Stereotactic frame-based guided brain biopsies: experience in a center at Latin America

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Resumen

Introducción: Las biopsias guiadas por estereotaxia se eligen para lesiones localizadas profundamente, así como para aquellas en áreas elocuentes, cuando el riesgo supera el beneficio de un procedimiento abierto o cuando la cirugía abierta no tiene ninguna ventaja sobre la sospecha de histología. **Objetivo:** Este estudio tiene como objetivo describir retrospectivamente el rendimiento diagnóstico y la morbilidad y mortalidad relacionadas con una serie de biopsias guiadas estereotácticas en un período de 6 años en un solo centro en América Latina. **Materiales y Métodos:** Se revisaron 62 historias clínicas de pacientes sometidos a biopsias cerebrales guiadas con estereotaxia. Se adquirieron las características clínicas, la morbilidad y la mortalidad asociadas a los procedimientos. **Resultados:** La tasa de complicaciones fue del 2,7% y el rendimiento diagnóstico alcanzó el 87%. La localización más frecuente del objetivo fue frontal y el diagnóstico más frecuente fue el glioblastoma. **Conclusiones:** La tasa de complicaciones y el rendimiento diagnóstico en esta serie fueron similares a los observados en diferentes series revisadas en la literatura, realizadas con procedimientos estereotácticos utilizando marco o realizados con neuronavegación en la literatura.

Palabras clave: Estereotaxia, biopsia guiada por imágenes, rendimiento diagnóstico, morbilidad, mortalidad, cerebro.

Abstract

Introduction: Stereotactic guided biopsies are chosen for deep-located lesions, as well as for those in eloquent areas, when the risk outweighs the benefit of an open procedure, or when open surgery has no advantage over the suspected histology. **Objective:** This study aims to describe retrospectively the diagnostic yield and the morbidity and mortality related to a series of stereotactic-guided biopsies in a 6-year period in a single center in Latin America. **Materials and Methods:** 62 medical records of patients who underwent stereotactic-guided brain biopsies were reviewed. The clinical features, the morbidity and mortality associated to the procedures were acquired. **Results:** The complication rate was 2.7% and the diagnostic yield reached 87%. The most frequent location of the target was frontal and the most frequent diagnosis was glioblastoma. **Conclusions:** The complication rate and the diagnostic yield in this series were similar to the observed in different series performed with frame-based stereotactic procedures or performed with neuronavigation in the literature.

Key words: Stereotaxic Technique, Image-Guided Biopsy, Diagnostic Yield, Morbidity, Mortality, Brain.

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Abbreviations: ICH = Intracranial Hemorrhage, CSF = Cerebrospinal Fluid, CT = Computerized Tomography, HIV = Immunodeficiency Human Virus, Subarachnoid Hemorrhage = SAH, TB = Tuberculosis.

Introduction

In the last decades different stereotactic-guided techniques have been developed for brain biopsies, including frame-based and frameless (neuronavigation) image-guided biopsies. Both techniques provide samples of intracranial lesions for histopathological analysis, with the intention of guiding the possible treatments and prevent any unnecessary further procedure. Although several studies showed that both techniques have same mortality rates and have similar diagnostic yield, traditionally the frame-based stereotactic-guided procedures have been the gold standard for taking these samples[1,2].

The largest series have shown that the frame-based procedures are safe, and have a general mortality between 1.0-6.5% and a general morbidity of 1-1.7%[3-5]. The most frequent complication associated to these biopsies is hemorrhage; about 60% of patients could bleed, even though the amount of blood differs and most bleedings are not considered complications *per se*. There is a wide range of clinical scenarios, including neurological deterioration with large volume bleedings that could need craniotomy for draining[3]. A different complication is any secondary neurological deficit related to a hemorrhage, however, incidence is very low[6]. Reported complications vary considerably[5,7].

The accepted complication rate in general is near 5%, and usually neurological deficits are transitory. A malignant histology appears to be a risk factor for hemorrhage[8,9].

It has been reported that frame-based and frameless stereotactic-guided biopsies have no significant differences in diagnostic yield or permanent morbidity, it has also been reported that these frameless procedures could be potentially advantageous for large lesions or for those with cortical location, while frame-based biopsies could be more effective for smaller lesions or those with deeper location[2]. However, frame-based stereotactic-guided biopsies remain the gold standard for sampling deep and eloquent area-located lesions[2,6,10,11].

Stereotactic Biopsies in Latin America and Spain

A Chilean group described the results of frame-based guided biopsies versus open biopsies, but the study is retrospective and did not attempt to demonstrate the diagnostic performance of procedures, it also showed no differences in complications and presented 5% of mortality and 13% of morbidity related to the frame-based procedures[12]. In other Spanish series, a diagnostic yield of 93% and 5% complications were reported[13]. These data relate to high similarity with the rest of the series reported in the literature. This study aims to describe retrospectively the diagnostic yield and the morbidity/mortality related to a series of stereotactic-guided biopsies in a 6-year period in a single center in Latin America.

Methods

A review of the medical records of patients who underwent frame-based stereotactic-guided biopsies in one institution in Latin America, from July 2009 to July 2015 was performed. Eligible patients were those who were on the neurosurgery department procedure list and those in the database of service registration for neurosurgical procedures that were performed during that period of time. All patients were selected with code terminology 'stereotactic brain biopsy' within these lists. The total number of patients found was 62. Then a complete search was done in the electronic system of medical records ("e-salud") and in the physical files stored in our facility. The medical records of each patient were reviewed completely. Clinical, microbiological findings, cerebrospinal fluid (CSF), and pathology results were analyzed as well. Approval of our Institutional Review Board was given, as well as permission of our institutional bioethics committee. STATA version 13® was used for applying Pearson-Chi^2 for analysis of the possible association of tuberculosis (TB) with the subgroup of patients with final pathology result of reactive gliosis, given the small sample of the study. All biopsies were performed by one senior neurosurgeon. Pre-operative guidance was performed with a contrast-enhanced head CT scan and/or with a contrast-enhanced brain MRI (Figure 1). One or two neurosurgery residents were assistants for each surgery. 16 samples were taken in each procedure for histological/inmunohistological analysis: 4 samples clockwise in the core of each lesion, 4 samples 5 mm out of the core, and 4 samples 10 mm out of the core (Figure 2).

Results

Among the 62 eligible patients 20 (32.3%) were female and 42 (67.7%) were men. The age range was 20 to 81 years, with an average of 47 ± 17 years. 4 (6.5%) patients had a previous diagnosis of infection with Human Immunodeficiency Virus (HIV) diagnosed with ELISA (2 samples) and 8 (13%) had antecedent of TB.

In all cases the final pathology result was determined in 54 (87%) of the 62 patients, the other 8 (13%) patients had biopsy specimens reported as 'reactive gliosis'. In this series the most frequent diagnosis was high-grade glioma in a total of 21 patients (34%). (Table 1).

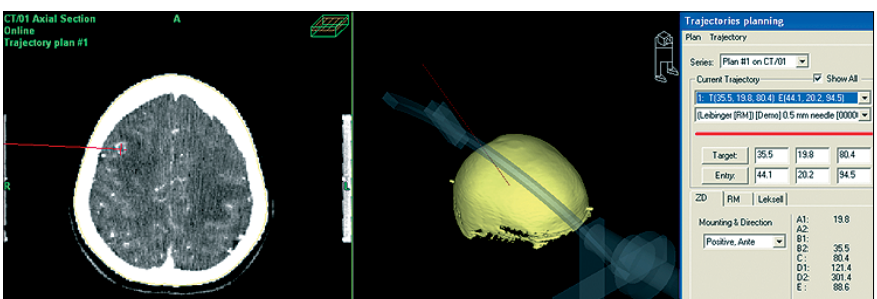

Figure 1. Pre-operative planning for Stereotactic Frame-based brain biopsy.

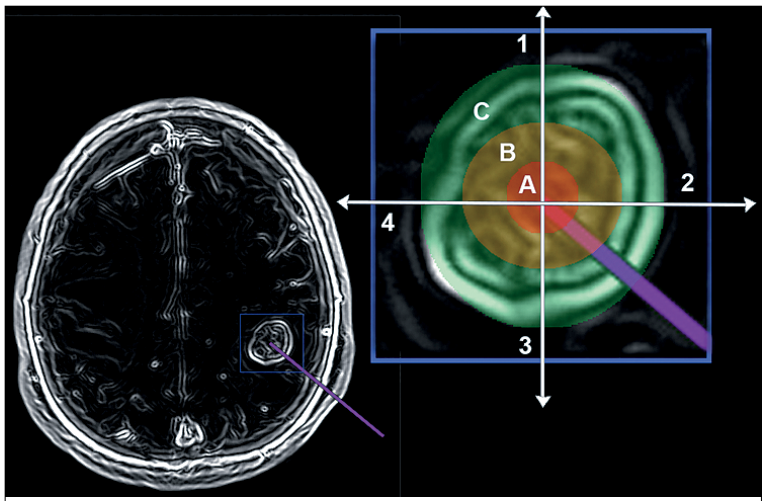

Figure 2. Illustrative sketch of the sample taking. A designed approach to the core of the lesion is performed (A). At this location 4 samples are taken in the four cardinal points (1, 2, 3, 4). Afterwards, the biopsy needle is repositioned 5 mm (B) and 10 mm (C) out of the core for the other 8 samples.

Table 1.
The final diagnosis of biopsies with positive result

Diagnosis	Number of patients (%)
High Grade Glioma	21 (34)
Low Grade Glioma	13 (21)
Reactive Gliosis/Inflammatory	8 (13)
Lymphoma	7 (11.2)
Abscess	7 (11.2)
Metastases	3 (4.8)
Cortical Dysplasia	3 (4.8)
Total	62 (100)

Table 2.
Location of the biopsied lesions

Localization	Number of patients (%)
Frontal	17 (27.5)
Thalamus	13 (20.9)
Basal Ganglia	10 (16.1)
Parietal	7 (11.2)
Brain stem	5 (8.1)
Temporal	4 (6.5)
Occipital	4 (6.5)
Cerebellum	2 (3.2)
Total	62 (100)

Moreover, the most common location for biopsies was in the frontal lobe (35%), the distribution is seen in Table 2.

The signs and symptoms of the patients were divided into three different groups (Table 3). Only 1 (2.7%) patient had a complication associated with the procedure: patient had a secondary brainstem intracranial hemorrhage and had a consequently fatal outcome.

Finally, an assessment of the functional outcome of patients in the short and medium term was performed. Being a very heterogeneous group, there is no any specific functional scale for an evaluation of this group of patients, therefore we decided to use the Glasgow Coma Scale (GCS), the Karnofsky Performance Scale (KPS), and the modified Rankin Scale (MRs) score to determine the functional outcome of the patients. No patient had deterioration of his or her functional capacity.

Discussion

In this paper the characteristics of 62 patients who were taken to stereotactic-guided biopsy with the Dujovny-Zamorano (ZD) frame for diagnostic purposes were evaluated. The diagnostic performance of procedures that focused the treatment of patients in this series was 87%, which is comparable with the performance of other large series in the literature, as shown in Table 5[14].

It is worth noting that several patients remain with a histopathological diagnosis with inflammatory changes only, which runs from 6 to 41% (Table 5), including samples with reactive gliosis[15].

In some series it is reported as gliosis or as inflammatory changes. For this study reported inflammatory changes and reactive gliosis were interpreted as inconclusive as it is not representative to define any medical treatment with the patient. The most common diagnosis was high-grade glioma, possibly related to their ability to infiltrate deep structures located in eloquent areas or locations that require the least invasive procedures without injury eloquent areas. CT scans were performed for post-operative neuro-radiological monitoring for the presence or absence of subarachnoid hemorrhage (SAH) or ICH, and to determine if the sample was taken from the pre-determined tar-

Table 3.
Signs and symptoms of patients

Signs and symptoms	Number of patients
Motor	46
Behavior/Cognitive	7
Sensitive	27

Table 4.
Features of biopsies reported as reactive gliosis

No	Age	Signs	Location	Antecedents
1	36	Sensitive	Thalamus	Pulmonary TB
2	56	Motor	Occipital	Pulmonary TB
3	60	Motor	Frontal	Myeloproliferative disease
4	42	Sensitive	Frontal	-
5	27	Sensitive	Frontal	Multiple Sclerosis
6	71	Behavior	Thalamus	Milliary TB
7	25	Motor	Brain Stem	Renal transplant
8	55	Behavior	Thalamus	-

TB (Tuberculosis).

Table 5.
Inflammatory/Unspecific stereotactic brain biopsies of different series

Author Year	Biopsies	Inflammatory/Unspecific (%)
Apuzzo ML, et al.[6] 1987	500	25 (21.4)
Kim JE, et al.[15] 2003	275	25 (21.4)
Woodworth GF et al[2] 2006	110	12 (10.2)
Zorro-Guío OF et al[7] 2013	44	7 (6)
Hawasli AH, et al.[19] 2013	170	48 (41)
Total	1,099	117 (100)

get in the procedure planning.
Making an analysis of the cases in the subgroup with reactive gliosis the following was found: 4 of the 8 patients had lesions located deep in the brain stem and in the thalamus, 3 of them had TB as an antecedent in common. Studies on the possible causes of failure in the biopsy result associated with the instrument or the way in which the sample is performed, the site where the sample is taken, the number of samples, the volume of the sample, taken or not frozen biopsy, tissue heterogeneity or the error in the sampling[16,17]. However, there is only one study related to clinical risk factors that could affect the results of the biopsy[18]. Some of these potential predictors that could be considered would be: antecedent of smoking, previously diagnosed with another type of cancer, prior diagnosis of diabetes mellitus, coronary heart disease, hypertension, anticoagulation or aspirin use prior to the procedure[18,19].
Regarding the findings of this subgroup of patients with reactive gliosis (Table 5), in our study we found that the antecedent of TB may also affect this result. The Chi^2 test was applied with a value $p = 0.048$ (Pearson-Chi^2 = 3,9102), therefore noting the possible association between the reactive gliosis and the presence of TB. However, it is necessary to perform other studies with larger samples to draw clear conclusions. This study has several limitations given its nature of a retrospective series, as well as being a small sample of patients. Additionally, only one surgeon performed all procedures and technique was not compared with neuronavigation. However, this study reveals a new possible risk factor for negative biopsies and it is an initial study for further prospective studies for evaluation of inconclusive biopsies. Finally, an important impact on patient care and health system economy would be improved with a special analysis of these patients. Are TB patients worth it for stereotactic frame-based brain biopsy? An open *versus* stereotactic study comparing samples would help neurosurgeons to make surgical decisions over those challenging cases.

Conclusion

Stereotactic-guided biopsies had a diagnostic yield in this series of 87% and the rate of complications was 2.7%, comparable to the largest series reported in the literature. Regarding the subgroup of patients with non-diagnostic biopsies, it could have clinical risk factors that could affect the diagnostic yield of the process, e.g. having a history of TB. However, it is necessary to perform additional studies to determine clinical risk factors that could affect the final pathology result.

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