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Original Article

Clinical and laboratory profile of serum sickness-like reaction in children

Reza Shiari[1,2], Fatemeh Adibe Eshgh[1], Ezzat Rowshanzamir[1], Hojjat Derakhshanfar[1]

ABSTRACT

Background: Classic serum sickness was initially reported after antitoxin therapy for diseases such as diphtheria and tetanus. The illness was shown to be due to an adverse reaction to the antigenic substance of the serum proteins of the animal in which the antitoxin was prepared.

Today, it is usually encountered as an adverse effect to certain medications, especially penicillin group of antibiotics. In these cases it is called a serum sickness-like reaction. The aim of this study was to determine the aetiological factors of serum sickness-like reaction, influence of age and sex and clinical manifestations of this disease in Iranian children.

Materials and Methods: The study included all children under 16-year-old who were diagnosed as serum sickness-like reaction and were admitted in the department of Paediatric Rheumatology in Mofid Children's Hospital between April 2009 and September 2010. Diagnosis was based on history of recent exposure to the antigenic substance that triggered the reaction and the development of signs and symptoms of typical serum sickness. Children with infections that result in a similar clinical picture of fever and rash were excluded from the study.

Results: Twenty-eight patients were included in this study. The most common medication causing serum sickness-like reaction in our study was furazolidone (5 cases, 18%). Cefixime (4 cases, 14%), amoxicillin, co-trimoxazole, cephalexin and co-amoxiclav, (with 2 cases each, 7%) were the other causes of serum sickness-like reaction in this study. The time interval between consumption of antigenic substance in 25 cases (89%) and the appearance of clinical manifestations was 1–3 weeks. Skin rash and angio-oedema was observed in all our patients. Arthralgia was observed in 85%, fever in 75% and arthritis in 36% of patients.

Conclusion: As any medication, especially antibiotics may cause serum sickness-like reaction; it is advisable to avoid prescribing unnecessary drugs in children.

Keywords: *Serum sickness, type III hypersensitivity, skin rash, furazolidone*

INTRODUCTION

Serum sickness vasculitis is a type III hypersensitivity reaction that was first reported in 1905 by Pirquet and Schick, following the treatment of tetanus and diphtheria patients by antitoxins.[1] Clinical manifestations of patients with this disease include fever, skin rash, lymphadenopathy, arthralgia, arthritis and unspecific lab findings. The diagnosis of serum sickness is based on a history of exposure to a substance with antigenic properties along with typical signs and symptoms of the disease.[2] Serum sickness is usually a self-limited disease and recovery occurs within 7–10 days

[1]Associate Professor, Division of Paediatric Rheumatology, [2]Paediatric Infectious Research Centre (PIRC), Shahid Beheshti University of Medical Sciences, Mofid Children Hospital, Tehran, Iran.
Correspondence: *Dr. Reza Shiari, email: shiareza@yahoo.com*
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after discontinuation of exposure to the antigenic substance. Rarely, vital organs such as heart and kidney could be involved.[3] Classic serum sickness was originally reported following administration of external antigenic substance from heterologous serum (usually from horse) as antitoxin. These days, it is usually seen as an adverse effect to certain medications, especially penicillin group of antibiotics. In such cases it is called a serum sickness-like reaction, which is clinically identical to serum sickness with regard to manifestations and management.[3,4]

This study aims to determine the aetiological factors of serum sickness-like reaction, influence of age and sex, clinical manifestation, and lab findings of this disease during the time period between April 2009 and September 2010 in a university-affiliated children's hospital.

METHODOLOGY

This is a descriptive research performed to define the aetiological factors, influence of age and sex, and clinical manifestation of serum sickness-like reaction. The study included all children under 16-year-old who were admitted in the Department of Paediatric Rheumatology in Mofid Children's Hospital in Tehran between April 2009 and September 2010. The diagnosis of serum sickness-like reaction was based on the history of recent exposure to antigenic substance that triggered the reaction and the development of signs and symptoms of typical serum sickness.

All children were fully checked for other causes of fever and rash such as infectious and collagen vascular diseases. The causes of infection and rash in children according to patient ages, clinical manifestation, Laboratory data and imaging were evaluated and children with Infectious mononucleosis, scarlet fever, systemic lupus erythematosus, and Kawasaki disease were excluded from the study.

Primary information collected from patients' case note was recorded on a pre-designed information sheet; this included demographic data, age, aetiological factors, clinical signs, time interval between exposure to the antigenic substance and commencement of clinical manifestations and laboratory finding. For each participant in the study a chart was made and analysis performed.

RESULTS

Within 1 year, 148 cases were admitted because of fever and skin rash and among them 28 patients were diagnosed as having serum sickness-like reaction. On the whole, 28 patients were enrolled, of which 17 were females. Average age was 3.5 years. The youngest patient of this study was a 15-month-old girl while the oldest was a 9-year-old boy. Most cases were in the age range of 2–3 years, (43%).

In all the cases under this study, agents causing the serum sickness in admitted patients were prescribed medications (Figure 1). The most common medication causing serum sickness-like reaction in our study was furazolidone (5 cases, 18%). Others were cefixime, (4 cases, 14%), amoxicillin, co-trimoxazole, cephalexin, and co-amoxiclav, (2 cases each; 7%). Among the cases in which serum sickness was due to the consumption of two or more medications, the combination of furazolidone and penicillin was the most common cause (2 cases, 7%).

The time interval between consumption of antigenic substance in 25 cases (89%) and appearance of the clinical manifestations was 1–3 weeks, in 2 patients (7%) it was < 1 week (3–4 days), and in one 2.5-year-old child (4%) an interval of > 3 weeks (25 days) was observed following oral consumption of cephalexin.

Widespread red to violaceous annular and serpiginous confluent plaques with dusky centres and intensely red borders (angio-oedema) with an acral and facial predominance were observed in all of our patients either at the time of admission or soon afterwards. Arthralgia was observed in 85%, fever in 75% and arthritis in 36%. Thirteen patients had urticarial rash, 9 patients developed maculopapular rash and the rest of the 6 patients developed a rash similar to erythema multiforme.

No lymphadenopathy was observed. In 13 cases (46%) leukocytosis was observed and no patient in this study developed leucopenia. In 3 cases (11%) platelets were more than normal range and in 1 case (4%), there was thrombocytopenia. Erythrocyte sedimentation rate (ESR) was measured in 25 patients; it was elevated in 19 cases (76%), and 6 cases (24%) had normal ESR. In all cases in which urine analysis was done, the results were normal except for 1 case that shows mild hematuria.

Echocardiography was performed in 4 cases, one showed pericardial effusion.

Complement studies were done to measure the levels of C3, C4 and CH50 in 24 case; the levels were reduced in 20 patients and normal in 4 patients. The mean duration of hospitalisation time was about 3 days with a minimum of 1 day and maximum of 5 days. Most of the cases were under conservative treatment but in 5 cases, steroid therapy was required.

All the patents were discharged in good general condition and no morbidity was reported on follow-up visits.