

Ectopic germinal centers in the thymus accurately predict prognosis of myasthenia gravis after thymectomy

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Abstract

The ability of thymic histopathology to predict the long-term impact of thymectomy in non-thymomatous myasthenia gravis (NTMG) is mainly uncharted. We applied digital pathology to quantitatively characterize differences of thymic histology between early-onset (EOMG) and late-onset MG (LOMG) and to investigate the role of thymic changes for thymectomy outcomes in MG. We analyzed 83 thymic H&E slides from thymectomized NTMG patients, of which 69 had EOMG and 14 LOMG, using digital pathology open-access software QuPath. We compared the results to the retrospectively assessed clinical outcome at two years after thymectomy and at the last follow-up visit where complete stable remission and minimal use of medication were primary outcomes. The automated annotation pipeline was an effective and reliable way to analyze thymic H&E samples compared to manual annotation with mean intraclass correlation of 0.80. The ratio of thymic tissue to stroma and fat was increased in EOMG compared to LOMG ($p=8.7e-07$), whereas no difference was observed in the ratio of medulla to cortex between these subtypes. AChRAb seropositivity correlated with the number of ectopic germinal centers (eGC; $p=0.00067$) but not with other histological areas. Patients with an increased number of eGCs had better post-thymectomy outcomes at two years after thymectomy ($p=0.0035$) and at the last follow-up ($p=0.0267$). ROC analysis showed that eGC area predicts thymectomy outcome in EOMG with an AUC of 0.79. Digital pathology can thus help in providing a predictive tool to the clinician, the eGC number, to guide the post-thymectomy treatment decisions in EOMG patients.