Serum Sickness Reaction Post-MMRV Vaccination in a Pediatric Patient

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Serum sickness is an immune-complex-mediated hypersensitivity reaction that classically presents with fever, rash, polyarthritis, or poly arthralgias. Damage is caused by formation or deposition of antigen-antibody complexes in vessels or tissues. Deposition of immune complexes causes complement activation and/or recruitment of neutrophils by interaction of immune complexes with Fc immunoglobulin G receptors. The condition was first recognized as an entity in the early 1900s in patients who had received heterologous antisera, which was historically used to treat infectious diseases. The symptoms typically occur one to two weeks after exposure to an offending agent and resolve within several weeks of discontinuation [1].

The mumps measles rubella (MMR) vaccine was introduced in the United States in 1971. It protects against three major diseases: measles, mumps, and rubella. All three of these diseases can cause serious health complications. In rare cases, they can even lead to death. It is given to all children in two doses, the first one at 1 year of age and a second dose at 6 years old. Possible side effects of the vaccination may include redness, swelling, and pain at the injection site. To the best of our knowledge, there are no reports of cases of serum sickness after mumps measles rubella varicella (MMRV) vaccination.

We present a case of a one-year-old girl with a serum sickness reaction one week after receiving her MMRV vaccination.

PATIENT DESCRIPTION

A one-year-old girl arrived at the emergency department (ED) with high fever for a week and an urticarial rash [Figure 1 A, B, C] 10 days after receiving her MMRV vaccination. Only paracetamol and non-steroidal anti-inflammatory drugs (NSAID) were administered after the appearance of the high fever, but no antibiotics.

The girl was healthy with normal development and vaccinations according to age. Chronic daily medication was not administered. There was no family history chronic illness, and no known allergies.

Her first vital signs were normal with fever 36.9°C, blood pressure 89/51 mmHg, heart rate 128 beats per minute, normal respiratory rate, and normal oxygen saturation.

On physical examination she presented with an urticarial rash over her arms and legs, back, and abdomen [Figure 1 A, B, C]. There were no signs of skin peeling, ulcers, enlargement of lymph node, or mucosal involvement. Her heart rate was normal with no heart murmur. Breath sounds were normal with no additional crackles or wheezing. There were no signs of meningeal disease or Kawasaki disease.

A blood sample revealed moderate neutropenia (900 × 10^3/μL), normal leukocyte count, normal hemoglobin, and severe thrombocytopenia (54 × 10^3/μL). Electrolytes were normal with low C-reactive protein (8 mg/L). There were no elevated liver enzymes. Complement systems revealed low C3 and C4 levels (60 and 2, respectively). Blood smear was normal. Serologic tests for Epstein-Barr virus, cytomegalovirus, and parvovirus were negative. Corona virus swap was negative.

The girl was admitted to the pediatric department and was treated with betamethasone and antihistamine dimethindene drops orally for itching with no exacerbation of her symptoms, no elevated inflammatory markers, and normalization of neutrophil and platelet levels. Her fever normalized and there was regression of her rash. Chest X-ray and abdominal ultrasound were normal.

One week later the patient returned for a follow-up to our immunology pediatric clinic. Her behavior was normal. New blood samples revealed improvement of her complement levels. Clinical signs were normal with no signs of a rash.

COMMENT

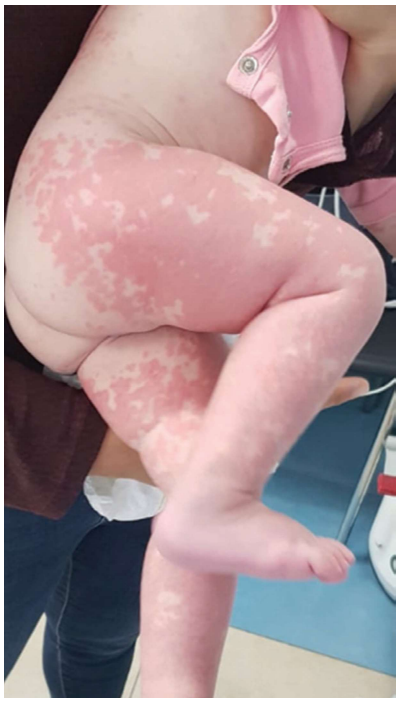
We acknowledge the importance of vaccination and do not question the efficacy of vaccines or the changes they have had in reduction of critical diseases worldwide.

According to the Institute for Vaccine Safety (IVC), vaccines routinely recommended to the general population of the United States have not been shown to cause serum sickness. A 2012 report by the Institute of Medicine (IOM), now the National Academy of Medicine (NAM),

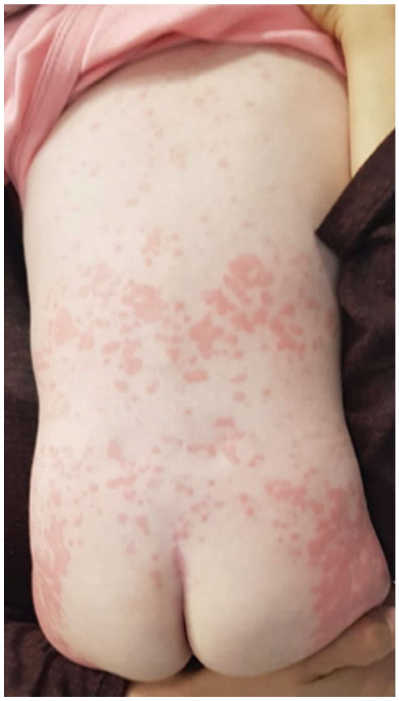
Figure 1. Urticaria with angioedema

[A] Wrist and hand

[B] Buttocks



[C] Lower back



found only one relevant study in the literature assessing serum sickness after diphtheria, tetanus, or pertussis vaccines vaccination [2]. However, the IOM concluded that this mechanistic evidence was weak. The IOM also concluded that there was no mechanistic evidence of an association between serum sickness and the pertussis vaccine [2].

From 2018 to 2020, three more reports of serum sickness after vaccination were reported. The most recent diagnosis of serum sickness was in January 2020 in which a 6-year-old girl presented with a one-day history of bilateral lower limb pain 2 days after getting her tetanus vaccine [3]. The other two cases were reported in February 2019 in which 19-year-old identical twins presented with low grade fever and rash 10 days after receiving equine rabies immunoglobulin as a post-exposure rabies treatment after cat scratches [4].

Vasculitis diseases such as Henoch-Schönlein purpura (HSP) have recently been found to be related to vaccination. A recent case report in Israel in 2020 described a diagnosis of HSP in a 4-year-old girl 8 days after receiving her first seasonal influenza vaccine [5].

Our patient presented with high fever arthralgia and urticarial rash 10 days after receiving the MMRV vaccination with low complement level. There were no inflammatory markers and all the symptoms, as well as the rash were normalized without any antibiotics. In addition, we did not find any positive viral serologic test, which would indicate an inflammatory disease. We did not find other symptoms or blood test results, which would have supported other systemic diseases such as Kawasaki disease, juvenile idiopathic arthritis, or systemic lupus erythematosus.

The facts that the symptoms began 10 days after the vaccine, that all clinical manifestation resolved, and that complement level improved after steroid administration strengthens the diagnosis of serum sickness.

MMRV vaccine is an attenuated vaccine. Adverse reaction could be caused by vaccine antigens, adjuvants, constitutes, preservatives, or stabilizers.

CONCLUSIONS

We presented a case of a serum sickness reaction after MMRV vaccination. Serum sickness in a patient who presents to the ED with fever and rash after getting a vaccination should be considered. There is a need for more case reports and studies to support this finding.

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Capsule

Lingering immune changes after obesity

A past period of obesity caused by a high-fat diet in mice produced persistent changes in innate immunity even after weight loss and normalization of metabolism. **Hata** and colleagues found that such diet-induced obesity in mice, even after it was resolved, led to persistent epigenetic changes in chromatin in macrophages associated with increased expression of genes that function in inflammatory responses. Experiments with transplants of adipose tissue or bone marrow implicated alterations of myeloid cells in exacerbating inflammatory responses to experimentally induced injury in the eye. If similar processes occur in humans, then the authors proposed that such changes could contribute to predisposition to age-related macular degeneration associated with obesity.

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Eitan Israeli

Capsule

SARS-CoV-2 infection and persistence in the human body and brain at autopsy

Stein and colleagues conducted complete autopsies on 44 patients who died from COVID-19, with extensive sampling of the central nervous system in 11 of these patients to map and quantify the distribution, replication, and cell-type specificity of SARS-CoV-2 across the human body, including the brain, from acute infection to more than 7 months following symptom onset. The authors show that SARS-CoV-2 is widely distributed, predominantly among patients who died with severe COVID-19, and that virus replication is present in multiple respiratory and non-respiratory tissues, including the brain, early in infection. Furthermore, they detected persistent SARS-CoV-2 RNA in multiple anatomic sites, including throughout the brain, as late as 230 days following symptom onset in one case. Despite extensive distribution of SARS-CoV-2 RNA throughout the body, they observed little evidence of inflammation or direct viral cytopathology outside the respiratory tract. These data indicate that in some patients SARS-CoV-2 can cause systemic infection and persist in the body for months.

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Eitan Israeli

Capsule

Autoimmunity-associated T cell receptors recognize HLA-B*27-bound peptides

Human leucocyte antigen B*27 (HLA-B*27) is strongly associated with inflammatory diseases of the spine and pelvis (e.g., ankylosing spondylitis [AS]) and the eye (e.g., acute anterior uveitis [AAU]). How HLA-B*27 facilitates disease remains unknown, but one possible mechanism could involve presentation of pathogenic peptides to $CD8^+$ T cells. **Yang** et al. isolated orphan T cell receptors (TCRs) expressing a disease-associated public β-chain variable region-complementary-determining region 3β (BV9-CDR3β) motif from blood and synovial fluid T cells from individuals with AS and from the eye in individuals with AAU. These TCRs showed consistent α-chain variable region (AV21) chain pairing and were clonally expanded in the joint and eye. The authors used HLA-B*27:05 yeast display peptide libraries to identify shared self-peptides and microbial peptides that activated the AS- and AAU-derived TCRs. Structural analysis revealed that TCR cross-reactivity for peptide-MHC was rooted in a shared binding motif present in both self-antigens and microbial antigens that engages the BV9-CDR3β TCRs. These findings support the hypothesis that microbial antigens and self-antigens could play a pathogenic role in HLA-B*27-associated disease.

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