Infectious mononucleosis

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Is the best-known clinical syndrome caused by Epstein-Barr virus (EBV). It is characterized by fatigue, malaise, fever, sore throat, and generalized lymphadenopathy. Originally described as **glandular fever**, it derives its name from the mononuclear lymphocytosis with atypical-appearing lymphocytes that accompany the illness. Other infections may cause infectious mononucleosis-like illnesses.

Etiology;

EBV, a member of the γ-herpesviruses, causes >90% of cases of infectious mononucleosis. Two distinct types of EBV, type 1 and type 2 (also called type A and type B),Type 1 is more prevalent worldwide than type 2, although type 2 is more common in Africa than in the United States and Europe. Both types lead to persistent, lifelong, latent infection. Dual infections with both types have been documented among immunocompromised persons. As many as 5–10% of infectious mononucleosis-like illnesses are caused by primary infection with cytomegalovirus, *Toxoplasma gondii*, adenovirus, viral hepatitis, HIV, and possibly rubella virus. In the majority of EBV-negative infectious mononucleosis-like illnesses.

Epidemiology;

EBV infects >95% of the world's population. It is transmitted via penetrative sexual intercourse, and in oral secretions such as “deep kissing.”

EBV is shed in oral secretions consistently for >6 mo after acute infection and then intermittently for life. As many as 20–30% of healthy EBV-infected persons excrete virus at any particular time. Immunosuppression permits reactivation of latent EBV; 60–90% of EBV-infected immunosuppressed patients shed the virus. EBV is also found in male and female genital secretions and can be spread through sexual contact.

This syndrome may be seen at all ages but is rarely apparent in children <4 yr of age,

Pathogenesis;

EBV initially infects oral epithelial cells, which may contribute to the symptoms of pharyngitis. After intracellular viral replication and cell lysis with release of new virions, virus spreads to contiguous structures such as the salivary glands, with eventual viremia and infection of B lymphocytes in the peripheral blood and the entire lymphoreticular system, including the liver and spleen. The atypical lymphocytes that are characteristic of infectious mononucleosis Epithelial cells of the uterine cervix may become infected by sexual transmission of the virus. EBV is consistently found intracellularly in smooth muscle cells of leiomyosarcomas of immunocompromised persons. **EBV was the 1st human virus to be associated with malignancy**. Malignant EBV-associated proliferations include nasopharyngeal carcinoma, Burkitt lymphoma, Hodgkin disease, lymphoproliferative disorders, and leiomyosarcoma in immunodeficient states, including AIDS. EBV is also associated with carcinoma of the salivary glands.

Clinical manifestations;

The incubation period of infectious mononucleosis in adolescents is **30–50 days**. In children, it may be shorter.

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The majority of cases of primary EBV infection in infants and young children are clinically silent. In older patients, the onset of illness is usually insidious and vague. Patients may complain of malaise, fatigue, acute or prolonged (>1 wk) fever, headache, sore throat, nausea, abdominal pain, and myalgia. This prodromal period may last 1–2 wk. The complaints of sore throat and fever gradually increase until patients seek medical care. Splenic enlargement may be rapid enough to cause left upper quadrant abdominal discomfort and tenderness, which may be the presenting complaint.

The **physical examination** is characterized by generalized lymphadenopathy (90% of cases), splenomegaly (50% of cases), and hepatomegaly (10% of cases). Lymphadenopathy occurs most commonly in the anterior and posterior cervical nodes and the submandibular lymph nodes and less commonly in the axillary and inguinal lymph nodes. Epitrochlear lymphadenopathy is particularly suggestive of infectious mononucleosis. Symptomatic hepatitis or jaundice is uncommon, but elevated liver enzymes are common. Splenomegaly to 2–3 cm below the costal margin is typical; massive enlargement is uncommon.

The sore throat is often accompanied by moderate to severe pharyngitis with marked tonsillar enlargement, occasionally with exudates. Petechiae at the junction of the hard and soft palate are frequently seen. The pharyngitis resembles that caused by streptococcal infection. Other clinical findings may include rashes and edema of the eyelids.

Rashes are usually maculopapular and have been reported in 3–15% of patients. Up to 80% of patients with infectious mononucleosis experience **"ampicillin rash"** if treated with ampicillin or amoxicillin. This vasculitic rash is probably immune mediated and resolves without specific treatment. EBV is also associated with **Gianotti-Crosti syndrome,** a symmetrical rash on the cheeks with multiple erythematous papules, which may coalesce into plaques, and persists for 15–50 days. The rash has the appearance of atopic dermatitis and may appear on the extremities and buttocks.

Diagnosis;

A presumptive diagnosis may be made by the presence of typical clinical symptoms with atypical lymphocytosis in the peripheral blood. The diagnosis is usually confirmed by serologic testing, Culture of EBV is tedious and requires 4–6 wk. The cultures are observed for 6 wk for signs of **cell transformation:** proliferation and rapid growth, mitotic figures, large vacuoles, granular morphology, and cell aggregation

Differential Diagnosis.

1-Infectious mononucleosis-like illnesses may be caused by primary infection with cytomegalovirus, T. gondii, adenovirus, viral hepatitis, HIV, or possibly rubella virus. Cytomegalovirus infection is a particularly common cause in adults.

2- pharyngitis may cause sore throat and cervical lymphadenopathy indistinguishable from that of infectious mononucleosis but is not associated with hepatosplenomegaly.

3- The most serious problem in the diagnosis of acute illness arises in the occasional patient with extremely high or low white blood cell counts, moderate thrombocytopenia, and even hemolytic anemia. In these patients, bone marrow examination and hematologic consultation are warranted to exclude the possibility of leukemia.

Laboratory tests ;

In >90% of cases there is leukocytosis of 10,000–20,000 cells/mm^3, of which at least ⅔ are lymphocytes; atypical lymphocytes usually account for 20–40% of the total number.

Other syndromes associated with atypical lymphocytosis include acquired cytomegalovirus infection, toxoplasmosis, viral hepatitis, rubella, roseola, mumps, tuberculosis, typhoid, *Mycoplasma* infection, and malaria, as well as some drug reactions. Mild thrombocytopenia to 50,000–200,000 platelets/mm^3 occurs in >50% of patients but only rarely is associated with purpura. Heterophile antibodies agglutinate cells from species different from those in the source serum. The transient heterophile antibodies seen in infectious mononucleosis detected by the **Paul-Bunnell-Davidsohn test**. **EBV-specific antibody testing** is useful to confirm acute EBV infection, especially in heterophile-negative cases, or to confirm past infection and determine susceptibility to future infection.

Treatment;

There is no specific treatment for infectious mononucleosis. **Rest and symptomatic treatments are the mainstays of management.**. Because blunt abdominal trauma may predispose patients to splenic rupture, it is advised against participation in contact sports and strenuous athletic activities during the 1st 2–3 wk of illness or while splenomegaly is present. **Short courses of corticosteroids (<2 wk) may be helpful for complications of infectious mononucleosis, but this use has not been evaluated critically.** Some appropriate indications include incipient airway obstruction, thrombocytopenia with hemorrhaging, autoimmune hemolytic anemia, seizures, and meningitis. A recommended dosage is prednisone 1 mg/kg/day (maximum 60 mg/day) or equivalent for 7 days and tapered over another 7 days..

Complications

The most feared complication **is subcapsular splenic hemorrhage or splenic rupture**, which occurs most frequently during the 2nd week of the disease. Rupture is commonly related to trauma, which often may be mild, and is rarely fatal. Swelling of the tonsils and oropharyngeal lymphoid tissue may be substantial and may cause **airway obstruction** that manifests as drooling, stridor, and interference with breathing..**Headache** is present in about half of cases, with severe neurologic manifestations, such as **seizures and ataxia**, in 1–5% of cases. There may be **meningitis with nuchal rigidity** and mononuclear cells in the cerebrospinal fluid, facial nerve palsy, transverse myelitis, and encephalitis. **Guillain-Barré syndrome or Reye syndrome may follow acute illness. Hemolytic anemia,** often with a positive Coombs test result and with cold agglutinins specific for red cell antigen i, occurs in 3% of cases. The onset is typically in the 1st 2 wk of illness and lasts for <1 mo. **Aplastic anemia** is a rare complication that usually presents 3–4 wk after the onset of illness, usually with recovery in 4–8 days, but some cases do require bone marrow transplantation. **Mild thrombocytopenia and neutropenia** are common, but severe thrombocytopenia (<20,000 platelets/μL) or severe neutropenia (<1,000 neutrophils/μL) are rare. **Myocarditis or interstitial pneumonia** may occur, both resolving in 3–4 wk. Other rare complications include **pancreatitis, parotitis, and orchitis.**

Prognosis;

The prognosis for complete recovery is excellent if no complications ensue during the acute illness. The major symptoms typically last 2–4 wk, followed by gradual recovery.. Prolonged and debilitating fatigue, malaise, and some disability that may wax and wane for several weeks to 6 mo are common. Occasional persistence of fatigue for a few years after infectious mononucleosis is well recognized.