

## **IgG4-related lung disease associated with concomitant adenocarcinoma of the lung**

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### **Background:**

A previous study purported that malignancy may be associated with subsequent development of IgG4-related disease (IgG4-RD). It has been also suggested that IgG4-RD predisposes patients to malignancy. However, the association of IgG4-RD with a simultaneous cancer has not been well known. Herein, we examined the presence of IgG4-RD associated with adjacent malignancy in a cohort of 156 resected lung adenocarcinomas over one year period (2009) at Mayo Clinic Rochester.

### **Methods & Materials:**

All slides from 156 resected lung adenocarcinoma cases were reviewed by two pathologists and a representative block was chosen for a panel of immunohistochemical stainings including IgG4, IgG, CD3, CD20 and MUM1 to examine the immune microenvironment as well as IgG4 positive cell infiltration. IgG4+ plasma cells were manually counted in three hot spots and presented as average number per HPF. IgG+ cells were enumerated in the corresponding fields to calculate IgG4/IgG ratio in each case. Histopathology was also evaluated for the features of IgG4-RD including lymphoplasmacytic infiltrates, storiform fibrosis, and obliterative phlebitis or arteritis.

### **Results:**

Image analysis for CD3, CD20 and MUM1 positive cells showed that the median (25-75%) numbers of CD3+, CD20+, MUM1+ cells per 1mm<sup>2</sup> of tumor were 1504 (846-2264), 570 (189-4413), and 323(184-711), respectively. Median ratio of B and T cells (CD20+/CD3+) and median proportion of plasma cells among the infiltrates (MUM1+/[CD3+, CD20+ &MUM1+]) were 0.38 (0.20-0.83) and 14% (8-25%), respectively. Thirty-nine of 156 cases (25%) had  $\geq 24.6\%$  (3 quartiles) of plasma cells among the infiltrates. Eighteen of 156 cases had at least one IgG4+ plasma cells in the sections and nine cases (5.8%) had  $\geq 10$  IgG4+ cells per HPF (ranging 15-68/HPF; 0.31–0.57 in IgG4/IgG ratio). One case (0.6%), from a 65 year-old man at the time of surgery, showed the histopathologic features of IgG4-RD with 68 IgG4+ cells per HPF with 0.49 in IgG4/IgG ratio, meeting the current morphologic criteria for IgG4-RD. IgG4 serum level or follow up information is not available in this patient.

### **Conclusions:**

Image analysis of tumor infiltrating immune cells revealed that high proportion of plasma cells ( $\geq 24.6\%$ ) was seen in 39 of 156 (25%) lung adenocarcinoma cases. Nine of 156 (5.8%) showed  $\geq 10$  IgG4+ cells per HPF and one of these cases met the current histopathologic criteria for IgG4-RD. This case suggests IgG4-RD features as a peculiar immune reaction to tumors or something akin to a paraneoplastic syndrome.