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Case study

Long-term utility and complication profile of open craniotomy for biopsy in patients with idiopathic encephalitis

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ABSTRACT

Neurosurgeons are often asked to perform open biopsy for diagnosis of encephalitis after medical investigations are non-diagnostic. These patients may be critically ill with multiple comorbidities. Patients and their families often request data regarding the success rates and complication profile of biopsy, but minimal literature exists in this area. Retrospective chart review of all patients undergoing open brain biopsy (burr hole or craniotomy) for encephalitis refractory to medical diagnosis between January 2009 and December 2013 was undertaken. Pathology records and outpatient follow-up were reviewed to determine most recent clinical status of each patient. A total of 59 patients were included with mean follow up of 20 months. The average age at biopsy was 55 years. The most common unconfirmed diagnoses leading to biopsy were vasculitis (44%), neoplasm (27%), infection (12%), autoimmune (12%), amyloidosis (5%). Tissue pathology was diagnostic in 42% of all cases. Overall, biopsy confirmed the preoperative diagnosis in 46% of cases and refuted the preoperative leading diagnosis in 25% of cases. At last follow-up, the tissue pathology resulted in a medical treatment change in 25% of cases. There was a 14% major neurological complication rate (postoperative stroke, hemorrhage, or neurological deficit) and 9% cardiopulmonary complication rate (delayed extubation and re-intubation) attributable to surgical intervention. In this limited series, diagnostic utility of biopsy in patients with idiopathic encephalitis is less than 50% and the major complication rate is 23%. Patients and providers must be counseled accordingly and weigh the risks and benefits of open biopsy for encephalitis cautiously.

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1. Introduction

Identification of the underlying cause of encephalitis is essential for its expedient treatment. Unfortunately, many cases of encephalitis are difficult to diagnosis despite an exhaustive battery of neuroimaging, cerebrospinal fluid, and serum testing [1–6]. In these cases, the neurology or neurocritical care team may request a brain biopsy to definitively diagnosis the underlying process responsible for the resultant encephalopathy. While these cases are uncommon, they occur frequently enough that the neuromedical and neurosurgical teams are often asked by patients and families to provide the diagnostic accuracy and overall utility of these

biopsies. They may also be asked to provide estimates of morbidity and at times mortality. While these components of neurosurgical intervention are clearly important, limited data exist on which to base these estimates [5,7–9]. In this study, we examined the short and long term utility of open brain biopsy for undiagnosed encephalitis and its associated complication profile.

2. Methods

After Institutional Review Board approval, all patients who underwent open craniotomy for biopsy of encephalitis refractory to medical diagnosis between January 2009 and December 2013 were reviewed. Routine demographics (Table 1) were compiled and included age, sex, race, use of anticoagulants, history of steroid use, and preoperative diagnostics were recorded. Additionally, preoperative demographics such as hypertension, diabetes, coronary artery disease, tobacco use, and BMI were compiled. Intraoperative,

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Table 1
Demographics.

<i>Characteristic</i>	n = 59
Age, years	55 (22–88)
Male	26 (44%)
Median follow-up (m)	11
<i>Race</i>	
Caucasian	31 (53%)
African origin	13 (22%)
Asian	2 (3%)
Latino	1 (1.5%)
Other	11 (18%)
<i>Comorbidities</i>	
CAD	11 (19%)
DM	11 (19%)
HTN	33 (56%)

CAD = coronary artery disease, DM = diabetes mellitus, HTN = hypertension.

perioperative, and immediate postoperative complications were evaluated for DVT and PE, cardiopulmonary decline, neurological decline, and surgical complications.

All neurology clinic follow-ups were reviewed and diagnostic changes and final therapeutic interventions were compared to initial treatment decisions and separated into two categories: (1) the biopsy result changed treatment definitively, (2) the biopsy result did not change treatment. For each case, the leading suspected diagnosis was derived from inpatient medical records prior to the biopsy and were separated into five categories: amyloid, vasculitis, neoplastic, infectious, and autoimmune. Final pathology reports were reviewed to obtain definitive diagnostic information.

Postoperative treatment was standardized for all patients reviewed based on established practice guidelines at our institution. These include the use of routine computed tomography scans on all patients postoperatively on day zero following biopsy and the initiation of subcutaneous, prophylactic dose heparin on postoperative day one if there was no interval hemorrhage present or suspected.

Patients were excluded on the basis of age less than 18 years, presence of solitary brain lesions as a suspected cause of encephalitis, stereotactic biopsies, or previous craniotomy for brain biopsy. This study was done in compliance with all guidelines put forth in the Declaration of Helsinki.

3. Results

A total of 59 patients met inclusion criteria (Table 1). The age range of these patients was between 22 and 88, and were predominantly female (56%). The medium follow-up was 11 months after biopsy. There was a high incidence of comorbidities (Table 1), with 56% having a history of hypertension, and 19% having history of coronary artery disease and diabetes. Preoperatively, 39% were on some type of anticoagulation, with 29% on aspirin, 5% on warfarin, and 5% on clopidogrel. 39% of patients had preoperatively been given steroids at some dose during hospitalization. Preoperative lumbar puncture was attempted in 37% of patients, and 34% had a preoperative ischemic event that was identified on cranial imaging (Table 2).

Prior to surgery, the leading diagnoses were evaluated (Table 3), and the most common identifiable leading diagnoses were vasculitis at 44%, and neoplasia at 27%. The result of the brain biopsy after final review by staff pathologist was then identified as either definitive or non-definitive based on the preoperative leading diagnosis. Only in 42% of cases was the final pathology review definitive for a diagnosis overall. The overall pathological yield of the surgical biopsy was broken down by the leading clinical diagnosis

Table 2
Preoperative parameters.

<i>Anticoagulant use</i>	23 (39%)
Aspirin	17 (29%)
Warfarin	3 (5%)
Clopidogrel	3 (5%)
<i>Steroid use</i>	23 (39%)
Preoperative LP	22 (37%)
Preoperative stroke	20 (34%)
<i>Leading preoperative diagnosis</i>	
Amyloid	3 (5%)
Vasculitis	26 (44%)
Neoplasm	16 (27%)
Infection	7 (12%)
Encephalitis NOS	7 (12%)

LP = lumbar puncture, NOS = not otherwise specified.

Table 3
Results.

<i>Postoperative diagnoses</i>	
Amyloid	3 (5%)
Vasculitis	13 (22%)
Neoplasm	14 (24%)
Infection	2 (3%)
Autoimmune	10 (17%)
Encephalitis NOS	17 (29%)
<i>Pathologically definitive</i>	25 (42%)
Amyloid	1 (33%)
Vasculitis	5 (19%)
Neoplasm	12 (75%)
Infection	3 (43%)
Encephalitis NOS	4 (57%)
<i>Diagnostic change at follow-up</i>	
Changed definitively	15 (25%)
Unchanged	27 (46%)
Remained inconclusive	17 (29%)

prior to the day of surgery (Fig. 1). In the case of vasculitis, 81% of biopsies were non-diagnostic. Biopsy was diagnostic in 33% of amyloid cases, 57% of encephalitis cases, and 43% of infectious cases. Biopsy was most likely to be diagnostic in cases of suspected neoplasm with a 75% postoperative pathological diagnosis. There was no association between biopsy yield and race, age, sex, coronary artery disease, diabetes, hypertension, anticoagulant use, or steroid use.

The differences between preoperative and postoperative diagnoses were also examined. In this case, the leading preoperative diagnosis was compared to the overall clinical diagnosis at time of discharge and at follow-up when examined as a percent of total cases in the cohort (Fig. 2). Amongst all cases, biopsy confirmed the preoperative diagnosis in 46% of cases, refuted the preoperative leading diagnosis in 25% of cases, and remained inconclusive in 29% of cases. (Table 3). Preoperatively, vasculitis was the most common leading diagnosis among all patients at 44%, but postoperatively comprised only 22% of the cohort. The second-largest changes in percent by diagnosis were idiopathic encephalitis (12% preoperatively, 29% postoperatively) and autoimmune encephalitis (no cases preoperatively, and 17% postoperatively). The diagnosis of infection was also less common after biopsy (12% versus 3%). Percentages of cases that were thought to be amyloidosis or neoplasia remained relatively constant (5% pre-and postoperatively for amyloidosis, and 27 and 24% for neoplasia).

At last follow-up, neurology clinic notes were reviewed to determine if the patient had received treatment changes as a result of the pathological diagnosis. If after biopsy was completed there was any change in medication status (addition or subtraction of

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