A 12-year-old black girl is hospitalized because of increasingly severe dyspnea and sore throat. The sore throat started about a week earlier and was accompanied by fever and chills. The patient was evaluated at an urgent care center when her symptoms worsened, where she was given ampicillin for a presumptive “strep throat.” A generalized maculopapular erythematous rash developed within 24 hours of the start of therapy, and the ampicillin was promptly withdrawn. The rash cleared gradually thereafter. Now the patient’s sore throat has worsened to the point that she has difficulty with drinking and eating. She has become increasingly dyspneic during the past 24 hours.

The child has no history of recurrent infections, cough, chest pain, palpitations, or seizures. She has been nauseated but has had no vomiting, hematemesis, or melena. She reports a dull aching pain in the left upper quadrant. She denies headache, vision problems, weakness, and neck stiffness. Her urinary output is scanty and highcolored. She has no known allergies, and her immunizations are up-to-date. The patient is a well-built, well-nourished young girl who looks ill and who is in moderate respiratory distress. Her pulse rate is 100 beats per minute; temperature, 38.1°C (100.6°F); respiratory rate, 30 breaths per minute; supine blood pressure, 90/60 mm Hg; standing blood pressure, 78/48 mm Hg. Skin, mucous membranes, and tongue are dry. The tonsils are grossly erythematous, enlarged, and almost touching each other in midline. There is a grayish white exudate over the tonsils. An expiratory stridor is audible. Skin shows fading rash. Cervical, anterior and posterior chain, submandibular, axillary, and inguinal glands are enlarged, discrete, nonmatted, and nontender. The ankles are not swollen. The chest moves symmetrically and is resonant to percussion; bronchovesicular sounds are audible bilaterally. No wheeze or rales are heard. Jugular venous pressure is normal; the apex is within normal limits, and both heart sounds are audible without any murmur or gallop. The liver is 3 cm below the costal margin, and the spleen is 9 cm below the costal margin. Bowel sounds are normal. The patient is neurologically intact.

The white blood cell (WBC) count is 21,000/μL, with 21% polymorphonuclear leukocytes, 72% leukocytes, and 16% atypical lymphocytes. Hemoglobin level is 12.6 g/dL; platelet count, 212,000/μL; erythrocyte sedimentation rate, 88 mm/h. What abnormalities does the peripheral smear show, and to which of the following disorders does the clinical picture point?

- Diphtheria
- Tangier disease
- Infectious mononucleosis
- Hodgkin lymphoma
- Vincent angina

**SYMPTOMS/COMPLICATIONS**

Clinical features of infectious mononucleosis are listed in the Table. Associated sequelae are rare; most patients recover fully in 4 to 6 weeks. When complications do occur, however, they can be dramatic and often lifethreatening.

- In severe cases, proliferation of lymphoid tissue leads to tonsillar enlargement; this may cause upper airway obstruction with stridor.
- Paratracheal adenopathy and pulmonary interstitial infiltration may also cause dyspnea.
- Splenic rupture occurs in 0.1% to 0.2% of cases; affected patients may require prompt splenectomy. In most cases, splenic rupture occurs after minor trauma during the second
Other hematologic complications include thrombocytopenia, hemolytic anemia (2% of cases), and granulocytopenia.

Neurologic complications include encephalitis; seizures; Guillain-Barr syndrome; peripheral neuropathy; myelitis; and cranial nerve palsies, including Bell palsy.

Other rare complications are severe hepatitis with grossly elevated liver function test results, myocarditis, and pericarditis.

**DIAGNOSIS**

In most infected patients, leukocytosis is observed; the WBC count ranges from 10,000/μL to 20,000/μL. Atypical lymphocytes may account for 10% to 80% of total lymphocytes. Mild thrombocytopenia is transient. In the great majority, there is mild to moderate elevation of liver enzyme levels—particularly transaminases—to about 2 to 3 times normal. Detection of heterophil antibodies with the monospot test is the characteristic laboratory abnormality. These antibodies are detected in 90% of patients with infectious mononucleosis, although the test takes up to 3 weeks to become positive. Therefore, repeated testing may be necessary—especially if the initial test is performed early. Several commercially available monospot tests are helpful in making the diagnosis. The heterophil antibodies usually disappear by 3 months but may be present for up to a year. False-positive monospot test results are rare but can occur in patients with varicella, influenza, or lymphoma. EBV infection can also be detected by the presence of other specific antibodies. Routine use of virus-specific antibody detection is not needed but may be helpful in patients with atypical cases of EBV infection or in young children who can be heterophil antibody-negative. Titers of IgM and IgG antibodies to EBV viral capsid antigen (VCA) are elevated in more than 90% of patients at the onset of the disease. Simultaneous detection of EBV early antigen also helps confirm the diagnosis.

**PROGNOSIS**

Infectious mononucleosis is usually self-limited. The duration of infection varies; the acute phase lasts about 2 weeks. Generally, about 20% of patients can return to work or school within 1 week, and 50%, in 2 weeks. Fatigue may not resolve fully for 2 to 4 weeks. Fewer than 1% of those infected die—usually from splenic rupture, encephalitis, or severe airway obstruction. **TREATMENT** Therapy is largely supportive. Patients need to rest during the acute phase. For those with splenomegaly, heavy lifting and contact sports should be avoided for 2 months (to protect against splenic rupture). Acetaminophen or an NSAID can be used as an antipyretic instead of aspirin (to prevent the remote possibility of Reye syndrome). The role of corticosteroids in uncomplicated cases has been extensively studied—and they are not advocated. Nevertheless, these agents have been very useful in patients with impending airway obstruction, myocarditis, hemolytic anemia, or encephalitis. Antiviral therapy with acyclovir has been shown to limit oropharyngeal viral shedding, but it has no impact on the clinical course. **OUTCOME OF THIS CASE** The patient in this case had a throat culture negative for group A streptococci; blood cultures were also negative. Results of urinalysis were normal, and urine culture was negative. Serum sodium level was 130 mEq/L; potassium, 3.1 mEq/L; chloride, 92 mEq/L; bicarbonate, 21 mEq/L; glucose, 98 mg/dL; urea nitrogen, 26 mg/dL; creatinine, 1.1 mg/dL; serum bilirubin, 2.6 mg/dL; bilirubin, direct, 1.9 mg/dL; protein, 6.9 g/dL; albumin, 4.3 g/dL; aspartate aminotransferase, 126 IU; alanine aminotransferase, 102 IU; alkaline phosphatase, 222 IU. Findings on chest films and an ECG were normal. The monospot test was positive. Epstein-Barr panel revealed early antigen, 1:150, VCA 1:280. Epstein-Barr nucleolar antigen was absent. The patient was given intravenous fluids, and treatment with parenteral hydrocortisone, 100 mg every 8 hours, was started. Within 24 hours she became afebrile, was breathing with less difficulty, and was able to take sips of water. Three days after the start of therapy, her tonsils were smaller and she was able to tolerate a soft diet. She was discharged on the fourth day on a regimen of oral prednisolone in tapering doses.

**References:**

- Straus SE, Cohen JI, Tosato G, Meier J. NIH Conference. Epstein-Barr virus infections: biology,


**Links:**