Pulmonary Extranodal Marginal Zone Lymphoma of Mucosa-Associated Lymphoid Tissue Associated with Granulomatous Inflammation in a Child with Chromosome 22q11.2 Deletion Syndrome (DiGeorge Syndrome)

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Patients with immunodeficiency disorders have an increased incidence of lymphoproliferative disorders; however, only 4 such patients with DiGeorge/chromosome 22q11.2 deletion syndrome have been reported. We report a case of a pulmonary Epstein-Barr virus–negative extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue in a child with this syndrome. *(J Pediatr 2012;161:954-8).*

The patient is a 15-year-old female with chromosome 22q11.2 deletion/DiGeorge syndrome diagnosed at age 9 years, documented by cytogenetic fluorescence in situ hybridization studies. She has cardiovascular defects with congenital ventricular septal defect, patent ductus arteriosus, and right-sided aortic arch, hypoparathyroidism, subtle dysmorphic facial features, immunodeficiency (including low peripheral $CD4^+$ T cell count, hypogammaglobulinemia, frequent recurrent pneumonias and other infections), and Evan syndrome diagnosed at the age of 3 years. She also has chronic eczema and lichen planus. Currently, she is maintained on amoxicillin and weekly to monthly gamma globulin.

Approximately 2 years ago, the patient presented with fever, chronic cough, and progressive respiratory symptoms. Chest radiograph revealed lung consolidation thought to represent pneumonia. Antibiotic therapy produced some improvement; however, follow-up chest radiograph remained abnormal, and a chest computed tomography (CT) scan showed consolidation involving the right lower lobe and multiple scattered bilateral pulmonary nodules. Pulmonary function testing revealed restrictive changes. Analysis of bronchoalveolar lavage fluid was nondiagnostic.

Three months later, progressive enlargement of the pulmonary nodules was noted. The patient underwent thoracoscopic wedge biopsies, which were initially diagnosed as inflammation and granulomatous disease. Two months later, a repeat chest CT showed that the pulmonary nodules had increased in size. Pathological re-review of the more abnormal right lower lobe biopsy specimen revealed an extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) lymphoma with plasmacytic differentiation (**Figure 1**, A-C). Elsewhere a patchier infiltrate, granulomas with negative acid-fast and Grocott staining, prominent intraalveolar macrophages, and some interstitial and pleural fibrosis were seen. Immunohistochemistry analysis identified many $CD20^+$ B cells in nodules; variable numbers of internodular $CD5^-$, $CD10^-$, $BCL6^-$, $CD43^-$, cyclin $D1^-$, and $BCL2^+$ B cells; IgM^+ λ light chain-restricted plasma cells in the main mass, and scattered $CD3^+$ T cells that were focally more numerous (CD4>CD8) (**Figure 1**, D-F). Elsewhere there were polytypic plasma cells and 2 small foci that appeared to be κ light chain-restricted (**Figure 1**, G and H). Epstein-Barr virus (EBV)-encoded RNA in situ hybridization for EBV and human herpesvirus 8 immunohistochemistry were negative. Polymerase chain reaction–based immunoglobulin heavy chain and T-cell receptor gene rearrangement analyses using BIOMED-2 protocols supported the presence of a monoclonal B-cell population but polyclonal T cells.[1] Staging of bone marrow, including flow cytometry studies, showed nonnecrotizing granuloma, but no evidence of lymphoma. Staging positron emission tomography (PET)/CT imaging showed extensive hypermetabolic lymphadenopathy and numerous hypermetabolic pulmonary nodules (**Figure 2**; available at www.jpeds.com).

The patient was treated with 6 cycles of rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisolone (R-CHOP), and achieved complete remission. Restaging bilateral bone marrow examinations were negative. Posttherapy skin biopsy analysis revealed only granulomas. Analysis of gastric biopsy specimens obtained

CT	Computed tomography
EBV	Epstein-Barr virus
LPD	Lymphoproliferative disorder
MALT	Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue
PET	Positron emission tomography
R-CHOP	Rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisolone

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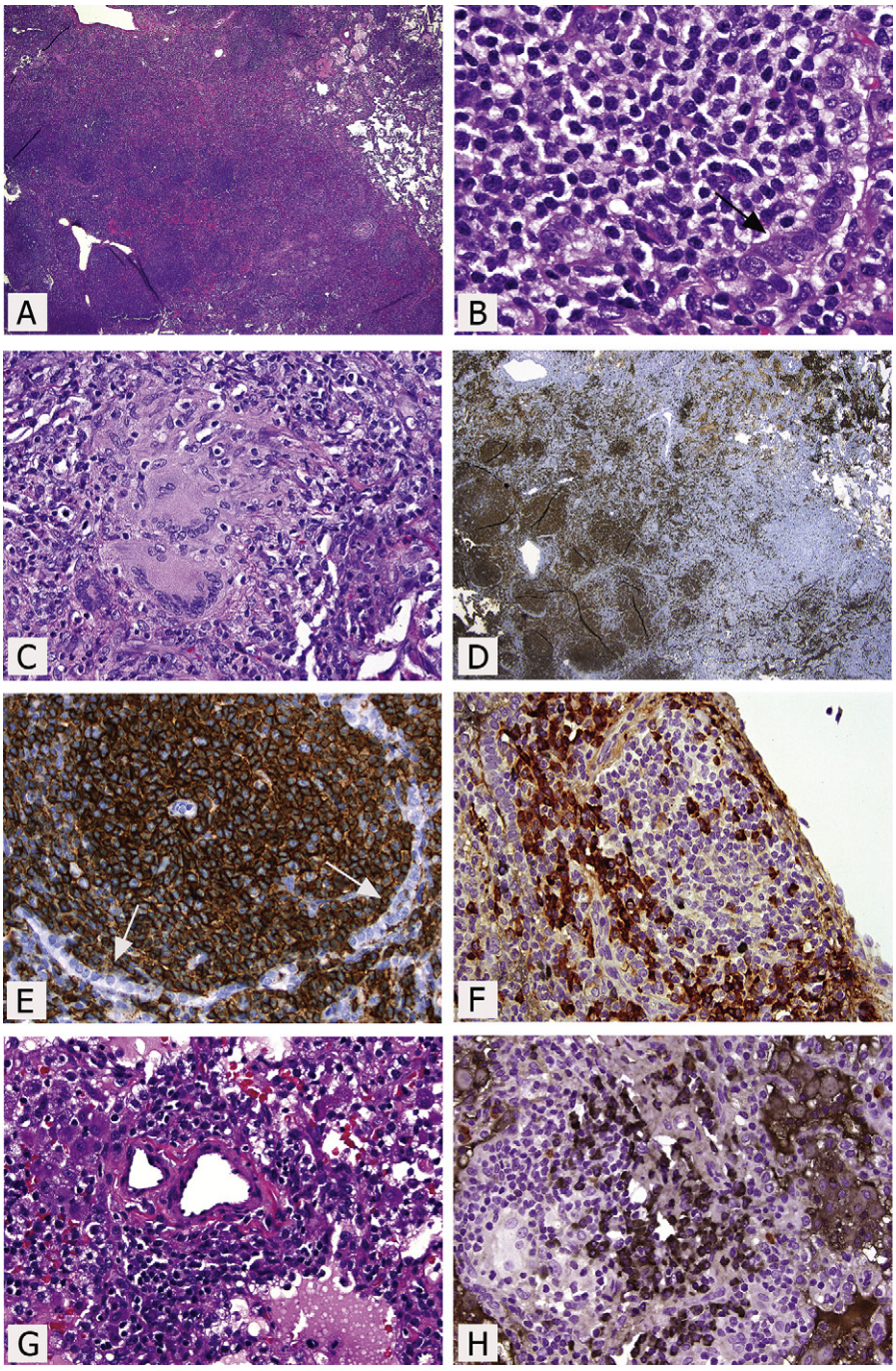

Figure 1. Pulmonary wedge excision of the right lower lobe. **A,** Mass-like dense infiltrate with scattered follicular-type structures. **B,** Predominantly small lymphoid cells, including some with monocytoid and plasmacytoid features, infiltrating the epithelium. Note the residual epithelial remnants (*arrow*). Other focal areas show numerous plasma cells. **C,** Epithelioid granulomas with Langhans giant cells. **D,** Numerous $CD20^+$ cells in the follicles and a moderate number in the interfollicular regions. **E,** At higher magnification, numerous $CD20^+$ small lymphocytes in and around the follicle, also surrounding the residual $CD20^-$ epithelial cells (*arrows*). **F,** Double immunostaining for κ and λ immunoglobulin light chains showing numerous λ^+ plasma cells (*red/brown*), but only rare κ^+ plasma cells (*black*). The λ restriction was confirmed by κ and λ single immunostains and in situ hybridization stains. The plasma cells were IgG^-, IgA^-, IgM^+, and IgD^-. **G,** Small aggregates of small lymphocytes and plasma cells away from the main mass. **H,** In contrast to the main mass, the plasma cells here show κ light chain restriction in this double-immunohistochemical stain. (**A, B, C,** and **G,** hematoxylin and eosin staining; **D** and **E,** immunoperoxidase staining for CD20; **F** and **H,** double-immunoperoxidase staining for κ and λ immunoglobulin light chains).