



A Stream in Glacier National Park

PIC QUESTION OF THE WEEK: 5/16/11

Q: What are some treatment options for Wegener's granulomatosis?

A: Wegener's granulomatosis (WG) is a rare autoimmune disorder associated with vasculitis and characterized by the formation of granulomas, that is, nodular inflammatory lesions infiltrated with numerous macrophages. The inflammatory changes reduce blood flow resulting in damage to the affected organs. WG can affect any organ system, but its destructive effects are primarily seen in the respiratory tract and kidneys. There is no known cause for this disease that occurs in approximately 3/100,000 individuals. It is more common in whites and the average age of those affected is 40 years. Because it affects less than 200,000 people in this country, WG is classified by the FDA as an *orphan disease*. The initial and most common symptoms involve the upper respiratory tract and include constant rhinorrhea, purulent discharge, epistaxis, and sinus pain. Other symptoms include arthralgia, cough, and hemoptysis. Pulmonary nodules, infiltrates, and cavitations may also develop. Initial respiratory symptoms can be rapidly followed by involvement of other organs, mainly the kidneys. If left untreated, WG can result in renal failure and death. There are limited treatment options for this disease and cure is rarely attained. Remission of WG has been attempted through use of immunosuppressive agents such as cyclophosphamide, methotrexate, glucocorticoids, and immunobiologic therapies such as TNF- α inhibitors. The FDA has recently approved the monoclonal antibody rituximab (Rituxan) in combination with glucocorticoids for the treatment of this orphan disease. Rituximab binds to the CD20 antigen on the surface of B-lymphocytes and results in a significant decrease in circulating and tissue levels of this cell type. In one clinical trial, rituximab plus glucocorticoids produced a remission rate of 64% compared to 53% in those treated with cyclophosphamide plus glucocorticoids. Patients in this study received only one course of therapy. Rituximab is administered once weekly for four weeks by IV infusion. Parenteral and oral corticosteroids should be given just prior to or simultaneously with rituximab. A *Black Box* warning describes the occurrence of severe hypersensitivity reactions during or within 24 hours after infusion. Adverse effects include lymphopenia, asthenia, anemia, and a number of other hematologic and immunosuppressive complications such as progressive multifocal leukoencephalopathy (PML). WG is a complex and potentially fatal disease. Hopefully, rituximab will prove useful in extending remission rates and improving outcomes for patients with this orphan disease.

References:

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