Case Report

Infectious Mononucleosis in a 3-year-old Male Child: A Case Report and Review of the Literature

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ABSTRACT

We present a case of Infectious mononucleosis in a 3-year-old male who presented to us with a one-day history of sore throat, difficulty breathing, fever and general malaise. Examination showed marked enlarged hyperaemic bilateral tonsils with white exudates, palatal petechiae, dyspnoea, drooling, periorbital oedema and generalised lymphadenopathy. However, on day 7 post admission and treatment he developed a clearly defined, maculopapular rash, pruritic in nature, which was accompanied with slight fever of 37.8*. His past history included an episode of otitis media which was treated with amoxicillin and prior to the above presentation the child was well. The rest of the history was unremarkable. Full blood count revealed monocytosis, lymphocytosis and thrombocytosis. PCR was positive for Epstein-Barr virus (EBV). The patient was treated and therapy was instituted with good recovery. He was discharged on day 11 post admission.

INTRODUCTION

Infectious mononucleosis (I.M) typically known as "kissing syndrome" is a clinical syndrome most commonly associated with Epstein-Barr virus infection and is transmitted through oral pharyngeal secretions. Naturally humans are the only reservoirs for EBV and although it is said to be less severe in children it always leads to lifelong persistence, furthermore when the immune system is impaired, reactivation is possible. Sero-epidemiologic Studies have shown that the majority of cases between 1 to 5 years of age occur during primary EBV infection.

Literature review

I.M was first described by Nil Filatov a Russian pediatrician in 1880s. The disease occurs worldwide with no seasonal preference. It is recognized most frequently in adolescents and young adults from developed countries for reasons that are not completely understood. Part of the explanation is lack of recognition of the syndrome in preadolescents. The heterophile antibody test is often unreliable in young children, particularly those under 4 years of age. Thus, assays specific for EBV must be performed in these cases, lest the diagnosis of infectious mononucleosis be missed. Infectious mononucleosis in preadolescents is not rare and a numerous number of cases in children younger than 12 years old have been seen.

A second reason could be that deep kissing transmits a large amount of infectious virus. In contrast, young children probably acquire the virus from asymptomatic parents or siblings who shed low levels of EBV in their oral secretions and transmit a smaller infectious inoculum.

Parents of young children (<6 years of age) have EBV in their oral secretions about 30% of the time.

According to Katinka Ónodi-Nagy et al. Journal of allergy and therapy 2015, the clinical features and a positive heterophil test are usually sufficient to differentiate the condition from bacterial infection and to make the diagnosis of IM. Cutaneous rash may develop during the infection. The incidence of skin eruption in acute IM is 4.2 to 13% without drug intake. By the frequent use of antibiotics within acute IM, the incidence of skin reactions rises,

ranging between 27.8% and 69%; in some past studies for ampicillin even 90%. According to the literature there is no obvious consensus on the cause of skin symptoms, whether a true drug sensitization or only transient immune-activation develops. Furthermore, studies showed that primary EBV infection appears predominantly in children, adolescents and young adults and that infection occurring before the age of 4 is considered to be asymptomatic or to resemble a nonspecific viral disease, while in adolescents and adults the classical features of the illness are prominent.

A research done by Chovel-Sella et al. Suggested that there was no association with age in the development of rash after antibiotic exposure [1]. The immune system of a few months old child is different from an adult, which may play an important role in the development of drug sensitization. It is possible that true drug sensitization occurs with much lower frequency in children, than in young adults. They concluded that further investigations were needed to answer whether the mechanism of maculopapular eruptions following antibiotic administration in IM differ in different age groups. Furthermore Chovel-Sella et al. found the aminopenicillin rash in children is significantly lower than the 90% incidence rate reported in earlier studies [1,3,6,7]. The skin eruptions are mostly diffuse, symmetric maculopapular exanthems on the whole body (Figure 2). Not only morbilliform lesions, but in some cases urticarial, purpuric and vesicular rashes, pustular erythematous rash, universal erythema or cutaneous vasculitis in the erythema multiforme pattern were also reported in connection with antibiotic use [16,17,20,27]. Severe cutaneous reactions such as erythema multiforme or Stevens-Johnson syndrome may be possible manifestations.

In another case report in the British medical journal done by Tsuneaki Kenzaka et.al a 24 year old patient treated for infectious mononucleosis also developed a clearly defined, maculopapular pruritic rash on day 4 post admission which was accompanied with slight fever .In addition, mild splenomegaly was observed. Drug history revealed that ampicillin was prescribed for sore throat and adenopathy 3 days prior to presentation. The conclusion was that Administration of ampicillin to a patient with infectious mononucleosis caused by EBV primary infection should be avoided. If ampicillin is administered 90-100% of patients have a high probability of developing a skin rash several days after the administration.

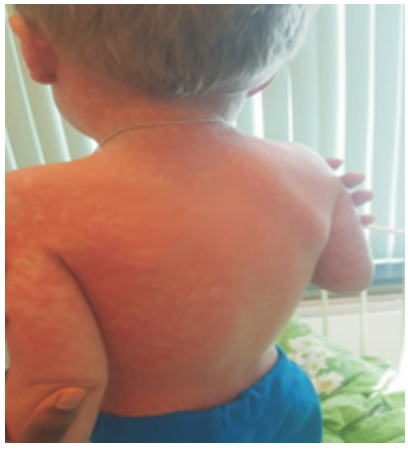
Previously published papers suggest that interactions of viruses and penicillin may predispose individuals to specific illness out-comes. It became an issue whether this phenomenon may lead to persistent, true drug hypersensitivity or it is just a temporary reaction. In the past, in general, it was believed that the morbilliform skin rash following antibiotic intake in patients with IM is a transient reaction, not a true allergic reaction. Webster et al. proposed the phenomenon to be penicillin specific. In their in vivo and in vitro investigations, they aimed to find evidence of specific humoral or cell-mediated immune responses to ampicillin in those patients who developed a rash following antibiotic therapy. They suggested that ampicillin polymer-mediated lymphocyte stimulation may play a role in the development of maculopapular rash. Although, the polymer has weak stimulating effect on lymphocytes, which is probably independent of previous exposure to the drug, they showed a dose dependent widespread lymphocyte stimulation resulting in skin eruptions with altered cell function occurring in IM patients. Antibodies could prevent this reaction. In vivo skin testing proved largely inconclusive, as did investigations of specific penicilloyl antibodies.

McKenzie et al. stated that the phenomenon was not true penicillin hypersensitivity, but a non-immunological reaction, because it did not re-appear after the re-administration of the drug. After their investigation of 20 IM (not all of them underwent previous antibiotic therapy) and 20 control patients they concluded that the ampicillin rash in IM resulted from a disseminated reaction of the small blood vessels to circulating ampicillin-antibody complexes. They detected elevated antibody-like activity against ampicillin in both IgM and IgG

immunoglobulin classes by means of a sensitive radio-immunoassay. They proposed that the ampicillin induced antibody developed in a similar manner to the Paul-Bunnell antibody, but it was immunologically unrelated. These antibodies occurred without obvious relation to prior ampicillin therapy. They suggested that ampicillin rash could result from interaction of ampicillin with the IgM or IgG antibody to ampicillin generated in the acute phase of infectious mononucleosis. The rash could result as a consequence of complement activation due to circulating antigen-antibody complexes.

DESCRIPTION OF CASE REPORT

3-year-old male who presented to us with a one-day history of sore throat, difficulty breathing, fever and general malaise. He was well-nourished and oriented febrile to touch with a fever of 38*C. Examination showed marked enlarged hyperaemic bilateral tonsils with white exudates, palatal petechiae, dyspnoea, drooling, and periorbital oedema, cervical, axillary and inguinal lymphadenopathy. His past history included an episode of otitis media which was treated with aminopenincilins for 5-7 day's before hospitalisation and it was said that the child was said to have been well prior. The rest of the history was unremarkable and other systems were essentially normal. On day 7 Post admission the patient developed a widespread, non-itchy maculopapular exanthema which appeared on the trunk and upper arms first, and a few days later extended to involve the face and forearms.



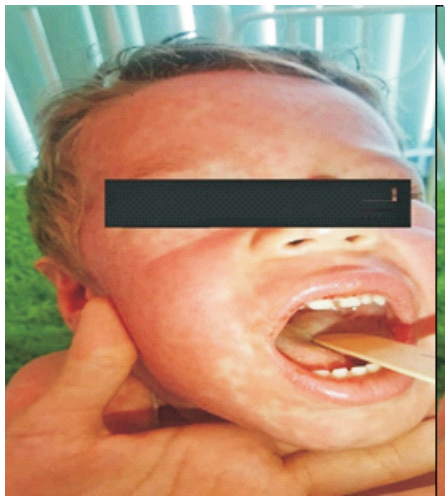


Image 1 and 2: Day 7 post admission with maculopapular

Exanthema on trunk, back and upper arms. A few days later it spread to the face and forearms

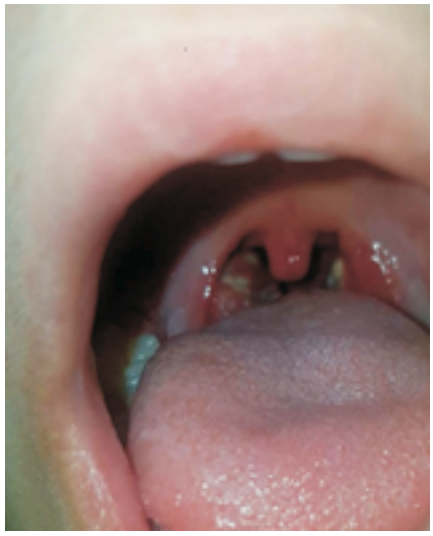


Image 3: Bilateral hyperemic markedly enlarged tonsils with exudates. (Images captured by Dr Mwela B.M)

Investigations

Full blood count showed a monocytosis, lymphocytosis and thrombocytosis.

The immunoenzyme analysis identified the Epstein-Barr virus (EBV) IgM and IgG

Throat swab was positive for streptococcus mitis.

Abdominal and pelvic ultra sound showed a mild hepatomegaly and mesenteric lymphadenopathy

Other investigations were essentially normal.

Treatment

On admission the patient was commenced on acyclovir 140mg IV 3 times daily and Ibuprofen 140 mg(given orally when temperatures were high.)

When the rash appeared on day 7 infusion therapy with saline solution, dexamethasone nasal drops 2 drops TDS,chloramphenicol 0, 25% nasal drops 3 times a day were added to the treatment. By day 10 of admission and treatment the fever subsided, exanthema improved markedly, there was reduced lymphadenopathy and the tonsils had reduced to almost normal size with minimal signs of inflammation.

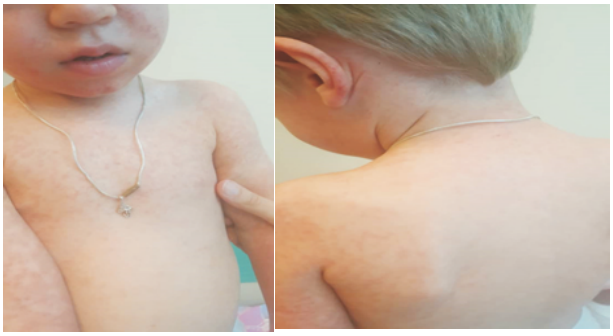


Image 4, 5: day 11. exanthema improved markedly (captured by Dr Mwela B.M)

The patient was discharged on day 11 with the following recommendations:

Follow up review by Pediatrician and local residence 1 week after discharge.

Planned otolaryngologist review (as all ENT related patients should be reviewed by ENT specialist)

Suprastin (Chloropyramine) 12.5 mg 2 times a day - 7 days; ECG after 3 months

DISCUSSION

Infectious mononucleosis is a clinical syndrome most commonly associated with Epstein-Barr virus infection and is transmitted through oral pharyngeal secretions. Although it is said to be less severe in children it leads to a lifelong infection and should always be excluded in children with symptoms of viral infection on admission. Our 3-year-old patient presented with a classical picture of IM (exudative tonsillitis, generalised lymphadenopathy, fatigue and fever.) PCR was positive for Epstein-Barr virus (EBV) IgM and IgG. According to the table shown below on the staging of EBV infection by enzyme immunoassay antibody results our patient would fall under subacute infection because the time and onset of illness was about 4 weeks to 3 months. In the past medical history, he was said to have been unwell with otitis media which was said to have been treated with antibiotics which also included oral amoxicillin and being a beta-lactam antibiotic, amoxicillin caused a rash which indicates a 'hypersensitivity reaction' to the antibiotic.

Table 1: Staging EBV infection by enzyme immunoassay antibody results

Stage of infection	*Time after onset of illness*	*VCA IgM*	*VCA IgG*	*EBNA-1 IgG*
EBV naive	—	Negative	Negative	Negative
Acute primary infection	0–3 Weeks	Positive	Negative or positive	Negative
Subacute infection	4 Weeks–3 months	Positive	Positive	Negative
Convalescent infection	4–6 Months	Negative or positive	Positive	Negative or positive
Past infection	>6 Months	Negative	Positive	Positive

Abbreviations: EBNA, EBV nuclear antigen; EBV, Epstein–Barr virus; IgM, immunoglobulin

M; VCA, VCA, viral capsid antigen.

According to literature there is no obvious consensus on the cause of skin symptoms, whether a true drug sensitization or only transient immune-activation develops but in our patient due to the drug history clinical presentation and onset of skin

symptoms we concluded that the skin eruptions were as a result of a 'hypersensitivity reaction' to the antibiotic in this case "amoxicillin" Although on discharge the skin rash and clinical picture had improved remarkably a diagnoses of infectious mononucleosis caused by EBV primary infection and skin rash caused by amoxicillin were made. The skin rash began to disappear by about 1 week, and it improved in over about 3 months.

CONCLUSION

- Infectious mononucleosis in preadolescents is not rare and a high index of cases in children younger than 12 years old have been seen.
- To make a definitive diagnosis of IM you need an immunofermental blood test of EBV virus antibodies.
- However approximately 40% of children 4 years of age or younger do not develop heterophile antibodies following a primary EBV infection.[23] If the heterophile is the only test ordered, the diagnosis will be missed or false.
- The simultaneous use of aminopenincilins in infectious mononucleosis increases the occurrence of skin eruptions. In patients taking these antibiotics the eruptions usually occur 2-10 days after starting the antibiotic treatment.However antibiotics of other groups are widely used in IM patients if necessary.

Never give aspirin to a child who has a viral illness because its use has been linked to Reye syndrome, which may lead to liver failure and can be fatal.

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