Solutions to **ANCA-Associated Kidney Disease: Secondary Causes**

1. **ISOTRETINOIN**: Retinoids such as isotretinoin and Vitamin A regulate cellular proliferation and differentiation in epithelial cells, monocytes, and lymphocytes. A variety of vasculitic syndromes such as pulmonary capillaritis, polyarteritis nodosa (PAN), and ANCA vasculitis have been described with retinoids. pANCA positivity has been reported in some of these cases. Other drugs such as hydralazine, etanercept, erlotinib, and PTU have been associated with vasculitis as well.

2. **SYSTEMIC SCLEROSIS**: Rarely systemic sclerosis (SS) has been associated with ANCA vasculitis. Some of reported SS cases with ANCA vasculitis are thought to exhibit the characteristic clinical manifestations of MPA, although ANCA positivity in SS is uncommon. When rapid kidney failure or RPGN with active urine sediments, pulmonary hemorrhage and/or systemic inflammatory manifestations are observed in patients with SS having positive ANCA, the possibility of MPA should always be considered.

3. **AORTIC REGURGITATION**: Cardiac valvular involvement in ANCA associated systemic vasculitides is rarely reported. Most of these valvular lesions are due to granulomatosis with polyangiitis (Wegener's), and half are present when the diagnosis of vasculitis is made. Aortic regurgitation is the most common valvular lesion, and often requires semi-urgent valve replacement.

4. **HYDRALAZINE**: Hydralazine is known to cause drug-induced lupus erythematosus, but has rarely been reported to cause ANCA positive vasculitis. Patients with hydralazine-induced vasculitis typically have a more severe course than those with hydralazine-induced lupus, predominantly due to renal vasculitis. The incidence of hydralazine-induced vasculitis is dose and exposure dependent, with a mean dose of 142 mg/day and mean duration of exposure 4.7 years. Numerous antibodies are associated with hydralazine including anti-MPO antibodies, ANA, anti-histone antibodies, anti-dsDNA antibodies, antiphospholipid antibodies, and anti-elastase antibodies. The possibility of hydralazine-induced vasculitis should be considered when patients treated with hydralazine develop a pulmonary-renal syndrome. Early diagnosis and prompt discontinuation of the drug is necessary for the treatment of hydralazine-induced ANCA vasculitis.
5. ETANERCEPT: Etanercept among other tumor necrosis factor inhibitors including infliximab and adalimumab used in the treatment of rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis are a rare cause of ANCA vasculitis and other autoimmune disorders including lupus like syndrome and autoimmune hepatitis. TNF alpha inhibitors have been shown to up-regulate some aspects of immune function, and the possibility that this agent may precipitate or exacerbate vasculitis in some individuals has to be considered.

6. LUPUS NEPHRITIS: Anti-MPO antibodies are not uncommon in lupus patients, but it is unclear if they are pathogenic. There are case reports of lupus nephritis that also presented with features of ANCA vasculitis and alveolar hemorrhage, suggesting a combination of lupus nephritis and ANCA disease. Although very rare, this can be devastating. In summary, there are many medication- and disease- related causes of secondary ANCA vasculitis. The majority of ANCA vasculitides are idiopathic, and no secondary cause is found.