

AB020. PS01.02. Identification of potential biomarkers in thymectomy specimen from myasthenia gravis patients in the MGTX-trial

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Background: The thymectomy trial in non-thymomatous myasthenia gravis (MG) patients receiving prednisone therapy (MGTX) showed that transsternal thymectomy combined with prednisone was more efficient than prednisone alone in terms of improving muscle weakness and quality of life, and reducing total prednisone dose of MG patients. The resulting surgical specimen underwent a rigid work-up, which allows us to look for correlations between histomorphological features and clinical parameters obtained for the study. The aim was to identify potential prognostic and predictive tissue biomarkers.

Methods: A total of 126 non-thymomatous MG patients underwent randomization to the prednisone-only or the thymectomy group. Fifty-six patients agreed to have their thymectomy specimens evaluated by reference pathologists. One patient was excluded because of detection of a B2 thymoma. For the other 55 thymectomy specimens all obtained tissue blocks (11±5 blocks per specimen) underwent a pre-defined standard diagnostic protocol: first, all sections were hematoxylin-eosin (HE)-stained and evaluated for e.g., percentage of fat tissue on the slide; percentage of intra-thymic

fat tissue; grading of cortical atrophy; grading of follicular hypertrophy; number of follicles, and percentage of cortical and medullary area. Second, slides containing thymic parenchyma were immunohisto-chemically stained for CD23 (expressed by follicular dendritic cells) using a routine immunoperoxidase technique. Then, numbers and morphology of lymphoid follicles were “manually” assessed on digitalized sections.

Results: So far the above work-up led to 17 histological variables of different measurement scales per slide (e.g., percentage of fat tissue as interval scaled data (0–100%); grading of thymic follicular hyperplasia (grades 0–4) as ordinal scaled data. Comparing the patient data to data from a historical, non-inflammatory collective showed a trend to hypertrophy of thymic tissue in the MGTX-collective. Non-physiological lymphofollicular hyperplasia (grades 2–4), i.e., the hallmark of thymuses of prednisone-naïve early onset MG patients was observed in only 27% of cases, reflecting the impact of prednisone on LFH.

Conclusions: Most “traditional” histological features (e.g., grade of lymphofollicular hyperplasia) showed no significant correlation to clinical parameters. However, we shall present and discuss more sophisticated morpho-metry-based features that hold promise for predictive significance in terms of MG outcome and recommendations for optimal and economical sampling of thymectomy specimens.

Keywords: MGTX; myasthenia gravis (MG); thymitis; histopathology

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