Brain Tumor Pathol (2006) 23:71–75
DOI 10.1007/s10014-006-0204-y

ORIGINAL ARTICLE

Deepali Jain · Mehar Chand Sharma · Chitra Sarkar
Prabal Deb · Deepak Gupta · A.K. Mahapatra

Correlation of diagnostic yield of stereotactic brain biopsy with number of biopsy bits and site of the lesion

Received: March 7, 2006 / Accepted: June 27, 2006

Abstract Our objective was to examine the reliability of histological diagnosis achieved vis a vis the number of biopsy bits obtained along a single trajectory of the stereotactic needle. A retrospective analysis of stereotactic biopsies performed in a single tertiary care neurosciences center, during a period of 11 years, between 1995 to 2005 was done. The overall diagnostic accuracy achieved on histopathology was correlated with the number of bits obtained by stereotactic biopsy. A total of 86 cases were analyzed, which consisted of 58 males and 28 females. Age ranged from 6 to 75 years, with a mean age of 36.1 years. Twenty percent of the patients were in the pediatric age group and 15% were ≥60 years of age. Most common sites biopsied were thalamus/basal ganglia (55.8%), followed by eloquent areas and other sites. A definitive histological diagnosis was established in 70 cases (diagnostic yield, 81.3%), which encompassed 65 neoplastic and 5 nonneoplastic lesions. Astrocytic lesions, the most common, include 10 pilocytic astrocytomas (PA), 29 diffuse astrocytomas (DA), 11 anaplastic astrocytomas (AA), and 7 glioblastoma multiforme (GBM). In 16 cases no definite histological diagnosis could be offered. The number of biopsies ranged between 1 and 6 bits (mean, 2; median, 1). The majority (68.7%) of the biopsies were 1 or 2-bits. The diagnostic accuracy increased from 76.5% for single biopsies to 84% and 88.2% for 2 and 3 bits, respectively, and 100% for biopsies with 5 to 6 bits. Overall, a trend of higher diagnostic yield was seen in cases with more biopsies when compared with single bit biopsies. Thus, this small series confirms that stereotactic procedures involving multiple bits are associated with a high diagnostic yield.

D. Jain · M.C. Sharma (✉) · C. Sarkar · P. Deb
Department of Pathology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India
Tel. +91-11-26593371; Fax +91-11-26588663
e-mail: sharmamehar@yahoo.co.in

D. Gupta · A.K. Mahapatra
Department of Neurosurgery, All India Institute of Medical Sciences (AIIMS), New Delhi, India

Key words Stereotactic biopsy · Brain tumor · multiple bits · Site · Histopathology · Diagnostic yield

Introduction

Stereotactically directed needle biopsy was one of the first minimally invasive procedures adopted in the field of neurosurgery. Since the introduction of the stereotactic frame by Leksell et al., this procedure has undergone numerous technical improvements.[1,2] Owing to the rapid advancements in neuroimaging techniques, a large number of small, slowly-growing and minimally invasive lesions are being increasingly diagnosed. Further, intraoperative magnetic resonance imaging (MRI) has transformed a blind stereotactic procedure into a visually controlled one.[3] Currently, stereotactic biopsy offers a rapid histological or cytological diagnosis with minimal morbidity and mortality, thus establishing its utility in the workup of neurosurgical cases for accurate diagnosis and subsequent management of lesions of the central nervous system.[4]

A wide variety of diagnostic methodologies have been utilized in the evaluation of the biopsy yield, ranging from crush cytology and frozen section to conventional histology of paraffin-embedded sections. Overall, stereotactic biopsy produced a correct diagnosis in 80%–99% of cases.[5] However, various workers combined one or more evaluation techniques (histology and cytology) in an attempt to increase the overall diagnostic yield.[6] Similarly, higher diagnostic yield without a corresponding rise in the complication rate was observed on increasing the number of biopsies per lesion.[7]

However, to the best of our knowledge, there is no available study that systematically compared the diagnostic yield of stereotactic biopsy with the number of tissue bits. Hence, this study was carried out to compare the diagnostic accuracy of conventional histology in relation to the number of biopsy bits obtained from different zones of the lesion along one single trajectory of the probe.

Materials and methods

A total of 130 brain biopsies were performed over a span of 11 years. Of these, biopsy bit information could be retrieved in 86 cases from the Neuropathology database of the Department of Pathology, All India Institute of Medical Sciences, New Delhi, between January 1995 and December 2005. Relevant clinical details pertaining to age, sex, and site of tumor were recorded for all the cases.

Procedure

In 81 patients, a contrast-enhanced computed tomography (CT) scan was performed after fitting the Leksell stereotactic coordinate frame, and the X, Y, and Z coordinates for the lesions to be biopsied were calculated from the CT computer. In the remaining 5 patients, image-guided (CT/MRI scan) frameless stereotactic biopsies were performed. Serial biopsies were obtained along a single trajectory of the probe, from the hypodense center to the margin of the tumor as seen on an enhanced CT scan, using a 2-mm Leksell–Sedan punch biopsy forceps. The procedure was performed under local anesthesia in frame-based and under general anesthesia in frameless biopsies. The burrhole site and the trajectory were selected as per location of the lesion.

Hematoxylin and eosin (H&E)-stained slides were reviewed by three independent pathologists (D.J., M.C.S., C.S.), and the diagnoses were reconfirmed.

Histopathological evaluation

Resected tissue from all cases was fixed in 10% neutral buffered formalin, routinely processed, and paraffin embedded. Sections 5-μm thick were stained by H&E stain. Three histopathologists independently reviewed the H&E slides along with relevant immunohistochemical/histochemical stains and reconfirmed the original histopathological diagnoses. Tumors were diagnosed as per the criteria of the World Health Organization (WHO) classification of central nervous system (CNS) tumors (2000).

Immunohistochemistry

Representative blocks of formalin-fixed paraffin-embedded tissue were selected, 5-μm-thick sections cut, and immunohistochemical (IHC) staining performed by LSAB technique (LSAB Kit) using monoclonal antibodies to glial fibrillary acidic protein (GFAP; dilution 1:800), leucocyte common antigen (LCA; dilution 1:100), CD3 T-cell marker (dilution 1:200), CD20 B-cell marker (dilution 1:200, M/s Neomarker), and cytokeratin (CK; dilution 1:25). All antibodies, except CD20, were obtained from M/s Dakopatts (Glostrup, Denmark). High-temperature antigen retrieval using microwave was carried out by immersing the sections in 10 mM citrate buffer (pH 6.0) and heating inside a 750-watt microwave oven on full power for 30 min wherever required.

Special stains

Ziehl–Neelsen stain for acid-fast bacillus, periodic acid–Schiff (PAS), and silver methenamine stain for fungus were done in all cases with granulomatous inflammation.

Results

A total of 86 patients were analyzed at this tertiary care neurosciences center during a study period of 11 years between January 1995 and December 2005.

Clinical profile

Age and sex ratio

Age ranged from 6 to 75 years (mean, 36.1 years). Most of the patients were in their third or fourth decade of life (37%); 18 patients (20.1%) were in the pediatric age group (≤18 years) and 13 patients (15.11%) were in the ≥60 years age group. There was male preponderance (58 cases) with a male-to-female ratio of 2.07:1. Interestingly, in the ≥50 years age group, all patients were male except 2 females (M:F, 21:2).

Location

Thalamus/basal ganglia was the most common location (55.8%), followed by frontal and parietal lobes (18.6%), corpus callosum (0.04%), and brainstem (0.04%) (Table 1). Two patients had multiple lesions; one 61-year-old man had bilateral thalamic involvement.

Histopathology

A definitive diagnosis could be offered in 81.3% of cases, which consisted of 65 neoplastic and 5 nonneoplastic lesions (Table 2). Astrocytic neoplasms, the most common, included 10 pilocytic astrocytomas (PA), 29 diffuse astrocytomas (DA), 11 anaplastic astrocytomas (AA), and 7

Table 1. Distribution of lesions at various locations with diagnostic accuracy

Site	Number of cases	Diagnostic accuracy (%)
Thalamus/basal ganglia	48	85.4
Cerebral hemisphere	16	75
Corpus callosum	4	75
Brainstem	4	75
Other	14	78.7
Totals	86	81.3

Table 2. Cases with definitive histological diagnosis ($n = 70$)

Diagnosis	No. of cases
Astrocytoma (WHO grade I)	29
Diffuse astrocytoma (WHO grade II)	10
Anaplastic astrocytoma (WHO grade III)	11
Glioblastoma multiforme (WHO grade IV)	7
Mixed glioma	2
Primary central nervous system lymphoma (NHL B cell)	5
Metastasis from adenocarcinoma	1
Tuberculosis	2
Mucormycosis	1
Abscess	1
Nonspecific inflammatory pathology	1

WHO, World Health Organization

Table 3. Distribution of astrocytomas ($n = 57$)

Location	No. of cases
Thalamic/basal ganglia	35
Hemispheric	11
Corpus callosum	4
Brainstem	4
Multiple lesions	2
Posterior fossa	1

Table 4. Cases without any definitive diagnosis ($n = 16$)

Diagnoses	No. of cases
Normal brain	6
Reactive gliosis	5
Inadequate for opinion	3
Scant necrotic tissue	1
Fibrocollagenous tissue	1

glioblastoma multiforme (GBM). Distribution of astrocytomas is summarized in Table 3.

Other neoplastic lesions included non-Hodgkin lymphoma, diffuse B-cell type (five cases), mixed glioma (two cases), and metastasis from an adenocarcinoma (one case); for nonneoplastic pathologies consisting of tuberculosis (two cases) and one case each of mucormycosis and brain abscess, one biopsy each showed nonspecific inflammation (Table 2).

Cases with noncontributory histology (Table 4) included normal brain (six cases) and reactive gliosis (five cases). In three cases, biopsy was inadequate for opinion as size was very small (less than 0.1 cm). In one case, the tissue was necrotic, and another biopsy consisted of fibrocollagenous tissue only.

Correlation of number of bits with diagnostic yield

The number of biopsies ranged between 1 and 6 (mean, 2.1; median, 1) for every patient. In 59 patients (68.7%), biopsies were single or 2 bits. However, in the remaining 27 cases (31.39%), the number of biopsies ranged between 3 and 6 (Table 5).

Table 5. Correlation of number of biopsy bits and diagnostic accuracy

No. of biopsy bits	No. of cases	Definitive diagnosis	Diagnostic accuracy (%)
One	34	26	76.5
Two	25	21	84
Three	17	15	88.2
Four	6	4	66.7
Five	3	3	100
Six	1	1	100
Totals	86	70	81.3

The overall diagnostic accuracy was 81.3%. The diagnostic accuracy increased from 76.5% for single biopsies to 84% and 88.2% for biopsies with 2 bits and 3 bits, respectively, and to 100% for 5 and 6 bits. Although statistically not significant ($P = 0.99$), in general, a trend of higher diagnostic yield was seen in cases with more biopsies when compared with single-bit biopsies. However, more cases need to be included in the 4- and >4-bit biopsies to obtain a definitive correlation.

Correlation of location of tumor with diagnostic yield

Diagnostic accuracy was highest in thalamus/basal ganglia lesions (85.4%), which was comparable to the overall 81.3% accuracy. Similarly, a 75% diagnostic yield of hemispheric, brainstem, and corpus callosum lesions was also comparable (see Table 1).

Discussion

Stereotactic biopsy of brain masses offers a safe and accurate technique of obtaining adequate tissue for histological evaluation. Currently it provides an effective method of managing cases with a lesion in the eloquent areas of the brain; or when craniotomy carries a significant risk of morbidity and mortality owing to an underlying medical condition; in patients for whom cytoreductive surgery is not contemplated; and in cases in which a pathological diagnosis is desired before definitive open surgery.[4,8]

However, to derive the maximum benefit from the tissue obtained by stereotactic biopsy, diagnosis needs to be rapid and accurate. Processing of frozen sections and cytology smears is rapid and generally preferred over permanent sections, which are more time consuming. These intraoperative diagnostic techniques ultimately help not only in confirming if the target lesion has been reached but also help in making a sufficiently reliable diagnosis.[9,10] Cytological evaluations are generally in the form of smears and squash preparations. In the presence of typical morphological features, cytological analysis of tumours can be rapid and reliable, although it often lacks identifying the grade of neoplasms. The overall diagnostic yield of cytology varies between 73% and 94%.[11–13] Tilgner et al. evaluated 5000 consecutive biopsies and noted an accuracy of 90.3%, of which 81.3% had complete correlation and 9% had partial

correlation with subsequent biopsies.[14] Similarly, Firlik et al. studied 595 cases and observed correlation of cytology with final diagnosis in 90% cases (52% complete and 38% partial correlation).[15] In contrast, Collaco et al. reported correlation between cytology and histology in 73% of solid lesions.[16]

Frozen section evaluation is generally preferred over cytology for intraoperative evaluation of larger biopsy samples. Brainard et al.[17] evaluated the diagnostic yield of frozen sections in 188 stereotactic brain biopsies; 11 (6%) biopsies were nondiagnostic, and in 119 (67%) of the remaining 177 cases, a definitive diagnosis was offered on initial section, whereas in 15 and 25 cases a correct diagnosis was made on subsequent second and fourth frozen sections, respectively. They emphasized that in 14 (11%) of 131 neoplastic lesions a sampling error relative to the lesion contributed to an inaccurate diagnosis. Further, Grunet et al.[18] reported a diagnostic yield of 98% while correlating the utility of intraoperative frozen sections with conventional paraffin embedding and staining techniques.

In comparison to intraoperative evaluation techniques, histological preparation of small biopsies helps in preservation of morphology and permits better assessment. However, proper fixation, optimal staining, and sectioning of small biopsies is often difficult and time consuming and is often fraught with reduced accuracy when compared with larger biopsy specimen. Evaluating the diagnostic validity of histological techniques with stereotactic biopsy yielded an accuracy rate ranging between 80% and 99%,[5] which is comparable to the present study of 81.3%, and in concordance with a previous study from this center that reported a yield of 81.1%.[19] Bernays et al.[3] offered a specific histological diagnosis in 111 of 114 tissues (97.4%), which is in contrast with a 79% accuracy reported by McGirt et al.,[20] evaluating 23 patients who underwent an open surgery within 60 days of stereotactic biopsy. However, in a recent study by Aker et al.,[21] the overall diagnostic yield of 94% was reduced to 83% when correlated with the diagnoses of the resected specimens.

The term diagnostic yield used by various workers in depicting their results has often been the source of conflicting data in the available literature. This term has been interchangeably used to denote the percentage of successful tissue sampling, rate of recovery of pathological tissue, or the percentage of cases in which a specific and conclusive histopathological diagnosis was obtained. However, in the present study, diagnostic yield refers to diagnostic accuracy in cases where specific diagnosis has been obtained.

The various crucial factors that influence the diagnostic yield include the technical problems related to the surgical procedure itself; subjective judgment of the operating surgeon; problems associated with tissue handling and processing; methodology adopted for evaluation; and finally inherent characteristics of brain tumor specimens.[22] The study by Feiden et al.[23] bears testimony to the importance of representative tissue sampling and proper histological processing in enhancing diagnostic accuracy of stereotactic biopsies. However, to enhance diagnostic accuracy of the stereotactic biopsy, various workers combined one or more methods of evaluation. In a survey by Firlik et al., 23% of 92 respondents utilized frozen section examination alone, compared to 13% selecting one or more cytological techniques; while the remaining 64% preferred combination of both frozen section examination and cytology.[15]

In contrast, a study by Fritsch et al.[7] supported the notion that high diagnostic yield can be attributed to the increased number of biopsies per lesion, which was also supported by Brainard et al.[17] The latter further recommended that stereotactic biopsies taken at the presumed target are not always diagnostic and multiple biopsies slightly off center of the lesion may be required to obtain diagnostic material. To improve the diagnostic yield, Cappabianca et al.[6] assessed multiple biopsies per patient in addition to utilizing a combination of diagnostic methods (histology and cytology). They noted that in comparison to the definitive diagnosis made on the whole tumor, a correct positive diagnosis on the biopsy sample alone by histology and cytology was made in 96% and 93% of cases, respectively; it increased to 96% when both methods were combined. Correct identification of tumor type and grade was achieved by histology or cytology alone in 82% and 80% of the cases, respectively, and increased to 85% when both methods were combined.

However, to the best of our knowledge, none of the studies with multiple biopsies compared diagnostic efficacy with respect to the number of tissue bits obtained along the single trajectory of the probe. In this regard, the present study shows a trend of enhancement in the diagnostic yield that was directly proportional to the number of tissue bits obtained per patient. Thus, an accuracy of 76.5% for single biopsy improved to 84% and 88.2% with 2 bits and 3 bits, respectively. Although diagnostic yield is biopsies greater in 5- or 6-bit (100%) in comparison to single-bit biopsy, the number of cases in 4 to 6 bits were few and thus no definitive correlation could be obtained. Thus, it is recommended to evaluate more number of stereotactic biopsies with multiple cores in order to achieve significant correlation.

Currently, owing to the advancements in neuroimaging techniques, stereotactic biopsy has a low risk even in deep brain regions such as basal ganglia, mesencephalon, and pons. A recent study by Shahzadi et al.[24] highlighted the role of stereotactic biopsy in evaluation of thalamic lesions, with an acceptable rate of complication and a high diagnostic yield. In the current study, 55.8% of cases had a lesion involving thalamus/basal ganglia, which was significantly higher than the 26.5% and 19.7% noted in the Bernays series[3] and Matsumoto series,[25] respectively. While correlating the diagnostic yield with location of lesions, it was observed that thalamic lesions had the highest diagnostic accuracy (85.4%); this was another feature that was not evaluated by any other series, but has significant importance in terms of diagnostic evaluation of deep-seated, small, slowly growing lesions diagnosed on neuroradiology that are not always amenable to open surgery.

Despite the shortfalls and problems associated with stereotactic biopsies, this study has established its utility in management of neurosurgical cases with minimal mortality and morbidity. However, the pursuit for selecting an optimal method for evaluating the biopsies and devising tech-

niques for enhancing the diagnostic yield remains an everlasting challenge to neuropathologists. As is evident from the present study, it is currently possible to obtain multiple biopsies per patient, thus improving overall diagnostic accuracy. However, more cases need to be evaluated with multiple biopsy bits to achieve a better diagnostic correlation.

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