Churg-Strauss syndrome occurring during omalizumab treatment

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To the Editor,

The Churg-Strauss syndrome (CSS) is a rare type of primary vasculitis that involves small- and medium-sized blood vessels (1). The diagnosis of CSS is based on the American College of Rheumatology (ACR) criteria, which includes asthma, eosinophilia >10%, paranasal sinusitis, pulmonary infiltration, histological proof of vasculitis, and mono- or polyneuropathy (2). Fulfillment of four out of these six criteria is adequate for a positive diagnosis. The clinical course of CSS includes three consecutive phases comprising a prodromal phase characterized by respiratory symptoms (rhinosinusitis and asthma), a second phase where peripheral blood eosinophilia and eosinophilic tissue infiltrates are observed, and a third phase characterized by systemic vascular manifestations (3). Fever is a symptom generally observed in all the patients, although it can be very irregular, ranging from temperatures below 39°C or even 38°C in the majority of the patients to 40°C in rare cases. The fever generally subsides some time before death (1). CSS is a rare disease and its prevalence is 13/1,000,000 in the general population (4). Omalizumab is a humanized monoclonal antibody against IgE that is effectively used to treat persistent severe asthma. Omalizumab significantly decreases asthma exacerbation rates in patients with severe persistent asthma (5).

A 31-year-old male patient was admitted to the hospital with a fever of 38.4 °C, dyspnea, and abdominal pain. He was under omalizumab treatment because of persistent asthma. He has also been suffering from recurrent nasal polyps for the past 2 years. His physical examination revealed bilateral rhonchi in his lungs and abdominal tenderness.

His laboratory results were as follows:
- Hemoglobin: 14.4 g/dL; white cell count: 15500/mm3; eosinophils: 45%(6990/mm3); thrombocytes: 270000/mm3;
- erythrocyte sedimentation rate: 51 mm/h; C-reactive protein: 106 mg/L; creatinine: 0.7 mg/dL;
- alanine aminotransferase: 66 U/L; aspartate aminotransferase: 34 U/L; international normalized ratio: 1.09;
- rheumatoid factor: 44.1 IU/mL (reference range: <15 IU/mL); and total immunoglobulin E (IgE): 1080 IU/mL (reference range: <100 IU/mL). The patient’s anti-neutrophil cytoplasmic antibody and other autoimmune markers were negative. His abdominal radiography and abdominopelvic ultrasonography were observed to be normal.

On his third day at the hospital, hyperesthesia and severe pain developed in his legs. The electromyography (EMG) results were consistent with polyneuropathy. In the following days, erythematous maculae, papules, and hemorrhagic vesicles appeared in his lower extremities. The histological examination of the skin biopsy showed widespread eosinophilic infiltrations on the vessel walls (Figure 1). In addition, pulmonary infiltrates were observed in the chest radiography and his thoracic computerized tomography (CT) showed a ground-glass appearance in the right lower lobe. The colonoscopic biopsy performed to assess a possible involvement of his colon revealed eosinophilic leukocytes in the submucosal layers of the vessels (Figure 2). Considering all these findings, the patient was diagnosed with CSS according to the ACR classification. At the time of the diagnosis, all the six diagnostic criteria were fulfilled. The patient was started on a regimen of high dose intravenous corticosteroids (methylprednisolone 1 mg/kg). Five days later, the skin lesions subsided, the eosinophil level decreased to 5%, and his fever returned to normal.

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The safety and efficacy of omalizumab in asthma treatment are controversial and additional data are required to evaluate this therapy option. Two main hypotheses have been considered by the authors. Firstly, omalizumab plays a direct causative role in the development of CSS, although its mechanism is yet to be cleared. Secondly, the CSS had become manifest after the withdrawal from the corticosteroid therapy. The first case of a patient who developed CSS under omalizumab treatment was reported by Winchester et al (6). In the
following years, similar cases were reported by clinicians where they discussed the causal relationship between CSS and omalizumab (7, 8). Wechsler et al. (9) has conducted a study on 13 patients and has concluded that omalizumab treatment may unmask CSS because of the weaning of corticosteroids in some asthma patients or may delay corticosteroid treatment allowing for CSS to manifest itself.

Clinicians should consider CSS in the differential diagnosis of the asthmatic patients who present with fever and dyspnea, particularly if they are under treatment with omalizumab.

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References