

Case Report

Polymorphic Exanthem Induced By Amoxicillin In A Child Case With Infectious Mononucleosis

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Abstract

Seven year old girl presented with sore throat, fever, fatigue; amoxicillin clavulanic acid therapy had been started in a clinic. In 7th day of treatment widespread rash all over her body began. On dermatological examination all over the body was covered by target-like, petechial lesions and in some areas maculopapular lesions with becoming faded by pressure. In laboratory examinations 3-5 times increased liver enzymes, complete blood count with lymphocytosis were found. In serological tests EBV Viral Capsid Antigen (VCA) IgG and IgM were positive. EBV IgM/EBV IgG ratio was found 3 times higher. Based on clinical, histopathological and laboratory examinations it was thought as Epstein Barr Virus (EBV) rash induced by amoxicillin.

Infectious mononucleosis caused by EBV infection, usually affects children and adolescents. Aminopenicillins used during this infection may cause maculopapular rash. Development of polymorphic lesions is relatively rare. Although rashes seen while the treatment with aminopenicillin, drug eruptions must be thought firstly; infectious mononucleosis must take place in differential diagnosis.

Introduction

Epstein Barr Virus (EBV) is a gamma herpes virus which can cause Infectious Mononucleosis (IM), nasopharyngeal carcinoma, Burkitt lymphoma, Hodgkin lymphoma, lymphoproliferative disease after transplantation and oral hairy leukoplakia in HIV positive patients [1,2]. Primary EBV infections are generally subclinical. The diagnosis is made by serological tests [3]. IM caused by EBV commonly has fever, sore throat and lymphadenopathy [2]. Rarely, there could be complications such as hepatomegaly, splenomegaly, icterus and splenic rupture [4]. While using especially aminopenicillin group antibiotics, maculopapular or urticarial rashes generally occur. In this case report, a 7 year-old child with polymorphic rashes after using amoxicillin treatment in acute IM has been presented.

Case

7 year-old girl was admitted to our clinic with disseminated rashes on her whole body after 7 day long amoxicillin treatment for sore throat, fever and fatigue complaints. From her personal history, it is learned that she could use amoxicillin therapy without having any reaction. The patient neither has another disease nor uses any medication.

In physical examination, hyperemic, hypertrophic and cryptic tonsils were found. There was tenderness on the right upper quadrant of the abdomen. Lymphadenopathy and hepatosplenomegaly were not detected. In dermatological examination, disseminated maculopapular rashes, target-like and petechial lesions were seen especially on upper extremities and torso (Figure 1,2).

The complete blood count showed leukocytosis as $12.1 \times 10^3 \mu\text{L}$ ($3,57 - 11,01 \times 10^3 \mu\text{L}$) predominantly composed of lymphocytes with %72,45 rate (%16,82 - 45,30). Liver function tests results were found

high as: AST: 154 U/L (9-48 U/L), ALT: 291 U/L (10-49 U/L), ALP: 435 U/L (45-129 U/L), GGT: 202 U/L (0-38 U/L), LDH: 684 U/L (120-246 U/L). Serologic tests results were found as: EBV VCA (Viral Capsid Antigen) IgM: 1,87 T. V (>0,12 T.V), EBV VCA IgG:0,63 T.V. (>0,10 T.V)

Histopathological examination of two punch biopsies obtained from skin lesions showed focal spongiosis in epidermis, vacuolar changes in basal layer, lymphocyte exocytosis, mononuclear cell infiltrations around vessels and in interstitial region, a few eosinophils, extravasated red blood cells and melanophages (Figure 3,4).

Based on clinical, laboratory and histopathologic examinations, the patient was diagnosed with polymorphic rashes induced by amoxicillin treatment associated with acute EBV infection.



Figure 1: Maculopapular rashes.



Figure 2: Target-like lesions.

Symptomatic treatment was given to the patient and liver function test values decreased to normal values 1 week later, also the rashes decreased simultaneously.

Discussion

IM generally affects children and adolescents with triad of fever, lymphadenopathy, pharyngitis [1,4]. Slight hepatic involvement is commonly seen in approximately %80-90 of all cases. This situation is generally asymptomatic although liver enzymes elevate 2-3 times typically [2]. Lymphocytosis, sometimes accompanied by atypical lymphocytes, can be seen [4].

Serological test positivities of VCA IgM and VCA IgG are important for diagnosis of the disease. Negative result of EBV VCA IgM is a strong evidence to exclude IM [4]. However, routine serologic tests may be insufficient to characterize EBV reactivation in some cases such as immunosuppressive cases [5]. In that cases, the sensitivities reported for Real-Time Polymerase Chain Reaction (RT-PCR) were high. RT-PCR and measurement of EBV viral load may be useful for the diagnosis of infectious mononucleosis in cases with inconclusive serological results [6].

Maculopapular rashes develop in %70-100 of IM patients with simultaneous usage of aminopenicillin treatment [7]. There are many hypotheses in mechanism of eruption. Antibodies against amoxicillin

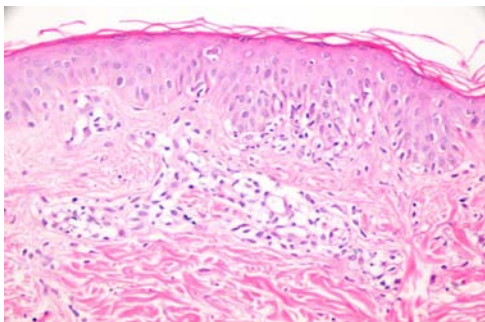


Figure 3: Vacuolar changes in basal layer, lymphocyte exocytosis, and mononuclear cell infiltrations around vessels and in interstitial region, a few eosinophils, extravasated red blood cells and melanophages (H&Ex40, H&Ex200).

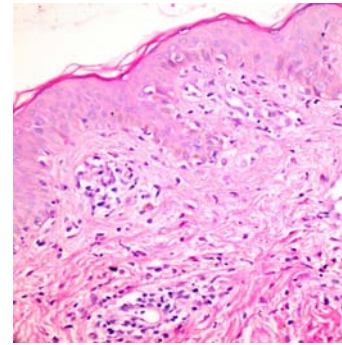


Figure 4: Vacuolar changes in basal layer, lymphocyte exocytosis, and mononuclear cell infiltrations around vessels and in interstitial region, a few eosinophils, extravasated red blood cells and melanophages (H&Ex40, H&Ex200).

were generated in IM patients [8]. Dysregulation of immune system is another mechanism that is accused of eruption [7]. Patients, who have developed hypersensitivity reaction against amoxicillin, generally had used aminopenicillin group treatment many times without having reactions before, such as the case of our patient [8].

EBV infection can cause %10 of eruptions which have a broad spectrum from nonspecific erythematous eruption to morbilliform, vesicular, polymorphic rashes. Whereas this eruption often begins at 4-6th days of the disease and clears up in 1 week, the eruption after starting amoxicilline treatment occur commonly in 7-10 days and it generally are seen on extensor surfaces as pinkish-cooper like pigmented or morbilliform [8].

Common presentation of aminopenicillin induced skin reactions in IM patients is macular or maculopapular rash. The three cases of erythema multiforme like rash associated with IM have been reported to date in literature. One of them was a 23-year-old woman without drug use [9], one was a 15-year-old boy who was taken cefotaxime [3] another was a 7-year-old girl who was taken oral amoxycillin similar to our case [10]. When polymorphic rash occurs, differential diagnosis becomes more important because it may be misdiagnosed as erythema multiforme. Differentiation of erythema multiforme from aminopenicillin induced polymorphic rash has critical importance as systemic corticosteroid therapy may inhibit EBV-induced autoantibody production and may induce a dose-dependent increase in viral replication [11,12].

Existence of tonsillar crypts that are non-responsive to antibiotherapy, 2-3 times elevated liver function test results and lymphocytosis in complete blood count may help to the diagnosis of the disease such as the situation of our patient. The serological tests for EBV verify the diagnosis. Level of IgM was found 3 times more than IgG level and both were positive in our patient.

Histopathology of IM lesions is nonspecific. Mild spongiosis, parakeratosis, perivascular lymphocyte infiltration, focal keratinocyte necrosis, mild vacuolar degeneration could be seen. In histopathology of hypersensitivity reaction against amoxycillin such as the case for the present case, generally vacuolar interface changes, spongiosis and dense dermal infiltrates are seen [8].

Consequently, aminopenicillin induced polymorphic rash associated with IM is rarely seen and differential diagnosis may be

challenged. We want to remind that the existence of IM should be considered also in the patients, especially in children, when drug induced polymorphic rash is seen; thus a detailed examination is required.

References

1. Arslan N, Akman H, Sayan M, Ozturk Y, Buyukgebiz B. Epstein-Barr virus enfeksiyonuna ikincil gelişen hepatik yetmezlik: bir vaka takdimi. *Çocuk Sağlığı ve Hastalıkları Dergisi*. 2003; 46: 47-49
2. Karaman O, Uslan I, Colbay M, Acarturk G, Yuksel S, Danalioglu A. Akut Hepatitin Nadir Sebeplerinden Biri Epstein Barr Virus: Olgu Sunumu. *Bakirkoy Tıp Dergisi*. 2007; 3: 115-117.
3. Zavar V, Chuh A, Sankalecha S. Erythema multiforme-like lesions in the course of infectious mononucleosis. *J Dermatol Case Rep*. 2009; 3: 44-46.
4. Ebell MH. Epstein-Barr virus infectious mononucleosis. *Am Fam Physician*. 2004; 70: 1279-1287.
5. Karadag Gecgel S, Ersoy A, Sevinir BB, Sınırtaş M, Goral G. [Evaluation of PCR results in the diagnosis of Epstein-Barr virus infections]. *Mikrobiyol Bul*. 2012; 46: 594-606.
6. Vouloumanou EK, Rafailidis PI, Falagas ME. Current diagnosis and management of infectious mononucleosis. *Curr Opin Hematol*. 2012; 19: 14-20.
7. Jappe U. Amoxicillin-induced exanthema in patients with infectious mononucleosis: allergy or transient immunostimulation? *Allergy*. 2007; 62: 1474-1475.
8. Mendoza N, Madkan V, Sra K, Willison B, Morrison LK, Tyring SK. Human Herpesviruses: In Bologna JL, Jorizzo JL, Schaffer JV, Callen JP, Cerroni L, Heymann WR, Hruza GJ, Mancini AJ, Patterson JW, Röcken M, Schwarz T *Dermatology*, 3rd ed, Elsevier, 2012; 1321-1365.
9. González-Delgado P, Blanes M, Soriano V, Montoro D, Loeda C, Niveiro E. Erythema multiforme to amoxicillin with concurrent infection by Epstein-Barr virus. *Allergol Immunopathol (Madr)*. 2006; 34: 76-78.
10. Hughes J, Burrows NP. Infectious mononucleosis presenting as erythema multiforme. *Clin Exp Dermatol*. 1993; 18: 373-374.
11. Andersson J, Ernberg I. Management of Epstein-Barr virus infections. *Am J Med*. 1988; 85: 107-115.
12. Chapman CJ, Spellerberg MB, Smith GA, Carter SJ, Hamblin TJ, Stevenson FK. Autoanti-red cell antibodies synthesized by patients with infectious mononucleosis utilize the VH4-21 gene segment. *J Immunol*. 1993; 151: 1051-1061.