Case 7-2014: A 27-Year-Old Man with Diarrhea, Fatigue, and Eosinophilia

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Presentation of Case

Dr. Tilak Sundaresan (Medicine): A 27-year-old man was admitted to this hospital because of diarrhea, fatigue, and eosinophilia.

The patient had been in good health until 2 weeks before admission, when fatigue developed. Eleven days before presentation, he had moved to the United States from Indonesia. After his arrival, he had bloating and nonbloody, loose bowel movements, without fever, chills, vomiting, cramping, or abdominal pain. One week later, the diarrhea persisted and his exercise tolerance sharply decreased. The day before admission, he was seen at his local health center. Testing included a complete blood count (Table 1) and stool examination. He was referred to this hospital for admission.

The patient reported weight loss of approximately 4.5 kg in recent weeks, without dyspnea, night sweats, fevers, chills, rash, arthritis, cough, pruritus, alcohol intolerance, or hypersensitivity to insect bites. Two years earlier, the patient had presented with intermittent diarrhea, abdominal cramping, tenesmus, nausea, and weight loss (9 kg); there had been microscopic blood in the stool, and a diagnosis of ulcerative colitis had been confirmed by colonoscopy and biopsy. Symptoms had responded to treatment with mesalamine. Complete blood counts at the time of the diagnosis and 7 months before this admission had been normal. On his admission to this hospital, the patient's medications included mesalamine (1.2 g daily) and acetaminophen as needed for headache. He had no known allergies. He was born in India and had lived in Indonesia and Australia during the previous 25 years. He had traveled to a rural area in India in the previous month. He was married, reported being monogamous with his wife, and had no children. He had moved to the United States to attend graduate school. He was a vegetarian, drank alcohol infrequently, had a remote history of light smoking, and did not use illicit drugs. His parents and brother were healthy. There was no family history of cancer or autoimmune disease.

On examination of the patient, the vital signs were normal. The spleen tip was palpable, and an erythematous papular rash was seen on the anterior thorax; the
remainder of the examination was normal. Blood levels of creatinine, magnesium, total and direct bilirubin, amylase, lipase, uric acid, fibrinogen, creatine kinase, vitamin B₁₂, and tryptase were normal, as were the activated partial-thromboplastin time and results of D-dimer testing; testing for total antibodies to hepatitis A virus was positive; and testing for hepatitis A virus IgM, antibodies to hepatitis C virus, hepatitis B virus surface antigen, and hepatitis B virus surface antibodies was negative. Other test results are shown in Table 1. Urinalysis was normal, and a chest radiograph was normal.

Computed tomography (CT) of the abdomen and pelvis revealed numerous enlarged mesenteric and retroperitoneal lymph nodes, as large

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<th>Table 1. Laboratory Data.†</th>
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<td>Variable</td>
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<tr>
<td>Hematocrit (%)</td>
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<td>Hemoglobin (g/dl)</td>
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<td>White-cell count (per mm³)</td>
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<td>Platelet count (per mm³)</td>
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<td>Mean corpuscular volume (μm³)</td>
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<td>Mean corpuscular hemoglobin concentration (g/dl)</td>
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<td>Red-cell distribution width (%)</td>
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<td>Prothrombin time (sec)</td>
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<td>Potassium (mmol/liter)</td>
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<td>Phosphorus (mg/dl)</td>
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<td>Alkaline phosphatase (U/liter)</td>
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<td>Aspartate aminotransferase (U/liter)</td>
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<td>Lactate dehydrogenase (U/liter)</td>
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as 1.4 cm by 2.2 cm by 3.1 cm. CT of the chest, performed after the administration of contrast material, was normal. Four days later, positron-emission tomography with the use of \(^{18}\)F-fluoro-deoxyglucose (\(^{18}\)F-FDG-PET) revealed intense uptake of FDG throughout the skeleton and in an enlarged spleen, with low-to-moderate uptake in retroperitoneal and mesenteric lymph nodes. A CT-guided core biopsy of a retroperitoneal lymph node was performed, and the specimen showed reactive hyperplasia with increased eosinophils and plasma cells but no evidence of lymphoma on morphologic studies or flow cytometry.

Stool specimens were negative for \textit{Clostridium difficile} toxin, protozoa, helminth ova, and enteric pathogens. Testing was negative for antibodies to strongyloides, toxocara, trichinella, and human immunodeficiency virus (HIV) and for cytomegalovirus nucleic acids. Cultures of the blood and urine were sterile.

Diagnostic procedures were performed.

### Differential Diagnosis

\textit{Dr. Amir T. Fathi}: All discussants were involved in the care of this patient, and the diagnosis is known to us. This 27-year-old man of Indian origin who had recently been living in Jakarta, Indonesia, and had a history of treated ulcerative colitis presented with diarrhea and fatigue. Laboratory evaluation revealed leukocytosis with eosinophilia.

The differential diagnosis of eosinophilia is broad. Eosinophils are derived from CD34+ progenitor cells in the bone marrow and differentiate in response to T-cell–derived cytokines, including interleukin-5, interleukin-3, and granulocyte–macrophage colony-stimulating factor. Mature eosinophils can persist for up to 24 hours in the circulation before migrating into extravascular sites, where they can survive for days.\(^1\)\(^2\) Eosinophilia is defined as an absolute eosinophil count of more than 500 per cubic millimeter, and hyper-eosinophilia as an absolute eosinophil count of more than 1500 per cubic millimeter.

### Infectious Causes of Eosinophilia

Infections, including tissue-invasive parasites, should be carefully considered in persons living in or frequently traveling to developing countries. Parasitic infections associated with eosinophilia include strongyloides, echinococcus, schistosoma, toxocara, and trichinella.\(^3\)\(^7\) Other causes of eosinophilia include infections with HIV and human T-cell lymphotropic virus type 1.\(^8\)\(^9\)

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\* To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for phosphorus to millimoles per liter, multiply by 0.3229. To convert the values for calcium to millimoles per liter, multiply by 0.250.

\† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.
ALLERGIC AND RHEUMATOLOGIC CONDITIONS

Eosinophilia can be a feature of allergic conditions, including atopic dermatitis, asthma, and medication hypersensitivity.10–14 Rheumatologic conditions such as idiopathic eosinophilic vasculitis and Churg–Strauss vasculitis may be associated with eosinophilia.15,16 Other nonmalignant causes include adrenal insufficiency and sarcoidosis.17,18 Peripheral-blood eosinophilia can occur in patients with ulcerative colitis,19,20 but the degree of hypereosinophilia seen in this case would be exceptionally uncommon, and this patient’s inflammatory bowel disease was controlled on treatment. The patient was taking mesalamine, which has been linked to eosinophilia.13

MALIGNANT CONDITIONS

Eosinophilia can be associated with a variety of malignant conditions, including solid tumors and nonmyeloid hematologic cancers, such as T-cell lymphomas, Hodgkin’s lymphoma, and acute lymphoblastic leukemia.21–25 The “lymphocytic variant” of the hypereosinophilic syndrome is an entity in which eosinophilia is a result of growth factors elaborated by an expansion of clonal, immunophenotypically aberrant T cells.26,27 Finally, eosinophilia may be associated with a number of myeloid cancers, including chronic myelogenous leukemia, systemic mastocytosis, and myeloid and lymphoid neoplasms with abnormalities in the genes encoding platelet-derived growth factor receptors alpha or beta (PDGFRα or PDGFRβ) or fibroblast growth factor receptor 1 (FGFR1).

This patient underwent extensive evaluation for underlying causes of eosinophilia. Microbiologic investigation, including serial stool evaluation for ova and parasites and strongyloides, was negative. No clonal B-cell or abnormal T-cell populations were detected through flow cytometry, and polymerase chain reaction detected no clonal T-cell–receptor gene rearrangement. A BCR-ABL1 rearrangement was not detected. Serum levels of tryptase, vitamin B12, rheumatoid factor, and anti-neutrophil cytoplasmic antibody (ANCA) were within normal ranges. Imaging revealed diffuse lymphadenopathy, but a lymph node–biopsy specimen did not reveal evidence of lymphoma or other malignant tumors.

Examination of bone marrow–biopsy and aspirate specimens is helpful in establishing or ruling out diagnoses of hematologic neoplasms with associated eosinophilia.28 In this case, a comprehensive evaluation had ruled out important underlying causes of eosinophilia, and we favored a diagnosis of either idiopathic hypereosinophilic syndrome or chronic eosinophilic leukemia.

CLINICAL DIAGNOSIS

Idiopathic hypereosinophilic syndrome or chronic eosinophilic leukemia.

PATHOLOGICAL DISCUSSION

Dr. Robert P. Hasserjian: Review of the peripheral-blood smear revealed marked leukocytosis with a predominance of mature eosinophils, including forms with three or four nuclear lobes and some with sparse or uneven granulation (Fig. 1A). The bone marrow–biopsy specimen was markedly hypercellular (95% cells, 5% fat), with numerous mature and immature eosinophilic forms (Fig. 1B). Megakaryocytes had normal morphologic features. Mast cell numbers were not increased, and there were no lymphoid aggregates or abnormal lymphoid infiltrates. The smear of the bone marrow aspirate revealed a preponderance of maturing eosinophils among normally granulated myeloid elements and a relative paucity of erythroid forms (Fig. 1C). Conventional cytogenetic analysis of the bone marrow revealed a normal male karyotype in 20 cells in metaphase.

The pathological features of the bone marrow can be helpful in ruling out some underlying causes of hypereosinophilia; in this case, there was no evidence of systemic mastocytosis or lymphoma involving the bone marrow. The normal karyotype and the absence of a BCR-ABL1 rearrangement ruled out chronic myelogenous leukemia, which on rare occasions may be manifested by a prominent eosinophilia. If other underlying causes of eosinophilia have been ruled out clinically, the main pathological differential diagnosis of eosinophilia rests between one of the myeloid neoplasms with eosinophilia (Table 2) and idiopathic hypereosinophilic syndrome.

The most common genetically defined eosinophilic myeloid neoplasms are those with rearrangements in PDGFRα (usually a FIP1L1-PDGFRα fusion due to an 800-kb cytogenetically cryptic deletion at the 4q12 locus),29–31 The number of mast cells in the bone marrow and the serum tryptase levels are usually increased in neoplasms with FIP1L1-PDGFRα rearrangement;32 neither was increased in this case, and analysis of the bone marrow biopsy specimen did not reveal any evidence of systemic mastocytosis.

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marrow with the use of fluorescence in situ hybridization did not reveal FIP1L1-PDGFRA rearrangement. Rearrangements of PDGFRB and FGFR1 also define specific neoplasms, but these rearrangements were ruled out in this case by a normal bone marrow karyotype.

Chronic eosinophilic leukemia, not otherwise specified, encompasses clonal eosinophilic neo-
Despite the presence of eosinophilia, the underlying cause of hypereosinophilic syndrome is not always easily identified. In some cases, clonal evidence may be identified through cytogenetic analysis, with or without morphologic evidence of dysplasia. In other cases, the presence of a clonal marker suggests that the eosinophilia is clonal, even in the absence of overt dysplasia. This clonality is often identified by the presence of a specific chromosomal translocation, such as 

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<th>Disease</th>
<th>Clinicopathological Features</th>
<th>Genetics</th>
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<tr>
<td>PDGFRα rearranged</td>
<td>Elevated serum tryptase level and increased number of bone marrow mast cells</td>
<td>Cryptic deletion at the 4q12 locus, creating FIP1L1-PDGFRα rearrangement</td>
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<tr>
<td>PDGFRβ rearranged</td>
<td>Peripheral mononcytosis</td>
<td>t(5;12)(q31–33;p12) with ETV6-PDGFRβ rearrangement</td>
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<tr>
<td>FGFR1 rearranged</td>
<td>Often concurrent or subsequent T-lymphoblastic lymphoma or acute myeloid leukemia</td>
<td>Translocations of 8p11, fusing FGFR1 with various partners</td>
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<td>Chronic eosinophilic leukemia, not otherwise specified</td>
<td>Persistent eosinophilia (≥1.5×10^5/liter) with evidence of a clonal myeloid proliferation (abnormal karyotype, increased blasts, or morphologic dysplasia)</td>
<td>No rearrangement of PDGFRα, PDGFRβ, FGFR1, or BCR-ABL1; may have normal or abnormal karyotype</td>
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DISCUSSION OF MANAGEMENT

MANAGEMENT OF THE HYPEREOSINOPHILIC SYNDROME

Dr. Fathi: Patients in hypereosinophilic states can present with varied signs and symptoms, including fatigue, cough, dyspnea, angioedema, rash, fever, and rhinitis.26,28,42 The degree of leukocytosis varies, with absolute eosinophilia ranging from 1500 to 400,000 eosinophils per cubic millimeter. Until recently, outcomes for patients with hypereosinophilic syndromes were very poor, with a reported median survival of 9 months and 3-year survival of less than 15%. Cardiac sequelae accounted for the majority of deaths.42,43 With better supportive care, more aggressive treatment approaches, and the development of new therapies, improved rates of 5-year survival (≥80%) have been reported, although longer-term survival does decrease over time, possibly due to the effects of eosinophilic end-organ damage.26,44 Certain prognostic factors are associated with poor outcomes, including male sex, a white-cell count of greater than 100,000 per cubic millimeter, peripherally circulating blasts, refractoriness to glucocorticoids, and cardiac injury.26

The conventional initial therapeutic choice for patients with the hypereosinophilic syndrome is glucocorticoids, which in most cases result in control of hypereosinophilia.26,44,45 If responses to glucocorticoids are suboptimal, hydroxyurea can be used26,44,46; alternatively, the administration of vincristine can produce rapid decreases in eosinophilia.47 Imatinib has been shown to produce rapid and clinically significant responses in patients with eosinophilic neoplasms and PDGFRα or PDGFRβ rearrangements34,48 and is also effective in a smaller subset of patients who have chronic eosinophilic leukemia or the hypereosinophilic syndrome without these rearrangements.49 Other tyrosine kinase inhibitors, such as dasatinib, have also been studied, with a suggestion of therapeutic activity in a subgroup of patients.50 Interferon alfa can be used as a single agent or in combination with glucocorticoids or hydroxyurea to produce remissions.51,52 Eosinophils express CD52, and the anti-CD52 monoclonal antibody alemtuzumab appears to have efficacy in patients whose disease has been refractory to conventional treatments.53 The anti–interleukin-5

plasms that have no rearrangements in PDGFRα, PDGFRβ, FGFR1, and BCR-ABL1. Clonality may be proven by showing any other cytogenetic abnormality or may be inferred by the presence of an increased percentage of blasts or overt morphologic dysplasia of maturing erythroid, myeloid, or megakaryocytic elements.28,41 It is important to note that morphologic abnormalities in eosinophils, such as hypogranulation and nuclear hyperlobation or hypolobation, are frequently seen in reactive eosinophilias and should not be considered as proof of clonality. The hypereosinophilic syndrome characterizes hypereosinophilic states in which underlying causes are not detected despite comprehensive evaluation, organ injury related to hypereosinophilia is present, and there is no evidence of clonality.26,28,42 In this case, no underlying cause of the eosinophilia was identified after extensive clinical evaluation, but there was also no proof of a clonal myeloid proliferation, leading to a diagnosis of idiopathic hypereosinophilic syndrome.
antibody mepolizumab has also shown promising results in clinical trials. The role of stem-cell transplantation is not well established, but prolonged survival with this treatment has been reported.

This patient had severe and persistent diarrhea. The gastroenterology service was consulted.

GASTROINTESTINAL COMPLICATIONS OF THE HYPEREOSINOPHILIC SYNDROME

Dr. James M. Richter: Gastroenterology was consulted early in this patient’s hospital course because of his diarrhea and history of ulcerative colitis. When the patient was in India, colonoscopy with biopsy revealed characteristic findings of ulcerative colitis, which responded well to mesalamine. After his arrival in the United States, the patient noted diarrhea with fatigue and weight loss. Although this diarrhea syndrome appeared to be different from his earlier illness, ulcerative colitis may be associated with eosinophilia, and we felt that it was important to make a clear distinction. At colonoscopy, the appearance of the colonic mucosa was distinctly abnormal but not characteristic of ulcerative colitis. The mucosa was edematous with patchy erythema but no ulceration. The mucosa of the upper gastrointestinal tract appeared normal.

Dr. Hasserjian: Biopsy specimens of the colon and rectum showed increased eosinophil numbers in the lamina propria (Fig. 1D); a biopsy specimen of the stomach also showed patchy clusters of eosinophils (Fig. 1E). There was no evidence of active colitis or gastritis.

Dr. Richter: We thought that these findings effectively eliminated classic ulcerative colitis as the cause of the patient’s current diarrhea. Several additional though unlikely gastrointestinal considerations remained. Mesalamine allergy is a rare cause of eosinophilia. Intestinal parasites, such as strongyloides, should be ruled out, as they were in this case. Eosinophilic gastroenteritis should be suspected in any patient with gastrointestinal symptoms that are associated with peripheral eosinophilia. The diagnosis of eosinophilic gastroenteritis is made in the appropriate clinical context and according to the results of endoscopic biopsy. However, the degree of eosinophilia in this case was beyond the range that is often observed. An eosinophilic gastroenteritis, characterized by abdominal pain, diarrhea, gastrointestinal bleeding, and colitis, may be seen in the hypereosinophilic syndrome, which was the best explanation for this patient’s gastrointestinal illness.

Dr. Fathi: During the initial week of hospitalization, gradually increasing doses of hydroxyurea were begun. Unfortunately, severe therapy-related mucositis and pancytopenia developed, requiring blood products, and the patient’s peripheral-blood eosinophil count remained elevated at 94,000 per cubic millimeter. The administration of methylprednisolone was also begun in an effort to decrease the eosinophil burden, but results were similarly suboptimal. Imatinib was then initiated, but this worsened the patient’s diarrhea and was discontinued after a few days. An episode of chest pain occurred at the start of the second week of hospitalization, in association with elevated cardiac enzyme levels. Echocardiography and cardiac magnetic resonance imaging (MRI) were performed.

CARDIAC COMPLICATIONS OF THE HYPEREOSINOPHILIC SYNDROME

Dr. Godtfred Holmvang: A cardiac MRI study (Fig. 2A and 2B) was performed to look for eosinophilic myocarditis, and mild left ventricular enlargement with diffusely impaired systolic function (left ventricular ejection fraction [LVEF], 39%) was seen. After the administration of gadolinium, there was patchy subendocardial and papillary-muscle hypoenhancement (Fig. 2C), also seen as more confluent subendocardial hypodensity in a contrast-enhanced CT scan 17 days later (Fig. 2D), suggesting subendocardial hypoperfusion and microvascular compromise. Two of three tissue variables that were evaluated for myocardial inflammation were abnormal. Global early enhancement of myocardium relative to skeletal muscle was elevated (myocardium:skeletal muscle ratio, 8.9; abnormal ratio, >4.0), the myocardium:skeletal muscle ratio of T1-weighted signal intensity was high normal (ratio, 1.8; abnormal ratio, >1.9), and there was diffuse, nearly circumferential subendocardial delayed enhancement, more prominent at the midventricular to apical levels. This pattern is associated with eosinophilia-related subendocardial injury or fibrosis.

Dr. Shmuel S. Schwartzenberg: The echocardiogram on the first hospital day showed excellent function of the right and left ventricles (Videos 1 and 2, available with the full text of this article at NEJM.org), with an LVEF of 71%, normal valvular function, normal-sized heart chambers, and a normal systolic pulmonary-artery pres-
Figure 2. Cardiac Imaging Studies.
Cardiac MRI images in a short-axis view (Panel A) and a four-chamber view (Panel B) show extensive subendocardial late gadolinium enhancement (arrows) not limited to a specific vascular territory. A short-axis cine image acquired early after the administration of gadolinium shows multifocal hypoenhancement (Panel C, arrows) suggestive of patchy subendocardial hypoperfusion. This hypoenhancement has become more confluent with circumferential subendocardial hypodensity in a subsequent image from a contrast-enhanced CT scan (Panel D, arrows; courtesy of Dr. Subba Rao Digumarthy). A short-axis view from an echocardiogram of the tricuspid valve during the patient’s fourth week in the hospital (Panel E) shows trace tricuspid regurgitation with an increased peak systolic gradient of 42 mm Hg across the tricuspid valve.
sure, estimated at 26 mm Hg. Serial echocardiograms showed progressive worsening of the ventricular function, which 4 weeks after admission had reached a nadir of 26% due to diffuse hypokinesis of the left ventricle; there was also right ventricular mild dysfunction, biventricular and biatrial enlargement, functional mild-to-moderate mitral regurgitation (Videos 3 and 4), and pulmonary hypertension with an estimated pulmonary-artery pressure of 52 mm Hg (Fig. 2E). No intracardiac thrombus was observed on any of the echocardiographic studies.

Dr. G. William Dec, Jr.: The differential diagnosis for the patient’s cardiac deterioration includes myocardial ischemia due to coronary arteritis, coronary arterial thromboembolism, acute myocarditis (lymphocytic or allergic in cause), and eosinophilic myocarditis due to his hypereosinophilic syndrome. In this patient who was recently receiving multiple medications, it is also important to differentiate allergic myocarditis from the hypereosinophilic syndrome. In this patient who was recently receiving multiple medications, it is also important to differentiate allergic myocarditis from the hypereosinophilic syndrome. Endomyocardial biopsy may be necessary to differentiate two conditions, although it was not considered necessary in this case. Eosinophilic myocarditis is the most likely diagnosis in this case, given the high frequency of cardiac involvement among patients who have the hypereosinophilic syndrome.55

Eosinophilic heart disease, which can occur from any cause, has three distinct pathological stages (Fig. 3). Stage 1 is acute myocarditis with intense eosinophilic infiltration, leading to systolic dysfunction. This stage is most likely in this patient and is supported by the cardiac MRI findings.56 Stage 2 is associated with intracardiac thrombotic lesions. Finally, stage 3 disease occurs late and is associated with endomyocardial and myocardial fibrosis.

Specific pharmacologic therapies aimed at reducing the eosinophilia have already been discussed; however, I would add that for patients with evidence of mural thrombi, systemic anticoagulation with warfarin is essential. Despite adequate levels of systemic anticoagulation (international normalized ratio, 2 to 3), some patients still have embolic complications, and the addition of an antiplatelet agent (e.g., aspirin or clopidogrel) is recommended.

Dr. Fathi: Because of the patient’s inadequate initial response to treatment, the administration of weekly vincristine was initiated, resulting in improvement of peripheral-blood and bone marrow eosinophilia. We noted that karyotypic analysis of the bone marrow now revealed a chromosomal deletion at 3p13 in 2 of 20 metaphases. This was believed to be a transient abnormality due to cytotoxic therapy, rather than a manifestation of a clonal myeloid neoplasm, since the abnormality was present in a small minority of metaphases, was absent at diagnosis and in two

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**Figure 3. Cardiac Response to Chronic Eosinophilic Injury.**
subsequent marrow samples, and is not a characteristic finding of any myeloproliferative neoplasm.

During the third week of hospitalization, the patient had progressive hemoptysis and respiratory decompensation and required intubation. Evaluation revealed diffuse alveolar hemorrhage, most likely with concurrent bacterial pneumonia. Coagulopathy had developed, with a prothrombin time of 118 seconds, attributed to severe vitamin K deficiency caused by intractable diarrhea. A repeat transthoracic echocardiogram revealed an LVEF of 26%. After respiratory improvement, the patient was extubated. He received a total of five cycles of vincristine, with marked reduction in the eosinophil count to 120 per cubic millimeter. He was discharged from the hospital after 47 days. A bone marrow–biopsy specimen revealed normal hematopoiesis with no increase in the eosinophil count. Vincristine was discontinued because of progressive neuropathy involving the legs. Hypereosinophilia soon recurred, and the eosinophil count reached 4930 per cubic millimeter within 2 weeks after the discontinuation of vincristine.

The patient was enrolled in a compassionate-use program through which mepolizumab was made available. Despite this treatment, the eosinophil count increased to 25,000 per cubic millimeter a week later. The patient was then readmitted to this hospital for aggressive cytoreduction with high doses of cytarabine. He had a complete remission after this course, with resolution of eosinophilia. Because he had improvements in functional status and cardiac function (LVEF, 43%), consolidative treatment was pursued with a reduced-intensity, HLA-matched unrelated-donor stem-cell transplant.

HEMATOPOIETIC STEM-CELL TRANSPLANTATION
Dr. Yi-Bin Chen: Hematopoietic stem-cell transplantation (HSCT) has been reported as successful treatment for the hypereosinophilic syndrome in single case reports. However, in view of the substantial risks associated with HSCT, it should be used only for cases, such as this one, that are refractory to conventional therapy. This patient’s only sibling was a partial HLA match. Given his ethnic background, the probability of finding a fully matched unrelated donor was approximately 20 to 30%, illustrating the need for minority volunteers to enroll in donor registries. Fortunately, in this case, we were able to identify an HLA-matched unrelated donor for this patient.

We elected to proceed with unrelated-donor HSCT with the use of reduced-intensity conditioning consisting of chemotherapy with fludarabine and melphalan and post-HSCT tacrolimus as graft-versus-host-disease (GVHD) prophylaxis. Because CD52 is strongly expressed on eosinophils and has been used in the treatment of the hypereosinophilic syndrome, we administered alemtuzumab during the conditioning chemotherapy to both deplete eosinophils and provide added protection against GVHD. Donor engraftment was successful; however, 3 weeks later, the patient presented with respiratory distress, and CT studies showed diffuse bilateral ground-glass opacities with nodularity. Bronchoalveolar lavage was unrevealing, and he was treated with broad-spectrum antimicrobial agents and high-dose glucocorticoids. His clinical and imaging abnormalities resolved over a 2-week period. The cause of the respiratory distress was probably viral pneumonitis or idiopathic pneumonia syndrome. Now, 2 years after HSCT, he does not require any immunosuppressive medications and has no signs of acute or chronic GVHD. He was able to return to business school 8 months after HSCT. He is here today, and we have invited him to comment.

The Patient: I feel as if you all know me already. When I was first told that I might be able to talk at this conference, I was pretty excited, because what better platform could I have to extend my thanks to the entire Massachusetts General Hospital (MGH) community that helped me start school again and be able to stand in front of you today. It was difficult to decide whom to thank, since it was a large multidisciplinary team and the not-so-great state of mind that I was in during my treatment made it hard to recall everyone’s name.

I do want to take a minute to reinforce just how important a role the nurses play for a patient. Almost 95% of your time in the hospital you spend with your nurses, and the quality of care from the nurses at MGH is simply exceptional. Their support, thoughtfulness, and unyielding optimism can make the difference between despair and hope in a patient.

The compassion that every staff member displays, on top of the professionalism, is what makes this a great hospital. It can be the doctors, the nurses, the people who deliver the meals, those who clean the rooms, the ambassadors who help patients from their cars, and
those who work at reception. You all face patients with serious illnesses on a daily basis, and you still manage to treat each patient with the utmost kindness and respect. You need to be made of special ingredients for that. You guys are special! It’s hard for me to believe that I am back at school doing exactly what I wanted to do back at school doing exactly what I wanted to do. It’s hard for me to believe that I am back at school doing exactly what I wanted to do.

Dr. Nancy Lee Harris (Pathology): Are there any questions?

Dr. Amin Arnaout (Medicine): Did you or can you send out cells for whole-genome or whole-exome sequencing to see whether there is a genetic abnormality?

Dr. Fathi: We attempted to perform sequencing on isolated eosinophils early in the patient’s course, but studies were suboptimal because of poor RNA quality. We will attempt to further analyze samples obtained before HSCT, with the use of next-generation sequencing, to search for a clonal genetic alteration.

**FINAL PATHOLOGICAL DIAGNOSIS**

Idiopathic hypereosinophilic syndrome.

**ACKNOWLEDGMENTS**

This case was presented at Medical Grand Rounds.

Dr. Fathi reports receiving consulting fees for serving on the advisory boards of Genzyme, Seattle Genetics, Concert Pharmaceuticals, Agios Pharmaceuticals, and Teva Pharmaceuticals; Dr. Richter, consulting fees from Policy Analysis; Dr. Chen, consulting fees from Seattle Genetics and Otsuka Pharmaceuticals and grant funding from Seattle Genetics, Otsuka Pharmaceuticals, and Bayer/Omys; and Dr. Hasserjian, consulting fees from Sanofi, Incyte, and Amgen. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

**REFERENCES**