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Computed Tomography Guided Stereotactic Biopsy of Cerebral Lesion: A Safe Diagnostic Procedure

CT guided Stereotactic biopsy (CTSB) is a minimally invasive procedure that uses three dimensional (3D) coordinated system for precisely locating a target within a space to obtain tissue sample for diagnostic and therapeutic purposes.

The main aim of this study is to analyze the role of CTSB in deep seated lesions, multi-focal lesions, lesions in eloquent areas as well as in frail patients at high risk for major cranial surgeries and small intra-cranial lesions which are otherwise hard to access.

The study was conducted in National Institute of Neurological and Allied Sciences, Nepal with retrospective data using non probability purposive sampling.

The study was done from January 2007 to December 2012. Analysis of frame based stereotactic biopsy over that period was done.

Descriptive statistics for patient demographics and distribution of lesions was used. Paired t-test was used to compare pre-operative and post-operative GCS to define the safety. Difference in post procedure diagnosis in terms of histology was analysed.

Of the 40 cases evaluated, 55% were males and 45% females. Lesions had lobar distribution in 62.5% and were deep seated in 37.5% cases. Three (7.5%) patients had multifocal lesions. Net diagnostic yield was 97.5% and diagnosis could not be established in one case. In five (12.5%) cases the preoperative diagnosis was revised by the procedure and in 13 (32.5%) a new diagnosis was established. Complications were observed in 10%, 7.5% cases having seizure and 2.5% having postoperative brain swelling. Procedure related mortality was seen in one (2.5%) moribund patient. There was no statistical difference in GCS at 48 hours post procedure as compared to preoperative state implying the safety of the procedure.

CTSB of cerebral lesion appears to be safe procedure of diagnostic advantage. It can significantly change the final diagnosis making it imperative when indicated.

Key Words: CT guided Stereotactic Biopsy, deep seated brain lesion, frame based biopsy

Accurate diagnosis of a brain lesion like in any other organ systems requires histological confirmation. With the advent of newer investigative modalities like CT scan, MRI scan and metabolic imaging, we can estimate with certain degree of confidence, the nature of a particular lesion.[19] However, in order to prognosticate a particular disease entity and furthermore, to plan the treatment guideline with certainty, histopathological confirmation is imperative.

It is not always easy to obtain sample from lesions in the brain, particularly if the lesion is deep seated, near the eloquent areas, multiple and in a frail patient who is

surgically a poor candidate. Stereotactic biopsy probably addresses the way out in such circumstances. In this era of minimally invasive surgery, it serves a promising role in acquiring tissue sample particularly in such difficult scenario.[4,5,7,8,11,15,19]

With CT scan, localization of intracranial target can be made with precision. Localization is based upon the calculation of coordinates with respect to the rods in the stereotactic system. This in turn can be translated from space localization to the target set point in a patient. The principle has evolved over years ever since Horsely and Clarke[14] performed the first stereotactic brain biopsy on the cerebellum of a rat and Spiegel-Wycis, later in 1947, displayed their first human stereotactic technique using three dimensional coordinate system using intracranial land mark defined by pneumoencephalography[22]. Maroon et al. first reported CT guided stereotactic system in 1977.[20]

The usefulness of stereotactic biopsy in terms of its safety and accuracy as demonstrated in our institution is shared here on the basis of our experience in 40 cases.

Materials and Methods

Study design

Analytical cross sectional, retrospective study.

Sampling technique

Non-probability purposive sampling.

Study Place

National Institute of Neurological and Allied Sciences, Kathmandu, Nepal.

Sample size

Forty two patients underwent CT guided Stereotactic biopsy for intracranial brain lesions. Two cases had to be excluded from the study due to missing clinical records. Hence, only 40 cases were analyzed.

Study Duration

January 2007 to December 2012

Inclusion criteria

All patients who underwent CT guided Stereotactic biopsy in this institute within the study duration with a lesion visible on contrast CT, lesion that was deep seated, multiple and in frail patients who are surgically poor candidates for for major cranial surgery.

Stereotactic brain biopsy procedures

Frame based stereotactic biopsy was performed either using Leksell frame. or Brown-Roberts-Wells (BRW) frame (Radionics, Burlington, Massachusetts).

Leksell frame based biopsy

Biopsy was performed under general anesthesia taking into consideration of patient's comfort. Preoperative thorough work up including coagulation profile was done in every case. Head was fully shaved so as to allow maximum sterile operative field and to provide surgeon a complete and unobstructed view of the cranium thus, facilitating optimal pin and platform placement.

Approach to entry point was individualized depending on the location of the lesion. Skin infiltration with 2% lignocane was done followed by incision and a small burr hole using Hudson perforator and burr. A small cruciate incision was made on the duramater. Burr hole site was covered temporarily with a betadine soaked gauze. Leksell stereotactic frame was then fixed with two aural pins and three aluminum pins screwed into the outer table of the skull.

Patient was then taken to CT scanner. Head and the stereotactic frame were supported on special head rest. Computer based calculation of target coordinates was performed. Amount of iodine contrast injected ranged from 1 to 2 ml/kg body weight. CT scan was then performed in 10 to 15 seconds. A lateral scout view was made and corresponding to that, the field of view was defined. CT-image acquisition was performed in slices of 2 mm thickness allowing a localization of the intracranial lesion with precision.

Coordinates were selected for at least two targets within the lesion. These coordinates localized the mass in a three dimensional space in relationship to the frame. While selecting a target, non-enhancing areas were avoided in heterogeneously enhancing lesion and a central target was selected in homogenously enhancing lesion.

Stereotactic arc was then placed on the frame and a 14-gauge cannula was advanced to the target site along the trajectory of the burr hole in rigid arc fixation. Stylet was removed; a blunt biopsy forceps was inserted through a trocar into the lesion, advanced up to the stopping marker, opened and closed to obtain tissues at various orientations. The probe can be inserted to hit the target from an infinite number of trajectories based on the same arc. Specimens were procured from four quadrants at each target and sent to a pathologist for cytological and histopathological examination.

Before dismantling, a small piece of contrast soaked surgicel was inserted into the target. Stereotactic frame was taken off the patient. Skin was closed with three stitches and each pin site with one stitch and covered with a handiplast. Post-procedure, CT scan was done to rule

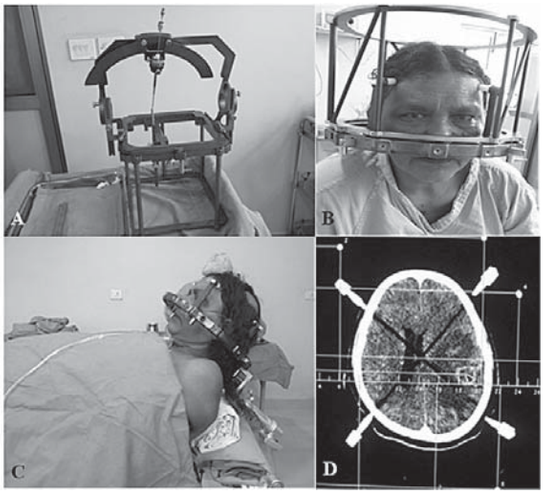

Figure 1: Stereotactic procedure. A) leksell Frame, B) fixation of Leksell frame, C) patient is ready for the procedure, D) CT scan after fixation of the frame and before the procedure

out intracranial hemorrhage and to confirm the biopsy site based on the identification of contrast soaked surgicel right at the previously chosen target.

BRW Frame based biopsy

Prior to computerized stereotactic biopsy all patients were clinically evaluated and available records such as CT scan, chest x-ray and all baseline investigations including coagulation profile were reviewed. Head of the patient was either shaved or thoroughly washed with antiseptic soap and base ring of BRW system was positioned and secured in to the outer table of the skull with four screws after infiltrating the required points with 2% lignocaine. Patient was shifted to CT scanner. Localizing ring was attached to base ring before CT scanning **(Figure 1, A-D)**. Region of interest was indicated to the CT technician and target was selected on CT console and pixel coordinates of nine localizer rods were derived and recorded. After removing the localizing unit patient was shifted to the operation room. In the mean time, x and y coordinates acquired from CT scanner was fed into the Radionic Sterocalc and three scales (Antero-posterior, Lateral and Vertical) were calculated in order to translate it to the phantom base. Setting of arc and phantom rehearsal was done. Entry point was infiltrated with 2% lignocane, incised and small burr hole made with Hudson perforator. A minor cruciate incision made over the dura and a 14-gauge cannula was advanced to the target site along the trajectory of the drill hole in rigid arc fixation. Stylet was removed, biopsy forceps advanced up to the stopping marker, opened and closed to obtain tissues at various orientations. Wound closed with one or two stitches and base ring removed and patients sent back to intensive care unit for monitoring. All the patients were followed for any complications.

Post operative CT scan was repeated only if patient deteriorated to rule out possible complications like hematoma or brain swelling.

Histological Evaluation

The tissue was sent to the laboratory in 10 % formalin. The specimen was processed for paraffin embedding and slides were prepared. Initially, they were stained with Hematoxylin & Eosin stain. Special stains were used only if deemed necessary.

Statistical Analysis

Postoperative complication if any was analyzed with univariate model. Categorical variables (sex, location, multiplicity and pathological nature) were analyzed using descriptive statistics. The continuous variables like pre-operative and post-operative GCS were analyzed using Paired T-test at 95 percent confidence interval.

Results

Patient's demographics

Of 40 patients who underwent stereotactic biopsy 22 (55%) males and 18 (45%) females. Most patients were from the age range of 41-60 years (72.5%) and the youngest and oldest patient were respectively 12 and 65 years.

Distribution of the lesion

Tumor had lobar distribution in 25 (62.5%) cases and deep seated in 15 (37.5%) cases. Three (7.5%) cases had multifocal lesions **(Table 1)**.

LOCATIONS	NUMBER OF PATIENTS
	Total (%)
Lobar	**25(62.5%)**
frontal	8
parietal	8
temporal	7
occipital	2
Deep-seated	**15(37.5%)**
basal ganglia	2
thalamus	6
ventricle	2
caudate nucleus	1
corpus callosum	1
multifocal	3

Table 1: Distribution of lesion

S. No.	Pre operative Diagnosis	Post operative Diagnosis	No of cases
NO CHANGE IN DIAGNOSIS			
1	Glioma	Glioma Grade IV	11
		Glioma Grade III	3
		Glioma Grade II	3
2	Metastasis	Metastasis	2
3	Ependymoma	Ependymoma	1
4	Granuloma	Granuloma	1
		Total	**21**
DIAGNOSIS REVISED			
1	Lymphoma	Glioma Grade IV	2
		Glioma Grade II	1
2	TB granuloma	Non Hogdkin's Lymphoma	1
3	Subependymal giant cell astrocytoma	Choroid Plexus papilloma	1
		Total	**5**
NEW DIAGNOSIS ESTABLISHED			
1	Inconclusive	High grade glioma Grade IV	7
		Metastasis	2
		High grade glioma Grade III	1
		Diffuse Astrocytoma WHO grade II	1
		TB granuloma	1
		Non Hodgkin's Lymphoma	1
		Total	**13**
NO CONFIRMATORY DIAGNOSIS			
1	Inconclusive	Inconclusive	**1**

Table 2: Comparision of Clinico-radiological and stereotactic diagnosis

Stereotactic Diagnosis

Positive results in histopathological examination were obtained in 39 (97.5%) cases **(Table 2)**. The patient in whom diagnosis could not be established was a 50 year old male with a small, hypodense lesion in the left postero-parietal region. The biopsy was reported as hyper plastic vascular and mild gliotic changes in neuroparenchyma and was non diagnostic even after a repeat biopsy.

In 21(52.5%) patients, the preoperative clinico-radiological diagnosis was in concordance with the stereotactic biopsy final diagnosis. In five (12.5%) cases the preoperative diagnosis was revised by the procedure. In 13 (32.5%) cases a new diagnosis was established.

Morbidity and Mortality

There was one procedure-related mortality in our series. She was a 46 year old lady who was in a state of poor general health pre-procedure with left frontal and parietal mass lesions. Following the procedure the patient had track hematoma, brain swelling and an episode of seizure. She was immediately intubated and ventilated, but she expired 48 hours after the procedure. Complications were seen in four other patients (10 %). Three (7.5%) patients had seizure. One patient having seizure also had intra-ventricular haemorrhage. One patient had brain swelling. Apart from the patient that died, all complications were managed conservatively and had subsequent improvement **(Table 3)**.

S. No.	Comparison of Pre-op and Post-op GCS	No of cases	Paired t-test
1	Preoperative and post operative GCS same	34	p-value <0.05
2	Preoperative GCS better than Postoperative GCS	2	
3	Postoperative GCS better than preoperative GCS	4	

Table 3: Comparison of Preoperative and postoperative GCS and the statistical treatment

Difference in Glasgow Coma Scale of patients postoperatively as compared to preoperative status compared using Paired t test was statistically not significant ($P<0.05$).

Discussion

Histopathological confirmation of intracranial lesion forms a sound base to draw further management plans and to prognosticate any patient with intracranial lesion. Though we can pick up intracranial lesions quite early on with the advancement of modern diagnostic tools like CT, MRI and metabolic scans, we cannot fully be certain of the given diagnosis in about a third of the cases.[19]

The site of the lesion, multiplicity, patient factors as poor general health and safety does not always allow us to access those lesions by open means. Many a times, unwanted deleterious effects might thus be encountered in such circumstances. Stereotactic biopsy provides tissue diagnosis with minimal disruption of brain parenchyma and high diagnostic accuracy.[6,9]

An analysis of over 3,800 cases from various series revealed an overall morbidity rate of 3.2% and a mortality rate of 0.6%.[19] No case of any overall morbidity was registered in the series of Bosch,[3] Hall et al.[10] and Heilbrun et al.[13] Davis[6] reported only two (0.4%) complications and one (0.2 %) death. Apuzzo et al.[1] reported a complication rate of 1% and a mortality rate of 0.2%. Debaene[7] reported 5% biopsy associated complications, while Brommeland[2] had complications in 5.1% cases.

Out of 36 patients reported by Winkler[24], bleeding occurred in 3(8.1%) patients, with one being a CT detectable intracerebral hematoma. The most common complication is hemorrhage at the biopsy site.[19] In many cases, damage to blood vessels in the trajectory of the biopsy is an unavoidable consequence. As reported by Krieger[19] out of 3500 stereotactic biopsies, they had one procedure related death, seven significant hemorrhages including subdural and epidural hematomas, five seizures and two infections.

In our own series of 40 patients, complications were seen in 4 (10 %) patients. 3 (7.5%) of the patients had seizure which were controlled with antiepileptic drugs, conservatively. Of patients having post procedure seizure, one had intra-ventricular hemorrhage. One (2.5%) patient had brain swelling and one (2.5%) patient died. The morbidity and mortality were hence comparable to the larger series.

We do not routinely use antibiotics following the procedure, though some authors prefer routine prophylactic antibiotic usage.[19] None of the patients in our series had infective complications. This strengthens the view that antibiotic prophylaxis is not necessary of sterotactic brain biopsy.

We do not use seizure prophylaxis routinely. We observed seizure in three patients in our series. One of them had Neurocysticercosis and two had lesions in frontal and parietal regions respectively which turned out to be high grade glioma on biopsy. As the episodes of seizure were controlled with antiepileptic medications, we still do not suggest routine use of antiepileptic drugs following the procedure.

Intra-ventricular hemorrhage as a complication was encountered in patients who had deep seated thalamic lesion with paraventricular target point. This makes us aware that targets close to choroid plexus and ventricle should be avoided as far as practicable and if really need to be biopsied, should be dealt with meticulously to avoid possible complications. Of 37 patients in Winkler's series, thalamic lesion was biopsied in only one case.[24]

The primary goal of a stereotactic biopsy is to provide a representative sampling of the lesion to neuropathologist for a diagnosis. We do not do frozen section biopsy prior to sending stereotactic biopsy obtained specimen to the laboratory, yet the diagnostic yield was high. In our series of 40 cases, the net diagnostic yield was in 39 (97.5%) cases and comparable to those achieved in various other series. [12,16,17,19,21,23] Failure to obtain diagnostic tissue during biopsy varied among documented series. An inconclusive result occurred in fewer than 10%.[18] Histological diagnosis was established in 96 % in Winkler's series[24], 94.8% in Brommeland's[2] and 87.5% in Debaene's.[7] Hence, CTSB seems to play a pivotal role in guiding us through the management of patients by providing diagnostic clue

Like any other procedure, CT guided Stereotactic biopsy is not free of complications. High degree of monitoring and preparedness is warranted specially in deep seated lesion where complication in the form of intra-ventricular bleeding can be encountered. There was no statistically significant difference in terms of preoperative and post operative Glasgow Coma Scale of the patients in our series implying safety of this procedure.

Conclusion

Histopathological diagnosis is the gold standard diagnosis and can most accurately guide the doctor in management of patients. Open surgical approach to multifocal, deep seated or lesion in eloquent areas of the brain is hazardous, more so in frail, debilitated patients. Sterotactic biopsy is a safe and ideal approach in these conditions though it is associated with complications as brain swelling, track hematoma, seizure and rarely death.

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