CASE REPORT

α1-Antitrypsin deficiency in a patient diagnosed with granulomatosis with polyangiitis

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SUMMARY

Granulomatosis with polyangiitis is a rare type of vasculitis that affects small-sized and medium-sized vessels. Any organ system can become affected, but it most commonly affects the upper airways, lungs and kidneys. The α1-antitrypsin deficiency is another rare disease that involves a genetic deficiency in the enzyme antitrypsin, which is produced in the liver and protects the lung against proteinases. The simultaneous occurrence of these two diseases is very rare and has been described. We present a case of granulomatosis with polyangiitis limited to the upper airways, and α1-antitrypsin deficiency occurring in the same patient. The patient presented with recurrent upper airway infections. The patient was treated with steroids and azathioprine which prevented recurrence of symptoms. High clinical suspicion of the concomitant occurrence of α1-antitrypsin deficiency in patients with vasculitis is essential to provide patients with adequate screening and treatment.

BACKGROUND

The case highlights the association between granulomatosis with polyangiitis and α1-antitrypsin (AAT) deficiency. This association is rare, and the mechanism remains unknown, but it has significant clinical implication. Patients with this association tend to have more aggressive systemic vasculitis. Increasing the awareness of such an association helps clinicians identifying AAT deficiency in vasculitis patients and thus starting adequate screening and treatment.

CASE PRESENTATION

A 25-year-old woman was referred to the rheumatology clinic with symptoms of recurrent sinusitis. The patient was fairly healthy, with no significant medical history. She did not smoke, drink alcohol or use illicit drugs. The patient was experiencing recurrent sinus infections for 3 years, requiring multiple courses of antibiotics. She also suffered from low-grade fevers, night sweats and chronic fatigue. She underwent an extensive ear, nose and throat evaluation including septoplasty and right maxillary antrostomy and right maxillary anterior window with no relief. Suspicion for an underlying autoimmune disease was raised.

INVESTIGATIONS

Biopsies from nasal mucosa and upper airways from two different occasions were non-confirmatory showing damaged vessels from cautery with no evidence of granulomas but could not exclude an underlying vasculitis.

Serology showed normal erythrocyte sedimentation rate, normal complement levels, negative antinuclear antibody and antidouble-stranded DNA, rheumatoid factor and anticyclic citrullinated peptide antibody.

The perinuclear antineutrophil cytoplasmic antibodies were negative and the cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) were positive at 1:80 (negative is<1:20). Her urinalysis was negative for dysmorphic red blood cells or casts.

She was also found to have AAT deficiency with PiZZ phenotype. A chest CT scan showed normal lung parenchyma. Her pulmonary function and liver function tests were normal. A right upper quadrant ultrasound showed a normal liver texture. Liver biopsy ruled out cirrhosis.

TREATMENT

The patient was treated with a prolonged course of prednisone and azathioprine.

OUTCOME AND FOLLOW-UP

The patient's symptoms completely resolved.

She is being followed by pulmonary and gastrointestional for her associated AAT deficiency.

DISCUSSION

The simultaneous occurrence of these two rare diseases would be very unlikely unless an association exists between the two. The AAT is a direct inhibitor of PR3 protein among other cytoplasmic enzymes. It has been postulated that deficiency of AAT leads to decreased inhibition of PR3 protein and thus increased stimulation of the immune system to produce autoantibodies against it known as cANCA.[1] It is also known that cANCA is increased in Wegner's granulomatosis and might be reflective of disease activity. However, Vincent Esnault *et al*[2] showed that patients with Pizz phenotype had ANCA not directed against PR3 and did not show symptoms of vasculitis, which indicates that the relationship is not straight forward. In addition, other studies have shown that a significant number of patients with increased levels of cANCA are found to have AT-deficiency phenotype,[3] mostly of the severe (ZZ) or moderately severe phenotypes (MZ, IS, MS). In many studies, the disease activity of the vasculitis was shown to be related to the AAT deficiency, with the ZZ phenotype being associated with the widespread and severe vasculitis irrespective of the AAT levels in blood.[4] The AT protein level in blood does not necessarily need to be abnormal or low.[5] One plausible explanation for that is the fact that

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AT is an acute phase reactant and levels in blood increase during inflammation. However, low levels have been also associated with more severe cases and widespread vasculitis.[5]

The exact mechanism of the occurrence of the two diseases remains unknown and requires further studies.[6] In addition, there are no guidelines that describe whether every patient with cANCA vasculitis should be tested for AT-deficiency or vice versa, and what would be the implication of this on the treatment of the two diseases. But it is important to highlight that clinicians should be aware of such an association and should test for AT-deficiency and phenotype in patients with severe widespread vasculitis or concomitant lung emphysema or liver disease.[4]

- OVID/MEDLINE search of granulomatosis with polyangiitis (Wegner's) and α1-antitrypsin deficiency reveals eight references.
- OVID/MEDLINE search of Vasculitis and α1-antitrypsin deficiency reveals around 30 references.

Learning points

- An association between vasculitis and α1-antitrypsin deficiency exists and both disease can concomitantly occur in the same patient.
- Patients with vasculitis who are found to have α1-antitrypsin deficiency of the ZZ allele tend to have more severe and systemic vasculitis.
- The mechanism of such an association remains unknown and studies are needed to determine when to screen vasculitis patients for α1-antitrypsin deficiency.

Contributors Both the authors were responsible for the overall content. SA is managing the patient. HI was responsible for doing the literature search.

Competing interests None.

Patient consent Obtained.

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