CASE 9.6
Human Immunodeficiency Virus Infection | Level 3

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1. What subjective and objective evidence supports the diagnosis of HIV in this child?

SUBJECTIVE FINDINGS: The patient presented with a chief complaint of fever, cough, difficulty breathing, and poor feeding. These symptoms are consistent with an acute pulmonary infection and could be indicative of *Pneumocystis jiroveci* pneumonia, given this patient's clinical condition. Infants with HIV infection are commonly diagnosed with *P. jiroveci* pneumonia. Developmental delay is frequent in untreated HIV in infants; this child is not crawling or babbling, according to his foster mother. The infant's biological mother engaged in risky behaviors, had a known history of sexually transmitted infections, and did not undergo prenatal care; therefore, maternal-to-child transmission of HIV is of great concern in this case.

OBJECTIVE FINDINGS: Findings consistent with *P. jiroveci* pneumonia are fever, tachypnea, cough, respiratory distress (presence of nasal flaring and retractions), and hypoxia. Lung auscultation revealed bilateral basilar rales and chest radiography obtained at the urgent care center showed bilateral diffuse parenchymal infiltrates, which are consistent with *P. jiroveci* pneumonia. Presence of *P. jiroveci* pneumonia or other opportunistic infections is a strong indicator of HIV infection or severe immune compromise; this child has leukopenia and a CD4 count <15%. Other findings consistent with HIV infection in this child include failure to thrive (weight-for-age <2%, length-for-age ~2%), microcephaly (head circumference <2%), malnutrition (hypoalbuminemia), candidal infections (thrush and diaper dermatitis), and anemia. Laboratory evidence of HIV is demonstrated by a positive HIV antibody test, positive Western blot, and HIV RNA level of 190,000 copies/mL.

2. Assess the treatment plan for this patient's pneumonia and recommend changes to the regimen, if necessary.

Definitive diagnosis of *P. jiroveci* pneumonia can be made only by isolating the organism from pulmonary tissue or fluid, which usually requires an invasive procedure such as bronchoscopy with bronchoalveolar lavage (BAL). Treatment can begin prior to definitive testing because results are often positive for at least 72 hours after initiating antimicrobial therapy. Intravenous trimethoprim/sulfamethoxazole (TMP-SMX) is the drug of choice and is dosed as 15 to 20 mg/kg/day (of trimethoprim component) divided every 6 hours. As the pneumo-

nitis resolves, children with mild-to-moderate disease who do not have malabsorption or significant diarrhea can be converted to oral TMP-SMX (same daily dose) for a total course of therapy of 21 days. Intravenous TMP-SMX has been difficult to procure in recent years because of manufacturing problems. Although it is currently available in specific vial sizes, future availability may be sporadic and hospitals should proactively identify alternative agents for use when it is not available. For this child, the initially prescribed antibiotic regimen is appropriate for his weight and renal function (37.5 mg IV every 6 hours is equal to 20 mg/kg/day). The diagnosis should be confirmed through appropriate microbiologic testing, and the child should be monitored for improvement (normalization of respiratory rate, oxygen saturation, breath sounds, temperature, and blood gasses; disappearance of nasal flaring and retractions) and, if possible, converted to oral therapy to complete a 21-day course. Oral TMP/SMX can be used when there is evidence of clinical improvement and the child is able to tolerate oral therapy (no malabsorption or significant vomiting or diarrhea). If he is unable to tolerate TMP/SMX or does not respond to it after 5 to 7 days of therapy, then IV pentamidine (4 mg/kg once daily) can be given.

This child is at risk for *P. jiroveci* pneumonia but could also be infected with other organisms such as *Streptococcus pneumoniae*, *Haemophilus influenzae* (nontypable or type b), *Mycoplasma pneumoniae*, or viral pathogens. His lack of immunization against common pathogens in community-acquired pneumonia (CAP) and his immunocompromised state increase the risk for pneumonia caused by these organisms. Empiric treatment for CAP (IV ampicillin 200 mg/kg/day divided every 6 hours with or without IV azithromycin 10 mg/kg/day) should be initiated concomitantly with TMP/SMX until the diagnosis of *P. jiroveci* pneumonia is confirmed because the rates of TMP/SMX resistance in *S. pneumoniae* and *H. influenzae* are high.

Corticosteroid therapy is recommended for children with moderate-to-severe *P. jiroveci* pneumonia because it has been demonstrated to reduce the rates of respiratory failure and mortality. Clear indications for corticosteroid treatment are PaO_2 <70 mm Hg or an alveolar-arterial gradient of >35 mm Hg on room air. This child was hypoxic on presentation to the urgent care center and placed on supplemental oxygen before transfer to the hospital. His venous blood gas revealed mild respiratory acidosis with some metabolic compensation, and there was concern for respiratory failure. Empiric initiation of corticosteroid therapy is appropriate for this child given the high likelihood of *P. jiroveci* pneumonia and the severity of presentation, but some healthcare providers may opt to delay steroid therapy if the diagnosis can be confirmed in the next 72 hours. If steroid therapy is initiated, prednisone or prednisolone can be used and are dosed as 7.5 mg (1 mg/kg/dose) for this child given twice daily for 5 days, followed by 3.75 mg (0.5 mg/kg/dose) given twice daily for 5 days and 3.75 mg (0.5 mg/kg) once daily through day 21. Prednisolone is preferred over prednisone in the liquid formulation because of its improved palatability. If oral therapy is not an option, IV methylprednisolone can be administered using 1 mg/kg dose every 6 hours on days 1 to 7, followed by 1 mg/kg/dose bid on days 8 to 9, then 0.5 mg/kg/dose bid on days 10 to 11, and 1 mg/kg/dose daily on days 12 to 16.

Finally, because of this child's immune status, secondary prophylaxis for *P. jiroveci* should be initiated after the acute infection has resolved. No antimicrobials used to treat *P. jiroveci* completely eliminate it from the body; therefore, prophylaxis is required after treatment for active infection in immunocompromised persons unless criteria to discontinue secondary prophylaxis are met. Prophylaxis with oral TMP-SMX (dosed as 5 mg/kg/day [of TMP] or 5 mg/kg 3 times weekly on consecutive days) should continue until the child is treated with antiretroviral therapy for at least 6 months and has CD4 ≥15% or CD4 ≥500 cells/mm^3. For this child, the dose should be 37.5 mg (TMP component) once daily. If he is unable to tolerate TMP/SMX, oral dapsone (2 mg/kg/day) can be used for secondary prophylaxis.