



P3.359: IMMUNE DYSREGULATION IN THYMOMA-ASSOCIATED MYASTHENIA GRAVIS: A DIGITAL IMAGE ANALYSIS-ASSISTED CLINICOPATHOLOGICAL STUDY

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INTRODUCTION

Background:

- Myasthenia gravis (MG) is the most common paraneoplastic syndrome associated with thymomas
- Dysregulation of the thymic immune microenvironment has been implicated in thymoma-associated MG (TAMG)
- However, quantitative characterization of these immune alterations using digital approaches and their relationship with clinical outcomes remain limited

Objective:

To compare the immune landscape of TAMG and non-myasthenic thymoma (NMT) using immunohistochemistry and digital image analysis, and correlate immune infiltration with clinical outcome.

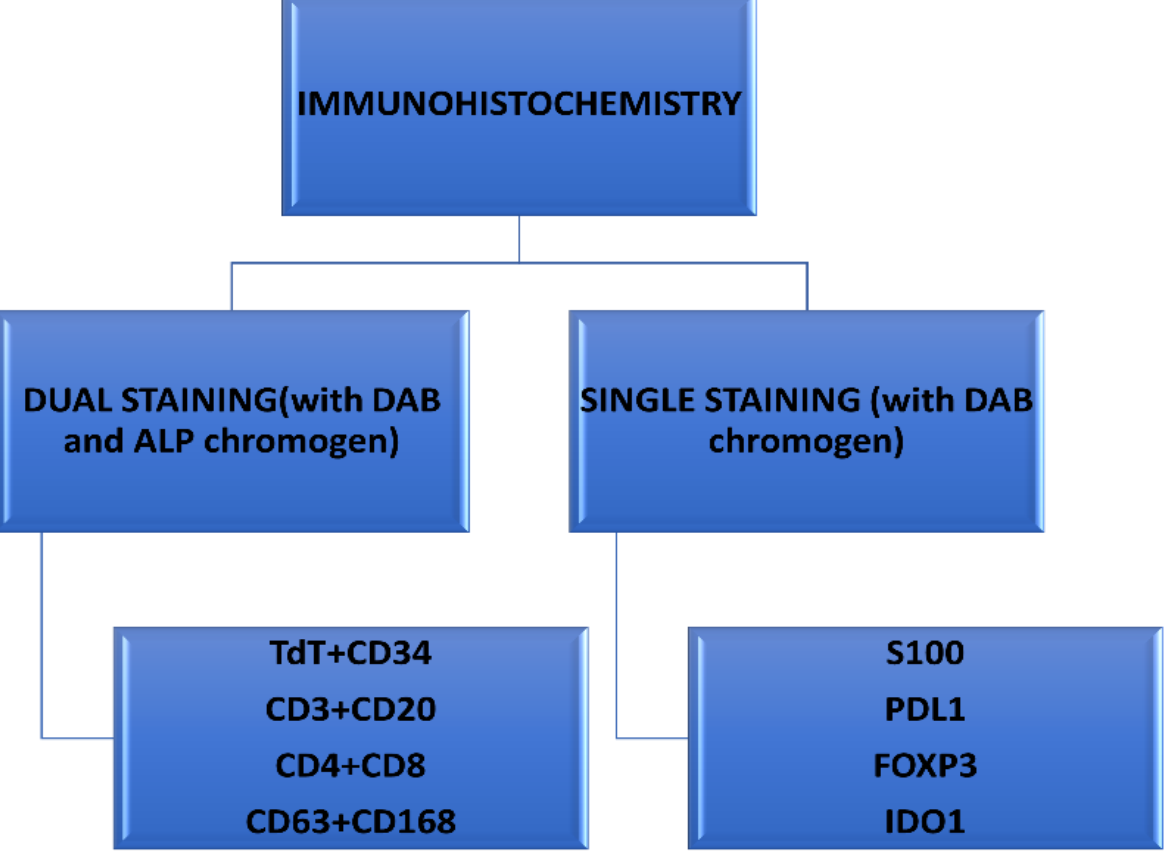
METHODS

Design:

Combined retrospective and prospective study (2014–2024) of 55 resected thymomas (36 TAMG, 19 NMT) at a single tertiary care center

IHC & Digital Image Analysis:

Twelve immune markers (CD3, CD20, CD4, CD8, TdT, CD34, FOXP3, IDO1, PD-L1, CD68, CD163, S100) assessed by IHC and quantified using QuPath across three spatial tumor zones (outer, middle, inner); each 0.1 mm² ROI (400 µm × 250 µm) summed to a 0.3 mm² composite density per case. PD-L1 scored by tumor proportion score (TPS)



DISCUSSION AND CONCLUSION

Discussion

- TdT+/CD34+ and CD3+ reductions in TAMG reflect **steroid exposure** consistent with known glucocorticoid-induced thymocyte apoptosis
- TAMGs with myasthenia persistence showed exploratory trends of decreased FOXP3+ immune cells, IDO1+, and CD20+ immune cells as compared to TAMG with remission-suggesting that persistent MG may reflect a less immunoregulated immune microenvironment
- PD-L1 is **significantly** higher in persistent vs. remission once steroid-exposed cases were excluded (p=0.0047, BH-adj p=0.0425)- a steroid-independent signal potentially reflecting reduced thymic negative selection

Limitations

- Small, single-institution cohort; remission subgroup underpowered (n=9)
- Incomplete steroid dosing/duration data
- No peripheral blood, functional, or normal-thymus

Conclusion

- Steroid exposure emerges as a key confounding factor influencing the immune microenvironment
- Other markers such as FOXP3+ immune cells, IDO1+, and CD20+ show an exploratory trend and needs validation in larger cohorts
- PD-L1 shows a steroid-independent association with MG persistence, highlighting its potential as a therapeutic target in this subgroup

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RESULTS

- Cohort:** Median age 45 years (16–69), male predominance (60%). Within TAMG: 15 (41.7%) had prior steroid exposure, 21 (58.3%) did not; post-thymectomy, 27 (75%) had persistent MG, 9 (25%) achieved remission
- Microscopy:** Hyalinization significantly more common in TAMG than NMT (p=0.045)
- Immune Cell Infiltration: TAMG vs. NMT:** TAMG showed significantly **lower** TdT+/CD34+ (p=0.0100, BH-adj p=0.0400) and CD3+ densities (p=0.0079, BH-adj p=0.0400) than NMT. FOXP3+ Tregs slightly higher in TAMG, but not significant (p=0.2643)
- Steroid Exposure: Three-group analysis** (TAMG with steroid vs. TAMG without steroid vs. NMT): steroid-exposed TAMG had significantly **lower** DP thymocytes, CD3+, and TdT+/CD34+ than other groups (all p≤0.0002)
- Outcome (Persistent vs. Remission):** TAMGs with myasthenia persistence showed exploratory trends of decreased FOXP3+ immune cells, IDO1+, and CD20+ immune cells as compared to TAMG with remission, however not significant
- PD-L1- the standout finding:** Varied significantly by histological subtype (p<0.0001), highest in high-grade thymomas. No significant association with outcome in the **full** TAMG cohort (p=0.104). **But** among the **21 non-steroid-exposed TAMG** specifically, PD-L1 was **significantly higher in persistent than remission** cases (p=0.0047, BH-adjusted p=0.0425)- a steroid-independent signal

