Immunoglobulin G4-Related Lymphadenopathy in a Patient with Rheumatoid Arthritis

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Background: Immunoglobulin G4-related disease (IgG4-RD) is a fibroinflammatory disease characterized by IgG4-positive plasma cells infiltrating one or multiple organs. The disease is difficult to diagnose because it is rare and appears with various manifestations such as lymphadenopathy, mass, pancreatitis, cholangitis, sialadenitis, retroperitoneal fibrosis, and lung nodules.

Case: A 57-year-old man taking tacrolimus for rheumatoid arthritis presented with multiple lung nodules and enlarged lymph nodes on computed tomography (CT) of the chest. He denied systemic and respiratory symptoms. Crackles were heard in both lower lung fields and there was no joint tenderness or swelling. Laboratory tests revealed the following: reversed albumin/globulin ratio, elevated serum IgG (3,310 mg/dL) and IgG4 (748 mg/dL) levels with polyclonal gammopathy, elevated erythrocyte sedimentation rate. Serum levels of C-reactive protein (CRP), angiotensin-converting enzyme, anti-nuclear antibodies were unremarkable and interferon-gamma release assay was negative. The chest CT demonstrated bilateral basal subpleural reticular opacity with indeterminate nodules and prominent mediastinal and axillary lymph nodes (Figure 1A). Positron emission tomography showed hypermetabolic lymph nodes in both neck, axillae, hilar, mediastinum, and intra-abdominal areas (Figure 1C). Axillary lymph node biopsy revealed lymphoid hyperplasia and IgG4-positive plasma cell infiltration with increased IgG4-positive/IgG-positive plasma cell ratio (>50%) (Figure 2A and B). Considering his medical history and CT findings, rheumatoid lymphadenopathy or lymphoma was suspected. However, in addition to histopathologic findings, elevated serum IgG4 level with normal CRP level suggests IgG4-RD. After treatment with high dose steroids for IgG4-RD, serum IgG4 level was normalized and the size of lymph nodes and lung nodules decreased (Figure 1B).

Conclusion: Lung nodules and systemic lymphadenopathy have various differential diagnoses, including malignant and benign etiologies. Although IgG4-RD is a rare disorder, clinicians should consider the possibility of IgG4-RD in these patients.

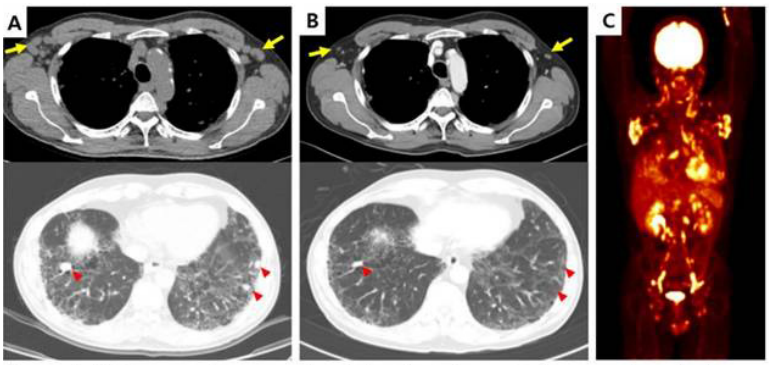

Figure 1. (A) Computed tomography of the chest demonstrating prominent both axillary lymph nodes (yellow arrows) and bilateral lung nodules (red arrow heads). (B) Decreased size of axillary lymph nodes (yellow arrows) and lung nodules (red arrow heads) after high dose steroid therapy. (C) Positron emission tomography showing hypermetabolic lymph nodes in both neck, both axillae, mediastinum, both hilar, abdominal areas.

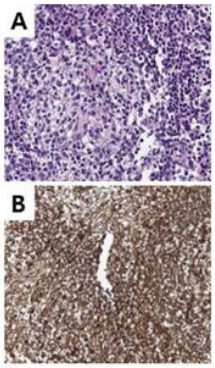

Figure 2. Histopathologic findings. (A) Hematoxylin-eosin stain showing atypical lymphoid hyperplasia. (B) Immunohistochemical stain of Immunoglobulin G4 (IgG4) showing IgG4-positive plasma cell infiltration.