Case report
c-ANCA-associated vasculitis in patients with ulcerative colitis: a case report

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ABSTRACT

The pulmonary manifestations of ulcerative colitis (UC) are rare and include inflammation of small and large airways, parenchymal disease and serositis among others. A substantial proportion of patients with inflammatory bowel disease, particularly those with ulcerative colitis present positive ANCA, most p-ANCA pattern. We present a case of patient with ulcerative colitis, with positive c-ANCA, which progressed to hemoptysis associated with radiological findings consistent with pulmonary vasculitis.

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INTRODUCTION

Pulmonary manifestations of ulcerative colitis (UC), which are rare, include pulmonary infections, bronchiectasis, chronic bronchitis and cryptogenic organising pneumonia (which was previously described as bronchiolitis obliterans organising pneumonia (BOOP)). Although pulmonary lesions are rarely recognised in UC patients, these lesions are not only capable of producing persistent and significant symptoms but also caus-
ing destructive and irreversible lesions in airways. It is difficult to diagnose these abnormalities in UC patients, largely because pulmonary manifestations can arise when UC is in remission and can even develop after colectomies have been performed. The presence of anti-neutrophil cytoplasmic antibodies (ANCA) suggests an immune system disorder. A cytoplasmic ANCA (c-ANCA) pattern is observed in 70-80% of patients with Wegener’s granulomatosis (WG), whereas a perinuclear ANCA (p-ANCA) pattern is primarily observed in patients with microscopic polyangiitis (MPA) or Churg-Strauss syndrome and in 60-70% of patients with UC. This phenomenon indicates that these autoimmune diseases may exhibit similar pathophysiological characteristics.

The authors describe the case of a c-ANCA-positive UC patient with pulmonary manifestations.

Case report

The patient was a 22-year-old female who had been diagnosed with UC for six years (based on bloody diarrhoea and abdominal pain). Two years prior to the current study, the patient presented with ulcerated skin lesions on the lower limbs; biopsy results were compatible with leukocytoclastic vasculitis (fig. 1).

The patient was admitted with complaints of one day of coughing, large-volume haemoptysis and dyspnoea following moderate- to low-effort activities. She did not present with fever or other symptoms, and neither recurrent sinusitis nor ocular/otological complications were reported.

Daily doses of 10 mg prednisone, 200 mg azathioprine, 50 mg amitriptyline and 20 mg omeprazole were prescribed.

A physical examination revealed pallor and tachypnoea (with a respiratory rate of 44). Pulmonary auscultation identified diminished breath sounds in the right hemithorax and diffuse crackles.

Laboratory tests upon admission produced the following results: Hb = 7.6 g/dL; haematocrit = 24.7%; 7,260 leukocytes/mm³ with 38% band neutrophils; 89,000 platelets/mm³; creatinine = 0.9 mg/dL; and ESR (erythrocyte sedimentation rate) = 100 mm. Electrolyte levels were normal. Two sputum samples were negative for acid-fast bacilli. Tests were positive for c-ANCA (titre not available). Partial urinalysis revealed leukocyturia, hematuria (without dysmorphic erythrocytes), nitrituria and bacteriuria but the absence of proteinuria. Urine cultures contained 100,000 CFU of Escherichia coli. Tests of 24-hour proteinuria produced negative results.

Chest X-rays revealed multiple alveolar condensations. Computed tomography (CT) scans of the chest indicated areas of confluent consolidation in the right lung, in the basal segments of the left lower lobe and in the lingula; this consolidation was associated with regions with a “ground-glass-like” appearance. In accordance with radiological descriptions, the CT findings suggested diffuse pulmonary haemorrhaging.

The multisystem clinical presentation suggested a diagnosis of vasculitis that predominantly involved small vessels. Other possible diagnoses, including WG, primary amoebic meningoencephalitis (PAM), Churg-Strauss syndrome, cryoglobulinaemia, systemic lupus erythematosus and systemic infections (such as leptospirosis), were also considered. The positive c-ANCA findings strongly suggested a diagnosis of primary vasculitis. Antibiotic therapy with ceftriaxone was initiated to treat the observed urinary tract infection. Due to the severity of the lung injury, we opted to perform pulse therapy with methylprednisolone and cyclophosphamide. The patient’s symptoms went into complete remission, and her tomographic results improved. Because the patient responded fully to treatment, no lung biopsy was performed. Maintenance treatment involved the administration of monthly cyclophosphamide pulses, which produced a sustained response.

The evolution of laboratory test results

Table 1 indicates how the patient’s laboratory test results evolved over time.

Discussion

UC and Crohn’s disease are idiopathic inflammatory bowel diseases that are associated with a variety of extraintestinal pul-

<p>| Table 1 – Patient’s laboratory test results. |</p>
<table>
<thead>
<tr>
<th>Tests</th>
<th>1st DA</th>
<th>3rd DA</th>
<th>5th DA</th>
<th>9th DA</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb</td>
<td>7.6 g/dL</td>
<td>9.4 g/dL</td>
<td>9.0 g/dL</td>
<td>10 g/dL</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>24.7%</td>
<td>29.5%</td>
<td>28.3%</td>
<td>31.7%</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>7,260 x 10³</td>
<td>11,290 x 10³</td>
<td>10,300 x 10³</td>
<td>7,370 x 10³</td>
</tr>
<tr>
<td>Tests for AFB in sputum</td>
<td>1st sample negative</td>
<td>2nd sample negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial urinalysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukocytes</td>
<td>32,000/mL</td>
<td>12,800/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBCs</td>
<td>40,000/mL</td>
<td>6,000/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>Negative</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterioscopy</td>
<td>Intense bacteriuria</td>
<td>Absence of bacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c-ANCA</td>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1 – c-ANCA-associated vasculitis in a patient with UC. A skin biopsy indicating leukocytoclastic vasculitis.
monary manifestations. In particular, upper airway stenosis, tracheobronchitis, bronchiectasis, constrictive bronchiolitis, nodules, interstitial lung disease, BOOP, pulmonary vasculitis, eosinophilic infiltration, WG and apical pulmonary fibrosis have been reported in UC patients. The most frequently reported pulmonary symptoms associated with UC are nonspecific and include cough, purulent sputum and dyspnoea. Mahadeva et al. studied UC patients and reported that the primary abnormality observed in high-resolution chest CT scans of these patients was bronchiectasis, followed by air trapping and “tree-in-bud” patterns. Among the series of cases examined by Mahadeva et al., only two patients exhibited abnormalities that were suggestive of fibrosis; in addition, no associations between bowel disease activity and lung injury were reported.

Extant literature has indicated that 70-80% of individuals with WG present with c-ANCA and that 10% of individuals with WG present with p-ANCA. ANCA positivity increases as disease involvement becomes more diffuse. Positive p-ANCA patterns have been observed in 60-70% of UC cases. This type of ANCA pattern is associated with MPA and Churg-Strauss syndrome. A c-ANCA pattern suggests the presence of anti-proteinase 3 ANCA in serum, whereas a p-ANCA pattern is defined as any perinuclear fluorescence associated with ANCA; this perinuclear staining mostly corresponds to anti-myeloperoxidase ANCA. The p-ANCA subtype found in individuals with UC does not react to the same antigens that are found in patients with WG. Instead, in the context of UC, p-ANCA appear to be directed against a myeloid cell-specific 50 kD nuclear envelope protein. The importance of this finding has not yet been completely characterised.

Rosa et al. determined that no renal injuries were reported during a one-year follow-up of ANCA-positive patients with UC. This finding supports the hypothesis that if ANCA have the potential to induce renal injury, this potential is dependent on the antigenic specificity of these antibodies, particularly given that ANCA have different antigenic targets in WG and UC. In the patient examined in the current case study, no renal involvement was detected.

Prior reports have described cases in which the coexistence of WG and UC has been confirmed by lung biopsies without accompanying ANCA tests. The extant literature has also described pulmonary complications in UC patients who are similar to the pulmonary complications observed in WG patients. In these UC patients, certain histopathological tests revealed the presence of BOOP. Focal areas of BOOP have been observed in 44% of WG cases, and the aforementioned BOOP-like manifestations observed in UC patients may represent a variant of WG.

The authors report the case of a c-ANCA-positive UC patient who presented with pulmonary manifestations and whose imaging results were consistent with pulmonary vasculitis. The patient exhibited excellent clinical response to conventional treatments for ANCA-associated vasculitis. The clinical presentation suggested an overlap between UC and c-ANCA-associated vasculitis isolated to the lungs, which may represent a limited form of WG.

REFERENCES

3. Targan SR. The Utility of ANCA and ASCA in Inflammatory Bowel Disease. Inflammatory Bowel Diseases. 1999;5:61-3.