

Microscopic polyangiitis (MPA) is an inflammation of the medium and small vessel walls that can affect different parts of the body including (but not limited to) the kidney, lungs, sinuses. Patients with MPA usually have the disease in their kidney and it is essentially indistinguishable from the kidney disease that patients with classic Wegener's granulomatosis (WG) often have.

The principal difference between MPA and WG is the absence of a specific type of inflammation called granulomatous inflammation that is what distinguishes WG from other forms of vasculitis, although the clinical features are similar in these two diseases. Patients presenting with kidney disease in the absence of disease in other parts of the body are generally classified as "renal-limited" vasculitis.

In the United States, the typical MPA patient is a middle-aged white male or female, but in fact the disease may occur in people of all ages, both genders, and all ethnic backgrounds.

The presenting **symptoms** include fever, joint and muscle pains, weakness, lack of energy and weight loss. Hematuria, the abnormal presence of blood in the urine, swelling and a decrease in the amount of urine may be manifestations of renal involvement which is one of the most frequently involved organs in MPA. In fact approximately 90% of patients with MPH have involvement of their kidneys (called glomerulonephritis, as called because the inflammation affects the part of the kidney that filters fluid to make urine and is called the glomerulus). Lung symptoms like shortness of breath, coughing up blood, and/or chest pain are experienced in about half of the patients. MPA is the most common cause of the so called pulmonary–renal syndrome, which is the common combination of inflammation and disease symptoms in both the lung and the kidney.

In MPA the symptoms of the upper airway (sinuses, ears) can occur, but are less common or milder than kidney or lung symptoms. The eyes and the nervous system can also be affected by the disease. A skin rash, usually with purplish bumps and spots mostly in the lower extremities, is sometimes seen. The stomach and intestinal tract can also be affected by the disease, resulting in pain or an alteration of the color of stools into black or bright red as a result of bleeding.

Over 80% of patients with MPA have ANCA.

The diagnosis of MPA is established with the biopsy, a small piece of tissue that is taken from the affected organ(s). The biopsy tissue is looked at under microscopes and reveals vasculitis. A skin or kidney biopsy is typically preferred, but can also be done in other organs such as the intestine.

The **treatment** of MPA is essentially the same as in WG especially when the major organs injured by the disease are the kidney and/or lung.

Induction therapy is the initial step for all patients diagnosed with MPA in order to reduce the inflammation of the disease. A minimum of three to six months induction phase is needed for most patients to reduce or get rid of the inflammation, which is often known as 'getting the disease into remission.'

Maintenance therapy is the following step and is meant to keep the disease in remission as long as possible and therefore reduce the chance that the inflammation will return (called a disease relapse). Maintenance therapy can be continued for 12 to 18 months, sometimes longer. For

patients who never completely get their disease into remission or who experience several disease relapses, ongoing maintenance therapy may be continued indefinitely.

Immunosuppressive regimens used in the induction phase of treatment usually include a combination of corticosteroids (prednisone) with either daily oral cyclophosphamide (Cytoxan) or monthly intravenous (given into a vein at a doctor's office or hospital) cyclophosphamide (Cytoxan).

Low-dose weekly oral methotrexate has been tried in patients with MPA without severe inflammation from the disease. Corticosteroids monotherapy is not generally considered for remission induction, since the reported remission rate is much lower. Patients who are dialysis-dependent at presentation seem to benefit from plasmapheresis. Although no controlled studies have been performed, patients with pulmonary hemorrhage may be treated with plasmapheresis also.

Maintenance therapy includes immunosuppressive agents such as mycophenolate mofetil, Rituximab, azathioprine, methotrexate, Cyclosporine, etanercept. Trimethoprim-sulfamethoxazole is an antibiotic agent used also relating with the fact that disease activity has been associated with both infection and the chronic nasal carriage of *Staphylococcus aureus*.

Treatment-associated toxicity: Cyclophosphamide treatment is associated with important toxicity. Women may stop having their menstrual cycles (periods) and men may have lowered or no sperm produced; either of which may not return to normal even after stopping treatment.

Inflammation of the bladder (cystitis), bladder cancer, myelodysplasia, (disorder of the function of the bone marrow, the part of the bone related to the production of blood cells) and lymphoma (type of cancer of the lymph nodes) can also occur with use of this drug. Some studies suggest that monthly intravenous cyclophosphamide (given by vein) may be as effective as daily oral treatment with the same drug in controlling symptoms and reducing inflammation, while reducing the overall cumulative dose and chance of side effects.

Long-term use of corticosteroids use can include cataracts (a clouding of the natural lens, the part of the eye responsible for focusing light and producing clear, sharp images), diabetes mellitus (disorder of the glucose levels in blood), osteoporosis (thin bones), fractures (small breaks in bones), aseptic necrosis of bone (condition in which poor blood supply to an area of bone leads to bone death) and severe pain and inflammation of the stomach.

Pneumonia and other infections are serious complications of any immunosuppressive therapy, including cyclophosphamide and corticosteroids.

Prophylaxis: Given the toxicities of cyclophosphamide, prophylactic therapy is usually provided with specific drugs to help prevent specific types of pneumonia, permanent loss of periods (menstrual cycles) in women of child-bearing, and bladder cancer. Given the toxicities of prolonged steroid use, prophylactic treatments may also be provided to help prevent for mouth infections, stomach pain and inflammation and bone loss.

The major lifetime effects in patients with MPA result from the combined effects of irreversible organ damage (such as kidney failure or lung scarring from the disease as well as the consequences of the cumulative dose and total period of each immunosuppressive therapy, whether utilized for initial disease, maintenance of remission, or management of relapses of the disease. Therefore the natural history of the disease is diverse among patients.