis (n, %)	3 (7.5)	5 (45.5)	8 (15.7)
Antivirals (n, %)	4 (10.0)	1 (9.1)	5 (9.8)
Antibiotics (n, %)	9 (22.5)	1 (9.1)	10 (19.6)
Total (n, %)	23 (57.5)	11 (100.0)	34 (66.7)
Timings (median, IQR) in days			
Symptoms – biopsy time	75.0 (30.0–161.0)	77.0 (36.5–198.5)	76.0 (32.25–159.25)
Admission – biopsy time	15.5 (4.0–35.5)	38.0 (31.0–60.0)	23.0 (7.0–42.0)

CT – computed tomography; MRI – magnetic resonance imaging; IQR – interquartile range; SD – standard deviation.

(IQR 4.0–35.5) days in HIV negative population and 38.0 (31.0–60.0) days in HIV positive population (p = 0.001).

All cases had an imaging-defined target to guide biopsy. Procedure was open in 35 (53.1%) patients. In HIV+ patients, stereotactic biopsy was performed in 10 (66.7%) patients, while in HIV negative patients, open biopsy was more frequently performed (29; 59.2%). This difference was not statistically significant (p = 0.07). The most frequent biopsy locations were brain hemispheres in 46 (71.9%) patients, followed by meninges (11; 17.2%), meninges and brain cortex (3; 4.7%), brainstem, (3; 4.7%), and anterior cerebral artery branch in one patient suspected to have vasculitis.

3.3. Initial hypothesis

The most common diagnostic hypotheses prior to biopsy were infectious diseases (48.4%), followed by meningitis of unknown aetiology (17.2%) and inflammatory diseases (12.5%) (Table 2). In HIV positive patients, infectious disease was the initial hypothesis in 13 (86.7%) of patients.

Some initial hypotheses were unspecific regarding aetiology or included multiple possibilities. In HIV negative patients, meningitis of unknown aetiology (meningeal gadolinium enhancement without parenchymatous lesions, of probable inflammatory or infectious aetiology) was the initial hypothesis in 11 (22.4%) patients, of which 7 were pachymeningitis. Non-infectious encephalitis (parenchymatous lesion of probable inflammatory aetiology) was the diagnostic hypothesis in 5 (10.2%) patients. In 3 (6.1%) immunocompetent patients, primary hypothesis was progressive multifocal leukoencephalopathy (PML).

3.4. Diagnostic success

In 46 (71.9%) patients, brain biopsy led to diagnostic success (75.5% in HIV negative patients and 60.0% in HIV positive patients). No difference was found in diagnostic success rate, regarding previous treatment (including steroids), year of biopsy or type of procedure. Final diagnoses are described in Table 3.

The most common diagnosis was infectious disease in 20 (31.2%) patients, followed by brain neoplasm in 12 (18.8%) and inflammatory disease in 8 (12.5%). Diagnosis confirmed the initial hypothesis in 26 (40.6%) patients: 4 out of 4 (100.0%) congophilic angiopathies, 1 out of 1(100%) multiple sclerosis, 11 out of 12 (91.7%) unspecific brain abscesses, 5 out of 7 (71.4%) pachymeningitis, 1 out of 2 (50.0%) pachyleptomeningitis, 2 out of 5 (40.0%) PML, 1 out of 5 (20.0%) encephalitis and 1 out of 6 (16.7%) vasculitis suspected cases. In 20 (31.3%) patients, result led to an unexpected definite diagnosis.

Regarding infectious pathologies, specific aetiological agents were isolated in half of microbiological cultures of brain abscess aspirate. In 10 (15.6%) cases, brain tissue was submitted to PCR techniques, and 7 (70.0%) positive results contributed to final diagnosis. In most cases, previous workup had included these techniques.

Regarding neoplastic diagnosis, initial clinical hypotheses were nonspecific inflammatory diseases in HIV negative patients, and infectious diseases in HIV positive patients. Considering the latter, two patients diagnosed with lymphoma had $CD4^{+}$ lymphocyte counts <200 cells/μL, and the remaining had between 200 and 500 cells/μL.

Regarding inflammatory pathologies, the most common inflammatory diagnosis was hypertrophic pachymeningitis in patients with previously known systemic autoimmune disorders.

3.5. Clinical impact

In 56 (87.5%) patients, neuropathological diagnosis had clinical impact on management, and most patients (57.8%) benefitted from treatment change because of this result. Clinical impact rates in HIV negative and positive patients were 91.8% and 73.3% respectively (Table 4).

Diagnostic success and clinical impact rates according to initial hypothesis and final diagnosis are displayed in Table 5. When final diagnosis confirmed the initial hypothesis, all diagnosis had clinical impact and 17 (65.4%) led to treatment change. When BB was nondiagnostic, 11 (61.1%) results still had a clinical impact, and 3 (16.7%) led to treatment change.

Table 2
Main diagnostic hypothesis prior to brain biopsy, according to HIV status.

Initial hypothesis (prior to biopsy)	HIV- population	HIV + population	Total
Infectious disease (n, %)	18 (36.7)	13 (86.7)	31 (48.4)
- Unspecific brain abscess (n, %)	12 (24.4)	0	12 (18.8)
- Progressive multifocal leucoencephalopathy (n, %)	3 (6.1)	2(13.3)	5 (7.8)
- Toxoplasmosis (n, %)	0	4 (26.7)	4 (6.3)
- Neurocysticercosis (n, %)	1 (2.0)	0	1 (1.6)
- Tuberculosis (n, %)	1 (2.0)	1 (6.7)	2 (3.1)
- Multiple hypotheses (n, %)	0	4 (26.7)*	4 (6.3)
- Unspecific (n, %)	1 (2.0)	2 (13.3)	3 (4.7)
Meningitis (n, %)	**11 (22.4)**	**0**	**11 (17.2)**
- Pachymeningitis (n, %)	7 (14.3)	0	7 (10.9)
- Leptomeningitis (n, %)	2 (4.1)	0	2 (3.1)
- Pachyleptomeningitis (n, %)	2 (4.1)	0	2 (3.1)
Inflammatory disease (n,%)	**8 (16.3)**	**0**	**8 (12.5)**
- Vasculitis (n, %)	5 (10.2)	0	5 (7.8)
- Multiple sclerosis (n, %)	1 (2.0)	0	1 (1.6)
- Unspecific (n, %)	2 (4.1)	0	2 (3.1)
Non-infectious encephalitis (n,%)	**5 (10.2)**	**1 (6.7)**	**6 (9.4)**
Congophilic angiopathy (n,%)	**4 (8.2)**	**0**	**4 (6.3)**
Multiple hypotheses (n,%)	**3 (6.1)****	**1 (6.7)*****	**4 (6.3)**

Multiple hypotheses were considered equally: * tuberculosis vs toxoplasmosis (n = 2), toxoplasmosis vs PML (n = 1) and bacterial vs tuberculosis vs toxoplasmosis abscess (n = 1) ** amiloidoma vs infection, demyelinating vs vascular lesion, demyelinating vs vascular vs infectious disease. *** acute disseminated encephalomyelitis (ADEM) vs toxoplasmosis.

Table 3
Final neuropathological results according to HIV status.

Final neuropathological diagnosis	HIV- population	HIV + population	Total
Infectious disease* (n, %)	16 (32.7)	4 (26.7)	20 (31.2)
- Bacterial brain abscess	11	1	12
- Progressive multifocal leukoencephalopathy	1*	2*	3
- Tuberculosis	2*	0	2
- Herpetic meningoencephalitis	2*	0	2
- Toxoplasmosis	0	1*	1
Neoplasm (n, %)	**7 (14.3)**	**5 (33.3)**	**12 (18.8)**
- Non-Hodgkin B cell Lymphoma	2	3	5
- Intravascular B cell Lymphoma	2	0	2
- Anaplastic astrocytoma	1	1	2
- Glioma	1	0	1
- Gliomatose cerebri	1	0	1
- Meningioma, grade I OMS	0	1	1
Inflammatory disease (n, %)	**8 (16.3)**	**0 (0)**	**8 (12.5)**
- Hypertrophic pachymeningitis	4	0	4
- Vasculitis	2	0	2
- IgG4 disease	1	0	1
- Multiple sclerosis	1	0	1
Other	**6 (12.2)**	**0 (0)**	**6 (9.4)**
- Congophilic angiopathy	4	0	4
- Meningitis	2	0	2
Non-diagnostic	**12 (24.5)**	**6 (40.0)**	**18 (28.1)**

Table 4
Clinical impact of brain biopsy, according to HIV status.

	HIV negative	HIV positive	Total
Clinical impact (n, %)	45 (91.8)	11 (73.3)	56 (87.5)
- Change of treatment	30 (61.2)	7 (46.7)	37 (57.8)
- Other[a]	13 (26.5)	4 (26.7)	17 (26.6)

[a] Other: better orientation or prognostic acuity.

Table 5
Diagnostic success and clinical impact rates according to category of diagnostic hypotheses and final diagnoses.

	Diagnostic success	Clinical impact	
		Total	Changed treatment
Initial hypothesis			
Infectious disease (n, %)	24 (77.4)	27 (87.1)	19 (61.3)
Inflammatory disease (n, %)	5 (62.5)	8 (100.0)	6 (75.0)
Meningitis (n, %)	8 (72.7)	10 (90.9)	6 (54.5)
Encephalitis (n, %)	3 (50.0)	5 (83.3)	2 (33.3)
Congophilic angiopathy (n, %)	4 (100.0)	4 (100.0)	2 (50.0)
Multiple hypotheses (n, %)	2 (50.0)	2 (50.0)	2 (50.0)
Final diagnosis			
Infectious disease (n, %)	–	20 (100.0)	15 (75.0)
Neoplastic disease (n, %)	–	11 (91.7)	11 (91.7)
Inflammatory disease (n, %)	–	8 (100.0)	6 (75.0)
Meningitis (n, %)	–	2 (100.0)	0
Congophilic angiopathy (n, %)	–	4 (100.0)	2 (50.0)
Nondiagnostic (n, %)	–	11 (61.1)	3 (16.7)

3.6. In-hospital follow-up

Information data about follow-up after biopsy was available in 60 patients (14 HIV+). In-hospital median stay after procedure was 12.0 (IQR 2.0–31.5) days. Seven patients had in-hospital occurrences between BB procedure and hospital discharge (Table 6). Four patients (6.6%) had procedure-related complications. One (7.1%) HIV+ patient had a complication after procedure, and three died during hospitalization, of not procedure-related causes. All cases of death occurred in patients with diagnostic biopsies. Procedure related mortality rate was zero.

4. Discussion

4.1. Diagnostic success

In over half of cases, brain biopsy led to diagnostic success, reaching 75% in non-HIV patients, which was higher than most previous studies (Bai et al., 2015; Josephson et al., 2007; Abdullah et al., 2017; Pulhorn et al., 2008; Schuette et al., 2010; Wong et al., 2010; Burns et al., 2009). Only recent studies have shown similar high diagnostic success rates (Noronha et al., 2019; Rice et al., 2011). A 2015 meta-analysis including 831 immunocompetent patients disclosed a diagnostic success rate of 54% with great heterogeneity depending on the initial hypothesis (Bai et al., 2015). Primary angiitis of CNS and atypical dementia hypotheses were associated with higher rates (over 60%), while only 30% of chronic meningitis hypothesis had a definite diagnosis. However, only 3/20 studies included were published after 2010. Recently, there seems to be a better selection of cases using non-invasive methods and improved surgical techniques, which is supported by a strong correlation between diagnostic success rates and time interval of the studies (Bai et al., 2015; Noronha et al., 2019).

Other aspects may explain our high diagnostic rate. In our study, all cases had an imaging-defined target, which is known to be associated with higher diagnostic yield (Bai et al., 2015; Noronha et al., 2019; Rice et al., 2011; Wong et al., 2010). PCR techniques in brain tissue led to final diagnosis in 7 cases, and previous studies do not mention the use of this technique. Also, some selection bias may have occurred, as the initial hypothesis was confirmed in more than one third of cases. However, this is common in the literature: biopsy confirmed preoperative diagnosis in 46% of encephalitis cases (Abdullah et al., 2017); in nonneoplastic disease, neuropathology confirmed 15.6% of all cases, including 23.5% of CNS inflammatory disease and 36% of CNS vasculitis (Noronha et al., 2019).

4.2. Clinical impact

The clinical impact of all final diagnoses (including those of confirmation) is therefore essential. Overall, we found that over 80% of BB had clinical impact on patient management, and most led to treatment change. Reported clinical impact rates have been very heterogeneous, between 8 and 30%, depending on indication (Bai et al., 2015; Schuette et al., 2010). However, recent quoted studies show impact rates between 60 and 80%, like ours (Noronha et al., 2019; Rice et al., 2011). Higher diagnostic success rates will likely lead to higher clinical impact rates. Also, better disease knowledge and treatment advances in the last decade could explain this difference to former studies.

In our cohort, almost one fifth of our patients were diagnosed with brain neoplasm, even though primary hypothesis was nonneoplastic. More than 90% of definitive neoplasm diagnosis influenced treatment change. This phenomenon seems to be widespread. It has been showed that lymphoma and astrocytoma were among the most common histologic diagnosis when nonneoplastic brain disease was the initial hypothesis (Noronha et al., 2019), whereas the second most common diagnosis in chronic meningitis hypotheses was neoplasm (Bai et al., 2015). It is not unusual to have neoplasm in the list of differential diagnosis of atypical neurological conditions, even when it is not the primary hypothesis. Diagnosis of brain neoplasm has a great clinical impact and treatment may improve prognosis if diagnosis is made soon

Table 6
Description of in-hospital occurrences after brain biopsy in seven patients.

HIV status	Admission-biopsy time (days)	Main diagnostic hypothesis	Biopsy type	Final diagnosis	In-hospital occurrences	Time after BB (days)
Pos.	154	Infectious lesion	S	Anaplastic astrocytoma	Not procedure-related death	2
Pos.	78	Toxoplasmosis	S	PML	Not procedure-related death	64
Pos.	35	Toxoplasmosis	S	Non-Hodgkin lymphoma	Not procedure-related death	20
Pos.	46	PML	S	Nondiagnostic	Symptomatic parenchymatous haemorrhage	1
Neg.	7	Brain abscess	S	Brain abscess	*De novo* ventriculitis	1
Neg.	44	Vasculitis	O	Small-vessel vasculitis	Symptomatic subdural haematoma	2
Neg.	14	Vasculitis	S	Nondiagnostic	Symptomatic parenchymatous haemorrhage	1

Pos. – positive; Neg. – negative; S – stereotactic; O – open; PML – progressive multifocal leukoencephalopathy; BB – brain biopsy.

enough, particularly in a young population as it was ours.

The clinical impact rates we present are higher than the diagnostic success rates. This is due to the fact that two thirds of nondiagnostic BB had clinical impact and 17% led to treatment change. Some information may redirect workup, exclude fewer probable conditions, allow withdrawal of useless treatments or simply better define prognosis, as others stated (Bai et al., 2015; Rice et al., 2011). On the other side of spectrum, not all definite diagnosis had significant clinical impact. Decision to submit a patient to such an invasive procedure should always have in mind its potential and clinical benefit, avoiding pure diagnostic ambitions.

4.3. HIV population

In the subgroup of HIV patients, almost two thirds of BB led to diagnostic success, and over 70% led to clinical impact. These rates are lower than those presented in the meta-analysis of 2016 (diagnostic success was 92% and management change was 58%), where most studies were pre-HAART (Lee et al., 2016). However, recent studies showed slightly lower diagnosis rates, between 68 and 77% (Noronha et al., 2019; Lee et al., 2016; Acosta et al., 2018). Stereotactic technique was performed in most HIV patients, similarly to our study, and did not influence diagnostic success (Lee et al., 2016).

Our cohort showed most common diagnosis was non-Hodgkin B cell lymphoma, followed by PML, toxoplasmosis and bacterial brain abscess, which is in line with other studies (Lee et al., 2016; Acosta et al., 2018). With HAART, there was a decrease in biopsy diagnosis of opportunistic infections, such as PML and toxoplasmosis, and increase in diagnosis of brain abscess from other aetiologies, while CNS lymphoma remained stable (Lee et al., 2016). Interestingly, even when neoplastic initial hypotheses were excluded, 70% of biopsies were diagnostic, and most common diagnosis was still CNS lymphoma in 20.6% (Noronha et al., 2019), which was comparable to our results.

Focal brain lesions in HIV patients are usually empirically treated as toxoplasmosis (Porter and Sande, 1992), and biopsy is only considered in refractory or atypical cases. In our cohort, most patients were previously treated with anti-toxoplasmosis treatment. On the other hand, lymphoma was still the most common diagnosis as expected, but its pathological confirmation is definitively required for oncological treatment.

4.4. In-hospital follow-up

During in-hospital follow-up, 4 (6.6%) patients had procedure-related complications. Procedure-related mortality was zero. This is in line with recent series where complication rates varied between 4% and 9% (Bai et al., 2015; Noronha et al., 2019; Rice et al., 2011; Pulhorn et al., 2008; Schuette et al., 2010; Wong et al., 2010; Gilkes et al., 2012). Most common complication in our cohort was symptomatic haemorrhage, as also shown in a recent meta-analysis (Bai et al., 2015), particularly in stereotactic procedures. Stereotactic biopsy is known to be associated with higher risk of parenchymatous haemorrhage (Livermore et al., 2014). These morbidity and mortality rates are lower than the ones associated to neoplastic disease biopsy (Livermore et al., 2014).

Although one might think HIV+ patients were more likely to have procedure-related complications, described morbidity and mortality rates for biopsy procedures in HIV + population are 5.7% and 0.92%, respectively (Lee et al., 2016). In our cohort, one HIV+ patient suffered a symptomatic parenchymatous haemorrhage after biopsy. During in-hospital follow-up, 3 HIV+ patients died of non-procedure-related causes. They were diagnosed with serious conditions (brain neoplasm and PML) and were in a very vulnerable condition during hospital stay. One of the patients was submitted to biopsy five months after admission. This suggests brain biopsy in HIV+ patients is equally safe, but timing of procedure may play a more important role to influence their prognosis.

4.5. Limitations

Being a retrospective study, it has limitations, particularly concerning missing data regarding previous workup and follow-up after procedure. Around 20% of patients were studied elsewhere and transferred to our centre temporarily for biopsy procedure, hampering data collection. Also, referral bias may have occurred towards the more challenging cases. Regarding neuropathological analysis, there was no minimal tissue sample volume required, and due to lack of collection of neuroimaging follow-up data, imaging was not reviewed by our team to confirm biopsy target accuracy. Although small, our cohort size is comparable to other studies in the same time length (Noronha et al., 2019; Rice et al., 2011; Acosta et al., 2018). Our HIV+ cohort is particularly small, but most of previous studies had wider inclusion criteria, such as neoplastic hypotheses. Finally, we cannot exclude some bias in patient inclusion and classification by the experts. Still, to minimize this, all cases were independently reviewed in a blinded process. We opted for a dichotomic decision (success: yes/no) to facilitate data analysis and interpretation. However, the degree of success also depends on the clinical course, previous workup and initial hypothesis considered and thus the expert decision on this outcome is ultimately subjective but reflects real-life clinical practice. Large prospective multicentric studies could add more information to help better select these patients.

5. Conclusion

Our study shows recent data about the usefulness of brain biopsy in nonneoplastic disease, including HIV+ population in post-HAART era. We reinforce the importance of extensive previous workup and empirical treatment, weighted against optimal timing for procedure, in order not to miss the therapeutic window. In selected cases, we show higher rates of diagnostic success and clinical impact, with few procedure-related complications.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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