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ORIGINAL ARTICLE

Concordance and diagnostic yield of stereotactic biopsies for posterior fossa: Technique and experience in a reference hospital

Concordancia y rendimiento diagnóstico de biopsias estereotáxicas para fosa posterior: técnica y experiencia en un hospital de referencia

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Abstract

Aim: *Describe our stereotactic brain biopsy (SBB) technique for intra-axial lesions of the posterior fossa, evaluate its effectiveness and safety, and compare them with other series.* **Material and methods:** *Retrospective study in ten consecutive patients, whose variables were age, gender, location of the lesions, clinical, radiological, and histopathological diagnoses, complications, and mortality, for analysis using descriptive statistics and tests of concordance and diagnostic validity.* **Results:** *Lesions were pontine in seven cases, and pontomedullary in three occasions, with histopathological diagnoses of four Grade II astrocytomas, two Grade IV astrocytomas, two infectious process, one neuroblastic tumor, and one cavernous malformation, whose frequency differs from the previous reports ($\chi^2 = 0.07$). The clinical-radiological concordance was poor ($\kappa = 0.20$). The validity of the clinical diagnosis had intermediate values (Sn = 66.7%, Sp = 75%), while radiological studies were more sensitive (Sn = 100%, Sp = 25%). A definitive diagnosis was obtained in all procedures, with no permanent morbidity or mortality because of the surgery.* **Conclusion:** *The SBB technique for posterior fossa implemented in our hospital shows high diagnostic yield, as well as absolute safety for the patient.*

Keywords: *Biopsy. Cranial fossa. Posterior. Stereotaxic techniques. Reproducibility of results.*

Resumen

Objetivo: *Describir nuestra técnica de biopsia cerebral estereotáctica (SBB) para lesiones intraaxiales de fosa posterior, evaluar su eficacia y seguridad y compararlas con otras series.* **Material y métodos:** *Estudio retrospectivo en 10 pacientes consecutivos, cuyas variables fueron edad, sexo, localización de las lesiones, diagnósticos clínicos, radiológicos e histopatológicos, complicaciones y mortalidad, para análisis mediante estadística descriptiva y pruebas de concordancia y validez diagnóstica.* **Resultados:** *Las lesiones fueron pontinas en 7 casos y pontomedulares en 3 ocasiones, con diagnósticos histopatológicos de 4 astrocitomas grado II, 2 astrocitomas grado IV, 2 procesos infecciosos, 1 tumor neuroblástico y 1 malformación cavernosa, cuya frecuencia difiere de reportes previos ($\chi^2 = 0.07$). La concordancia clínico-radiológica fue mala ($\kappa = 0.20$).*

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La validez del diagnóstico clínico tuvo valores intermedios (Sn = 66.7%, Sp = 75%), mientras que los estudios radiológicos fueron más sensibles (Sn = 100%, Sp = 25%). Se obtuvo un diagnóstico definitivo en todos los procedimientos, sin morbimortalidad permanente por la cirugía. **Conclusión:** *La técnica SBB para fosa posterior implementada en nuestro hospital muestra un alto rendimiento diagnóstico, así como una seguridad absoluta para el paciente.*

Palabras clave: *Biopsia. Fosa craneal. Posterior. Técnicas estereotáxicas. Reproducibilidad de resultados.*

Introduction

Stereotactic brain biopsy (SBB) in adult patients was established several decades ago and advanced together with the advent of head computed tomography (CT). Its utilization increased by including pediatric patients, with multiple reports revealing a high diagnostic value, as well as a low rate of complications[1-8]. Various techniques are known to perform SBB, with the patient in supine or semi-sitting positions through a precoronal burr-hole for transcerebral approach, and in prone position through transcerebellar-transpeduncular approach[3,7,9,10]. Lesions located on pons, medulla oblongata, cerebellar peduncles, as well as deep cerebellar, may correspond to various clinical entities with high diagnostic and therapeutic difficulty, such as primary and secondary neoplasms, and infectious, inflammatory, vascular, and demyelinating diseases, among others[5,9].

At present, magnetic resonance imaging (MRI) is an important and daily tool in the practice of neurosurgery and neurology, it allows locating small lesions in the brainstem, and integrates sequences such as spectroscopy, providing valuable characteristics for an approximation to the specific diagnosis[2,7,11]; reports combining this with positron emission tomography (PET) may improve interpretation of lesions[11]. Even with all these elements, sensitivity (Sn) and specificity (Sp) are not high enough, and SBB is a fundamental procedure to establish definitive diagnosis and treatment of neoplastic and non-neoplastic pathologies of the brainstem, difficult to access through a conventional craniotomy due to their location, and associated with a high risk of permanent neurological deficits and increased mortality[4,5,11-14]. Furthermore, SBB diagnostic yield varies, and occasionally a second procedure is required to determine a histopathologic diagnosis or no definitive results could be obtained[8,14-16]. Detailed information from several groups for the SBB technique used for intra-axial lesions of posterior fossa structures is available[8,15,10], although there is no consensus about atypical clinical or radiological characteristics, such as focal appearance or contrast enhancement of lesions subject to this procedure[1,14,15,17,18]. Associated adverse events are hematomas[7], sensory deficits, ophthalmoparesis, nystagmus, facial paresis, and anacusis, which may be transient or persistent[15].

The aims of this study are to describe the technique performed in our national reference center, including advantages and disadvantages, evaluate its effectiveness and safety, and establish comparisons with other series.

Material and methods

A retrospective study was carried out for evaluation of concordance and diagnostic yield of SBB for posterior fossa lesions in the period from February 2014 to June 2018. Patients with disorders on pons, medulla oblongata, cerebellar peduncles, and deep cerebellar were included, which did not allow to take biopsy samples by open and direct technique, without age restriction. Individuals with midbrain and pineal gland lesions were excluded since in these cases our preferred procedure is transcerebral SBB using a precoronal burr-hole.

Before performing surgeries, all patients and their caregivers signed an informed consent with approval from the bioethics committee following the 1964 Helsinki Declaration, who had a brain contrast-enhanced T1-weighted MRI, with 1 mm slices (Fig. 1). Under local anesthesia with 2% lidocaine at the site of each pin, the Zamorano-Dujovny stereotactic frame (ZD; FL Fischer, Freiburg, Germany) was placed, aligned to the orbitomeatal line, with its fiduciary system inverted (Fig. 2). Subsequently, a contrast-enhanced head CT was performed, with 2 mm slices without interval, for exportation to Praezis Plus Version 3.1.0.112 software (TatraMed s.r.o., Bratislava, Slovakia) for fusion with MRI, and stereotactic planning of two targets on the lesion, defining trajectories to evade vascular, ventricular or cisternal structures, as well as areas with diffusion restriction because they were considered of poor diagnostic value. Successively, at the operating room, general anesthesia was administered to

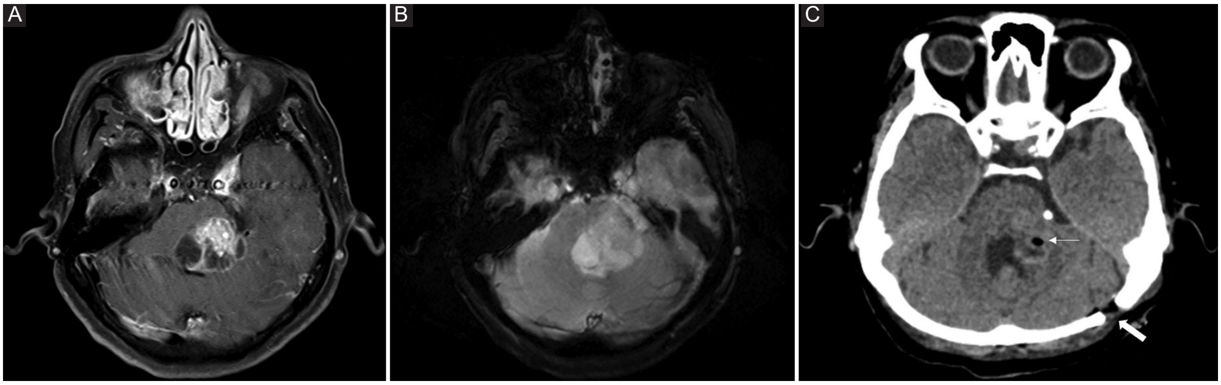

Figure 1. *Brain magnetic resonance imaging (MRI) in axial sections, contrast-enhanced T1-weighted sequence, in which a heterogeneous image is observed at pontine level with intense enhancement to gadolinium in its solid portion, associated with hypointense areas suggestive of necrosis* **(A)***, while in T2-weighted sequence shows similar heterogeneity and irregular borders* **(B)***, whose histopathological diagnosis was Grade IV astrocytoma. Post-surgical head simple computed tomography (CT) demonstrates the biopsy site (thin arrow) and the burr-hole (thick arrow)* **(C)**.

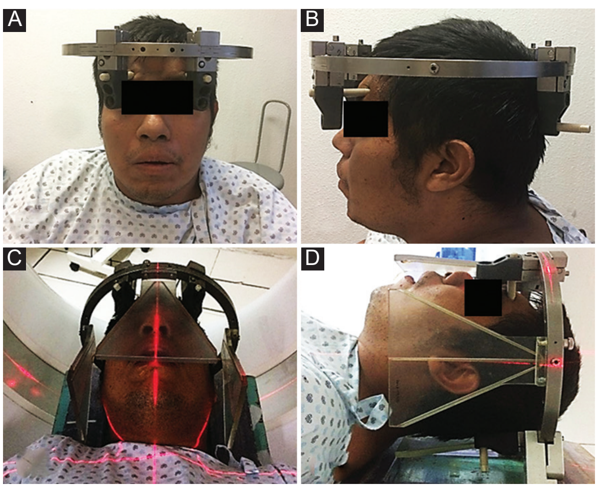

Figure 2. *Placement of the Zamorano-Dujovny (ZD) stereotactic frame with inverted mounting under local anesthesia* **(A and B)***. Using the laser from the gantry, head contrast-enhanced computed tomography (CT) allows confirming the adequate position of the frame and the alignment of the fiducials* **(C and D)**.

all patients for prone positioning and head coupled to the fixation device, with the surgical table in the semi-Fowler arrangement. When we treated pediatric patients, the ZD stereotactic frame was placed at the operating room under general anesthesia and endotracheal intubation, to later transfer them to CT, and then return to proceed with SBB. Negative right or left mounting of the stereotactic arch was achieved after verification of pre-established stereotactic coordinates. After the skin incision, an occipital burr-hole was made with a 14 mm auto-stop drill to allow dural opening by monopolar electrosurgery electrode applied to the tip of the Sedan-type biopsy needle (FL Fischer, Freiburg, Germany) to prevent cerebrospinal fluid (CSF) drainage that could cause brain shift (Fig. 3). Through a transcerebellar-transpeduncular approach, according to the planned trajectory, the biopsy needle was inserted for tissue aspiration from the 4 quadrants of the target through its 2.5 mm lateral window. Intraoperative changes in heart rate (HR) and blood pressure (BP) that might arise were always monitored.

The neuropathology team, present in the operating room, collected, and labeled the samples, used Hematoxylin-Eosin (H&E) staining for microscopic analysis, and examined the sufficiency of the material; if it was considered insufficient, the second target was biopsied for a similar new evaluation. Once the sample was declared satisfactory and the intraoperative result was reported, all samples were immersed in paraffin and transported to the neuropathology unit for specific immunohistochemical staining and testing. The incision was closed in two planes, the stereotactic system was dismantled, the patient was discharged to the general room for observation and, in the following 24 h, a simple head CT was obtained to rule out subclinical complications and corroborate the biopsied site by fusion of studies.

Statistical analysis was carried out using Microsoft Excel for Microsoft 365 MSO Version 16.0.13328.20262 software (Microsoft Corporation, Redmond, WA, USA) using descriptive measures such as percentages, means, confidence intervals (CI), standard deviations (SD), and Chi-square tests (χ^2); for clinical-radiological agreement, Cohen's kappa coefficient (κ) was used; and for diagnostic validity of clinical and radiological tests regarding the histopathological study (gold standard),

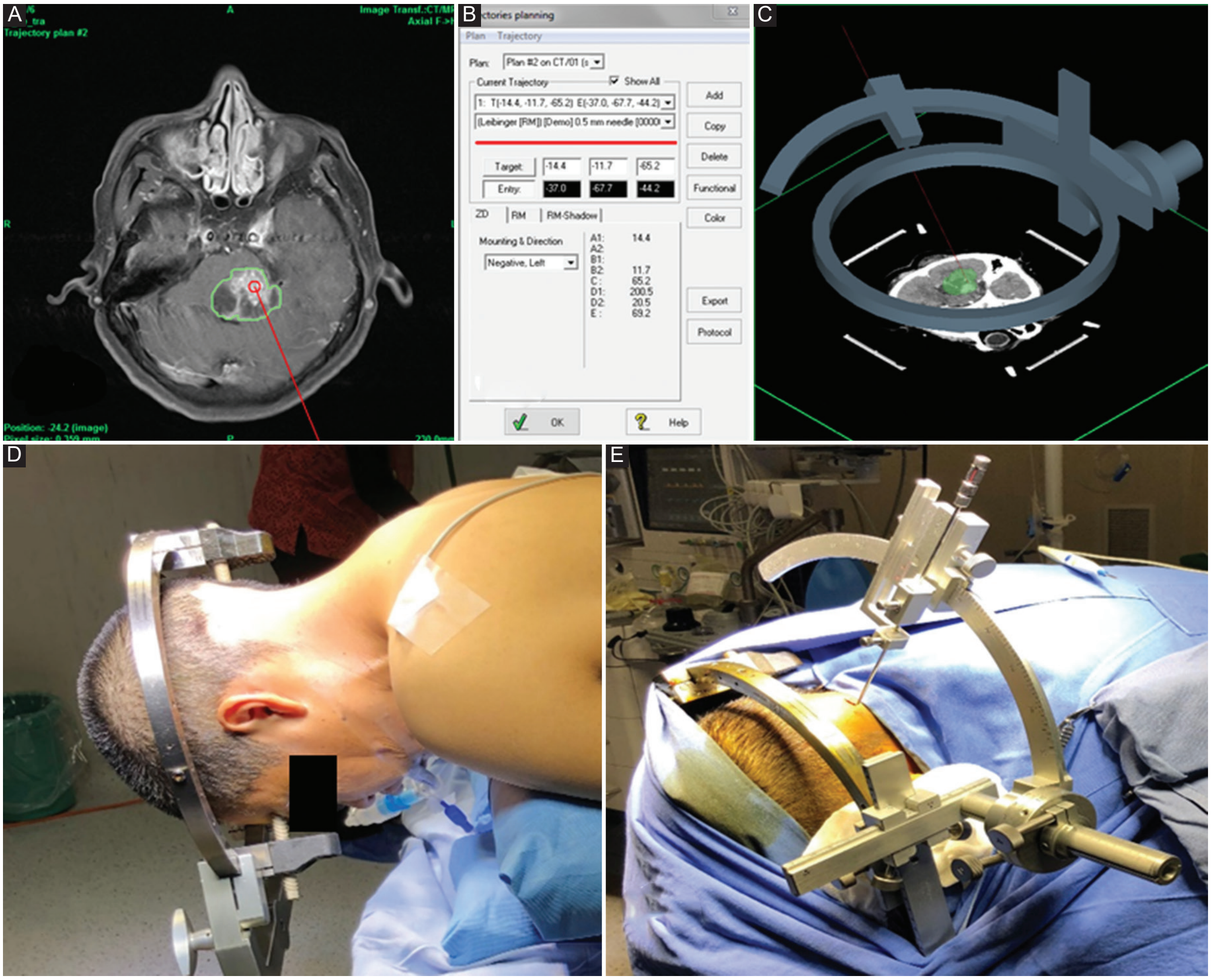

Figure 3. *Digital planning and contouring of the target, defining the trajectory of the biopsy needle* **(A)** *by linear and angular stereotactic coordinates* **(B)**. *Zamorano-Dujovny (ZD) stereotactic frame three-dimensional reconstruction and the trajectory in head contrast-enhanced computed tomography (CT)* **(C)**. *Patient in the prone position with the stereotactic frame coupled to the fixation device* **(D)**. *A post and pin have been removed to concede better access of the biopsy needle to the posterior fossa* **(E)**.

Sn, Sp, positive (PPV) and negative predictive values (NPV), as well as positive (LR+), and negative likelihood ratios (LR-) were obtained.

Results

During the established period, 140 consecutive SBB were executed. Ten patients with posterior fossa lesions met the inclusion criteria, of whom six were men and four were women. The mean age was 32.6 years (± 14.6; range, 10-55 years; 95% CI: 10.5), of whom three patients were at pediatric age. The locations were pontine in seven cases, and pontomedullary in three occasions.

Clinical diagnoses were five gliomas (astrocytoma and brainstem glioma), one demyelinating disease, and four neuroinfections (one neurotoxoplasmosis and three nonspecific). The diagnoses from radiological studies were ninie gliomas (astrocytoma, diffuse astrocytoma, and brainstem glioma) and one tuberculoma. Histopathological diagnoses were six gliomas, two neuroinfections, one cavernous malformation, and one neuroblastic tumor; among gliomas, four Grade II astrocytomas, and two Grade IV astrocytomas were found, while neuroinfections included one neurotoxoplasmosis and one non-specific infectious process (Table 1).

Frequency of clinical and histopathological diagnoses differed from other previously published series ($\chi^2 = 0.00$ and $\chi^2 = 0.07$, respectively). Clinical-radiological concordance was poor or insignificant ($\kappa = 0.20$). The validity of the clinical diagnosis regarding the histopathological analysis had intermediate values (Sn = 66.7%, Sp = 75%, PPV = 80%,

Table 1. Demographic characteristics of the patients and aspects related to their intra-axial posterior fossa lesions.

Patient	Gender	Age (years)	Anatomic location	Clinical diagnosis	Radiological diagnosis	Histopathological diagnosis
TSD	Male	10	Pontine	Astrocytoma	Astrocytoma	Grade II astrocytoma
RCA	Male	34	Pontomedullary	Demyelinating disease	Tuberculoma	Neurotoxoplasmosis
JGJ	Female	13	Pontine	Brainstem glioma	Brainstem glioma	Cavernous malformation
CGH	Male	34	Pontomedullary	Neuroinfection	Astrocytoma	Grade II astrocytoma
MOE	Male	42	Pontomedullary	Neurotoxoplasmosis	Astrocytoma	Neuroblastic tumor
GME	Female	43	Pontine	Astrocytoma	Glioma	Grade IV astrocytoma
AMH	Male	33	Pontine	Neuroinfection	Glioma	Nonspecific infectious process
EVM	Male	44	Pontine	Astrocytoma	Glioma	Grade II astrocytoma
HHP	Female	55	Pontine	Neuroinfection	Glioma	Grade IV astrocytoma
EAE	Female	18	Pontine	Astrocytoma	Diffuse astrocytoma	Grade II astrocytoma

NPV = 60%, LR += 2.7, LR- = 0.4), while radiological studies were more sensitive (Sn = 100%, Sp = 25%, PPV = 66.7%, NPV = 100%, LR += 1.3, LR −= 0.0). Diagnostic yield was 100%.

No patient died or had persistent and aggregate neurological deficits secondary to the neurosurgical procedure. However, one patient had intraoperative bradycardia (HR = 20 beats/min) at the time of biopsy sampling, with immediate recovery and no subsequent sequelae.

Discussion

At our center, we have decided to establish the SBB technique for pontine, medullary, cerebellar peduncles, and deep cerebellar lesions under general anesthesia, in the prone position and head coupled to fixation device, to avoid patient discomfort, allow better control of airway by anesthesiology, and avoid air embolism that could originate from semi-sitting position[8,10]. The transcerebellar-transpeduncular approach, despite being considered a long path to access pons or medulla oblongata, is safe[6], demonstrated by the absence of permanent morbidity related to the procedure in our experience. We had no associated mortality, and a correct diagnosis was obtained for specialized treatment in all cases[11,13,16], although the frequency of these may differ from other series carried out in similar populations[8]. The high diagnostic yield obtained is related to the presence of neuropathology staff during surgery, since under their criteria it was possible to determine the sufficiency of the tissue extracted for analysis; therefore, no procedure had to be repeated. Furthermore, we must indicate the high Sn and NPV of radiological studies, which allows identifying most of the tumors and other disorders of the brainstem with great certainty through a pattern of serial testing, which compensates for the poor concordance between clinical and radiological criteria.

Despite being a national reference center and having a long recruitment period for pediatric and adult patients, the number of SBB for posterior fossa is low, which had an impact on pathologies found[8], since in our sample, we were unable to observe some previously described tumors or we found a cavernous malformation, rarely subject to SBB. It is worth mentioning that most of the series reported also include lesions located on the midbrain, pineal region, and thalamus, which we have excluded because we prefer to use the transcerebral approach through a precoronal burrhole[3,5,7,9]. Multiple stereotactic frames, positions, and approaches have been used in SBB for posterior fossa, although none of them had statistical significance to determine their superiority[16].

Globally, there is a possibility that many patients are receiving inadequate treatments, incorrect diagnoses[2], or are simply denied reaching an accurate diagnosis due to the anatomical location of their lesions. We recommend the utilization of our SBB for posterior fossa method based on the retrospective design and results of this study, but each center must be effective with their local technique to achieve accurate diagnoses and minimize complications, for which we encourage to replicate our findings in their patient series. We suggest carrying out prospective, blind, and multicenter studies to have an adequate cohort of subjects subjected to the same procedure and to acquire more appropriate conclusions.

Conclusion

The SBB technique for intra-axial lesions of the posterior fossa implemented in our hospital with ZD stereotactic frame in inverted mounting, general anesthesia, and patient in prone position shows high diagnostic yield, as well as absolute safety.

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There is no affiliation with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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