G124 Acute Eosinophilic Myocarditis in a Churg-Strauss Syndrome Case Treated With Montelukast: Immunohistochemical Study to Explain Pathophysiology

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The goal of this presentation is to present an uncommon fatal case of acute eosinophilic myocarditis in a 18-year-old man with Churg-Strauss Syndrome (CSS) treated with Montelukast. A complete methodological forensic approach by means of autopsy, histological, and immunohistochemical examinations led us to the conclusion of for a CSS with massive cardiac involvement.

This presentation will impact the forensic science community by showing how the absence of specific symptoms of cardiac involvement in a multiorganic CSS in active phase can make an early diagnosis difficult. This case report illustrates the importance of early diagnosis of CSS and underlines the possible relationship between LRA and CSS and its etiopathogenetic mechanism.

CSS is a systemic vasculitis with multiorganic involvement and represents a rare disorder with an incidence between 1.3 and 6.8 cases per 1,000,000 patients per year. It evolves through a prodromal phase characterised by asthma and atopic allergies (rhinitis) and eosinophilic infiltrative disease, a second phase with eosinophilic infiltration of tissues, and a third phase (vasculitic) characterized by systemic vasculitis. Three main histological features characterize it: necrotizing vasculitis, tissue infiltration by eosinophils, and extravascular granulomas. All organs may be involved (peripheral nerves, lungs, skin), but severe gastrointestinal, renal, cardiac, and central nervous system manifestations are associated with a poor prognosis. The heart is the major target (16% – 50% of cases) and its involvement is the major cause of death in CSS (48%), usually associated with an ANCA-negative status. Cardiac disease includes myocarditis, coronary vasculitis, valvular heart abnormalities, congestive heart failure, and pericarditis. The aetiology and pathogenesis of eosinophilia and tissue damage is unknown. On a cellular level, a strong shift toward a Th2-like response with massive T-cell activation and IL-4, IL-13, IL-10, and IL-5 production is evident. CSS patients usually have high serum levels of IgE. In the active phase, high levels of eotaxin-3 (a chemokine-involved organ damage) were found. The diagnosis of CSS is problematic, because none of the disease features are themselves pathognomonic and the numerous findings may have presented and evolved over a period of years. There are six clinical criteria proposed by the American College of Rheumatology (asthma, blood eosinophilia greater than 10% on differential white blood cell count, mono or poly neuropathy, migratory or transient pulmonary infiltrates detected radiographically, paranasal sinus abnormality, biopsy containing a blood vessel with extravascular eosinophils) with four being necessary for CSS to be diagnosed. However, these criteria are not pathognomonic in the absence of histologically proven vasculitis (eosinophil-rich and granulomatous inflammation involving the respiratory tract and necrotizing vasculitis associated with asthma and eosinophilia). There are two different phenotypes, one “vasculitic,” with manifestations due to small-vessel vasculitis (purpura, mononeuritis multiplex, glomerulonephritis), and one “eosinophilic,” in which organ damage mainly results from tissue eosinophilic infiltration (pulmonary infiltrates, cardiomyopathy). ANCA positive patients usually show a more vasculitic phenotype. Although CSS is a rare disease, the number of reports increased in the last two decades after Leukotriene Receptor Antagonists (LRA) became available. In fact, in recent years several studies have reported the possible relationship between use of LRA and CSS expression. However, whether these drugs have a direct pathogenic role remains controversial.

Reported is a case of an 18-year-old man who was found lifeless at home in the bathroom by his parents. During the night he presented sweats, pain, and numbness in the leg. The extended family hadn’t a history of sudden death or atopic disease. Two years before rhinitis, sinusitis, eosinophilia, and, above all, asthma were compared and treated with corticosteroids, antibiotic and antileucotrienic therapy (montelukast). The prick tests were negative. Serologic and PCR tests were negative for respiratory viruses and for *Legionella*, *Chlamydia,* and *Mycoplasma*. ANCA blood test was negative; the serum concentration of IgE was high. The last CT scan revealed bilateral ground-glass nodular lung opacities.

A complete postmortem examination was performed. The internal examination revealed only a polivisceral congestion and pulmonary edema. The surface of the heart showed opacity of the epicardium. The heart had a normal shape, size, and weight. The coronary arteries were normal and without significant stenosis or thrombotic occlusion. The valves were not thickened. The myocardium was flabby and pale with scattered patches of red and yellow-gray discoloration. The histological examination of the heart revealed diffuse and extensive infiltration by eosinophils with extensive loss of myocardial cells, pericarditis, necrotizing eosinophilic vasculitis, including small and epicardial coronary arteries, and colliquative myocytolysis.

The lungs showed eosinophilic pneumonia, necrotizing vasculitis with intimal and medial infiltration by eosinophils and extravascular granulomas, consisted of epithelioid macrophages and giant cells around large necrotic centers in a densely packed area of eosinophils with presence of the specific granules and nuclear debris. These granulomas were surrounded by eosinophils. The kidneys showed scattered necrotizing vasculitis and infiltration by eosinophils. Other organs, including the brain, showed no lesions.

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An immunohistochemical examination of heart, lung, and kidneys samples with antibody anti CD4, CD8, CD45, EMBP (eosinophil major basic protein), IL10, TNF-alfa, and anti eotaxin-3 was performed to confirm diagnosis. The death was attributed to acute heart failure due to acute eosinophilic myocarditis in CSS.

Churg-Strauss Syndrome, Eosinophilic Myocarditis, Montelukast Therapy

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