

(cont) side effects, they can still exacerbate parkinsonism. If antipsychotic therapy is needed, quetiapine (Seroquel) is often well tolerated in low doses (starting with 12.5-25 mg) by PD patients. Given their propensity to develop delirium, older PD patients should not be treated with anticholinergic agents or benzodiazepines, since they may trigger or exacerbate acute confusion and delirium.

Nonpharmacologic Interventions. Patient with parkinsonism are prone to orthostatic hypotension, constipation, urinary difficulties, falls and deconditioning. Inpatient care should include a plan for early and daily mobilization with early involvement of physical and occupational therapists. Indwelling catheters and other tethers should be avoided. Nonmotor complications of PD, such as constipation, depression and orthostatic hypotension are generally treated as with other patients. For patients with longstanding PD, complex medication regimens, disease complications or inability to take oral medications, early involvement of the patient's neurologist or expert in movement disorders is advised.

HOSPITALIST CONFERENCE & LUNCHEON

MISSOURI ACP MEETING

SATURDAY, SEPTEMBER 26, 12:15 PM

TAN-TAR-A RESORT, LAKE OF THE OZARKS

TOPIC: HOSPITAL ACQUIRED INFECTIONS

<http://www.acponline.org/meetings/chapter/mo-2009.pdf>

CASE OF THE MONTH

Ahmad Tuffaha MD, UMKC

P-ANCA Vasculitis in a Patient with Alpha-1-Antitrypsin Deficiency: A Possible Mechanism

Introduction:

Antineutrophil cytoplasmic antibody (ANCA) testing plays a critical role in the diagnosis and classification of vasculitis. These antibodies are strongly associated with Wegener's granulomatosis, microscopic polyangiitis and Churg-Strauss syndrome. They are directed against a variety of autoantigens, including proteinase 3 (PR3) and myeloperoxidase (MPO) [1]. On the other hand, alpha-1-antitrypsin (AAT) is the major inhibitor of PR3 while MPO is an inhibitor of AAT. It is well known that AAT deficiency is associated with emphysema and liver disease. The protein is encoded by a gene with multiple different alleles classified by the protease inhibitor (PI) system (PI*MM = homozygous normal, PI*ZZ = homozygous deficient). The PI*ZZ phenotype carries a high risk for development of emphysema and liver disease [2]. (continued, page 3)

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Case Report:

A 50 year old white female presented with progressive myalgia involving the lower extremities, associated with malaise and anorexia. She complained of bilateral jaw pain with chewing but had no abnormalities of vision. She did not have cardiopulmonary or upper respiratory symptoms. She eventually developed numbness of the lower extremities and a left-sided foot drop, consistent with mononeuritis multiplex. The patient was known to be homozygous for the PP*ZZ phenotype of ATT deficiency. However, she did not have any evidence of active lung or liver disease. Her past medical history was also significant for hypothyroidism and migraines. Family history was remarkable for ATT deficiency in her sister, who had both emphysema and liver cirrhosis.

Physical exam revealed a left sided foot drop and decreased sensation to light touch distal to the knees. No other neurologic deficits were identified. Small knee effusions were evident but no rash was observed.

Testing for p-ANCA and anti-MPO antibodies yielded positive results. Her CRP was 48 mg/dl and her ESR was 85mm/hr. Temporal artery biopsy was normal. The patient was diagnosed with ANCA associated vasculitis and treated with prednisone and cyclophosphamide. Her symptoms resolved and her foot drop markedly improved within 6 months.

Discussion:

The biologic mechanisms which result in this association are unknown but it has been postulated that AAT deficiency leads to increased PR3 in a pro-inflammatory environment [3,4]. On the other hand, AAT is inactivated by the release of myeloperoxidase from activated neutrophils. Any mechanism that inactivates MPO would result in increased AAT activity. This might mean that antibodies directed against MPO may interfere with its function and result in amplified AAT activity (and a lowered risk of tissue damage in AAT deficiency); this could explain the lack of emphysema in this patient. In other words, it is known that patients with PI*ZZ phenotype have an AAT activity level that is 10-20% of normal. Anti-MPO antibodies inhibit MPO mediated inactivation of AAT, resulting in higher levels of AAT activity (above the 10-20% range), which may protect against the development of early onset emphysema, commonly associated with the PI*ZZ phenotype.

This case thus highlights the association between two relatively rare diseases and postulates a mechanism for this association. It also helps us to understand the nature of autoimmune disease and the potential for future treatment modalities.

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References:

1. Sghiri et al., Antineutrophil cytoplasmic antibodies and associated diseases, *Pathol Biol*, July, 2009; 57:398-402
2. Camelier et al., Alpha-1 antitrypsin deficiency: diagnosis and treatment, *J Bras Pneumol*, July, 2008; 34:514-27
3. Patterson et al., Alpha-1 antitrypsin deficiency and Henoch-Schonlein purpura associated with anti-neutrophil cytoplasmic and anti-endothelial cell antibodies of immunoglobulin-A isotype, *J Cutan Pathol*, Apr 2005; 32:300-306
4. Adrian et al., Analysis of ANCA: Frequency and specificity in a sample of 191 homozygous PI*ZZ alpha-1 antitrypsin deficient subjects, *Nephrol Dial Transplant*, 2001; 16:39-44