

## CASE REPORT

# An Interesting Case of Fever with Rash

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### ABSTRACT

Infectious mononucleosis (IM) caused by Epstein–Barr virus (EBV) is well known to occur in adolescents and is also termed as kissing disease. However, children in developing countries acquire the infection in first few years of life, and universal seroconversion is seen by ages 3–4 years. Transmission in this age group is through saliva from seropositive adults on fingers or toys. Recognition of disease is important as potentially life-threatening complications occur. Awareness of the disease occurrence in this age group also avoids antibiotic use for pharyngitis that mimics streptococcal sore throat. The presence of rash intrinsic to the disease along with other clinical features may give a clue to the diagnosis. Data from India on IM in children is scarce, perhaps due to lack of awareness or availability of diagnostic tests. We present a case in a preschooler who presented with fever, pharyngitis, lymphadenopathy, and rash without any prior antibiotic use and was managed on supportive therapy.

**Keywords:** Diagnosis, Infectious mononucleosis, Preschoolers, Rash.

*Pediatric Infectious Disease* (2019): 10.5005/jp-journals-10081-1220

### INTRODUCTION

Fever with rash is a common presentation in outpatient pediatric clinics. The diagnosis may vary from common illnesses to those that are life-threatening. We report a case of infectious mononucleosis (IM), a viral disease that mimics a bacterial infection and which is increasingly being diagnosed in preschoolers in the developing world.

### CASE DESCRIPTION

A 4-year-old male child presented with intermittent fever for 5 days, maximum temperature measured being 101°F. Mother noticed swellings on both sides of neck, 3 days back. He also developed pain on swallowing and had drooling of saliva for the last 2 days. On the day of presentation, he developed a maculopapular rash on face and trunk and became dull and hence was brought to the hospital. On examination, the sensorium was normal and vitals were maintained. Child had bilaterally palpable, nontender, and firm posterior cervical lymph nodes. Approximate size of these lymph nodes was 15 mm × 15 mm. There was no axillary or inguinal lymphadenopathy. Eye and ear examination and neck movements were normal. Throat examination revealed bilaterally enlarged tonsils with exudates. There were no palatal petechiae or ulcers in the oral cavity. The child had a morbilliform rash over face and trunk, non-itchy, and nonpetechial. There was a history of intake of acetaminophen and cetirizine prior to admission. A systemic examination was done which showed hepatomegaly (liver palpable 3 cm below costal margin). There was no splenomegaly, and the rest of the systems were normal. A provisional diagnosis of IM was made, and the child was admitted. Intravenous fluids and analgesics were started. Investigations were sent and reports are as follows: complete blood count showed a total leukocyte count of 24000 cells/mm<sup>3</sup>. There were 60% lymphocytes with 37% neutrophils and 3% eosinophils. Absolute lymphocyte count was 14,400 cells. Hemoglobin and platelet counts were normal. C-reactive protein was less than 5 mg/L. Peripheral smear examination revealed atypical lymphocytes with few monocytoïd cells. These were 11% of total cells. No abnormal cells were seen. Liver function test was also normal. Epstein–Barr virus (EBV) serology tests, i.e., IgG and IgM

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**How to cite this article:** Kukreja S, Gupta T, Bagania A. An Interesting Case of Fever with Rash. *Pediatr Inf Dis* 2019;1(3):129–130.

**Source of support:** Nil

**Conflict of interest:** None

antibodies to viral capsid antigen (VCA), were sent. Viral capsid antigen IgM report came positive, titers were >160 U/mL (reference range: negative, <20.0/borderline, 20.0–40.0/positive, >40.0), VCA IgG also came positive, i.e., 40.0 U/mL (reference range: negative, <20.0/positive, >20.0), and blood culture was sterile after 48 hours. A final diagnosis of IM was made, and the child was managed with supportive care. As his activity and oral intake improved, he was discharged after 3 days of hospital stay.

### DISCUSSION

Infectious mononucleosis is usually subclinical during childhood years. The incidence of symptomatic infection starts rising in adolescence through adult years. The size of viral inoculum or cellular immune response evoked by host may determine asymptomatic vs clinical infection. However, the factors that determine host response to EBV exposure are largely unknown.<sup>1</sup>

Humans are reservoirs of EBV, and disease spreads by intimate contact between EBV shedders and susceptible hosts. Worldwide, almost 90–95% of adults are EBV seropositive. It is interesting to note that in the developing countries, EBV seroprevalence is almost 100% by 4 years of age.<sup>2</sup> This is attributed to intense personal contact, poor personal hygiene, and overcrowding.<sup>3</sup> Data on profile of children with IM in India are scarce, and available data indicate that the disease is more common in preschool children than previously thought.<sup>4</sup>

Classic clinical features of IM are fever, sore throat, and fatigue. On physical examination, lymphadenopathy and

tonsillopharyngitis are seen. The frequency of these signs and symptoms is similar across all age groups. Rash may be seen more commonly in preschool children (34%) than in children older than 4 years (17%).<sup>5</sup> Rash in children with IM is maculopapular; however, it may be urticarial or scarlatiniform. Rarely, erythema nodosum or erythema multiforme may be seen.

Historically, as ampicillin was first used for sore throat, it was linked to appearance of rash in patients of IM. Two large case series indicated that administration of ampicillin or amoxicillin precipitated an exanthem in most adolescents with IM.<sup>6</sup> This was less common in children.<sup>7</sup> This rash was maculopapular, present all over the body, appeared 5–10 days after treatment was started and disappeared on discontinuation of medicines. The rash has also been reported occasionally with other antibiotics like cephalexin, azithromycin, etc. The mechanism may be a virus-induced transient and reversible, delayed-type hypersensitivity to the drug. Recent studies indicate that the rate of drug-induced rash may be much lower (32%) than previously thought (70–90%).<sup>8</sup> Another report suggested that there was an equivalent rate of rash in both those treated with a penicillin derivative and those patients with IM who did not receive any drug.<sup>9</sup>

Laboratory tests that indicate IM are as follows: a white blood cell (WBC) count showing lymphocytosis (absolute count >4500 cells/mm<sup>3</sup> or a differential count >50%) is suggestive. Peripheral smear showing significant atypical lymphocytosis (>10% of total lymphocytes) gives a good clue to the diagnosis. Total WBC count in IM ranges from 12000 to 18000 cells/mm<sup>3</sup>. At times, mild neutropenia and thrombocytopenia may be present, which is self-limiting. Rarely, patients may develop hemophagocytic lymphohistiocytosis. Raised aminotransferases in a child with pharyngitis should always alert the clinician to a strong diagnostic possibility of IM.

The diagnosis must be confirmed by heterophile antibody test (monospot) or by EBV-specific antibodies. Monospot test is a latex agglutination assay, and if results are positive, further confirmation is not necessary. However, heterophile tests are often negative in children less than 4 years; hence, EBV-specific antibodies (antibody to VCA IgG and IgM) must be tested in this age group. These antibodies are present on day 1 of clinical illness. IgM levels decrease 3 months later, while IgG persists for life.

For diagnostic confirmation, simultaneous testing for IgG antibodies to EBV nuclear antigen (EBNA) must be done. These appear 6–12 weeks after the onset of symptoms and persist throughout life. Their presence early in an illness rules out acute

EBV infection. Hence, a positive VCA antibody test with negative EBNA antibody test is diagnostic of IM.

Diagnosis is useful as serious complications like splenic rupture and airway obstruction can be anticipated and informed to caregivers. Management is supportive with acetaminophen, adequate hydration, and nutrition. Antibiotics and antivirals have no role. Corticosteroids may be used in children with impending airway obstruction (difficulty in breathing or dyspnea in lying down position).

## CONCLUSION

We report a case of IM in a 4-year-old child who presented with fever, exudative tonsillopharyngitis, and rash which was not drug induced. Recent studies indicate that rash may be more commonly a symptom of the disease, in young children. Awareness of the occurrence in preschoolers, disease presentation, and diagnostic tests is important for judicious use of antibiotics in sore throat and to prevent catastrophic complications like splenic rupture or airway obstruction.

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