

Stereotactic Biopsy of Brainstem Lesion in Children: Techniques, Efficacy and Safety: Case Review of Single Institutional Experience

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Abstract

Introduction: Stereotactic biopsy of brain stem lesions in children evolved from a controversial background but the current trend seems towards a safe procedure that will yield diagnostic accuracy to guide targeted and individualized treatments.

Aims and Objectives: To confirm safety, accuracy and usefulness of biopsy of brain stem lesions using our institutional experience on two index cases that underwent stereotactic procedures.

Methodology: A review of two case reports were conducted to expose diagnostic success and procedure-related highpoints.

Results: In both cases presented the procedure was uneventful, yielded the desired diagnostic tissue and there were no procedure related complications.

Conclusion: Stereotactic biopsy of pediatric brain stem lesion is safe. Tissue sampling was accurate in both cases and served as a prerequisite more targeted oncology referral and potentially individualized treatment.

Key words: pediatric brain stem lesions, stereotactic biopsy, diagnostic yield

Introduction

With the entrance and perfection MRI sequences in diagnostic neuroimaging since the early 1980s, there was a near complete detachment from diagnostic biopsy procedures for Brain stem lesions. It was then suggested that MRI was sufficient to establish a diagnosis upon which judgement on adjuvant treatments could be anchored. Oncologists were dissuaded from insisting on tissue diagnosis before deploying cancer treatment modalities including chemotherapy and radiotherapy. They were rather persuaded to rely on evidence derivable from MRI. This management philosophy was further buttressed by the fact that biopsy or indeed any previous surgical strategies did not influence convincingly the outcome of not only brainstem lesions but also most pediatric brain tumors. It was also argued that the morbidity and mortality does not match the potential benefits. The assumption was that all brain stem lesion were tumors especially gliomas and should be treated as such. This position was corroborated in 1993 by Albright et al in their report on the results of the Children's Cancer Group DIPG study and concluded that MRI was

adequate in making the diagnosis, since tissue sampling did not alter the treatment or impact outcome [1].

There is a resurgence in current thinking that Brain stem lesions could and should be biopsied. Since 2015, the evidence derived from Hamish et al [2]. formed the basis for a paradigm shift back to the traditional clinical methods of diagnostic tissue guided adjuvant treatments. The attendant complications of diagnostic biopsy procedures were largely eliminated by the adoption of stereotactic biopsy procedures. Furthermore, the safety, efficacy and high diagnostic yield made it worthwhile. A sound understanding of first neuroanatomy and second the principles of neuronavigation is key to success. A trans cerebellar route, image-guidance through the cerebellar peduncles provides a safe corridor to lesions on the pons and indeed other parts of the brain stem. This trajectory must and is usually below the transverse sinus. Stereotactic biopsy is either frame based such as the Leksell system or Frameless such as the Brain Lab, Stealth Navigation system etc. It is also instructive to note that the successes recorded in stereotactic biopsy have been extended

to the application of Robots and Cobots to enhance degree of precision. For this series of two cases reported below, we have deployed the Medtronic Stealth Neuro-navigation system. The technical nuances, safety, complications, and diagnostic yield form the experiences we hereby share. The aim of this report is therefore to present the safety, diagnostic success, and procedure related complications of stereotactic biopsy from experience gathered from two cases of pediatric brain stem lesions.

Methodology

Ethical clearance was sought for and obtained from the institution involved in this study namely the Wellington Neurosurgical Centre Abuja. Following a clinical and radiological suspicion of brain stem lesion as detailed by the case reports below, council and consent was obtained to proceed with a diagnostic stereotactic biopsy. Frameless Stealth guided procedures using the Medtronic USA neuronavigation Treatment Guidance system was used for the two cases.

It is important to understand the basic principles of this procedure in order to conduct it in an orchestrated manner. It starts with establishment of physical coordinates by application of about ten sticky fiducial markers or surface landmarks at designated points on the head of the patient on the day of the surgery. This is to reduce the chances of losing the sticky fiducials which has a tendency to fall off the longer it stays. Then the patient is taken to the CT suite where a contrasted CT Brain is obtained in axial slices only to establish imaging coordinates. Patient is then transferred to the operating theatre for pre-induction anesthesia checks and insertion of mandatory monitors. At about same time the stealth CT images already loaded on a CD is installed on the Stealth Machine and the imaging coordinates appropriately registered. The next stage which is probably the most important and thus considered the backbone of stereotactic procedures is co-registration of the pre-operatively acquired imaging coordinates with the physical coordinates which is the patient's head. For this to happen the patient who is already anesthetized will have the head fixed on Mayfield pins and positioned appropriate to the intended procedure. In both cases presented here, a prone position was adopted with head and neck flexed in military flexion to expose the nape of the neck. The entry point for the planned trans cerebellar approach is sufficiently exposed. The cranial reference frame with the optical reflecting balls is attached to the Mayfield articulating system and positioned close to the head but on the contralateral side of the lesion. A special optical tracking system is used to perform the actual co-registration which basically involves the point-to-point synchronization of the Fiducials on the patients head with the exact designated points on the registered imaging coordinates on the stealth machine. Following a successful co-registration, the process of navigation and stereotactic

surgery commences with surgical planning. This involves the application of sound neuroanatomic knowledge in combination with Stealth computer guidance to define safe entry points, trajectory path and exact distance to surgical targets as shown on pre-op scans (CT, MRI). Then, the site is prepared with standard sterile precautions and draped accordingly. Stealth guided mini skin incision is made usually on the suboccipital region below the transverse sinus. Then burr hole and durotomy follows. Stealth Biopsy kit is assembled and the procedure is conducted with the designated biopsy needle set at a predetermined length based on prior calculations during stealth guided surgical planning. Three specimens of core tissue are usually collected and placed on formalin specimen bottle and sent off immediately to the histopathology lab with appropriate documentation. The durotomy site is covered with hemostatic surgicell while the burr hole site is plugged with bone wax. The mini-incision is closed with vicryl 3-0 sutures and wound dressed. Estimated blood loss is usually less than 5 mls. IV Rocephin is administered at induction of anesthesia at a dose calculated from the body weight of the child.

Case Report 1:

A three year old female referred from a General Hospital on account of one month history of progressive weakness of right upper and lower limbs, more pronounced in the upper limbs but still able to walk though with some difficulty due to imbalance. There is a deviation of the head to the left side which is worsened by attempted gaze towards the left side.

Neurological examination revealed a fully conscious child with normal pupils. Cranial nerve VI palsy was noted on the left side causing her to turn the neck to the left side to focus on any object on that side. The rest of the cranial nerves were essentially normal. Power on most muscle groups on the left upper and lower limbs were MRC 4/5 but full power on the right.

MRI Brain revealed a 2 cm diameter cystic lesion on the left CP angle with low signal on T1 but high signal on T2 and Flair and displaying fairly regular ring enhancement and causing mass effect on the ponto-medullary region of the brain stem on the left side but no associated hydrocephalus (Figure 1). Following multiple differential diagnosis including GBM, Brain abscess, TB, the basis for the referral for Stealth guided biopsy was made by the referral institution.

She successfully underwent a Transcerebellar Stealth Guided biopsy (Figure 2) of this lesion using the technical nuances outlined above. There were no associated complications. Check CT scan (Figure-3b) confirmed biopsy trajectory and no post op hematoma complications. Despite the plethora of differentials as outlined above, Histology report confirmed choroid plexus papilloma (Figure 4). He is presently on both oncology and surgical follow up for more than one year with a stable neurology.

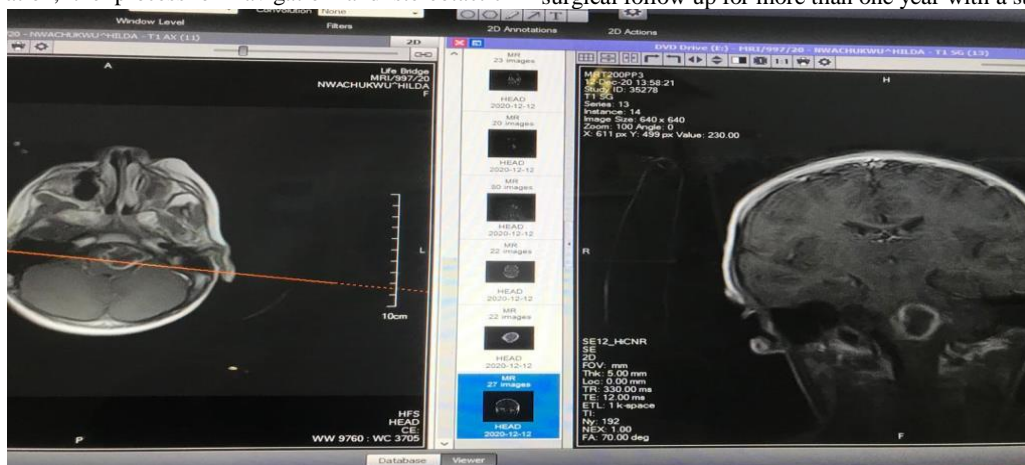


Figure 1. Cystic lesion Left CP angle.

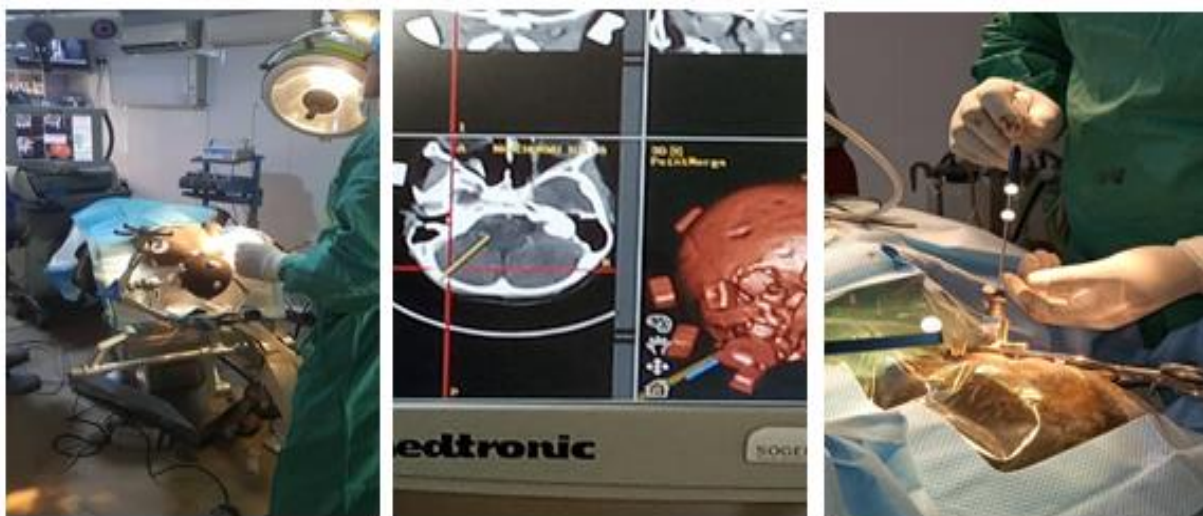


Figure 2. Transcerebellar Stealth Guided Biopsy



Fig 3a-Post op scar

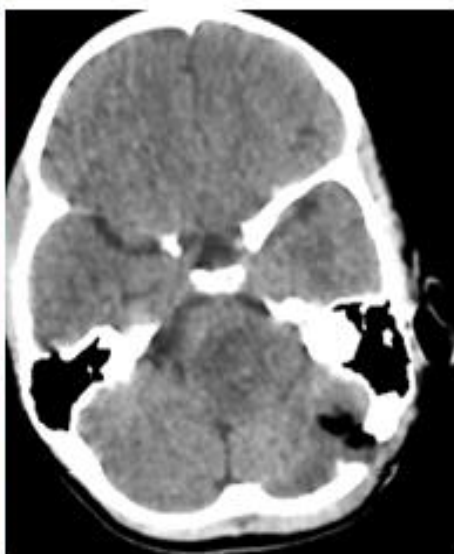


Fig 3b- Check CT head

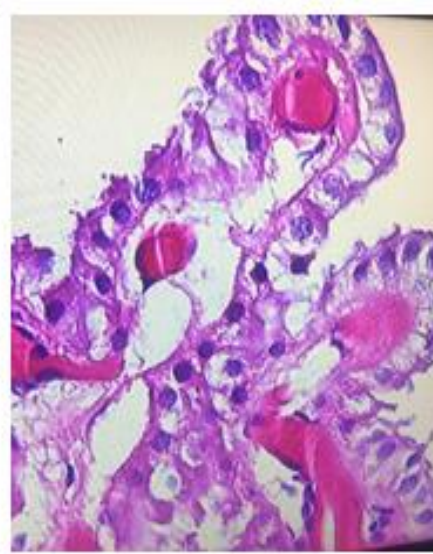


Fig 4-Choroid plexus papilloma

Case Report 2

11 years male with insidious onset, progressive and rather persistent headache for three years prior to presentation. There was associated right hemiparesis, progressive imbalance and difficulty with mobility. He was having increasing swallowing difficulty and also profound dyspnoea worsened by any exertion. Progressive difficulty with speech articulation has worsened in the last few months. He had voracious appetite and virtually feeds ad libitum and had become morbidly obese on presentation.

Examination on presentation revealed respiratory distress evidenced by flaring of alar nasi, orthopnoea, respiratory rate of 26/min. He was fully conscious, but incoordinated movements and imbalance requiring support at all times. Pupils were normal and reactive. No visual field defects but bilateral impairment of abducent nerves was present. The uvula was found to be slightly deviated to the right side but with profound limitation of movements of the whole soft palate signifying cranial nerve IX. There was also impaired movements of the vocal cords on indirect laryngoscopy signifying cranial nerve X palsy

MRI brain(Fig 5) revealed on T1 a diffuse expansion of the brain stem especially the pons with an intrinsic mass which takes up contrast inhomogenously. It brightens up on T2 and Flair sequences to heighten the suspicion of a Diffuse Intrinsic Pontine Lesion (DIPG).

A clinical and radiological suspicion of DIPG was already made at the referral hospital before but further oncology treatments required histological confirmation. Following adequate counselling of parents and consent procedures, he was scheduled and successfully underwent Stealth Guided Transcerebellar Biopsy of Brain Stem Lesion as detailed in the technical section above. It is instructive to note that although the procedure was essentially uneventful, post op extubation was difficult due to already existing respiratory challenges. He was however gradually stepped down to tracheostomy and subsequently discharged with it and carried it all through period of adjuvant treatments.

Histology report confirmed Anaplastic Astrocytoma which necessitated Oncology referral where he completed adjuvant treatments including chemotherapy and radiotherapy. He was reviewed again 12 months post

discharge and was found to be morbidly obese due to voracious appetite. Despite the trachostomy tube still in place he was found to be having

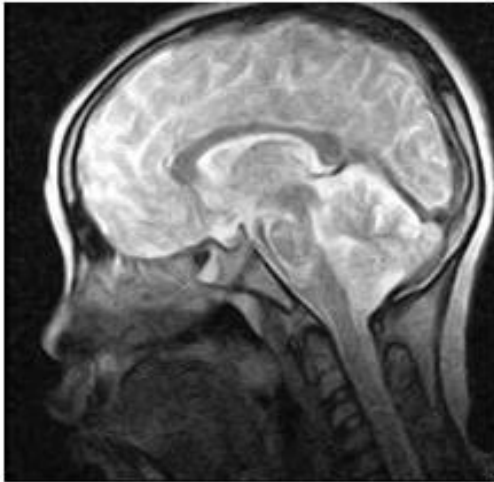


Figure 5a

Discussion

Brain stem tumors constitute about 10%–20% of all pediatric brain tumors [3]. They are extremely rare in adults. Diffuse Intrinsic Pontine Gliomas (DIPG) have been reported as the most common with a high mortality as less than 10% of afflicted children are alive at 2 years. From this background of seemingly hopeless prognosis, emerges a controversy over the appropriateness of any invasive diagnostic biopsy procedures especially since Albright posited that relevant MRI sequence was just about enough diagnostic procedure to appropriate adjuvant treatments. Furthermore, based on conclusions from previous studies, the risk profile of brain stem stereotactic biopsy procedures were transient morbidity (28%), permanent morbidity (9%) [5], while mortality rate was up to 4%, they comprise approximately 10%–20% of all pediatric brain tumors [3]. Consequent upon this, tissue sampling was rarely performed. Recently the desire for definitive histology and molecular characterization seems to have reawakened the drive towards diagnostic biopsy procedures. It is instructive to note that these molecular biology analyses have unraveled a unique genetic makeup of DIPGs that is quite distinct from other pediatric high-grade gliomas or adult high-grade gliomas [6]. The major issues to content with were the attendant complications brain stem surgical procedures which is being addressed by adopting the minimally invasive stereotactic options. This is corroborated by a meta-analysis of 735 patients which confirms that stereotactic biopsy is a safe diagnostic procedure, associated with a low rate of procedure-related complications (overall morbidity 6.7%, permanent morbidity 0.6%, mortality 0.6%) [2]. Furthermore, it allows adequate tissue sampling in 96.1% of cases, which is a prerequisite for histological diagnosis as well as for the molecular characterization of these tumors [2].

For both cases on this report, stealth guided biopsy was successfully conducted via a transcerebellar route. Although the preferable biopsy policy- transcerebral or transcerebellar, frame-based or frameless navigation is still debatable, adherence to the basic principle of neuronavigation is key and this is clearly outlined above. Frame-based stereotactic biopsy was previously regarded as standard procedure but with the advance of software and image quality, the application of frameless navigation system eg Stealth, is increasing [7]. It is important to report that frameless Stealth system was used in this series and contrasted CT was used for establishment of imaging coordinates in both cases, although other imaging modalities have been used including MRI, PET, SPECT [8]. Molecular characterization was not the primary focus,

increasing respiratory difficulty. Unfortunately he passed on approximately 18 months from presentation.

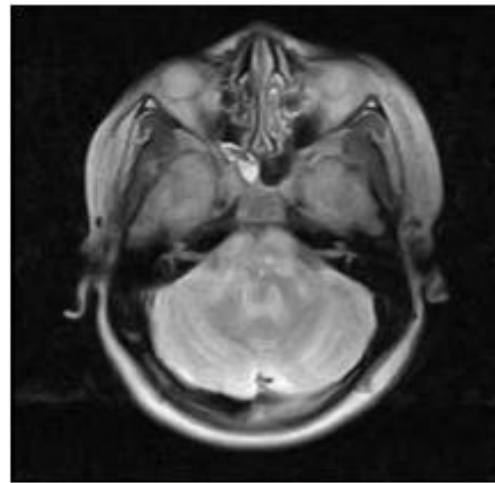


Figure 5b

but tissue diagnosis facilitated evidenced based oncology referral. The child with anaplastic astrocytoma thus had complement adjuvant treatments including radiotherapy and chemotherapy. But unfortunately, disease progressed until demise 18 months later.

One of the cases was confirmed choroid plexus papilloma. CPP is commonly seen in the lateral and third ventricle, but rare form has been identified extending to the Cerebella-Pontine angle close to the opening of the fourth ventricle. CPPs comprise about 1% of intracranial neoplasms but 2–4% in children. Rare locations have been reported and include the third ventricle, cerebellopontine (CP) angle, and cerebral parenchyma [9]. It is instructive to note that no further treatments have been advised following oncology referral of the case due to the very benign nature of this lesion.

Conclusion- Stereotactic biopsy of pediatric brain stem lesions is safe procedure but requires meticulous planning and execution. In both cases presented here tissue sampling was accurate and facilitated targeted oncology referral and individualized treatment. It is worthwhile and advisable to refer such cases timely to centers with such capacity.

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