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Original contribution

Remote infarct of the temporal lobe with coexistent hippocampal sclerosis in mesial temporal lobe epilepsy☆,☆☆

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Summary In patients undergoing surgery for temporal lobe epilepsy, hippocampal sclerosis remains the most commonly observed pathology. In addition to hippocampal sclerosis, 5% to 30% of these resections on magnetic resonance imaging contain a second independently epileptogenic lesion, commonly referred to as dual pathology. A second etiology of seizure activity, as seen in dual pathology, may serve as an important cause of treatment failure in striving for post-operative seizure control. Dual pathology, consisting of hippocampal sclerosis and a remote infarct of the adjacent cortex, has been rarely reported. Cases of pathologically confirmed hippocampal sclerosis diagnosed between January 2000 and December 2012 (n = 349) were reviewed, and 7 cases of coexistent infarct (2%) formed the study group. Seven individuals (mean age, 29 years; range, 5-47 years) with a mean epilepsy duration of 12.5 years (3.3-25 years) and a mean pre-surgery frequency of 15 seizures per week (range, 0.5-56 seizures/week) were followed up postoperatively for a mean duration of 64 months (range, 3-137 months). Pathologically, the most common form of hippocampal sclerosis observed was International League against Epilepsy type Ib or severe variant (n = 4). Four of the six individuals with post-surgery follow-up were seizure free at last encounter. The reported incidence of dual pathology, including hippocampal sclerosis and remote infarct, is low (2% in the present study) but may indicate a slightly increased risk of developing hippocampal sclerosis in the setting of a remote infarct. Surgical intervention for such cases anecdotally appears effective in achieving seizure control.

1. Introduction

Hippocampal sclerosis is the most common pathology seen in patients undergoing surgical resection for chronic temporal lobe epilepsy. While surgical resection of the epileptogenic tissue can provide marked improvement in seizure frequency for most patients, it fails to provide adequate seizure control in up to 20% to 30% of mesial temporal lobe epilepsy patients [1]. Current opinion is that this failure may be the result of residual epileptogenic tissue

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(eg, inadequate resection or dual pathology), the unmasking of new epileptogenic foci, or more diffuse cortical dysfunction [2,3]. A second focus of independent seizure activity, as seen in dual pathology, may serve as an important cause of treatment failure in obtaining seizure control in up to 10% of patients [3]. On pathology, 5% to 30% of surgical specimens are found to have dual pathology, eg, hippocampal sclerosis in combination with focal cortical dysplasia, tumors, or vascular lesions [1,4]. The most commonly reported pattern of dual pathology comprises hippocampal sclerosis and adjacent focal cortical dysplasia [5]. The coexistence of hippocampal sclerosis and remote infarct is less commonly observed. One large series observed a frequency of hippocampal sclerosis and ipsilateral remote infarct of the temporal lobe in 2.7% of patients [4]. Although rare, this combination may be a potential source of treatment resistance in individuals with surgical failure.

This study reports 7 cases of dual pathology comprised of remote infarct with hippocampal sclerosis in patients with a history of intractable epilepsy of the mesial temporal lobe and who underwent surgical resection of the epileptogenic focus.

2. Materials and methods

Institutional review board approval of the authors' home institution was obtained prior to identification of eligible study cases. The Cleveland Clinic Department of Anatomic Pathology surgical specimen files were retrospectively reviewed to identify cases of hippocampal sclerosis in patients undergoing resection for intractable mesial temporal lobe epilepsy. Hippocampal sclerosis was defined and diagnosed according to criteria set forth by International League against Epilepsy (ILAE) guidelines [6]. Three hundred forty-nine cases were identified during the study period of January 1, 2000, to December 31, 2012. To meet inclusion criteria, screened cases must have included full hippocampal and ipsilateral temporal lobe resections. Patients with a prior history of brain surgery were excluded to prevent false positive reporting of iatrogenic injury. Seven screened cases had coexistent remote infarct of the excised ipsilateral temporal lobe. The study group comprised 7 eligible cases including 4 males and 3 females, ranging in age from 5 to 47 years (mean age, 29 years). Observed patterns of cortical disorganization adjacent to the remote infarct were classified using both the Palmini et al and ILAE consensus classifications of focal cortical dysplasia [7,8]. Relevant clinical data were abstracted from the patients' medical record with most recent data retrieval being June 2015.

3. Results

All patients had medically intractable medial temporal lobe epilepsy refractory to pharmacologic intervention. Table 1 summarizes the preoperative clinical features of the study group. Seizure duration prior to surgery ranged from 3.3 to 25 years (mean duration, 12.5 years). The mean age at seizure onset was 16.7 years (age range, 21 months to 40 years). The most common pre-surgical seizure subtype was complex partial seizures (n = 5). Pre-surgical seizure frequency ranged widely from 1 to 56 weekly seizures (median frequency 15). Prior to surgery, the cohort was on a mean of 3 daily anti-epileptic drugs (range, 2-4 medications).

Mean duration of postoperative follow-up was 64 months (range, 3.5-138 months). One subject was an international patient who was lost to follow-up after surgical resection. At last follow-up, 4 (67%) of the 6 remaining patients were seizure free. Of the patients with seizure recurrence, one experienced a generalized tonic-clonic seizure during anti-epileptic drug withdrawal but, at last follow-up, was anti-epileptic drug free with no recurrent symptoms. The second patient experienced recurrent absence seizures occurring at an average of 35 per week; at last follow-up, this patient remained on 3 anti-epileptic medications. Of the 4 patients with no post-surgical seizure recurrence, one remained on anti-epileptic medication at last follow-up.

Six of the cases (86%) had a history of prior head trauma, with motor vehicle accident being the most common etiology. None of these patients underwent surgical evacuation or placement of clips for intracranial hemorrhage. The remaining case had a known history of a perinatal ischemic event.

All 7 patients underwent temporal lobe resection and displayed ipsilateral hippocampal sclerosis. Each hippocampus was completely submitted for sectioning. Table 2 summarizes the pathologic findings in the study group. The most commonly observed pattern of hippocampal sclerosis was of the ILAE type Ia or classic subtype (n = 4, 57%). These cases were marked by severe neuronal loss and astrogliosis of the CA1 region with variable amounts of neuronal loss in the remaining hippocampal subsectors CA2-4 (Fig. 1). Two patients (28.6%) presented with the severe pattern of hippocampal sclerosis, consistent with the ILAE Ib subtype; these hippocampi displayed greater than 50% neuronal loss in all hippocampal sectors. One case of hippocampal sclerosis showed a predominantly CA1 distribution of neuronal loss with relative sparing of the remaining hippocampal sectors consistent with the ILAE type II (Fig. 2A and B).

Of the 7 temporal lobes with evidence of remote infarct, three were completely submitted for sectioning. Commonly observed post-infarct changes included evidence of cavitary change, reactive astrogliosis, and atrophy of the adjacent cortex (Figs. 3-5).

Five resections showed focal disruption of the cortical architecture (focal cortical dysplasia) adjacent to the remote infarction (Fig. 6). These lesions would be analogous to type IA focal cortical dysplasia using the Palmini et al schema [7]. The lesions phenotypically resemble ILAE focal cortical dysplasia type Ib, but technically do not fit into the current consensus classification system. Of the five focal cortical