

## **THERAPEUTIC OPTIONS IN ACUTE PRESENTATION OF EOSINOPHIL INDUCED RESTRICTIVE CARDIOMYOPATHY**

Hypereosinophilic syndrome is a heterogeneous group of disorders characterized by persistent eosinophilia with evidence of organ dysfunction. Cardiac involvement is frequent and is the most common cause of death (1, 2, 3, 4). The eosinophil induced cardiac disease includes initial myocarditis and endocarditis eventually leading to endomyocardial fibrosis. The intermediate stage may include subendocardial endothelial damage with capillary thrombosis, mural thrombosis and progressive endomyocardial thickening (3). Clinical presentation is usually that of insidious onset of congestive heart failure due to restrictive cardiomyopathy (1). We present a case of rapidly progressive congestive heart failure due to restrictive cardiomyopathy without evidence of active myocarditis. Clinical course was highlighted by marked clinical and hemodynamic improvement upon left ventricular thrombectomy.

### **CASE REPORT:**

A 46 year old previously healthy caucasian male presented to his local community hospital with 2 to 3 week history of fever, episodes of chest pain, shortness of breath and a dry cough. The absolute eosinophil count was found to be in 14 to 1500/ $\mu$ L range. Echocardiogram showed a left ventricular mass. Coronary angiogram showed no significant disease. There was no improvement despite treatment with ace-inhibitors, diuretics, nitrates and glucocorticoids.

Upon transfer to our institution the patient was in moderate respiratory distress with initial physical examination significant for bibasilar rales, S3 gallop and systolic murmur consistent with mitral regurgitation. Resting gated radionuclide angiography showed left ventricular ejection fraction of 52% *EDV 191 cc, ESV 91 cc, SV 99 cc, EDVI 84 cc/m<sup>2</sup>, ESVI 140 cc/m<sup>2</sup>, SI 44 cc/m<sup>2</sup>. Mitral valve regurgitant fraction was 10%. A filling defect involving the inferoposterior and apical regions was noted. Transthoracic and transesophageal echocardiograms showed moderate mitral regurgitation and confirmed the large echodense mass. It was overlying the anterolateral wall and the apex, significantly reducing the left ventricular cavity size and causing restrictive pattern of cardiomyopathy. The septum, inferior wall as well as the right ventricle was spared. Right heart catheterization revealed severe pulmonary hypertension (pulmonary artery pressure of 78 mm Hg systolic and 38 mm Hg diastolic) and elevated left sided filling pressure (pulmonary capillary wedge pressure of 35 mm Hg). Cardiac index was 2.68 L/min per m<sup>2</sup> body surface area. Result of right ventricular endomyocardial biopsy was non-diagnostic showing hypertrophied fiber, some focal endocardial thickening and no increase in eosinophil.*

No secondary cause of eosinophilia could be identified despite thorough diagnostic evaluation. The eosinophil count during the hospitalization was found to be well controlled with combination of hydroxyurea and glucocorticoids and was noted to rebound upon withdrawal of these agents (maximum absolute eosinophil count was 1600/ $\mu$ L). Despite control of eosinophilia the patient exhibited rapid worsening of congestive heart failure. A combination of intravenous vasodilators, inotropic and adrenergic agents was used in various combinations with aggressive diuretic regimens. The best response was obtained using high dose intravenous furosemide infusion (500

mg to 1 gm per day) which was continued uninterrupted for several weeks. Attempts to discontinue the infusion resulted in acute pulmonary edema on more than one occasion.

Surgical removal of the left ventricular mass with preservation of the mitral valve was performed because of unsatisfactory response to medical therapy. The pathological examination revealed organizing mural thrombus. In addition, left ventricular needle biopsy showed endocardial fibrosis with rare eosinophils and no evidence of active myocarditis. Hemodynamic indices were excellent postoperatively including a cardiac index of 4.5 L/min per m<sup>2</sup> of body surface area, pulmonary artery pressure of 37 mm Hg systolic, 18 mm Hg diastolic and pulmonary capillary wedge pressure of 14 mm Hg. Repeat transthoracic echocardiogram showed mild mitral regurgitation and significant reduction of the left ventricular mass. Left ventricular systolic function remained normal. Resting gated radionuclide angiography revealed normalization of left ventricular dimensions. XXXXX XXXXX XXXXXX XXXXXX XXXXXX XXXXXX XXXXXX XXXXXX XXXXXX XXXXXX XXXXXX .

Congestive heart failure was well controlled postoperatively without vasodilator or inotropic support and the patient was discharged to home on oral diuretic regimen.

## **DISCUSSION:**

Empirically established diagnostic criteria for idiopathic hypereosinophilic syndrome include persistent eosinophilia of 1500 eosinophils/ $\mu$ L for at least six months (4). The acute nature of presentation in our patient did not allow enough time for strict diagnosis to be established. Treatment of eosinophilic heart disease included control of hypereosinophilia and management of heart failure. Digitalis, diuretics and afterload reducing agents have been used for the latter (1, 3). Corticosteroids appear to eosinophil induced acute myocarditis (2). Corticosteroids and cytotoxic drugs (hydroxyurea in particular) have been shown to control eosinophilia and improve survival (2, 3, 5).

Acute or subacute presentation of eosinophilic heart disease causing congestive heart failure has been associated with systolic dysfunction from acute myocarditis(6).Our case was unusual because of rapid clinical course despite no evidence of active myocarditis. It is conceivable that such a presentation may be related to reduction in size of the left ventricular cavity by formation of a large thrombus. This could have offset the hemodynamic balance in previously unrecognized sub clinical restrictive cardiomyopathy due to eosinophilic heart disease.

*Benefit of surgical endocardectomy and replacement of mitral valve for predominant left sided endomyocardial fibrosis in the chronic setting have been discussed in numerous reports (7, 8, 9, 10). To our knowledge this is the first detailed report of isolated left ventricular thrombectomy without scar excision or atrioventricular valve replacement. The procedure has previously been reported for right ventricular thrombus and also for left ventricular thrombus with mitral valve replacement (11, 12). We feel that this form of treatment should be considered as a viable as a viable option in patients with eosinophilic endomyocardial disease in the acute setting when medical management fails.*

Continuous intravenous infusion of furosemide has been suggested to be safe and more efficacious as compared to bolus therapy in congestive heart failure (13, 14). To our knowledge continuous prolonged high dose intravenous furosemide therapy like our case has not been previously documented in the literature.

*We believe this is the first report of combined clinical, hemodynamic, gated nuclear and echocardiographic feature before and after left ventricular mural thrombectomy for eosinophilic heart disease.*

## **REFERENCES:**

1. Parillo JE et al. The cardiovascular magnification of hypereosinophilic syndrome: prospective study of 26 patients, with review of the literature. *Am J Med* 1979; 67(4): 572-82.
2. Olsen EG and Spry CJF. Relation between eosinophilia and endomyocardial disease. *Prog. Cardiovasc Dis.*1985; 27: 241.
3. Fauci AS, Harley JB, Report WC, Ferrans VJ, Gralnick HR, Bjornson BH. The idiopathic hypereosinophilic syndrome: Clinical, pathophysiologic, and therapeutic considerations. *Ann Intern Med* 1982; 97:78-92.
4. Chusid MJ, Dale DC, West BC, Wolff SM. The hypereosinophilic syndrome: Analysis of fourteen cases with review of the literature. *Medicine* 1975; 54:1-27.
5. Arnold M, McGuire L and Lee JC. Loeffler's fibroplastic endocarditis. *Pathology* 1988; 20:79.
6. deMello DE, Liapis H, et al. Cardiac localization of eosinophil-granule major basic protein in acute necrotizing myocarditis. *N Engl J Med.* 1990; 323:1542-45.
7. Metras D, Coulibaly AQ, et al. Recent trends in the surgical treatment of endomyocardial fibrosis. *J Cardiovasc Surg* 1987;28:607.
8. Martinez EE, Venturi M, et al. Operative results in endomyocardial fibrosis. *Am J Cardiology.* 1989; 63:627.
9. Valithan Ms Balakrishnan KG, et al. Surgical treatment of endomyocardial fibrosis. *Ann Thoracic Surg.* 1987; 43:68.
10. Mady C, Pereira Barretto AC, et al. Effectiveness of operative and nonoperative therapy in endomyocardial fibrosis. *Am J Cardiology.* 1989; 15:1281.
11. Wrights RS, Simari RD, Orszulak TA, Edwards WD, Gleich GJ and Reeder GS. Eosinophilic endomyocardial disease presenting as cyanosis, platypnea, and orthodeoxia. *Ann Intern Med* 1992; 117; 482-83.
12. Ikaheimo MJ, Karkola PJ and Takkunen JT, Surgical treatment of Loeffler's eosinophilic endocarditis *Br Heart J* 1981; 45:729-32.
13. Lahav M, Regev A, et al. Intermittent administration of furosemide vs continuous infusion preceded by a loading dose for congestive heart failure. *Chest* 1992; 102; 3:725-31.
14. Gerlag PGG, van Meijel JJM. High-dose furosemide in the treatment of refractory congestive heart failure. *Arch Intern Med* 1988; 148:286-291.