BRIEF COMMUNICATIONS

HYPEREOSINOPHILIC SYNDROME: CAUSE OF PROSTHETIC VALVE OBSTRUCTION

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In 1975, Chusid and colleagues¹ defined hypereosinophilic syndrome as an unexplained eosinophilia lasting more than 6 months in the presence of end-organ involvement. Cardiac involvement occurs in more than 75% of patients with the hypereosinophilic syndrome. We report a case of prosthetic valve thrombosis caused by eosinophilic endocarditis.

Case report. A 23-year-old girl of Ghanan origin was referred to us for mitral regurgitation suspected to be of rheumatic origin. She was admitted in an acute condition with pulmonary edema, and an urgent mitral valve replacement with a 29 mm St. Jude Medical prosthesis (St. Jude Medical, Inc., St. Paul, Minn.) was performed. At operation, the gross appearance of the valve suggested a rheumatic origin. Incompetence was caused by lack of leaflet mobility and was not thought suitable for repair. Preoperative echocardiography did not reveal any significant findings apart from gross mitral regurgitation.

On postoperative day 2, she had pyrexia of 38° C. Her leukocyte count was 41.1×10^6 cells/ml with 81% eosinophilia. She also had diarrhea. Results of blood cultures, urine culture, and stool examination and cultures did not suggest any cause. Early morning on day 4, the patient became acutely breathless and was transferred to the intensive treatment unit. A diagnosis of mitral valve prosthetic obstruction was made. She was taken to the operating room and cardiopulmonary bypass was quickly established. At operation, there was heavy pannus formation over a previously placed prosthetic valve. This obstructed both leaflets. The valve was excised and replaced with a further 27 mm St. Jude Medical mechanical prosthesis. During attempts to wean the patient from cardiopulmonary bypass, there was gross right ventricular dysfunction. The lungs looked and felt granular and were extremely difficult to inflate. Because ours is an active extracorporeal membrane oxygenation (ECMO) center, the patient was given ECMO. She continued to receive ECMO for a period of 10 days. Her eosinophil count remained high. Meanwhile, all serologic tests for various parasites were done, with negative results. Steroid treatment were ultimately commenced. Because of bleeding

complications and failure to respond to ECMO, ECMO was removed, and the patient died on postoperative day 12.

Histologic examination of the native valve showed thickening of the valve cusp by dense, hyalinized, fibrous tissue. There was an increase in small-caliber blood vessels within the valve cusp. These vessels contained abundant eosinophils. At autopsy, the left ventricle showed apical endomyocardial fibrosis and marked fibrosis and thickening of the posterior mitral valve annulus. The histologic findings in the lungs were grossly masked by the ECMO and could not be commented on. The overall finding fits well with the diagnosis of eosinophilic endocarditis.

Discussion. Patients with idiopathic hypereosinophilic syndrome have a variety of clinical presentations. The most common is a systemic disorder in which cardiac disease is one component. High serum levels of eosinophilic cationic proteins, with potential hypercoagulable effects, contribute to the increased prevalence of thromboembolic episodes among these patients.

We had diagnostic difficulty with our patient. Hypereosinophilic syndrome is typically seen in men in their fourth decade who live in a temperate climate. Our patient was a young girl from a tropical country who had symptoms highly suggestive of rheumatic heart disease. Echocardiography did not reveal any evidence of endomyocardial fibrosis. The only positive finding was eosinophilia. Mild eosinophilia was recorded once 3 months before her operation, when the patient was seen with tenosinovitis of her wrist joint. In retrospect, all her symptoms could have been caused by eosinophilic endocarditis, as suggested by the histologic characteristics of her valve.

Review of the literature reveals that nine patients to date have undergone operation for hypereosinophilic syndrome involving the cardiac valves. Eight underwent mitral valve replacement and one underwent annuloplasty repair. Most of the authors reported using a xenograft in their patients. Harley and coworkers² in 1982 used a Björk-Shiley valve in their first patient and had to replace it as a result of thrombotic obstruction by a porcine Hancock valve. Davies and colleagues³ reported two cases, one of which involved mitral valve replacement with a Starr-Edwards valve, with no complications. The choice of valve prosthesis for this group of patients is difficult. Because of the rarity of the disease and the difficulty of diagnosis, as in our case, there are no data to evaluate the thrombotic potential and long-term structural integrity of available prosthetic valves in these patients. Mechanical valves are thrombogenic and mural thrombi are characteristic of hypereosinophilic endocarditis, so it would

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appear that a porcine heterograft prosthesis with additional anticoagulation would be beneficial. However, the toxic effects of eosinophilic granules on the xenograft remain to be evaluated. At autopsy in one such patient (Harley and colleagues²), although there were no mural thrombi, small thrombi were present on the bioprostheses despite treatment with warfarin.

Review of the literature⁴ further suggests that the exacerbations of symptoms in these patients, as in ours, should be treated with prednisolone 1 mg/kg and hydroxy urea 500 mg daily. Once the endocarditis is under control and remission of systemic symptoms has occurred, operation should be planned for relief of cardiac symptoms.

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A DEHYDROMONOCROTALINE-INDUCED PULMONARY HYPERTENSION MODEL IN THE BEAGLE

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Pulmonary hypertension (PH) is a poorly understood disease process for which no adequate therapy exists. Trials to gain a better understanding of PH have been hindered by the lack of relevant animal models. Although monocrotaline and hypoxia have both been used to generate PH in rats,^{1,2} rats are too small to allow hemodynamics to be evaluated accurately. We therefore tried to establish a model of PH in a larger animal, the beagle. However, a homogeneous model could not be produced in dogs by the administration of monocrotaline or by the long-term exposure to hypoxia. It is considered that monocrotaline is activated to a reactive metabolite in the liver and is then transported by red blood cells to the lung, where it initiates endothelial injury. The difference regarding the effect of monocrotaline on the lung between a rat and a dog, which might be due to the hepatic metabolic system, encouraged us to examine the reactive hepatic metabolites. The purpose of this study was to evaluate the cardiopulmonary hemodynamic alterations that developed in beagles after the direct administration of dehydromonocrotaline (DMCT), a putative toxic metabolite of monocrotaline, which was made in vitro.

Twenty purebred beagles with a mean age of 3 months and weighing 4 to 6 kg were used for the study. DMCT was prepared as described by Mattocks³ and was dissolved in dimethylformamide just before injection. After the baseline hemodynamics were measured, a single injection of DMCT, 1.5 mg/kg ($n = 7$), 3 mg/kg ($n = 10$), or 4.5

mg/kg ($n = 3$), was performed. Hemodynamic data and blood samples were obtained 8 weeks after injection. For each hemodynamic measurement, the beagles were anesthetized with sodium pentobarbital (25 mg/kg intravenously) and permitted to breathe spontaneously. Under stable conditions, a Swan-Ganz catheter (Baxter Healthcare Corporation, Edwards Div., Santa Ana, Calif.) was placed from the femoral vein to the pulmonary artery for measurement of pressure in the right side of the heart, and another catheter was placed in the femoral artery for measurement of systemic pressure. So that the weight ratio of the right to left ventricle could be calculated, the interventricular septum was included with the left ventricle. Portions of each lung and right ventricle were fixed, cut, and stained for histologic study. All animals received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources and published by the National Institutes of Health (NIH Publication No. 86-23, revised 1985). Data and variables were compared by multiple analysis of variance to determine the effect of study groups and time points. Differences were considered significant at $p < 0.05$ by the Scheffe F test. All data in the text are presented as the mean $\pm$ the standard deviation.

Because two beagles receiving 3 mg/kg injections and all receiving 4.5 mg/kg injections died of acute pulmonary edema within the first week of the DMCT administration, seven beagles receiving 1.5 mg/kg injections and eight receiving 4.5 injections were available for analysis. No significant differences were noted between the groups with respect to hemodynamic variables at baseline. The systolic pulmonary arterial pressure, mean pulmonary arterial pressure, and pulmonary vascular resistance in beagles

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