Neuronal loss and neurofibrillary tangles (NFT) are characteristically severe in the medial temporal lobe, including the hippocampus (Hp), in Alzheimer’s disease (AD). Antemortem hippocampal atrophy correlates with conversion of at-risk individuals to AD and clinical progression of AD. At autopsy, however, subsets of AD cases do not follow Braak-type staging and have relative preservation or susceptibility to atrophy. The purpose of this study was to examine the frequency, as well as the demographic and pathologic features of AD with relative sparing (HpSp) and limbic-predominance of Hp pathology. AD cases with NFT counts from thioflavin-S staining and a Braak NFT-stage of V or VI included 409 men and 480 women, ranging in age from 37 to 103 years. The HpSp group (n=61) had significantly higher NFT densities in superior temporal, mid-frontal and inferior parietal cortices, with significantly fewer NFT in CA1 and subiculum (all, p< 0.001). The converse was true for the limbic-predominant group (n=64), where NFT pathology was lower than typical AD in cortical areas and higher in the Hp (all, p< 0.001). The HpSp group had a larger posterior hippocampal area than typical AD (9%) and limbic-predominant AD (18%) (p< 0.001). The HpSp group was significantly younger and the male:female ratio was greater, whereas the limbic-predominant group was older and higher proportion female. APOE and MAPT genotype differed between the two variants (both, p< 0.01). Our data suggests that these two variants of AD account for about 14% of AD cases and are important to consider in biomarker studies.