CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 39-2024: A 30-Month-Old Boy with Recurrent Fever

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CME

PRESENTATION OF CASE

Dr. Vandana L. Madhavan: A 30-month-old boy was admitted to this hospital for the third time in 4 weeks because of recurrent fever.

The patient had been well until 4 weeks before the current presentation, when fever, dry cough, nasal congestion, and decreased intake of solid foods developed. The next day, while he was playing in a park with his siblings, he began limping. No trauma had preceded the onset of limping. The patient's parents brought him to the emergency department of this hospital for evaluation.

The patient was afebrile. He was interactive but appeared tired and walked with a limp, favoring the left leg. The lungs were clear on auscultation. The white-cell count was 28,440 per microliter (reference range, 4500 to 11,000), the erythrocyte sedimentation rate 63 mm per hour (reference range, 9 to 14), and the C-reactive protein level 31.3 mg per liter (reference range, 0.0 to 8.0). Urinalysis was normal. Other laboratory test results are shown in Table 1. Blood was obtained for culture, and imaging studies were obtained.

Dr. Evan J. Zucker: Ultrasonography of the hip and radiography of the pelvis showed no abnormalities. Radiography of the chest (Fig. 1A) revealed peribronchial cuffing and patchy perihilar opacities.

Dr. Madhavan: The patient was admitted to the hospital. On the second hospital day, he remained afebrile, had a normal energy level, and was walking normally. Blood cultures showed no growth. He was discharged home.

Two days after discharge, fever recurred. The patient's mother brought him back to emergency department of this hospital. The patient was afebrile, but leukocytosis and elevated levels of inflammatory markers persisted. Tests of a nasopharyngeal swab were positive for coronavirus (not severe acute respiratory syndrome coronavirus 2) and for human rhinovirus and enterovirus. Other laboratory test results are shown in Table 1. Blood was again obtained for culture, and additional imaging studies were obtained.

Dr. Zucker: Ultrasonography of the abdomen (Fig. 1B) revealed multiple hypoecho-

Table 1. Laboratory Data.*

Variable	Reference Range†	On First Admission, 4 Wk before Current Presentation	On Second Admission, 3 Wk before Current Presentation	On Current Presentation
Hemoglobin (g/dl)	10.5–13.5	9.7	9.6	7.7
Hematocrit (%)	33.0–40.0	29.8	30.0	24.2
White-cell count (per μl)	4500–11,000	28,440	20,120	42,390
Neutrophils	1800–7000	16,320	12,680	32,260
Lymphocytes	3000–9500	8160	4830	6360
Monocytes	200–1900	1990	1610	2630
Eosinophils	50–450	1480	800	380
Basophils	0–500	480	200	380
Platelet count (per μl)	140,000–440,000	564,000	432,000	440,000
Erythrocyte sedimentation rate (mm/hr)	0–14	63	93	78
C-reactive protein (mg/liter)	0.0–8.0	31.3	55.0	107.9
Sodium (mmol/liter)	133–145	140	135	138
Potassium (mmol/liter)	3.4–4.7	4.5	3.9	4.2
Chloride (mmol/liter)	98–115	102	98	101
Carbon dioxide (mmol/liter)	22–27	23	25	21
Urea nitrogen (mg/dl)	4–18	13	7	8
Creatinine (mg/dl)	0.30–1.00	0.34	0.30	0.37
Glucose (mg/dl)	65–99	104	107	96
Calcium (mg/dl)	8.8–10.8	9.7	9.6	9.5
Lactate dehydrogenase (U/liter)	110–295	265	—	3443
Aspartate aminotransferase (U/liter)	22–58	24	35	29
Alanine aminotransferase (U/liter)	10–40	13	15	17
Alkaline phosphatase (U/liter)	110–302	805	1090	718
Total bilirubin (mg/dl)	0.0–1.2	<0.2	<0.2	0.2
Albumin (g/dl)	3.1–4.8	4.1	3.7	3.5
Total protein (g/dl)	6.1–8.1	7.6	7.1	7.4

* To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for calcium to millimoles per liter, multiply by 0.250. To convert the values for bilirubin to micromoles per liter, multiply by 17.1.

† 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 children who do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

ic splenic lesions, measuring up to 6 mm in diameter. No cholelithiasis, thickening of the gallbladder wall, or biliary ductal dilatation was present. Computed tomography (CT) of the chest (Fig. 1C), abdomen, and pelvis, performed after the intravenous administration of contrast material, was notable for mediastinal lymphadenopathy mostly involving the paratracheal and subcarinal lymph node stations, as well as right hilar lymphadenopathy.

Dr. Madhavan: The patient was readmitted to the hospital. During the next 3 days, he had intermittent fever, which abated after the administration of ibuprofen. Blood cultures showed no growth. On the fourth hospital day, the patient was discharged home with recommendations for continued supportive care and instructions to undergo additional laboratory testing and imaging studies.

During the subsequent 3 weeks, the patient

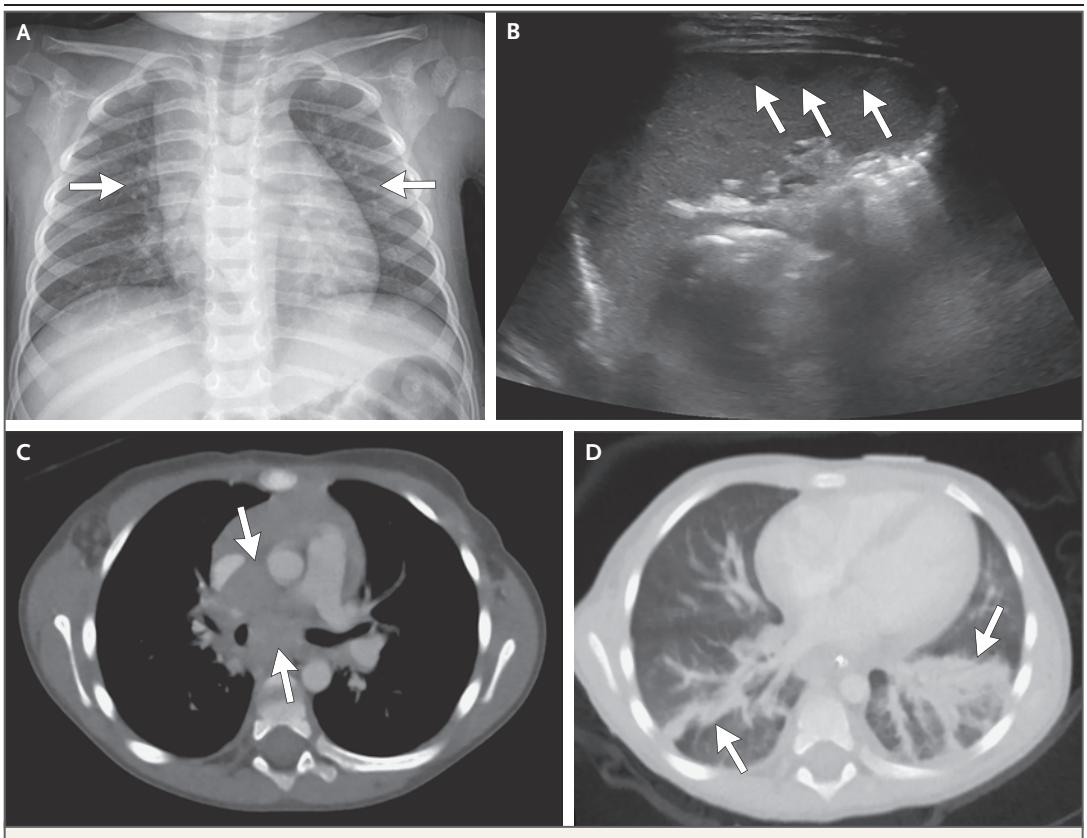

Figure 1. Imaging Studies of the Chest and Abdomen.

A frontal chest radiograph obtained during the patient's first admission (Panel A) shows mild bilateral peribronchial thickening and ill-defined perihilar opacities (arrows). An abdominal ultrasound image obtained during the patient's second admission (Panel B) shows multiple subcentimeter hypoechoic lesions (arrows) in the spleen. An axial contrast-enhanced CT image of the chest that was also obtained during the second admission (Panel C) shows extensive paratracheal and subcarinal mediastinal lymphadenopathy (arrows). An axial contrast-enhanced CT image of the chest obtained during the patient's third admission (Panel D) shows new basilar-predominant opacities in both lungs (arrows).

continued to have intermittent fever. On the day of the current presentation, planned outpatient laboratory testing was performed. The white-cell count was 42,390 per microliter, and the patient's mother was asked to bring him back to the emergency department for evaluation.

The patient's mother reported that the patient had fever once or twice daily. The episodes of fever were associated with chills, and the patient seemed averse to being held or touched. When he had no fever, he was playful and behaved normally. He had persistent dry cough, nasal congestion, and decreased intake of solid foods. There was no vomiting, diarrhea, or blood or mucus in the stool.

The patient had had normal growth and had met normal developmental milestones. He had iron-deficiency anemia. He took no medications and had no known drug allergies. Immunizations were up to date. His parents had immigrated to the United States from Central America. The patient and his siblings had been born in the United States, lived in a suburban area of New England, and had not traveled outside the region. His parents and older sister were healthy. One older brother had developmental delay and sensorineural hearing loss of unknown cause. Three and a half years before the patient's current presentation, another older brother had received a diagnosis of disseminated *Mycobacterium avium* complex infection at 31 months of age.

On examination, the axillary temperature was

40.2°C, the blood pressure 131/61 mm Hg, the pulse 180 beats per minute, the respiratory rate 55 breaths per minute, and the oxygen saturation 88% while the patient was breathing ambient air. The patient was crying but consolable. Breathing was normal, without grunting or intercostal retractions, and the lungs were clear on auscultation. The abdomen was soft and nontender. There was palpable right axillary lymphadenopathy; he resisted examination of the left axilla. No cervical or inguinal lymphadenopathy was noted. No focal tenderness on palpation of the arms, legs, or joints was present, and there was no rash.

Dr. Zucker: Radiography of the chest revealed an opacity in the right lower lobe. Subsequent CT of the chest, performed after the intravenous administration of contrast material (Fig. 1D), revealed multifocal pulmonary opacities with a basilar predominance in both lungs, along with lymphadenopathy that was relatively unchanged from that observed on previous CT imaging.

Dr. Madhavan: Administration of supplemental oxygen through a nasal cannula was initiated at a rate of 1 liter per minute. The patient was readmitted to the hospital.

A diagnostic test was performed.

DIFFERENTIAL DIAGNOSIS

Dr. Alicia Casey: This previously healthy and fully vaccinated 30-month-old boy presented with a 4-week history of recurrent fever in the context of persistent cough and intermittent limping. He was found to have hypoxemia and progressively worsening leukocytosis (with a white-cell count of 42,390 per microliter on the day of the current presentation), and he had a history of iron-deficiency anemia. Imaging studies revealed diffuse lung parenchymal opacities, multifocal lymphadenopathy, and multiple hypoechoic splenic lesions.

FEVER OF UNKNOWN ORIGIN

This patient had the syndrome known as fever of unknown origin, which is defined as a temperature exceeding 38.3°C at least daily for more than 8 days. In developed countries, a diagnosis is identified in most children with fever of unknown origin after extensive evaluation. Infection is the most common cause of fever of unknown origin in children of all ages, but in children older than 1 year of age, inflammatory, malignant, and miscellaneous conditions account for a substantial percentage of cases in developed countries. Overall, cancer is a less common cause of fever of unknown origin in children than in adults. In resource-limited countries, infection is the most common cause of this syndrome in children of any age, and noninfectious causes are less prevalent in resource-limited countries than in developed countries.[1,2]

The differential diagnosis of fever of unknown origin in this patient can be narrowed by focusing on diseases that typically involve the lungs, given the patient's cough, hypoxemia, and imaging findings of lymphadenopathy and diffuse lung parenchymal opacities. Cancer involving the respiratory tract or lymphoma with mediastinal involvement are unlikely in this patient, given his age. In addition, he did not have weight loss, fatigue, or cytopenias — findings that would be suggestive of cancer. Children with systemic lupus erythematosus, granulomatous–lymphocytic interstitial lung disease, antineutrophil cytoplasmic antibody–associated vasculitis, lung disease associated with inflammatory bowel disease, other immune-mediated interstitial lung diseases, or Castleman's disease can present with fever and pulmonary involvement. However, these diagnoses would be unlikely in a child of this patient's age.

SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

Systemic juvenile idiopathic arthritis (JIA) can occur at any age, but the peak age at presentation is between 1 and 5 years.[3] Most patients with systemic JIA have fever, arthritis, and an evanescent, macular, salmon-colored rash. Viral infections complicated by postinfectious arthritis can also be associated with fever; therefore, systemic JIA is not a consideration unless fever has been present for more than 2 weeks. Fever in patients with systemic JIA typically occurs on a daily basis and is characterized by a high spike in temperature with a return to a normal or subnormal temperature for the remainder of the day. Arthritis can occur in any joint, and some patients have arthralgias without evidence of arthritis; either of these conditions could explain this patient's limp.[4] Lymphadenopathy occurs in approximately one third of affected patients.[5]

This patient had a white-cell count of greater than 20,000 per microliter with a polymorpho-

nuclear predominance, an elevated erythrocyte sedimentation rate and C-reactive protein level, and initial thrombocytosis, all of which are consistent with systemic JIA. The blood level of ferritin was not provided for this patient, but markedly elevated levels can be seen in patients with systemic JIA. A few features of this patient's presentation are not consistent with systemic JIA, including the absence of rash and the presence of imaging findings that would not be typical of systemic JIA–associated lung disease; however, the spectrum of systemic JIA manifestations is broad, and this patient could have early, mild disease.[6,7] He did not have clubbing with erythema of the fingertips, which is often seen in patients with systemic JIA–associated lung disease. However, systemic JIA remains a possible diagnosis in this case.

KAWASAKI'S DISEASE

Kawasaki's disease is caused by widespread inflammation of medium-sized arteries and is typically diagnosed in children between 1 and 3 years of age. Kawasaki's disease is an important consideration in this patient because it is commonly associated with fever and lymphadenopathy. However, this patient did not have the classic mucocutaneous features of Kawasaki's disease, such as conjunctivitis, mucositis with cracked lips and strawberry tongue, and polymorphous rash.[8] In addition, although patients with Kawasaki's disease can have pulmonary edema due to cardiac dysfunction, parenchymal lung disease would be atypical.[8]

INFECTION

Infection is the most likely cause of fever of unknown origin in this patient, given his age. His symptoms and imaging findings are most consistent with a lower respiratory tract infection. Typical bacterial infections are unlikely because of the prolonged and indolent course. The time course of this patient's illness is more consistent with atypical bacterial infection (e.g., mycoplasma pneumonia), mycobacterial infection (e.g., tuberculosis or infection with a nontuberculous mycobacterium), viral infection (e.g., cytomegalovirus infection or Epstein–Barr virus infection), or fungal infection (e.g., blastomycosis, cryptococcosis, coccidioidomycosis, histoplasmosis, or aspergillosis). During the patient's second admission to the hospital, tests for coronavirus and human rhinovirus and enterovirus were positive; however, I suspect that these were probably "red herrings," given that his symptoms progressed during the next 3 weeks.

INBORN ERRORS OF IMMUNITY

One unusual feature of the patient's family history is that his older brother had received a diagnosis of disseminated *M. avium* complex infection at 31 months of age. His brother had no other history suggestive of any conditions that might confer a predisposition to atypical mycobacterial infection, such as structural abnormalities of the lung and airways (e.g., cystic fibrosis or bronchiectasis), acquired conditions leading to immunodeficiency (e.g., human immunodeficiency virus infection or the use of immunosuppressive medications), or difficulties in airway clearance (e.g., neuromuscular weakness or thoracic or skeletal abnormalities).[9] This history suggests that the patient's brother had an inborn error of immunity with susceptibility to atypical mycobacterial infections. Could this patient have the same inborn error of immunity?

Inborn errors of immunity should be considered in patients with infections that are severe, complicated, recurrent, occurring in multiple anatomical locations, resistant to treatment, or caused by unusual pathogens.[10] Even if this patient had not had a family history that included infection with an unusual pathogen, inborn errors of immunity should be considered because he had been hospitalized three times with a presumed infection that involved multiple locations including the lungs, lymph nodes, and spleen.

Inborn errors of immunity encompass a group of nearly 500 disorders.[11] Identification of the organism that is causing infection may provide a clue that leads to the specific type of inborn error of immunity.[12] Infection with an atypical mycobacterium in an otherwise healthy child warrants investigation for abnormalities in the number and function of T cells, defects in interferon-γ signaling, or defects in macrophage function. Mendelian susceptibility to mycobacterial disease (MSMD) is a group of genetic disorders that result in impaired production of interferon-γ or impaired phagocyte response to interferon-γ. Disseminated mycobacterial infection may develop in patients with MSMD after

the administration of the bacille Calmette–Guérin vaccine. In addition, these patients may begin to have local and systemic recurring infections with weakly virulent environmental organisms, including mycobacteria, fungal organisms, and viruses (particularly herpesviruses).[13]

Given this patient's presentation with fever of unknown origin, diffuse lung parenchymal opacities, multifocal lymphadenopathy, multiple hypoechoic splenic lesions, and leukocytosis, I am concerned that he may have an atypical mycobacterial infection like that seen in his older brother. To establish this diagnosis, I would perform bronchoscopy and bronchoalveolar lavage to obtain a microbiologic diagnosis. On the basis of his family history, I suspect that the patient and his brother have an inborn error of immunity, specifically MSMD. To establish this diagnosis, the next steps would be immunophenotyping and genetic testing for MSMD.

HOSPITAL COURSE AND CLINICAL IMPRESSION

Dr. Madhavan: Multiple radiologic studies obtained over the course of the patient's three admissions showed multifocal lesions in the lungs and spleen as well as diffuse lymphadenopathy, findings consistent with a disseminated fungal or mycobacterial infection. Suspicion for disseminated tuberculosis was low, given the absence of history of travel, congregate living, or contact with persons with tuberculosis.

When the patient's older brother had received a diagnosis of disseminated *M. avium* complex infection, he had also received a diagnosis of MSMD after genetic sequencing revealed homozygous pathogenic mutations in the gene encoding subunit 2 of the interferon-γ receptor (*IFNGR2*). The parents had not agreed to genetic testing for other family members at that time and again declined genetic testing both when the patient's mother was pregnant with the patient and after the patient was born. An immunodeficiency similar to that of the patient's brother was possible in this patient, and atypical mycobacterial infection was considered to be the most likely cause of his lower respiratory tract infection.

Given the unknown bacillary burden and extent of disease, it was crucial to assess as many sites as possible to increase diagnostic yield and the likelihood of sufficient data for therapeutic decision making. Numerous specimens were obtained, including blood, urine, stool, bronchoalveolar-lavage fluid, gastric aspirates, and biopsy specimens from a left axillary lymph node and from bone marrow.

CLINICAL DIAGNOSIS

Probable mycobacterial infection and mendelian susceptibility to mycobacterial disease.

DR. ALICIA CASEY'S DIAGNOSIS

Atypical mycobacterial infection in the context of probable mendelian susceptibility to mycobacterial disease.

DIAGNOSTIC TESTING

Dr. Madhavan: Gram's staining of the biopsy specimen from the left axillary lymph node revealed acid-fast bacilli. Cultures of the blood, bone marrow biopsy specimen, bronchoalveolar-lavage fluid and gastric aspirate samples, and left axillary lymph node biopsy specimen eventually grew *M. kansasii*, which confirmed the diagnosis of disseminated mycobacterial infection. This species is rarely pathogenic in immunocompetent persons but can cause serious infections in patients with underlying immunodeficiency.

Dr. Jocelyn R. Farmer: A diagnosis of disseminated mycobacterial infection should prompt consideration of underlying immunodeficiency (Fig. 2).[14] Causes of secondary immunodeficiency were considered, and, in this patient, none were identified; screening tests for human immunodeficiency virus were negative, no cancers were identified, and the patient was not receiving any iatrogenic forms of immunosuppression, such as treatment with a tumor necrosis factor α inhibitor.[15] Therefore, testing for inborn errors of immunity was performed, as detailed below.

In considering the type of inborn error of immunity that might be present in this patient with disseminated mycobacterial infection, we focused on immune pathways that are protective against mycobacterial infection in immunocompetent hosts, principally the pathway involving CD4+ type 1 helper T cells and effector phagocytes. Type 1 helper T cells respond to foreign antigens

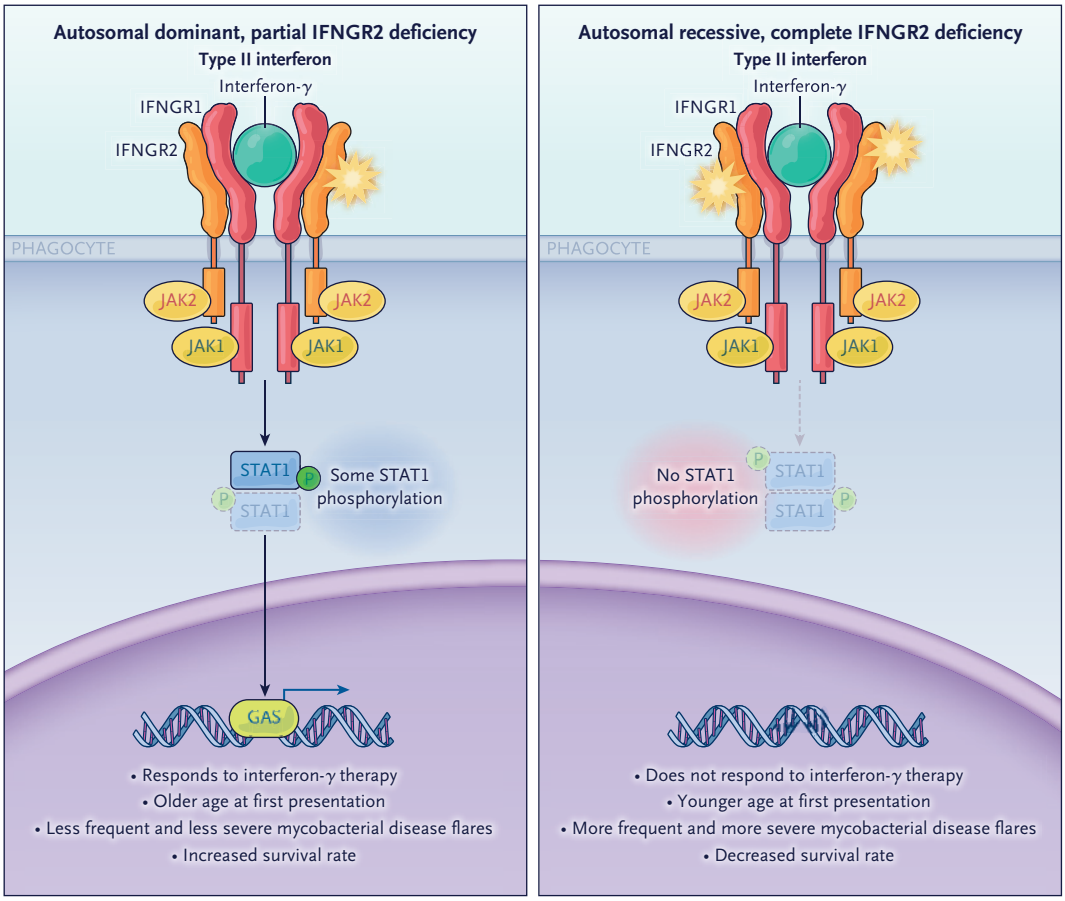

Figure 2. Mechanisms of Disease in Patients with Mendelian Susceptibility to Mycobacterial Disease.

Mendelian susceptibility to mycobacterial disease due to autosomal recessive, complete interferon-γ receptor 2 (IFNGR2) deficiency, which was diagnosed in this patient (right panel), is compared with autosomal dominant, partial IFNGR2 deficiency (left panel). GAS denotes interferon-γ–activated site, JAK1 and JAK2 Janus kinase 1 and 2, P phosphorylation, and STAT1 signal transducer and activator of transcription 1.

and produce interferon-γ. Effector phagocytes respond to interferon-γ, initiate the bactericidal oxidative burst, and further stimulate type 1 helper T cells through the production of interleukin-12.

This patient was found to have a normal CD4+ T-cell count in peripheral blood, along with intact CD4+ T-cell function as assessed by in vitro T-cell proliferation in response to anti-CD3 antibody alone and in association with interleukin-2 stimulation. These findings rule out a primary defect in the T-cell compartment or a combined immunodeficiency. In addition, the patient was found to have intact bactericidal oxidative burst function in phagocytes as measured with the use of dihydrorhodamine testing after in vitro stimulation with phorbol myristate acetate, a finding that ruled out a diagnosis of chronic granulomatous disease. However, on in vitro stimulation of peripheral-blood monocytes with interferon-γ, the cellular response as measured with the use of STAT1 (signal transducer and activator of transcription 1) phosphorylation was completely absent. These data were consistent with a diagnosis of MSMD, wherein the patient's phagocytes were unable to appropriately respond to interferon-γ.

Although genetic sequencing for MSMD was offered, the patient's parents did not agree to such testing. In light of the patient's immunophenotyping results and the findings from the

previous genetic sequencing in the patient's older brother, a diagnosis of MSMD due to autosomal recessive, complete IFNGR2 deficiency was made.

MICROBIOLOGIC AND IMMUNOLOGIC DIAGNOSIS

Disseminated *Mycobacterium kansasii* infection due to mendelian susceptibility to mycobacterial disease.

DISCUSSION OF MANAGEMENT

Dr. Madhavan: When treating mycobacterial disease, a combination of agents is used to mitigate the development of resistance. The inclusion of parenteral therapy is based on resistance patterns and the extent of infection.[16] In this patient, after Gram's staining of the lymph node biopsy specimen identified acid-fast bacilli and the culture grew *M. kansasii*, treatment with parenteral amikacin plus oral rifampin, ethambutol, and azithromycin was started. This treatment regimen was based on typical resistance patterns, given the expected long turnaround time needed to perform antimycobacterial susceptibility testing on an *M. kansasii* isolate. It is notable that 2 months after the initial diagnosis, culture of the bone marrow biopsy specimen grew *M. abscessus*; intravenous imipenem was subsequently added to the treatment regimen.

The patient underwent routine monitoring for potential toxic effects of each of the medications individually and in combination, and the results remained reassuring. Challenges with oral administration of medications are especially common in children, and therapeutic drug monitoring in this patient confirmed that he was receiving the intended doses. Problems with maintenance of central venous access are also frequent; this patient had three brief hospital admissions for repair and replacement of a peripherally inserted central catheter.

The duration of treatment of atypical mycobacterial disease depends on the clinical and radiologic response to therapy, along with changes in laboratory test results, with longer courses anticipated in the context of underlying immunodeficiency. The long-term prognosis in patients with atypical mycobacterial disease and MSMD and the treatment recommendations for such patients depend on the specific immunologic defect and its severity.

Dr. Farmer: The epidemiologic features of MSMD have been described in cohorts of patients who were followed predominantly at large referral centers. These data have been used to ascertain the frequency of genetic causes of MSMD. Autosomal recessive, complete IFNGR2 deficiency — as was diagnosed in this patient — is an extremely rare disorder, accounting for approximately 3 to 7% of cases of MSMD.[17,18] This level of immunodiagnostic clarity, down to the specific genetic driver of disease, has direct clinical implications for patient care.

Patients who have MSMD with autosomal recessive complete deficiency of the interferon-γ receptor have worse clinical outcomes than those with autosomal dominant partial deficiency, including an earlier age at first presentation, a higher overall risk of death, and more frequent and severe acute episodes of mycobacterial infection.[19] In patients who have MSMD with autosomal recessive complete deficiency of the interferon-γ receptor, there is limited ability to augment signaling further with interferon-γ therapy; this was the case particularly in this patient, in whom cellular response as assessed with the use of STAT1 phosphorylation was not merely reduced but completely absent.

We participated in a discussion with colleagues at the National Institutes of Health about this specific patient. The recommendation was to consider bone marrow transplantation after clinical stabilization for definitive management of his condition, given both the high-risk nature of the underlying mutation and the lack of available immune augmentation strategies to mitigate the risk of infection.

On account of health disparities, demographic factors, including a patient's ethnic background, may confer an independent higher risk of complications and death. This patient's family identified as Hispanic, and both parents were born in Central America. Data from the last four decades have shown that we do not know the true worldwide prevalence of MSMD, specifically including the frequency in Central America, owing to the paucity of national registry data regarding inborn errors of immunity as well as the lack of access to advanced diagnostic techniques such as genetic testing.[20] Therefore, the true fre-

quency of MSMD among persons of this patient's specific ethnic background is not known. Moreover, patients with inborn errors of immunity who identify as Hispanic have a higher risk of early death (before 24 years of age) than non-Hispanic patients with inborn errors of immunity.[21] These data highlight an urgent and unmet need to ensure equitable care for this patient's family specifically and, more broadly, for all patients with inborn errors of immunity.

Dr. Madhavan: After the patient completes his acute treatment regimen for the atypical mycobacterial infection, stem-cell transplantation would be curative. However, several factors have greatly influenced care for this family. Medical conversations, particularly those addressing longer-term considerations, are complicated by the parents' low health literacy. In addition, the parents are deeply religious and often prioritize placing their children's health "in God's hands" over partnering with the medical team. The coronavirus disease 2019 pandemic began 4 months after the patient's brother's diagnosis, a factor that decreased in-person oversight. At that time, the parents chose to discontinue the brother's medications; this led to worsening disease, and he continues to receive therapy nearly 5 years after his diagnosis. Changes in health care infrastructure have caused decreased home health care and staffing availability; their mother now needs to travel weekly to bring the children to a health care clinic for laboratory testing (to monitor for drug-related toxic effects) and for central catheter care.

There have been creative efforts to involve the family's primary care pediatrician, Spanish-speaking staff, chaplaincy, palliative-care personnel, and medical subspecialists in conversations with the family regarding the importance of antimicrobial therapy and regular visits for monitoring for an indeterminate length of time. The parents remain reluctant to escalate care, and discussions about curative stem-cell transplantation have been difficult to move forward.

One year after the initial diagnosis, the patient continues to receive intravenous amikacin and imipenem and oral rifampin, azithromycin, and ethambutol. He has remained afebrile and has had no respiratory symptoms except those involving the identified respiratory viral illnesses. The levels of inflammatory markers have normalized. Recrudescent central nervous system disease that occurred in the patient's brother 4 years and 4 months after his initial diagnosis resulted in the resumption of treatment with amikacin in addition to his previous oral therapy regimen; he continues to receive intravenous amikacin and oral rifampin, azithromycin, and moxifloxacin. Although the patient and his brother are currently in clinically stable condition and have had few unacceptable drug-related toxic effects, their long-term prognoses are far from reassuring.

FINAL DIAGNOSIS

Disseminated *Mycobacterium kansasii* and *Mycobacterium abscessus* infections due to mendelian susceptibility to mycobacterial disease.

This case was presented at Pediatric Grand Rounds.

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

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