Infectious mononucleosis

BACKGROUND Infectious mononucleosis is caused by the ubiquitous Epstein-Barr virus. It is a common condition usually affecting adolescents and young adults. Most cases are mild to moderate in severity with full recovery taking place over several weeks. More severe cases and unusual complications occasionally occur.

OBJECTIVE After presenting a case of severe infectious mononucleosis, the spectrum of disease is given. Diagnosis and complications are reviewed as well as management including the possible role for antiviral medications or corticosteroid therapy.

DISCUSSION The majority of cases of infectious mononucleosis are self limiting and require only supportive care. More severe cases, although unusual, may require admission to hospital and even to an intensive care unit. Corticosteroid therapy may be indicated for severe airway obstruction or other severe complications, but should be avoided unless the benefits outweigh potential risks. Antiviral therapy has no proven benefit.

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Case history

A 21 year old exchange student was admitted with a week long history of sore throat, fever, lethargy, anorexia and headache. His intake of food and fluids had been markedly reduced. He sought medical advice when he noticed he had become jaundiced. He had no risk factors for, nor contact with, viral hepatitis.

Initial examination revealed he was volume depleted and clearly icteric. He was febrile at 38.6°C and had generalised lymphadenopathy, hepatosplenomegaly and markedly enlarged tonsils that were mildly inflamed. There was no tonsillar exudate or palatal petechiae.

His blood film showed many atypical lymphocytes as well as red cell agglutination suggestive of cold agglutinins. Liver function tests revealed a predominantly hepatitic pattern and a bilirubin of 300 µmol/L (normal range 0–19 µmol/L). An infectious mononucleosis monospot test was positive.

He was commenced on intravenous fluid replacement and symptomatic relief with paracetamol and aspirin gargles. The following day his tonsillar hypertrophy had increased and he was commenced on intravenous hydrocortisone and was reviewed by the intensive care unit. He remained on the infectious diseases ward and after two days his corticosteroids were changed to oral. Twenty-four hours later, he deteriorated with further tonsillar hypertrophy and inability to take in oral fluids. A throat swab grew group C streptococcus, intravenous penicillin was commenced and hydrocortisone continued. He recovered over the following week and was discharged with a weaning course of prednisolone plus penicillin to complete a 10 day course.

Epstein-Barr virus (EBV) infects more than 90% of the world's population and most people do not have symptomatic infection. Infectious mononucleosis is the most common presentation and was described in the late 19th century by Filatov and Pfeiffer and was initially called 'Drusenfieber' (glandular fever).[1]

Transmission

Epstein-Barr virus can be found in throat washings of patients with infectious mononucleosis and for about 18 months after the infection. It can also be cultured from throat washings of 10–20% of healthy adults.[1] Transmission in young adults occurs through salivary contact such as kissing or

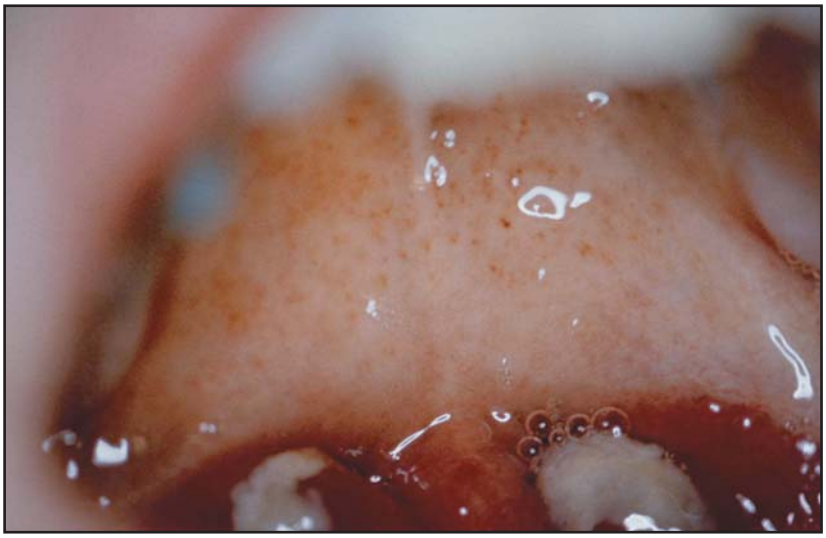

Figure 1. EBV infection

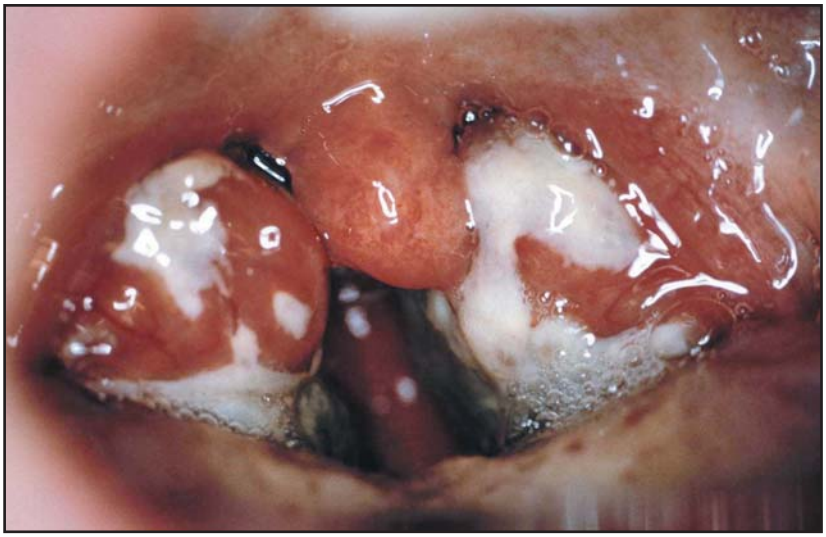

Figure 2. Streptococcal infection

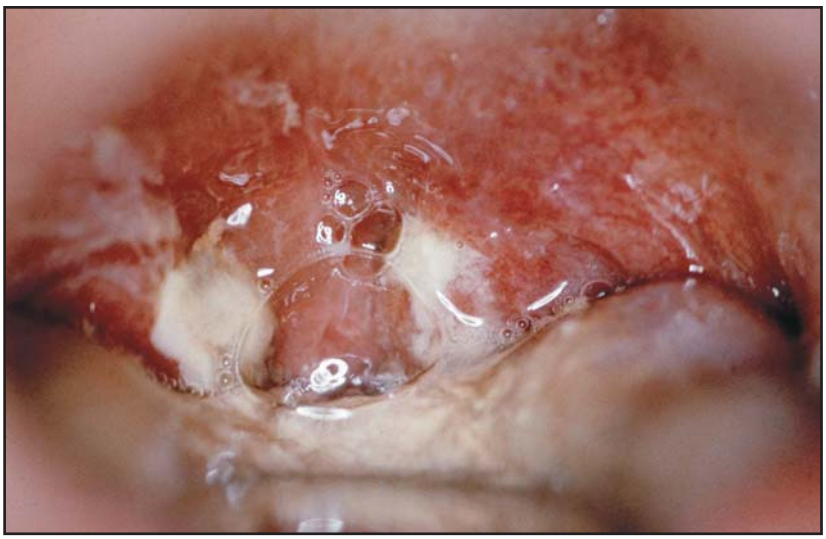

Figure 3. Epstein-Barr virus related palatal petechiae

sharing food and drinks but only a minority of patients recall contact with a known case.

Clinical features

When infection with EBV occurs during infancy or childhood, it is usually either asymptomatic or a nonspecific illness. The syndrome of infectious mononucleosis typically occurs when primary infection occurs in adolescents or adults[2] and consists of the triad of fever, sore throat and generalised lymphadenopathy. Fever is highest in the first week and resolves over a 10–14 day period. Other common symptoms are chills, sweats, anorexia, fatigue and malaise. Myalgias, headaches and abdominal fullness may also be seen and can be prodromal features.[1]

It is not always possible to differentiate EBV (Figure 1) from streptococcal infection (Figure 2) on the basis of the appearance of the patient's throat. Associated clinical features are important when this is the case. For example, it is common for cervical nodes in the posterior triangle to be involved in EBV infection. This is not usually the case in streptococcal pharyngitis, which is more likely to have very tender submandibular nodes. Epstein-Barr virus related palatal petechiae, located at the junction of the hard and soft palates, occurs in 25–60% of cases (Figure 3). Periorbital oedema is another possible feature and is shown in Figure 4. Splenomegaly occurs in about half of all cases. It peaks in the second week of illness then regresses over the next 7–10 days. Hepatomegaly is present in 10–15% of cases.[1] Maculopapular rashes are seen in 90% of patients with EBV who receive amoxycillin or ampicillin.[1] These rashes, which are shown in Figure 5, can be a problem as patients may be falsely thought to have a beta-lactam allergy which may compromise future antibiotic choices.

Complications

More severe infectious mononucleosis, such as in the case history, occur in a minority of patients. Intensive care management may be required when the tonsils are sufficiently enlarged that they endanger the airway. If there is associated bacterial pharyngitis, the blood film may not be typical of infectious mononucleosis. Fulminant liver failure is extremely unusual. Splenic rupture can occur so care should be taken with palpating the spleen and contact sports should be advised

against in the first three weeks or until the splenomegaly resolves.[3] Auto-immune haemolysis occurs in up to 3% of cases, can be severe but is rarely life threatening.[1] Other serious complications are severe neutropenia and aplastic anaemia.[3] Very severe cases involving marked disturbances in liver and renal function as well as severe cytopaenias may be manifestations of the haemophagocytic syndrome which generally requires tissue biopsy to make a diagnosis.[4]

Other complications include myocarditis, rashes and genital ulcers. Neurological complications of EBV are rare but include encephalitis, meningitis, transverse myelitis, Bell's palsy and Guillain-Barré syndrome. They tend to have a good prognosis.[1] There is also an X-linked recessive lymphoproliferative disease which involves a selective immune deficiency to EBV. This leads to Duncan's syndrome with manifestations of haematological deficiencies, clotting disturbances and lymphomas and is often fatal.[3]

Prolonged fatigue following infectious mononucleosis is common and often persists for months. There is no useful serological marker to show that EBV is the cause of this condition. There have been hypotheses that chronic fatigue syndrome is caused by EBV but these have now been abandoned.[5]

Diagnosis

Most cases do not offer too much diagnostic difficulty. The appropriate clinical picture associated with the presence of atypical lymphocytes and mildly abnormal liver function tests and possibly red cell agglutination makes the diagnosis very likely.

Investigations

Investigations in the acute illness reveal a raised white cell count with increased lymphocytes. The lymphocytosis peaks in the second or third week of illness. Atypical lymphocytes are usually seen on blood film and can vary between 0–90% of all lymphocytes. These are T-cells which change their morphology in response to EBV infected B-cells.[2] Other illnesses that can lead to the presence of atypical lymphocytes include cytomegalovirus infection, toxoplasmosis, acute viral hepatitis, rubella, roseola, mumps and drug reactions.[1] Mild neutropenia or thrombocytopenia are both common. The haematology laboratory may notice the presence of cold agglutinins. Liver function tests are abnormal in at least 80% of patients and usually consist of mild to moderate elevations of transaminases, alkaline phosphatase and bilirubin; Frank jaundice is seen in 5% of patients. Because of polyclonal activation of B-cells by EBV infection, a broad range of antibodies are produced and false positive tests for antinuclear antibodies and rheumatoid factor may be seen if tested for.[2]

Simple tests for the presence of heterophile antibodies (eg. the traditional Paul-Bunnell test or the

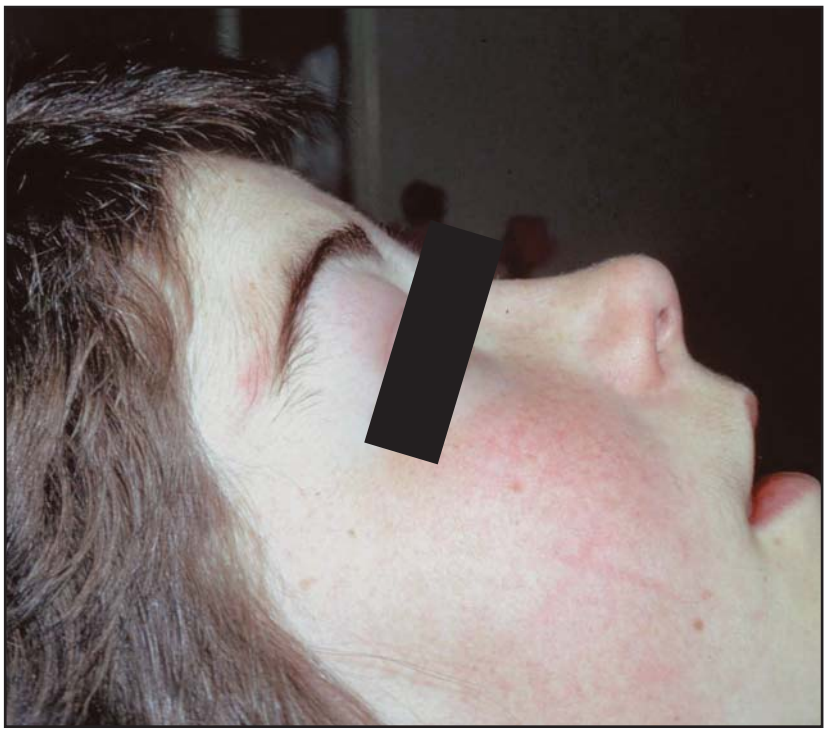

Figure 4. Periorbital oedema

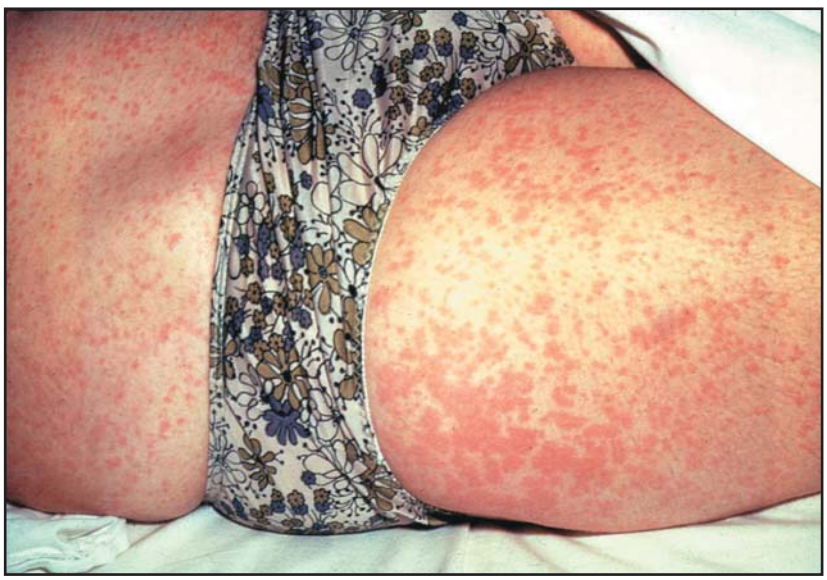

Figure 5. EBV maculopapular rash following amoxycillin

more sensitive EBV monospot test) are usually sufficient to confirm the diagnosis. Difficulties arise in cases where the presentation is atypical or where the test for heterophile antibodies is negative. Appearance of heterophile antibodies often does not occur until the second week of illness and is also less likely in younger patients compared to young adults.[1] Heterophile antibodies are present in 90% of cases and persist for about a year. False positives are seen in 6–10% of the population. In cases where the diagnosis is unclear, EBV specific serology will usually make the diagnosis. IgG and IgM antibodies against the viral capsid antigens (VCA) appear early on. The IgM antibodies are present for several months and do not reappear so are the most useful for diagnosing acute infection.[3] Titres of anti-VCA IgG do not always rise, so it is not a useful marker of recent infection. IgG antibodies against Epstein-Barr nuclear antigens usually take 3–4 weeks to appear so their appearance can sometimes be useful in diagnosing recent infection. Once present, they persist for life.[1] Viral culture or polymerase chain reaction are rarely indicated.

Management

The treatment of infectious mononucleosis is mainly supportive. Aspirin or paracetamol are useful for both the sore throat and fever. Admission may be required in severe cases or where oral intake is inadequate. Controlled trials of aciclovir with or without prednisolone have not shown benefit.[6,7] Given that EBV is known to have oncogenic potential,[8] immunosuppressive therapy such as corticosteroids should be avoided unless really needed. The indications for using corticosteroids are severe upper airway obstruction, acute haemolytic anaemia, severe thrombocytopenia, severe cardiac involvement or neurologic disease.

There is no specific therapy for prolonged fatigue following infectious mononucleosis. Again the treatment is supportive and those affected can be reassured that in the vast majority, this frustrating condition eventually has a good prognosis .

Conclusion

Infectious mononucleosis is a common illness in adolescents and young adults with the majority of cases resolving in several weeks without specific therapy. The diagnosis is usually straightforward. The patient with a more severe or complicated course of EBV may require admission to hospital, particularly if fluid intake is inadequate or the airway is compromised. Corticosteroid therapy has a very limited place in patient management.

SUMMARY OF IMPORTANT POINTS

- Infectious mononucleosis is a common illness of adolescents and young adults.
- The majority recover uneventfully over several weeks.
- Severe or complicated cases occasionally occur and may require hospital admission.
- There is no rule for antivirals and only a few specific indications for corticosteroids.

Conflict of interest: none declared.

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