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Clinical History:
A 51 year old man with asthma and intermittent eosinophilia presented with chest symptoms. He died on the same day despite treatment with antibiotics and steroids. Admission blood count showed a raised neutrophil count of 8.2, normal eosinophils and ESR of 2mm/hr.

Pathological Findings:
The heart was large and dilated (700g) with a haemorrhagic pericardial effusion. The coronary arteries looked diffusely thickened and focally narrowed. There were areas of scarring in the free wall of the left ventricle particularly subendocardially.
Nil else described at autopsy.

Microscopic Findings
Histologically, the epicardial arteries show extensive arteritis with a prominent eosinophilic component as well as plasma cells and lymphocytes. There was marked intimal and adventitial involvement with focal involvement of the media . No thrombosis is noted. Inflammation is focal . There are focal collections of macrophages. Subtle area of eosinophilic necrosis in the media is noted but there are no definite granulomas or giant cells seen. There is a mild focal interstitial eosinophil and lymphocyte infiltrate within the myocardium but no intramural vasculitis. There is widespread subendocardial fibrosis admixed with focal mixed inflammation and fatty metaplasia. The pericardium shows reactive changes with eosinophilic infiltrate .

Diagnosis:
Eosinophilic coronary vasculitis with myocardial fibrosis .
? Churg Strauss syndrome with eosinophilic coronary vasculitis. He had a raised eosinophil count of 3 and an ESR of 7 five months prior to death.
The big differential is spontaneous dissection of the coronary arteries which will have a prominent adventitial eosinophilic infiltrate but there is medial dissection with intramural haematoma formation at sites of the adventitial inflammation. Away from dissection no inflammation is noted. Also media and intima is not involved by eosinophils .(1)

EOSINOPHILIC VASCULITIS

Eosinophilic vasculitis is seen in the context of Churg Strauss syndrome. Isolated eosinophilic vasculitis involving the coronary arteries is rare with case reports(2),(3)

Churg-Strauss Syndrome

Churg-Strauss syndrome (CSS) is a necrotizing systemic vasculitis with extravascular granulomas and eosinophilic infiltrates of small vessels. CSS is usually revealed by nonspecific signs of necrotizing vasculitis in a context of late-onset asthma and blood eosinophilia. It is considered a systemic vasculitis with the highest prevalence of

cardiac involvement and can lead to rapid-onset heart failure due to specific cardiomyopathy. Pericardial effusion may also occur during CSS. CSS may present as tamponade, with or without other visceral involvement. Remission was obtained with corticosteroids and cyclophosphamide. (4) Churg-Strauss syndrome (CSS), first described in 1951, is a rare vasculitis of small- and medium-sized vessels. It is characterized by a constant association with asthma and eosinophilia, and by the presence of anti-myeloperoxidase (MPO) anti-neutrophil cytoplasmic antibodies (ANCA) in ~40% of the patients. Vasculitis typically develops in a previously asthmatic and eosinophilic middle-aged patient and most frequently involves the peripheral nerves and skin. Other organs, however, may be affected and must be screened for vasculitis, especially those associated with a poorer prognosis, such as the heart, kidney, and gastrointestinal tract, as assessed by the recently revised Five-Factor Score (FFS). Overall survival of CSS patients is excellent, but relapses are not uncommon and require maintenance or steroid-sparing therapies, depending on the original FFS-based prognosis at diagnosis. All patients require corticosteroids, often for prolonged periods, combined with immunosuppressants [e.g., induction (cyclophosphamide) and maintenance therapy (azathioprine)], for those with poorer prognoses. Recent insights, especially concerning clinical differences associated with ANCA status, showed that CSS patients might constitute a heterogeneous group, both clinically and pathogenically. (5)

If the heart is involved patients may present with fever and progressive heart failure due to pericarditis, eosinophilic endomyocarditis, and myocardial necrotizing vasculitis(6) Cardiac involvement may also lead to acute and constrictive pericarditis, myocarditis and endocarditis, as well as ischemic cardiomyopathy. Endomyocardial fibrosis similar to Loeffler's syndrome also occurs. (7)The outcome can be fatal(8).It may also present as sudden death with no prodromal symptoms or history.(9) I can form a significant number of sudden death cases in non atherosclerotic coronary pathology (10)The aorta may also be involved as well as cardiac valves (11)

A wide range of disorders give rise to eosinophil counts greater than 1.5 X 10(9)/l (hypereosinophilia) and cardiac injury. The best known of these is eosinophilic endomyocardial disease (Loffler's endomyocardial fibrosis), which occurs as a major complication of the idiopathic hypereosinophilic syndrome. Here the heart damage appears to be a direct result of tissue injury produced by toxic eosinophil granule proteins within the heart. However, it is not known what causes the eosinophilia in these patients, why the eosinophils degranulate, or why the endocardium is especially susceptible to this type of injury. A number of parasitic infections may give rise to eosinophilic myocarditis. This is usually the result of the presence of the parasites within the myocardium where they die within inflammatory lesions, which may be extensive. Occasionally, drug reactions and rejection of a transplanted heart may

produce eosinophilic myocarditis. Allergic granulomatosis and vasculitis (the Churg-Strauss syndrome), which gives rise to granulomas involving the myocardium, and eosinophilic (hypersensitivity) myocarditis usually respond rapidly to treatment with steroids. However, diffuse myocardial involvement may lead to heart failure, and some of these patients may later develop dilated cardiomyopathy. (12)

Reference List

(1) Desai S, Sheppard MN. Sudden Cardiac Death: Look Closely at the Coronaries for Spontaneous Dissection Which Can Be Missed. A Study of 9 Cases. Am J Forensic Med Pathol 2010; 34(3):234-243.

(2) Arena V, Valerio L, Arena E, De Giorgio F, Stigliano E, Monego G et al. Isolated eosinophilic coronary arteritis. J Clin Pathol 2010; 63(5):469-471.

(3) Taira K, Tsunoda R, Watanabe T, Fujino A, Ogyu A, Ashikawa K. An autopsy case of isolated eosinophilic coronary periarteritis: a limited form of Churg-Strauss syndrome or a new entity? Intern Med 2005; 44(6):586-589.

(4) Agard C, Resident ER, Leguern V, Ponge T, Masseau A, Barrier JH et al. Churg-Strauss Syndrome Revealed by Granulomatous Acute Pericarditis: Two Case Reports and a Review of the Literature. Semin Arthritis Rheum 2007.

(5) Dunogue B, Pagnoux C, Guillevin L. Churg-strauss syndrome: clinical symptoms, complementary investigations, prognosis and outcome, and treatment. Semin Respir Crit Care Med 2011; 32(3):298-309.

(6) Frustaci A, Gentiloni N, Chimenti C, Natale L, Gasbarrini G, Maseri A. Necrotizing myocardial vasculitis in Churg-Strauss syndrome: Clinicohistologic evaluation of steroids and immunosuppressive therapy. Chest 1998; 114(5):1484-1489.

(7) Heger M, Bergler-Klein J, Zehetgruber M, Parschalk B, Thalhammer F, Maurer G et al. [Left ventricular dysfunction in Churg-Strauss syndrome]. Z Kardiol 2003; 92(8):677-681.

(8) Rupani A, Amonkar G, Deshpande J. Eosinophillic myocarditis and coronary arteritis in a fatal case of asthma. Indian J Pathol Microbiol 2010; 53(4):790-792.

(9) Val-Bernal JF, Mayorga M, Garcia-Alberdi E, Pozueta JA. Churg-Strauss syndrome and sudden cardiac death. Cardiovasc Pathol 2003; 12(2):94-97.

(10) Hill SF, Sheppard MN. Non-atherosclerotic coronary artery disease associated with sudden cardiac death. Heart 2010; 96(14):1119-1125.

(11) Segal OR, Gibbs JSR, Sheppard MN. Eosinophilic aortitis and valvitis requiring aortic valve replacement. Heart 2001; 86(3):245.

(12) Spry CJ, Take M, Tai PC. Eosinophilic disorders affecting the myocardium and endocardium: a review. Heart Vessels Suppl 1985; 1:240-242.