Idiopathic hypereosinophilic syndrome presenting with multiple organ damage

A case report

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1. Introduction

Idiopathic hypereosinophilic syndrome (IHES) is a group of myeloproliferative disorders with unknown etiology that is characterized by eosinophilia in peripheral blood and inflammatory damage of multiple organs, including the heart, lungs, skin, nervous system, and gastrointestinal tract.[1,2] The clinical manifestations include myocardial injury, heart failure, respiratory failure, intracardiac embolism, arrhythmia, pericarditis, and gastrointestinal damage.[3] We report IHES in a patient who presented with multiple organ damage (MOD).

Patient concerns: A 52-year-old male presented with MOD, including myocardial damage suggestive of myocardial infarction, cardiac tamponade, respiratory failure, skin damage, and gastrointestinal damage.

Diagnoses: The absolute eosinophil count was 12,920/mm³, much higher than occurs in other diseases associated with eosinophilia (1500/mm³), and suggesting a diagnosis of IHES.

Interventions: Prednisone combined with hydroxyurea.

Outcomes: At 6 months after completion of drug treatment, the patient had no chest pain or dyspnea, and the results of a blood panel, chest computed tomography, and gastroscopy were normal.

Lessons: MOD is very rare in patients with IHES. Patients receiving prompt diagnosis and treatment have very good prognoses.

Keywords: eosinophilia, idiopathic hypereosinophilic syndrome, multiple organ damage

2. Case report

A 52-year-old male was admitted with chest pain for 1 week that was aggravated by dyspnea for 3 days. His medical history and family history of cardiovascular disease were unremarkable. His initial body temperature was 36.6 °C, respiratory rate was 24 breaths/min, pulse rate was 112 beats/min, blood pressure was 111/87 mm Hg, and oxygen saturation in room air was 90%.

An electrocardiogram (ECG) showed sinus tachycardia; T wave inversion in II, III, AVF, and V1 to V6; elevation of ST segment in I and AVL; and a poor increase of R wave in the thoracic leads (Fig. 1A). The initial laboratory tests indicated an absolute eosinophil count of 12,920/mm³, high-sensitivity troponin (hsTn) level of 2037.7 pg/mL (normal: <14 pg/mL), brain natriuretic peptide level of 758 pg/mL (normal: <100 pg/mL), and D-dimer level of 57 μg/dL (normal: <55 μg/dL). Arterial blood analysis also indicated hypoxemic respiratory insufficiency (pH 7.43, pCO₂: 26.7 mm Hg, pO₂: 72.6 mm Hg).

We considered AMI and performed coronary angiography immediately. There was no significant stenosis in the right coronary artery (Fig. 2A), left main artery, anterior descending artery, or circumflex artery (Fig. 2B). However, X-ray fluoroscopy indicated a bright band at the bottom of the heart, possibly due to pericardial effusion (Fig. 2A). An urgent bedside transthoracic echocardiogram demonstrated left ventricular endomyocardial thickening, and a dark area in the pericardial cavity. Thickness measurements indicated the anterior pericardium was 1.0 cm, the posterior pericardium was 1.7 cm, and the apex was 1.0 cm. There was no valvular dysfunction, but the left ventricular systolic function was obviously reduced, with an estimated ejection fraction of about 31%.
We performed emergency pericardiocentesis, and drained about 100mL of yellow, cloudy fluid. Examination of the pericardial effusate showed that the Rivalta test was positive (indicating an exudate). A chest computed tomography (CT) exam showed bilateral pleural effusion, scattered patches, and exudate in both lungs (Fig. 3A). We performed bilateral thoracentesis, and drained an additional 600mL of yellow, cloudy fluid. Laboratory examination of his hydrothorax showed that Rivalta test was positive, the nucleated cell count was 9260/mm³ with 65% eosinophils (Fig. 5A), total protein was 34.9g/L, lactate dehydrogenase was 201IU/L, and adenosine deaminase was 4.8U/L.

On the third day, the patient developed a bright red purpuric-like rash on both lower limbs (Fig. 4A), which rose above the skin, fused partially, and then spread to the whole body (Fig. 4B). A second ECG indicated sinus tachycardia; pathological Q-wave formation in I and AVL; T-wave inversion in II, III, AVF, and V1-V6; and a poor increase of R wave in the thoracic leads (Fig. 1B). The patient was negative for male tumor markers (AFP, CA72-4, NSE, CYFRA21-1, TPSA, FPSA, CEA, CA-199), antinuclear antibody, thyroid dysfunction, and TB infection. We thus excluded causes of reactive eosinophilia (fungal infections, parasitic infections, hypersensitivity reactions, and malignant diseases). Antineutrophilic cytoplasmic antibodies were also negative. We administered oxygen, an anti-inflammatory agent (Piperacillin and Sulbactam, 4.5g, every 8hours), a diuretic (Furosemide, 40mg, once a day), an anti-allergy medication (Loratadine, 10mg, once a day), a proton pump inhibitor for acid suppression (Omeprazole, 40mg, once a day).

On the fifth day, the patient developed gastrointestinal bleeding. Thus, we administered an intravenous infusion of somatostatin and omeprazole by micropump, performed fluid infusion, and provided other treatments to alleviate symptoms. A bone marrow examination indicated marked myelodysplastic activity and significantly increased eosinophils (42.5%). Flow cytometry showed there was “no significant abnormal phenotypic cell population,” and a biopsy showed that “bone marrow hematopoietic cells are proliferating and active, mainly eosinophils” (Fig. 5B). Examination of the peripheral blood using polymerase chain reaction indicated no abnormal expression of PDGFRα, PDGFRβ, FGFRI or PCMI-JAK2, and no JAK2V617F point mutation. These results led to a clear diagnosis of IHES. High-dose methylprednisone (1mg/kg/d), which began on the first day of admission, was apparently ineffective by itself, so we added hydroxyurea (days 1–2: 0.5g per day; days 3–12: 0.5g twice per day).

Figure 1. ECG at admission, showing T wave inversion in II, III, AVF, and V1 to V6; elevation of ST segment in I and AVL; and poor increase of R wave in the thoracic leads (A). ECG on day 3, showing sinus tachycardia; pathological Q-wave formation in I and AVL; T-wave inversion in II, III, AVF, and V1-V6; and poor increase of R wave in the thoracic leads (B). ECG = electrocardiogram.

Figure 2. Coronary angiography at admission, showing no significant stenosis in the right coronary artery (A), left main artery, anterior descending artery, and circumflex artery (B). Red arrow: suspected pericardial effusate.
Figure 3. Chest CT at admission, showing bilateral pleural effusion, scattered patches, and exudate in both lungs (A). Follow up chest CT at 2 months, showing complete absorption of lung exudate (B). CT = computed tomography.

Figure 4. Bright red purpura-like rash on both lower limbs at 3 days after admission (A), which rose above the skin, fused partially, and then spread to the whole body (B).

Figure 5. Hematoxylin and eosin staining of pericardial fluid at admission, showing chronic inflammatory cells, including eosinophils (arrow) (A). Bone marrow biopsy of the posterior superior iliac spine on the fifth day, showing proliferation of bone marrow hematopoietic cells and eosinophils (arrow) (B).
After 2 weeks, his eosinophil count dropped to normal and the rash subsided. Painless gastroenteroscopy showed multiple duodenal ulcers (stage A1), chronic nonatrophic gastritis with erosion, bile reflux, the presence of *Helicobacter pylori*, mild chronic mucosal inflammation of the terminal ileum, and focal lymphoid tissue hyperplasia. Antibiotic treatment (bismuth potassium citrate tablets 0.6 g, tinidazole tablets 0.5 g, clarithromycin tablets 0.25 g, twice a day) for *H pylori* was given. On day 20, we discharged the patient with a gradual tapering of corticosteroids.

A blood panel was reviewed once a week after discharge, and once a month after 2 months. The patient’s eosinophil level remained within the normal range during follow-up. Two months later, a chest CT examination showed that the lung exudate was completely absorbed (Fig. 3B). A painless gastroscopy indicated chronic nonatrophic gastritis.

3. Discussion

Hypereosinophilic syndrome (HES) was redefined in 2010 as more than 1500/mm³ eosinophils without a discernible secondary cause (eg, HIV infection, parasite or worm infection, allergic diseases, drug allergies, and nonhematologic malignancies). The eosinophil count in this patient was consistently higher than 1500/mm³, with a maximum of 12,920/mm³. To exclude secondary eosinophilia, we performed pretransfusion examinations with testing for tumor markers, antinuclear antibody, parasitic infections, allergic reactions, and abnormal expression of genes typical of other diseases associated with eosinophilia. We found eosinophilic infiltration in the pleural effusate and performed a bone marrow examination. The characteristics of our case coincide with the current diagnostic criteria for HES.

HES leads to organ dysfunction due to eosinophil infiltration and to various clinical manifestations which differ among individual patients. About 60% of patients with HES suffer from heart damage. Our patient had chest pain, an abnormal ECG, and elevated hsTn, suggestive of AMI, but the coronary angiography results were normal. Previous studies reported similar changes in ECG and hsTn in patients ultimately diagnosed with HES. A small number of patients with HES are positive for PDGFRα or PDGFRβ, and the transcribed proteins were sensitive to imatinib treatment, which may promote partial recovery of left ventricular function.

Although there are a variety of clinical manifestations in patients with IHES after cardiac injury, it is rare that pericardial tamponade occurs at disease onset. Our patient was admitted with clinical manifestations of pericardial tamponade, including sinus tachycardia and a decreased pulse pressure difference (11/87 mm Hg). Pericardial puncture led to significant alleviation of the symptoms. The typical echocardiographic results in patients with IHES include decreased systolic and diastolic function, thickening of the myocardial intima, and thrombosis. Our patient had endocardial thickening and significant left ventricular dysfunction, but no intracardiac thrombosis.

Acute eosinophilic pneumonia is characterized by diffuse pulmonary parenchymal lesions. An X-ray examination can reveal pulmonary patches and exudation; excessive exudation can lead to pleural effusion, to gas exchange abnormalities, and eventually to severe respiratory failure. Our patient had respiratory failure upon admission, with clinical manifestations of shortness of breath, dyspnea, and hypoxemia. Bilateral pleural effusion was evident in his chest CT results, and many lung patches had evidence of local exudation.

Wells et al. first described eosinophilic cellulitis (Wells syndrome) in 1971. More recently, Caputo et al. proposed classification of seven types of eosinophilic cellulitis: fixed drug eruption-like, plaque-type, bullous, annular granuloma-like, papulovesicular, papulonodular, and urticaria-like. Our patient began to develop loose red or dark purpura-like rashes on both lower limbs, which rose above the skin, partially fused, and then spread to the whole body.

IHES is a rare disease characterized by damage to the entire gastrointestinal tract, including eosinophilic gastritis, gastroenteritis, and colitis. The mechanism is presumably related to the presence of dense mucosal eosinophilia. Our patient underwent painless gastroenteroscopy, and we detected erosive gastritis, multiple duodenal ulcers, and colitis.

The aim of IHES therapy is to reduce the eosinophil granulocyte count in tissues, and glucocorticoids are often recommended. However, some patients with IHES do not respond to glucocorticoids, and cytotoxic drugs can be used as an alternative. Interferon and monoclonal immunomodulatory therapy may be considered in refractory cases. If an IHES patient has congestive heart failure, conventional therapy for heart failure should be administered. If IHES is accompanied by thrombosis, including thrombus in the heart or pulmonary artery thrombosis, anticoagulant therapy is necessary.

Our patient is still in follow-up. After nearly 5 months, his physical condition is basically normal. He continues to receive therapy for reversal of ventricular remodeling, including valsartan (80 mg/d), metoprolol tartrate (100 mg/d), and spironolactone (20 mg/d), as well as prednisone (10 mg/d).

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