Montelukast-associated Churg-Strauss syndrome with mononeuritis multiplex

Sir,

A 59-year-old man presented to us with numbness of legs of 3 months duration. He had a history of diabetes mellitus since 1 year. He had developed spontaneously resolving hyperpigmentation over forehead, back, hands, and legs and erythematous rashes over the trunk 3 months earlier followed by gradual onset of numbness and weakness in both legs and difficulty in buttoning. Over the last 1 week it had suddenly worsened and became chair-bound. He had a history of late onset asthma (for the past 2 years), which was controlled with inhaled corticosteroids, beta agonists, and a combination of montelukast and cetirizine; and late onset hypothyroidism on treatment with levothyroxine 100 μg. On examination, he had pedal edema and scattered erythematous rashes over back, buttock, right leg, and right forearm without nerve thickening. He had bilateral claw hand and foot drop with grade 0 weakness in both distal legs. There was sensory impairment in right fifth finger, left finger tips, and both lower limbs (LL) upto knees. Blood reports showed the following; hemoglobin (Hb) 11.7 g%, total count (TC) 11,700, eosinophils 14% (absolute eosinophil count 1,500), platelets 300,000, erythrocyte sedimentation rate (ESR) 77 mm/h, C-reactive protein 29mg/L, human immunodeficiency virus (HIV)/hepatitis B surface antigen (HBsAg)/hepatitis C virus (HCV) were negative, perinuclear anti-neutrophil cytoplasmic antibodies (P-ANCA)/cytoplasmic ANCA (C-ANCA) were negative, anti-double stranded deoxyribonucleic acid (dsDNA) was 29.7 IU/ml, rheumatoid arthritis (RA) factor 345 IU/ml, liver function test (LFT) showed albumin-globulin reversal, and creatinine was 0.7 mg%. Urine microscopy showed granular casts with 20-25 red blood cells (RBCs)/high power field (HPF) without proteinuria and HbA1c was 6.4%. Chest X-ray and paranasal examination were normal. Nerve conduction studies showed absent sensory nerve action potentials (SNAPs) in the sural nerves and left ulnar nerve and absent compound muscle action potentials (CMAPs) in both peroneal and right ulnar nerves. The study was suggestive of mononeuritis multiplex.

A sural nerve biopsy showed perineural fibrosis and epineural medium sized blood vessels with endothelial cells destruction and fibrinoid necrosis on the luminal aspect, perivascular and transmural dense infiltration of neutrophils and eosinophilic mixed with lymphocytes with karyorrhectic debris [Figure 1a-c]. There was epineural vascular proliferation with perivascular lymphoplasmacytic inflammatory infiltration and hemosiderophages. An occasional thrombosed blood vessel was seen with transmural and perivascular infiltration of eosinophils [Figure 1d]. The clinical and histopathology findings were consistent with Churg–Strauss syndrome (CSS). As he was taking montelukast 10mg for the past 2 years, a Naranjo adverse drug reaction probability scale score of 5 was calculated and suggested a high probability of montelukast-associated CSS.[1] Montelukast was discontinued and he was started on intravenous (IV) methylprednisolone 1 g/day × 5 days followed by 40 mg per os (PO) of prednisolone. Over the next 10 days, he improved and started ambulating independently.

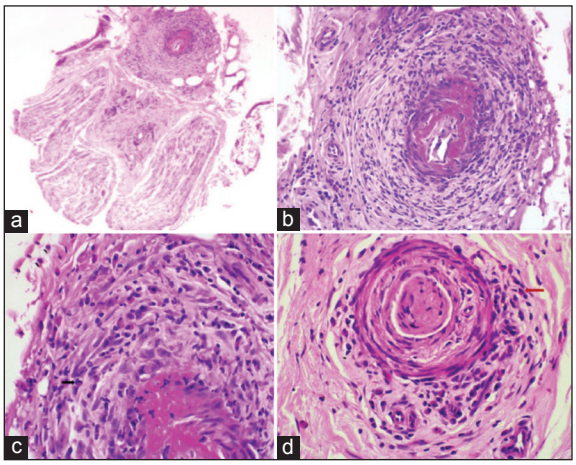

Figure 1: (a) Showing epineural, medium-sized blood vessel with features of leukocytoclastic vasculitis with infiltration of eosinophils (hematoxylin and eosin (H and E), ×5). (b) Fibrinoid necrosis, endothelial destruction, karyorrhectic debris, and transmural infiltration of neutrophils, lymphocytes, and eosinophils (H and E, ×20). (c) Transmural infiltration of neutrophils and eosinophils (black arrow; H and E, ×40). (d) Thrombosed blood vessel with transmural and perivascular infiltration ofeosinophils (red arrow; H and E, ×10)

Montelukast and other leukotriene-receptor antagonists (LTA) use are associated with a 4.5-fold higher risk of CSS.[2] Montelukast is a selective competitive antagonist of cysteinyl leukotriene receptors and increases levels of the leukotriene LTB4 leading to vasculitis by virtue of its potent chemoattractant property for neutrophils and eosinophils. CSS can be diagnosed if at least four out of six American College of Rheumatology (ACR) 1990 criteria are fulfilled; asthma, eosinophilia >10%, mononeuropathy (including multiplex) or polyneuropathy, nonfixed pulmonary infiltrates on chest X-ray, paranasal sinus abnormality, and biopsy containing a blood vessel with extravascular eosinophils.[3] More than four of these criteria had a sensitivity of 85% and a specificity of 99.7% for CSS. Mononeuritis multiplex is one of the most common peripheral nervous system manifestations of CSS and early treatment with steroids can stop disease progression.[4] Our patient fulfilled four of the ACR criteria and improved after drug withdrawal and steroid administration. It is essential to recognize secondary CSS as discontinuation of the offending agent is also imperative.

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