

Prevalence of B-cell clonal disorders in patients with IgG4-related disease: single-center experience

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Objective:

Lymphoplasmatic infiltrate, an essential attribute of IgG4-RD, frequently form MALT-tissue - a well-known underlying condition in lymphoma formation in Sjogren's syndrome. There is evolving data that IgG4-RD is associated with lymphomas as well.

Methods:

Single center open study. We reviewed medical records of 57 patients with biopsy proven IgG4-RD treated in Nasonova Research Institute of Rheumatology from 2010 to Oct-2016, 28 patients were included in the present study (19 with definite IgG4-RD, 9 with possible/probable IgG4-RD according to comprehensive diagnostic criteria). At baseline B-cell clonality in tissue (on frozen tissue section or paraffin embedded) was tested in 14 patients by PCR analysis of immunoglobulin (Ig) V-D-J genes heavy chain rearrangements (FR1, FR2, FR3); monoclonal secretion was tested in serum protein electrophoresis with immunofixation in 21 patients. Both were tested in 8 patients.

Results:

The mean age was 46.4 years (range 19-73), median duration of the disease before evaluation was 44 months (range 3-204). The mean number of organs involved was 2.4 (range 1-5): orbit 20, salivary glands 17, lymph nodes 16, biliary tract 2, pancreas 2, lungs 2, retroperitoneum 2, breast 1, bones 1, soft tissues of the neck 1, nasal cavity or paranasal sinuses 1, coronary arteries 1. Twenty five (89.3%) had elevated serum IgG4 levels >135 mg/dl at baseline (median 715 mg/dl, range 110 -7200 mg/dl). Paraproteinemia was detected in 3 patients (14.3%, tracer IgG κ -1, tracer IgG λ -1, monoclonal IgM κ 3.2 g/l-1). Two of these patients demonstrated B-cell clonality in the tissue specimens as well (in bone marrow and submandibular salivary gland). However, pathological and immunohistochemical examination didn't prove the existence of lymphoma. Overall B-cell clonality in the tissue was detected in 3 patients (21.4%): by PCR analysis of Ig heavy chain rearrangements in 2 cases (in submandibular salivary gland-1 and in bone marrow – 1), by PCR analysis of Ig kappa chain rearrangements (V κ -J κ and V κ -KDE/Intron RSS-KDE) in 1 case. The latter patient exhibited pathological characteristics of MALT-lymphoma of the lacrimal gland with κ -chain restriction. One patient had local AL-amyloidosis in orbit.

Conclusions:

It seems that IgG4-RD can act as a background for lymphoproliferative disorders which is further supported by the fact that in our cohort there was 1 patient with IgG4-associated MALT-lymphoma of lacrimal gland and 1 patient with AL-amyloidosis. B-cell clonality does not necessarily constitute lymphoma, but these patients require very close follow-up.