Massive Thromboembolism Owing to the Left Ventricular Thrombus Associated with the Hypereosinophilic Syndrome

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CASE REPORT

A 39-year-old man was transferred to Seoul National University Hospital with complaints of cough, chest discomfort, and weight loss. A weight loss of 12 kg in a 3-month period. Initial laboratory findings before referral revealed that the white blood cell (WBC) and eosinophil counts were 48,000/μL and 14,880/μL (31% of the WBC count), respectively. Possible etiologies of eosinophilia were excluded on the basis of the patient’s history and laboratory findings such as liver enzyme, serum electrolytes, parasite-specific immunoglobulin G, and toxocariasis antibodies. The patient was diagnosed with the hypereosinophilic syndrome (HES), and methyl prednisolone (mPD) therapy with a dose of 2 mg/kg/day was started. An echocardiographic evaluation was also performed due to increased cardiac enzyme levels (creatine kinase 138 IU/L, creatine kinase-MB 23.63 ng/mL, and troponin I 9.919 ng/mL). Massive thrombus filling the left ventricular cavity with hypermobile portion and mitral regurgitation of a moderate degree were found (Fig. 1). Intravenous anticoagulation therapy was started immediately. The mPD dose was increased to 500 mg/day due to the increasing eosinophil counts. Bone marrow biopsy and gene assay including BCR-ABL, FIP1L1/PDGFRα1, and PDGFRβ/5q32 were al-
so performed. After confirming the PDGFRB/5q32 gene rearrangement, a combination therapy of hydroxyurea and imatinib (Glivec, Basel, Switzerland) was added to the treatment protocol. The patient was then transferred to our hospital with a recommendation of urgent surgical left ventricular thrombectomy. The initial laboratory test after referral demonstrated elevated levels of WBC and eosinophils with absolute counts of 85,600/μL and 4,280/μL (5% of the WBC count), respectively. Follow-up echocardiography conducted 5 and 8 days after the initial evaluation showed a progressively decreasing left ventricular mass and the disappearance of the mobile mass at the inferobasal area (Fig. 1). There was no evidence of systemic embolism. Continuing medical treatment rather than urgent surgical treatment was decided upon.

Fourteen days after the initial diagnosis (5 days after referral), acute right leg pain with a diminished right dorsalis pedis pulse developed. Computed tomography angiogram (CTA) of the lower extremities revealed arterial occlusions at multiple levels including the infrarenal abdominal aorta, right common iliac artery, left iliac bifurcation, and right popliteal artery (Fig. 2). In addition to the great vessel occlusions, multiple both renal infarctions were found. An emergency operation was performed to resolve the thromboembolic complications. To prevent recurrent embolic events, simulta-
neous left ventricular thrombectomy was also planned. First, thromboembolectomy of the infrarenal abdominal aorta and bilateral iliac and right popliteal arteries was performed via femoral incisions by using a Fogarty catheter. After the completion of this thromboembolectomy, left ventricular thrombectomy followed via a median sternotomy and under aorto-bicaval cannulation with cold cardioplegic arrest.

The left ventricle was entered through left atriotomy. Further, the left ventricular thrombus was more solid than the usual fresh thrombus, and the margin between the thrombus and the endocardium was unclear. All visible thrombus was removed with care so as to not injure the endocardium and the myocardium (Fig. 3A). Although there was a moderate degree of mitral regurgitation at the preoperative echocardiography, intraoperative findings after thrombectomy revealed an intact mitral annulus without abnormal thickening or elongation of the subvalvular apparatus. The saline test also demonstrated only a minimal leakage. Due to these findings and the concern of a recurrent thrombosis around the prosthetic mitral ring, the mitral valve procedure was not performed. Cardiopulmonary bypass and aortic cross-clamp times were 68 and 32 minutes, respectively. The operation and the postoperative course were uneventful. The patient was extubated 12 hours after the surgery. A combination therapy of hydroxyurea and imatinib was sustained with the tapering of mPD. Postoperative CTA performed at postoperative day 2 and echocardiography at postoperative day 15 revealed the disappearance of the abdominal and iliac thromboembolism, and left ventricular thrombus, respectively (Fig. 3B, C). Mitral regurgitation was also improved to less than a mild degree. Although we performed a pathologic evaluation of the removed thrombus, there was no definite finding of eosinophil
infiltration since we tried to avoid any endomyocardial resection. The patient was discharged at 18 days after the surgery with the WBC and eosinophil counts of 7,280/μL and 349/μL (4.8% of the WBC count), respectively. He has undergone follow-up at an outpatient clinic for 2 months without any evidence of disease relapse and recurrence of thromboembolism. Further medical management plans included oral anticoagulation for 6 months after the surgery and adjustment of the immunosuppressant by tapering off methyl prednisolone and continuing the imatinib medication.

**DISCUSSION**

HES was defined as a persistent, unexplained elevation of peripheral blood eosinophils (≥1,500/μL) lasting at least 6 months with eosinophil-related end-organ damage [1]. However, in 2010, Simon et al. [2] suggested that a 6-month duration is not necessary if unexplained eosinophilia is documented on more than one occasion. The revised definition of HES is as follows: 1) blood eosinophilia (≥1,500/μL) on at least two occasions or evidence of prominent tissue eosinophilia associated with symptoms and marked blood eosinophilia; 2) exclusion of secondary causes of eosinophilia, such as parasitic or viral infection, allergic diseases, drug-induced or chemical-induced eosinophilia, hypoadrenalism, and neoplasms [2].

Recently, HES has been considered a myeloproliferative disorder, and an evaluation of the genetic mutation is helpful in selecting a treatment regimen [1]. Cardiac involvement of the HES occurs in more than 50% of the patients with various symptoms, such as dyspnea, chest pain, cardiac murmur, and congestive heart failure [3,4]. Cardiac involvement of HES is classified in three stages: first is the acute necrotic stage, which is characterized by myocardial necrosis with eosinophilic infiltration into the myocardium. Second is the thrombotic stage, which is triggered by the damaged endocardial surface in any cardiac chamber. The last is the fibrotic stage, which occurs with the replacement of thrombus by endomyocardial fibrosis. As a result, restrictive cardiomyopathy and valvular incompetence, such as mitral regurgitation, could occur [1,5]. Medical treatment of the HES included anticoagulation and immunosuppressive therapy. When the PDGFRα or various PDGFRB fusion genes are identified, imatinib shows good long-term efficacy with a low incidence of grade III/IV toxicity [1]. In addition, myeloid neoplasms associated with the rearrangement of PDGFRB are responsive to imatinib [6]. Therefore, in the present case, the patient harbored PDGFRB/5q32 gene re-arrangement and imatinib was included in the treatment regimen.

Most reported cases of HES with cardiac involvement underwent cardiac surgery due to restrictive cardiomyopathy and mitral regurgitation at the chronic stage [7,8]. In addition, although previous reports presented HES patients with the left ventricular thrombus, data preferring medical or surgical treatment are lacking [4]. The patient in the present study suffered from non-specific symptoms, such as cough, weight loss, chest discomfort, and dyspnea. Echocardiography was performed due to increased serum levels of creatine kinase-MB and troponin I. Despite the diagnosis of the left ventricular thrombus and referral for urgent surgery, medical management was the initial choice rather than surgical correction. The reasons for this choice were the concerns of recurrent thrombosis when performing thrombectomy before the control of the disease activity and the echocardiographic findings of the decreasing mass without any signs or symptoms of systemic embolism. However, the result was a massive thromboembolism occluding the abdominal aorta and the lower extremity arteries. Concomitant surgeries including the thromboembolectomy of the low extremities and left ventricular thrombectomy were performed on an emergency basis. Intra-abdominal and low-extremity arterial thrombi were effectively removed using a transfemoral approach without residual thrombus, because the thrombus was solid in nature, in contrast to the usual fresh thrombus. In addition, although the margin between the left ventricular thrombus and the endocardium was difficult to identify, perhaps due to the inflammatory involvement of the endocardium, left ventricular thrombectomy was successfully performed without residual thrombus on follow-up echocardiography. The postoperative course was uneventful without any signs and symptoms of recurrent left ventricular thrombus and systemic embolization. Although there has been no guideline for anticoagulation in such patients, we planned to continue oral anticoagulation until 6 months after the initial treatment, which might be suffi-
ciently long for the stabilization of the disease activity.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES