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Original contribution

The role of histopathologic subtype in the setting of hippocampal sclerosis–associated mesial temporal lobe epilepsy☆,☆☆

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Summary Hippocampal sclerosis (HS) and focal cortical dysplasia (FCD) are among the most common neuropathological findings in those undergoing surgery for refractory mesial temporal lobe epilepsy. Existing data regarding differences among the most recent International League Against Epilepsy (ILAE) HS subtypes remain limited. This study sought to characterize the roles of HS subtype and coexistent FCD. Epilepsy surgery pathologic specimens in 307 cases of temporal lobe epilepsy with HS were reviewed (mean age ± SD, 37 ± 15 years; 56% women). HS and coexistent FCD were classified according to ILAE guidelines. Medical records were reviewed for data on seizure recurrence and seizure burden (clinical follow-up mean duration ± SD, 5 ± 4 years). Cases of typical HS (ILAE type I) predominated (ILAE type Ia: 41%, Ib: 47%, II: 11%, and III: 0.7%]. The HS subtypes shared similar demographic and etiologic characteristics, as well as associated pathology and postoperative seizure outcomes. Individuals with type Ib HS were more likely to remain seizure free at long-term follow-up when compared with other subtypes, and they had a later age of seizure onset. Two hundred forty-three cases (79%) demonstrated FCD within the adjacent temporal lobe. Its presence was associated with a significantly decreased risk of seizure recurrence ($P = .02$). When present, FCD was predominantly type I (98%). HS subtype does not appear to affect epilepsy surgery outcomes despite some clinical differences between the subgroups. FCD is often observed in association with HS in mesial temporal lobe epilepsy; the finding of FCD was associated with better postoperative outcomes.

1. Introduction

Hippocampal sclerosis is the most common neuropathological finding among those undergoing surgery for refractory mesial temporal lobe epilepsy (MTLE). Since its first description, investigators have noted unique patterns of hippocampal neuron loss and architectural change within the adjacent temporal lobe [1-5]. Prior series have suggested that these distinct patterns of hippocampal sclerosis may represent subgroups with unique disease etiology, natural history, and treatment outcomes [2,4,6]. The generalizability of these studies has been limited by a lack of uniformity in terminology and diagnostic criteria. In 2013, the International League Against Epilepsy (ILAE) developed consensus classification criteria in an

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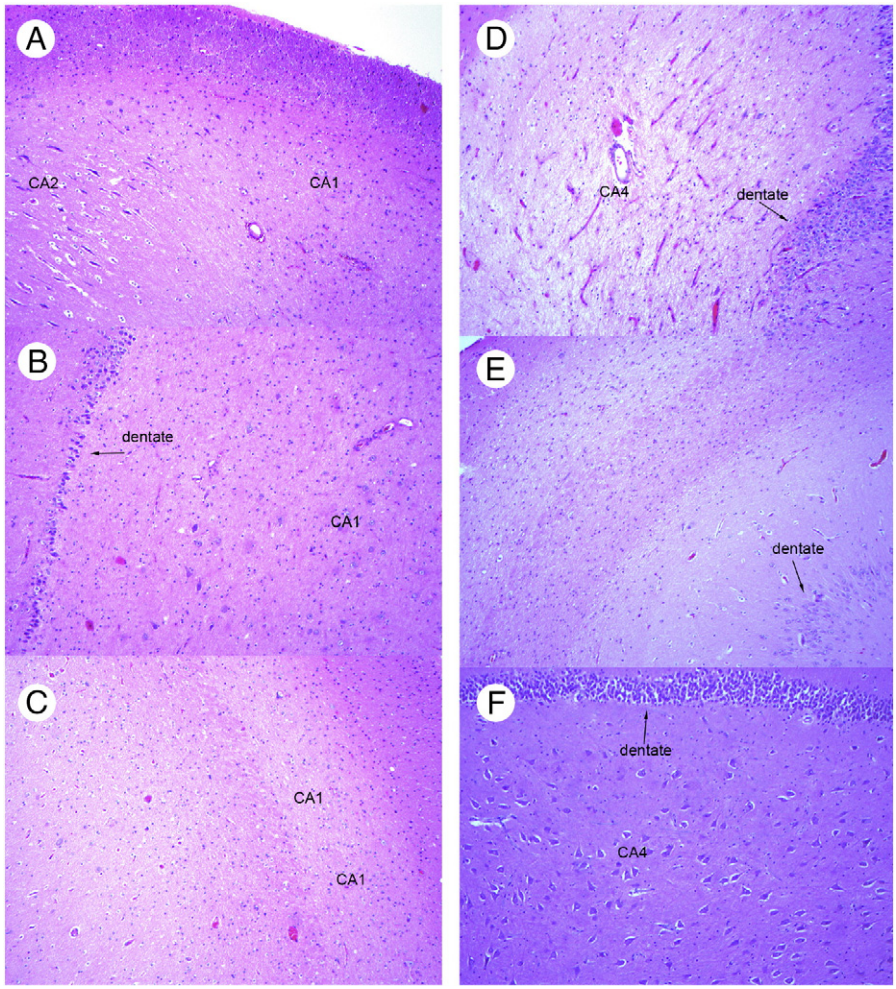

Fig. 1 A, ILAE type Ia hippocampal sclerosis marked by loss of neurons in the CA1 (Sommer sector) region (right) and a relative preservation of neurons in the CA2 region (left) (hematoxylin and eosin, original magnification ×100). B, ILAE type Ia hippocampal sclerosis with some loss of neurons in the CA1 region and in the dentate (left) (hematoxylin and eosin, ×100). C, ILAE type Ib hippocampal sclerosis characterized by a marked loss of neurons in the CA1 region (hematoxylin and eosin, ×100). D, ILAE type Ib hippocampal sclerosis also marked by marked loss of neurons in the CA4 region (hematoxylin and eosin, ×100). E, ILAE type II hippocampal sclerosis with a marked loss of neurons primarily in the CA1 region, seen here (hematoxylin and eosin, ×100). F, ILAE type II hippocampal sclerosis showing a relative sparing of neurons in the CA4 region (Luxol fast blue, ×100).

effort to guide diagnostic and research efforts [7]. A uniform method of histopathologic description may be valuable, as the mechanisms behind poor postoperative outcome remain to be fully characterized [8,9]. Limited data exist regarding the clinical and postoperative differences among the ILAE hippocampal sclerosis subtypes [6,10,11]. The ILAE criteria highlight the role of secondary pathology within the setting of hippocampal sclerosis, as individuals with coexistent epileptogenic lesions of the adjacent temporal lobe are distinguished from those with isolated disease. The role of focal cortical dysplasia (FCD), the most common coexistent pathology in MTLE-related hippocampal sclerosis, remains controversial [12]. To our knowledge, this study represents the largest hippocampal sclerosis series and is the first to investigate the impact of histologic subtype upon long-term outcomes.

This study seeks to correlate commonly observed pathological subtypes of hippocampal sclerosis in the setting of MTLE with clinical presentation, coexistence of FCD, and postoperative outcome.

2. Materials and methods

We obtained Institutional Review Board approval prior to commencement of this study. We searched the Cleveland Clinic Department of Anatomic Pathology surgical pathology files to identify cases of hippocampal sclerosis during the period 2000-2012 inclusive. This study period allowed for a potential minimum of 3-year follow-up after resective epilepsy surgery done for drug-resistant seizures while limiting study bias based upon changes in standard of clinical care. Only cases of standard anterior temporal lobectomy were considered. All microscopic sections were reviewed for each case to confirm the diagnosis of hippocampal sclerosis. A total of 357 cases, with unilateral hippocampus, amygdala, and temporal lobe resected, were screened for study inclusion. Twenty-one cases were excluded, as the quality or orientation of the hippocampal tissue precluded making a definitive diagnosis of hippocampal sclerosis. Thirteen cases were excluded