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Review Article

Endoscopic biopsy of brain tumors: Does the technique matter?

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Abstract

Background: Endoscopic biopsy of brain tumors is an important part of the armamentarium of management of intra- and periventricular tumors that is generally considered an acceptable and, in some situations, a preferred method for tissue sampling. The diagnostic yield of the procedure has been variably reported. Technical aspects of the procedure should undoubtedly reflect on its success rate and accuracy. Such impact on diagnostic yield of endoscopic brain biopsy is infrequently discussed in the literature.

Methods: A search of the medical literature was conducted for publications on endoscopic brain biopsy. These reports were analyzed regarding the various technical aspects.

Results: In the 43 publications analyzed, lenscopes were exclusively used in 22 reports and a tissue diagnosis was possible in 362 out of 387 endoscopic biopsies with a diagnostic yield of 93.54%. Only fiberscopes were used in 8 reports and a tissue diagnosis was possible in 100 out of 132 endoscopic biopsies with a diagnostic yield of 75.76%. The diagnostic yield in the mixed and unspecified groups was 88.95 and 88.04%, respectively. Very few details on the histopathological methods and tumor molecular genetics could be found.

Conclusion: Endoscopic biopsy of brain tumors has a higher diagnostic yield when lenscopes are used. Neuronavigation seems to add to the diagnostic accuracy of the procedure. Studies detailing molecular genetic features of biopsied tumors are necessary in the future.

Key Words: Biopsy, brain, endoscopic, fiberscope, flexible, intraventricular, lenscopes, periventricular, rigid, tumor

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INTRODUCTION

Fukushima was the first to introduce endoscopic brain biopsy in 1973 using a flexible fiberoptic ventriculofiberscope.[12] Five years later, he reported a series of 21 endoscopic biopsies for intraventricular tumors, of which a correct histopathological diagnosis was achieved in 11 patients.[13] Currently, the procedure is an important part of the armamentarium of management of intra- and periventricular tumors[10,22,31,35,37,40,42,47,49,51] that is generally considered an acceptable and, in some situations, a preferred method for tissue sampling. Notwithstanding this, the diagnostic yield of endoscopic brain tumor biopsy has been variably reported.[2-5,7,9] As

technical aspects of the procedure undoubtedly reflect on its success rate and accuracy, a review of the literature was conducted in order to shed light on the technical aspects of endoscopic biopsy of brain tumors as they pertain to the diagnostic yield of the procedure.

MATERIALS AND METHODS

A search of the English literature was conducted and 43 reports were retrieved from 1990 to July 2013 [Table 1]. The following technical aspects were evaluated in each study: Type of endoscopes used, use of stereotactic guidance, and histopathological methods utilized for diagnosis.

Regarding the type of endoscopes used, the published studies were subdivided into four groups according to the use of lenscopes versus fiberscopes [Tables 1 and 2]. These four groups included: (1) Lenscopes only, (2) fiberscopes only, (3) mixed group, where both types were used without specification of the diagnostic yield for either type, and (4) unspecified group, where the type of endoscope was not reported by the authors. The diagnostic yield in each group was then calculated as the percentage of biopsies leading to a histological diagnosis to the total number of biopsies performed. When both types of endoscopes were used in one report, results were considered to belong to either the lenscopes or the fiberscope group only if the authors specified the diagnostic yield according to the type of the endoscope used. Unfortunately, a specific diagnostic yield based on the type of endoscopic device was rarely reported in these mixed studies.[15,17,29,34,36]

RESULTS

The results of the study are presented in Tables 1-3 and Figure 1.

In the 43 reports analyzed, lenscopes were exclusively used in 22 reports and a tissue diagnosis was possible in 362 out of 387 endoscopic biopsies with a diagnostic yield of 93.54%. Only fiberscopes were used in 8 reports and a tissue diagnosis was possible in 100 out of 132 endoscopic biopsies with a diagnostic yield of 75.76%. The diagnostic yield in the mixed and unspecified groups was 88.95 and 88.04%, respectively [Table 2 and Figure 1].

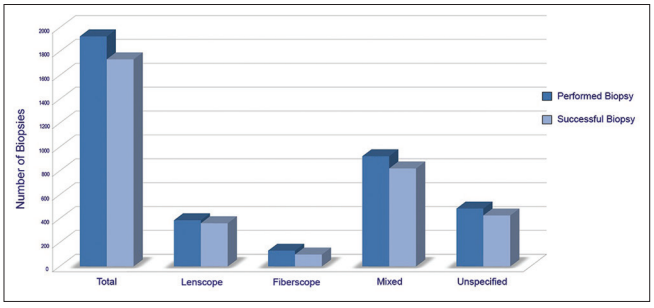

Figure 1: Bar graph of the performed and successful endoscopic biopsies in each group of published reports

DISCUSSION

Endoscopic biopsy of brain tumors is currently regarded an effective tool that is sometimes indispensable in establishing tissue diagnosis and tailoring further treatment [Figures 2-4].[1,15,23,26,28,45] Using the procedure for lesions within the ventricular system or in its vicinity offers direct visualization of the intraventricular anatomy and enables precise sampling of areas of the lesion that are highly likely to be pathologically representative, a feature that has been found to improve diagnostic accuracy. Additionally, biopsies from areas with an overlying blood vessel can be avoided, and areas with high vascularity can be coagulated to reduce bleeding during the procedure.[25]

The literature is currently replete with reports of endoscopic brain biopsies in which success rates range from as low as 61% up to 100%.[2-4,7,9,14,19,20,23,26,33,41,43,48,50] Analysis of the published reports retrieved a total of 1927 endoscopic brain biopsies in which the procedure led to a diagnostic information in 1735 cases, a collective diagnostic yield of 90.04% [Table 2]. In 2008, Fiorindi and Longatti calculated a collective success rate of 88% in 206 endoscopic brain biopsies compiled from eight published series.[11] In the largest two series published so far, Constantini *et al.*[5] reported diagnostic yield of 90.4% in 691 biopsies and Hayashi *et al.*[15] reported a diagnostic yield of 89.7% in 293 procedures.

From the technical point of view, one of the drawbacks inherent to neuroendoscopes of today's technology is

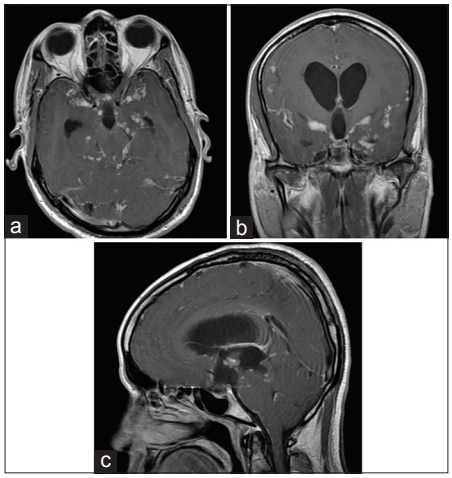

Figure 2: Preoperative magnetic resonance imaging (MRI) of the brain with contrast in axial (a), coronal (b), and sagittal (c) planes of a patient who presented with low-grade fever, headaches, confusion, and papilledema. A diffuse process involving the subarachnoid space and ependymal surface is evident in all images. Note the aqueductal obstruction (a) with triventricular enlargement. The enhancing third ventricular floor in the coronal image (b) was planned for endoscopic biopsy and endoscopic third ventriculostomy (ETV)

Table 1: Overview of the literature on the diagnostic yield of endoscopic biopsy detailing types of endoscopic equipment and the histopathological methods reported

	Endoscopic equipment	No. of biopsies*	Tumor location	Diagnostic yield (%)	Histopathological exam used
Tanei *et al.* (2012)	Lenscope navigation	6	Intraparenchymal	100	NA
Domínguez-Páez *et al.* (2011)	Lenscope	28	Intra- and/or periventricular	89	NA
Tsuda *et al.* (2011)	Lenscope Navigation	9	Intraparenchymal	100	NA
Morgenstern *et al.* (2011)	Lenscope	15	Pineal region	86.67	NA
Chibbaro *et al.* (2012)	Lenscope navigation	8	Pineal region	100	NA
Song *et al.* (2010) (Jkns)	Lenscope navigation	5	Intra- and/or periventricular	100	NA
Song *et al.* (2010) (Ch.N.S)	Lenscope	49	Intra- and/or periventricular	95.9	NA
Akai *et al.* (2010)	Lenscope navigation	3	Intraparenchymal	100	GFAP
Al-Tamimi *et al.* (2008)	Lenscope	8	Pineal region	75	NA
Kim *et al.* (2004)	Lenscope navigation	5	Pineal region	100	NA
Kim *et al.* (2013)	Lenscope navigation	23	Suprasellar (around 3rd ventricle	95.7	NA
Wong *et al.* (2011)	Lenscope	25	Pineal region	84.0	NA
Naftel *et al.* (2011)	Lenscope navigation	20	Intraventricular	90	NA
Tirakotai *et al.* (2007)	Lenscope Frame-based, frameless stereotaxy	29	Peri- and intraventricular	100	NA
Prat and Galeano (2009)	Lenscope navigation	22	Intraventricular	100	NA
Yurtseven *et al.* (2003)	Lenscope	18	Peri- and intraventricular	100	NA
Wellons *et al.* (2004)	Lenscope	7	Third ventricular	100	NA
Robinson and Cohen (1997)	Lenscope	3	Pineal region	100	NA
Najjar *et al.* (2010)	Lenscope	8	Intraventricular	100	NA
Roopesh Kumar *et al.* (2007)	Lenscope	24	Posterior 3rd ventricle	100	NA
Luther *et al.* (2006)	Lenscope	6	Pineal region and suprasellar	83	NA
Nagahisa *et al.* (2013)	Lenscope navigation	21	Intraventricular intraparenchymal	100	H/E, Olig2, CGH
Depreitere *et al.* (2007)**	Lenscope fiberscope	31 (+1 case not operated, excluded)	Intraventricular	Total 69 Lenscope 19/25=76 Flex 3/7=43	NA
Ahn and Goumnerova (2010)**	Lenscope fiberscope	33	Intra- and/or periventricular	Total 23/33=70 Rigid 17/21=81.0 Flexible 5/11=45.5	NA
Fiorindi and Longatti (2008)	Fiberscope	23	Intra- and/or periventricular	82.6	NA
Endo *et al.* (2009)	Fiberscope	1	Pineal region	100	CD20, CD79α, CD3
Gangemi *et al.* (2001)	Fiberscope	5	Pineal region	100	NA
Shono *et al.* (2007)	Fiberscope	12	Third ventricle	100	H/E Immunostaining
Oka *et al.* (1994)	Fiberscope	12	Intraventricular	100	NA
O'Brien *et al.* (2006)	Fiberscope	33	Intra- and/or periventricular	76	NA
Ferrer *et al.* (1997)	Fiberscope	4	Pineal region	75	H/E
Macarthur *et al.* (2002)	Fiberscope	28	Intra- and/or periventricular	61	NA
Mohanty *et al.* (2010)	Lenscope fiberscope	87	Intra- and/or periventricular	83	NA
Oppido *et al.* (2011)	Lenscope fiberscope	60	Intra- and/or periventricular	90	NA
Hayashi *et al.* (2011)	Lenscope fiberscope	691	Intra- and/or periventricular	89.7	NA
Souweidane *et al.* (2000)	Lenscope fiberscope	12	Third ventricle	92	NA
Yamini *et al.* (2004)	Lenscope fiberscope	6	Pineal region	66.67	NA
Pople *et al.* (2001)	Lenscope fiberscope	34	Pineal region	94	NA

Table 1: Contd..

	Endoscopic equipment	No. of biopsies*	Tumor location	Diagnostic yield (%)	Histopathological exam used
Kinfe *et al.* (2010)	Lenscope fiberscope	17	Periventricular	100	NA
Jinguji *et al.* (2013)	Lenscope fiberscope	11	Pituitary stalk	100	NA
Husain *et al.* (2010)***	Unspecified	178	Multiple	80.3 77.4 93.55	GFAP, NSE, synaptophysin, EMA, desmin, cytokeratins S-100, LCA, PCR
Constantini *et al.* (2013)	Unspecified	293	Intra- and/or periventricular	90.4	NA
Pettorini *et al.* (2013)	Unspecified	14	Pineal region	92.8	NA

CGH: Comparative genomic hybridization; EMA: Epithelial Membrane Antigen; GFAP: Glial Fibrillary Acidic Protein; LCA: Leukocytic Common Antigen; NSE: Neuron Specific Enolase; PCR: Polymerase Chain Reaction. *Number of actually biopsied tumors; not the total number of patients in the study; abandoned procedures excluded, **Ahn and Goumnerova (2010) and Depreitere *et al.* (2007) used fiberscope and lenscopes and segregated the diagnostic yield for each, ***In the retrospective group, 80.27%; in the prospective group with endoscopic biopsy alone, 77.42%; and with tumor irrigation fluid along with biopsy, 93.55%

Table 2: Segregation of diagnostic yield of biopsy by the type of endoscopic equipment used in 43 literature reports

	Total	Lenscope	Fiberscope	Mixed	Unspecified
Number of reports	43	23 (22+½+1/2)*	9 (8+1/2+1/2)*	8	3
Performed biopsies	1927	387§	132	923	485
Successful biopsies	1735	362	100	821	427
Diagnostic yield (%)	90.04	93.54	75.76	88.95	88.04

*Ahn and Goumnerova (2010) and Depreitere *et al.* (2007) used fiberscopes and lenscopes and segregated diagnostic yield for each, §One case from the series of Depreitere *et al.* (2007) excluded (biopsy not done because of poor visualization of tumor)

Table 3: Diagnostic yield of endoscopic biopsy using lenscope endoscope with and without navigation

	With navigation	Without navigation
Performed biopsies	151	191
Successful biopsies	148	177
Diagnostic yield (%)	98	92.67

their narrow working channels which may compromise the size of tissues retrieved and result in pathological interpretation challenges due to small fragmented or inadequate samples.[5,16] In one series of 31 patients from the Hospital for Sick Children, Toronto, Depreitere *et al.*[6] reported the small size of the biopsy samples as the primary reason for failure and problematic histological interpretation in 5 cases. The diagnostic yield of endoscopic biopsy was noted to increase when lenscopes were used instead of fiberscopes.[1,6] Lenscopes allow using larger-diameter biopsy forceps and, therefore, obtaining larger tumor samples. Moreover, they offer higher quality endoscopic images which enable obtaining samples from various regions of the exposed tumor surface.[4,24,25,39] Notably, however, no prospective assessment of the comparative diagnostic yields of lenscopes versus fiberscope endoscopic brain tumor biopsy has been carried out yet. Based on our analysis of the literature, a conclusion in favor of using a lenscope to obtain biopsy of brain tumors can clearly be drawn. Similar to our results, Mohanty *et al.* noted a correlation between the use of a fiberscope and a relatively higher nondiagnostic biopsy versus higher success rates being uniformly demonstrated with the use of lenscope endoscopes.[25]

It is of note that in the majority of reports, the authors have not specified the number of samples taken from the tumor. Some have pointed out that the number of samples was governed by intraoperative pathological interpretation with no more tissue than absolutely necessary taken in order to reduce intraventricular hemorrhage.[26] Others have reported two or more,[50] a minimum of three,[20] or just multiple specimens[28] during the biopsy procedure.

The reason for a preference to use a lenscope versus a fiberscope was also infrequently clarified in many articles reviewed. Superior image resolution[38,46] and larger working channels were stated by some authors using lenscopes,[4,26,46] while in some reports where fiberscopes were used, the justification was the possibility of safely reaching the posterior third ventricle.[3,44]

It was evident from literature analysis that using stereotactic guidance resulted in higher chances of obtaining a pathologically diagnostic material. The success rate for neuronavigation-guided endoscopic biopsy was 98% versus 92.67% when lenscopes were used alone. It is of note that although intraventricular anatomical structures would normally serve as the anatomical landmarks which give the neurosurgeon a spatial orientation, navigated endoscopy would be very important in cases with small or distorted ventricles, posterior third ventricular and periventricular tumors.[46]

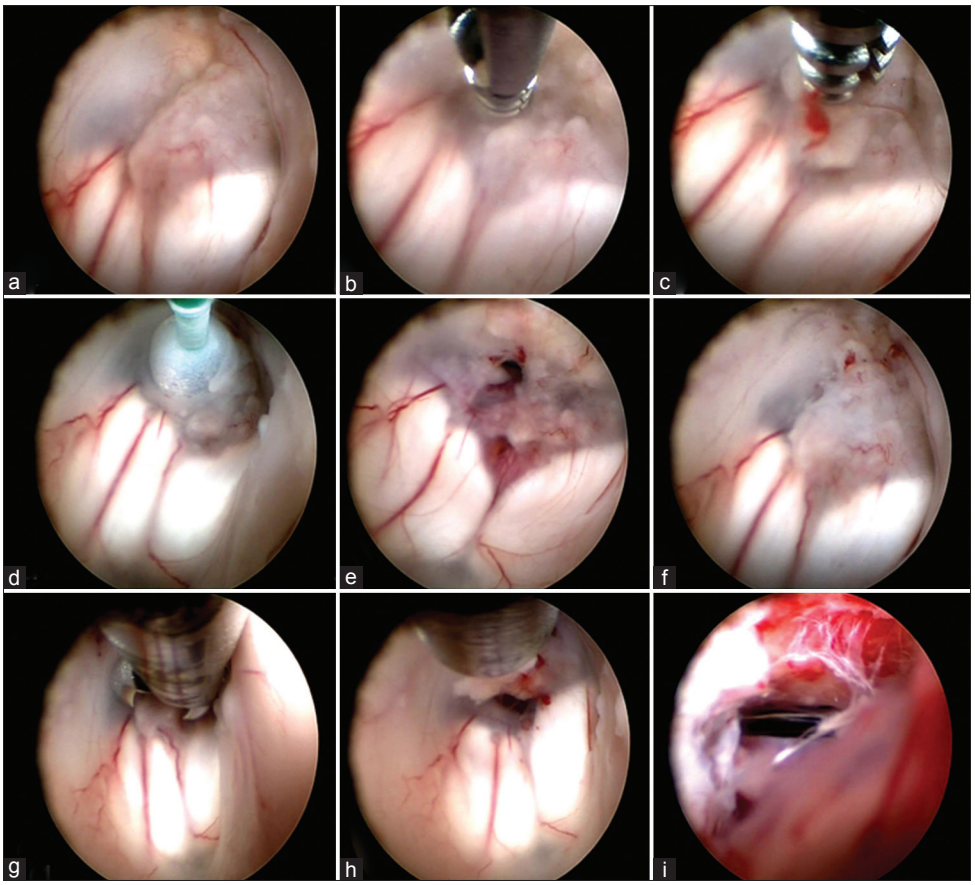

Figure 3: Endoscopic biopsy and endoscopic third ventriculostomy (ETV) of the patient presented in Figure 2. (a) Initial appearance of the pathological involvement of the third ventricular floor. (b–f) The area relatively clear of pathology is chosen for an initial ETV. Biopsy is taken from the involved tuber cinereum (g and h). View of the prepontine cistern after the ETV and biopsy are completed (i)

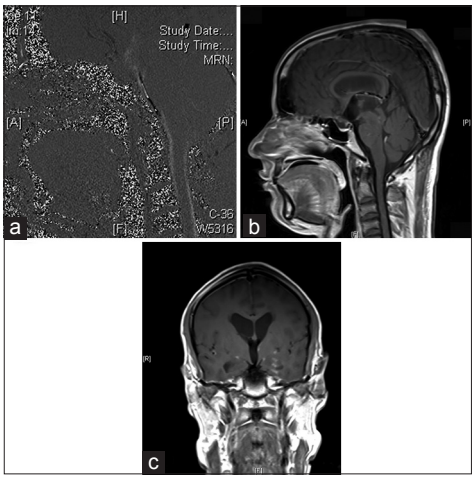

Figure 4: Postoperative MRI of the patient in Figures 2 and 3. Cine-phase contrast MRI (a) demonstrating flow of CSF from the third ventricle via the stoma. Sagittal (b) and coronal (c) MRI brain with contrast depicting the area of biopsy and stoma

Although the objective of this review was not to investigate all variables related to the diagnostic accuracy of endoscopic brain biopsy, it is important to point out that tumor location seems to play a role in the success rate of the biopsy. Ahn and Goumnerova reported success rates of 100%, 87.5%, 57%, and 25% for lateral ventricular, pineal region, thalamic, and tectal plate lesions, respectively.[1] High failure rates for superior vermian biopsies[25] and posterior fossa tumors[6] have also been reported. Such suboptimal success rates can probably be ascribed to difficulty of access to some areas.[25]

More importantly, the pathological approach to endoscopic brain tumor biopsy has not previously been detailed.[16] In none of the studies did the authors refer to uncertainties expressed by the pathologist regarding the final diagnosis, which may partly explain the variations in biopsy success rates.[6] Upon reviewing the literature, it was noticed that the histopathological diagnostic methods are seldom discussed and always overlooked, especially with respect to the molecular and immunohistochemical features of brain tumors. Except for one study by Husain *et al.*[16] published in 2010, only very few studies with scarce information[2,9,29] or single case reports[27] are available.

Molecular subtyping of brain tumors is becoming increasingly recognized as a valuable tool with diagnostic, prognostic, and therapeutic significance. For instance, the inactivating abnormalities of *hSNF5/INI1/*

SMARCB1/BAF47 tumor suppressor gene on chromosome 22q11.2 allowed segregating atypical teratoid rhabdoid tumors (ATRTs) from potential mimickers,[8,30] and the fusion between *KIAA1549* and *BRAF* oncogene specific to pilocytic astrocytomas is becoming an area for potential novel treatments.[18] To date, almost all assessments of successful endoscopic biopsy have been based upon conventional histopathological criteria.[5,15,17,21] To the best of our knowledge, only one report[16] on endoscopic biopsy of brain tumors has documented the immunohistochemical characteristics and in none of the studies have the molecular subtypes of tumors been reported. As some of these advanced pathology assays are dependent to a degree on the volume of tissue and the method of tissue processing, the technique of sampling and the equipment utilized may have an impact on the ability to obtain such increasingly important pathologic information. Prospective studies comparing the different contemporary endoscopic techniques as they relate to the molecular subtyping of brain tumors may help guide the surgeons' selection of biopsy technique.

CONCLUSION

Endoscopic biopsy of brain tumors has a higher diagnostic yield when lenscopes are used. Neuronavigation seems to add to the diagnostic accuracy of the procedure. Studies detailing molecular genetic features of biopsied tumors are necessary in the future.

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