P3-4 | THE TL1A/DR3 axis in the presence of TSLP induces steroid resistance of ILC2

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Background and Aims: Corticosteroids are mainstay of treatment for patients with asthma. There are subset of patients with severe asthma who have persistent symptoms despite high dose corticosteroid treatment. There is evidence to suggest that type 2 innate lymphoid cells (ILC2s) are involved in the severe asthma with steroid-resistance. Precise mechanisms of steroid resistance induction on ILC2s has not been elucidated. The aim of this study is to address the role of DR3 (death receptor 3), expressed on ILC2s and its ligand, TL1A (tumor necrosis factor-like protein 1A), in the mechanism of steroid resistance induction.
Methods: Enriched blood ILC2s, from mild asthmatics were stimulated with IL-2 (10 ng/mL) in combination with either TL1A (10 ng/mL)or TSLP (0.1 ng/mL), then treated with dexamethasone (10−9 M), to assess the steroid responsiveness of the TL1A/DR3 axis. Harvested cells were subject to immunofluorescence staining and enumerated by flow cytometry.
Results and Conclusions: Dexamethasone significantly reduced IL-5 production by ILC2s in the IL-2 + TL1A (16.4 ± 4.6 vs. 4.4 ± 1.8%) or IL-2 + TSLP (27.7 ± 7.9 vs. 15.2 ± 5.7%) conditions. In contrast, no significant inhibitory effect was noted when TL1A and TSLP were added together. In conclusion the TL1A/DR3 axis in the presence of TSLP induces steroid resistance of ILC2.

P3-5 | Serum periostin levels and periostin immunostaining were useful in the evaluation of eosinophilic granulomatosis with polyangiitis patients

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Background and Aims: There are several biomarkers for an acute exacerbation phase in eosinophilic granulomatosis with polyangiitis (EGPA), but none are valid for the relapsing phase in EGPA patients. Additionally, although confirmation of eosinophilia in the pathological tissue leads to diagnosis, pathological diagnosis after treatment is difficult because eosinophils disappear promptly after steroid administration. Therefore, we investigated whether the relationship between periostin and disease activity during the relapsing phase in EGPA patients.
Methods: We conducted a retrospective cohort study of EGPA patients who were diagnosed and treated at the Department of Allergy, National Sagamihara Hospital from January 2009 to May 2014, using serum periostin levels and periostin immunostaining of pathological tissues.
Result: Serum periostin levels in EGPA patients with acute exacerbation phase and with relapse phase were significantly higher than in those with remission phase. Additionally, periostin was significantly correlated with peripheral blood eosinophil counts during remission phase ($r = 0.438$, $p < 0.01$). Moreover, eosinophils were significantly reduced in histopathology after steroid administration (100% vs 14.0%, $p<0.01$). However, there was no significant difference in periostin expression in histopathology between with and without steroid administration (86.1% vs 79.1%, $p=0.141$).
Conclusion: Our results suggest that serum periostin may be a biomarker for relapse phase as well as biomarker at acute exacerbation phase in EGPA patients. Furthermore, our results suggest that immunostaining with periostin may be a diagnostic aid in pathological tissues that are difficult to diagnose as EGPA after steroid administration.

P3-6 | A clinical analysis of PAP (pulmonary alveolar proteinosis) s diagnosed with difficulty in the COVID-19 pandemic

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Background and Aims: Respiratory care during the COVID-19 Pandemic is very difficult. In this study, we attempted to clinically analyze two cases of patients who were initially diagnosed as COVID-19 based on imaging findings, but were ultimately diagnosed as autoimmune PAP.
Methods: Medical records, imaging findings, and pathological findings were reviewed retrospectively and with reference to the literature.
Results: One patient was a 55-year-old male and one was a 21-year-old female. The symptoms were abnormal chest shadows on physical examination in March and acute

gastroenteritis symptoms in July, respectively. Both patients presented to the triage outpatient clinic with bilateral ground glass infiltrates on chest CT, and were judged to have COVID-19. SARS-CoV-2-PCR was performed a total of three times. Antibody tests were also performed on the man. The results were all negative. However, the suspicion of COVID-19 did not disappear from the imaging findings, so outpatient CT follow-up was continued, and after the third month, we started to think of diseases other than COVID-19. Although there was a relatively large distribution in the mantle region, the shade was a crazy paving pattern, so we decided that PAP should be differentiated first in both cases. Both patients had high levels of autoantibodies against granulocyte-macrophage colony-stimulating factor (GM-CSF)(male: 138U/ml, female: 16U/ml), and the bronchoscopy results were compatible with PAP.

Conclusions: It is currently very difficult to diagnose respiratory diseases other than COVID-19, which shows a crazy paving pattern, and this experience during the COVID-19 Pandemic is very valuable and suggestive.

P3-7 | Mepolizumab may not induct long term remission in patients with eosinophilic granulomatosis with polyangiitis with high relapse rates

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Background: We evaluated the predictive factors of clinical efficacy of mepolizumab in patients with eosinophilic granulomatosis with polyangiitis (EGPA), a rare disease characterized by the presence of allergic granulomatosis and necrotizing vasculitis, in whom remission could not be induced despite treatment with corticosteroids (CS) and immunosuppressants.

Methods: Of the 66 EGPA patients who visited Hiratsuka City Hospital, 35 received mepolizumab and were classified into two groups: 24 (68.6%) who experienced a 'marked effect' (the daily dose of CS or IS could be decreased or the interval between intravenous immunoglobulin treatments could be prolonged) and 11 (31.4%) who experienced a 'weak effect' (these measures were not feasible). In both groups, we evaluated the number of eosinophils in the peripheral blood, relapse rates, daily dose of CS at disease onset and before and after administration of mepolizumab.

Results: All patients who received mepolizumab had clinical effect on vasculitis symptoms. Relapse rates before mepolizumab administration and dose of CS after mepolizumab administration in the 'marked effect' group was significantly lower than that in the 'weak effect' group ($p < 0.01$). The number of eosinophils in the peripheral blood at disease onset in the 'marked effect' group was higher than that in the ''weak effect'' group ($p < 0.05$), but not before and after administration of mepolizumab. Relapse rates in marked effect group significantly decreased after administration of mepolizumab, but did not change in weak effect group.

Conclusion: Patients with EGPA with high relapse rates could not induct long term remission even if after administration of mepolizumab.

P3-8 | Clinical application of serum and sputum YKL-40 in asthma, ACO and COPD

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Background and Aims: We have previously reported sputum YKL-40 could be a biomarker for predicting neutrophilic airway inflammation in asthma, asthma-COPD overlap (ACO) and COPD. (Suzuki Y. JSA Congress 2019). However, little is known about relationship between serum and sputum YKL-40. Therefore, we evaluate associations between these biomarkers and parameters related to disease activity in asthma, ACO and COPD.

Methods: Forty two asthmatics, 21 ACO patients and 21 COPD patients were recruited. Blood samplings, induced sputum tests, spirometry, FeNO measurements, and questionnaires (ACT, CAT, and mMRC dyspnea scale) were performed.

Results and Conclusions: There was a trend correlation between serum and sputum YKL-40. Serum as well as sputum YKL-40 levels in the COPD group were significantly higher than those in the asthmatic group ($p<0.01$). Additionally, serum YKL-40 levels in the ACO group were significantly higher than those in the asthmatic group ($p<0.05$), but sputum YKL-40 levels were not. YKL-40 in both sputum and serum showed positive correlations with sputum neutrophils ($p<0.05$). Serum YKL-40, but not sputum YKL-40, were negatively correlated with FEV_1/FVC ($p<0.01$). In terms of relationships between YKL-40 and symptom questionnaires, sputum YKL-40 levels in the COPD group with CAT score≥10 or mMRC score≥2 were higher than those with CAT score <10 or mMRC<2 ($p<0.05$). YKL-40 can be a marker of neutrophilic airway inflammation. Additionally, YKL-40 in sputum and serum may reflect distinct clinical features in asthma, ACO and COPD. Concomitant use of these biomarkers may provide more useful information on evaluating disease activity.

P3-9 | Allergy in IgG4-related disease

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