

Pediatric Serum Sickness — Symptoms and Treatment

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Serum sickness can happen as a complication to the administration of certain antisera, such as antitoxins, antivenoms, and antibiotics. The condition is characterized by the presence of a rash that is associated with fever, arthritis, and systemic organ involvement. The condition is believed to be immune-complex mediated. Early recognition of the syndrome and adequate treatment have been associated with an excellent clinical outcome. The causative agent should be discontinued and symptomatic treatment is indicated. Immunosuppression with corticosteroids might be needed in more severe cases. Patients who are unresponsive to corticosteroids should be offered plasma exchange therapy.



Overview

Serum sickness is an **immune-mediated hypersensitivity reaction due to the injection of non-human antitoxins** that is characterized by rash, arthritis, and fever and commonly associated with other systemic features.

Epidemiology of Pediatric Serum Sickness

The incidence of serum sickness and other immune-mediated reactions to drugs or other antisera agents has been consistently reported to be **higher in children compared to adults**. Additionally, the incidence of serum sickness in girls is higher compared to males.

The incidence of serum sickness is **largely dependent on the antisera being administered to the patient**. Those receiving antisera for diphtheria and scarlet fever have a high incidence of developing serum sickness syndrome that is estimated to be around 30%. The current incidence of serum sickness in children exposed to antivenom for snake bites is estimated to be around 7%.

All patients receiving **anti-thymocyte globulin (ATG)** developed serum sickness. The incidence of serum sickness in children treated with cefaclor is estimated to be around 2 per 100,000.

The prognosis of serum sickness syndrome after adequate diagnosis and prompt treatment is excellent.

Pathogenesis of Pediatric Serum Sickness

Antitoxins, antivenoms, and ATG which are a group of heterologous serum proteins, are recognized as the most common cause of serum sickness in children. Biologic agents, such as **humanized monoclonal antibodies, human monoclonal antibodies, streptokinase, and the pneumococcal vaccine**, can also cause serum sickness in children.

Antibiotics such as **cephalosporins, ciprofloxacin, penicillins, sulfonamides, tetracyclines, and metronidazole** can cause serum sickness, especially in children. **Carbamazepine and other antiepileptics** might cause serum sickness in children.

The exact pathogenesis of serum sickness is still poorly understood, but recent studies have formed a basic understanding of the most likely mechanisms of the condition. After the administration of one of the possible causative proteins or drugs, the **host tries to neutralize this antiserum by binding it with specific antibodies**. Within one to two weeks, **immunoglobulin M antibodies against the administered protein are usually formed**.

It is believed that the antigen load in the different antisera described above is slightly higher than our antibodies reserve. When this happens, cross-linking happens and the development of complex large immune complexes ensues. Our mononuclear phagocytes are usually capable of clearing these immune complexes, but when they exceed their ability, serum sickness happens.

The previously mentioned **large immune complexes tend to aggregate and are deposited in various tissues**. They can be deposited within the renal glomeruli causing acute kidney injury within the skin causing typical skin rashes, or in the perivascular regions. When they are deposited within the perivascular regions, they can cause vasculitis.

Other immune-mediated responses related to immunoglobulin E and the activation of mast cells and basophils have also been described in patients with serum sickness and can attribute to the systemic clinical picture of the syndrome.

Clinical Features of Pediatric Serum Sickness

Because of the nature of the pathology in serum sickness, it is understandable that the symptoms of the condition would not occur before one to **two weeks after the administration of the triggering agent**. This can be explained by the need for the immunoglobulin M antibodies to form, and for a significant number of large immune complexes to form and start depositing in different tissues and cause significant damage.

Patients usually present with **fever, malaise, and headaches**. If the condition is not recognized yet, patients can go on to develop a skin rash, joint pain, peripheral and facial edema, abdominal pain and proteinuria or hematuria.

The **rash is typically pruritic** and usually starts from the site of the injection of the antisera involved. **Urticaria, erythema, petechiae, and purpura** can all be seen in patients with serum sickness.

Patients can have a **limited range of motion in the affected joints** due to arthritis or merely arthralgia. **Pericardial effusions, shortness of breath and chest wheezing** can also be seen. Peripheral lymphadenopathy has been also described in patients with serum sickness.

A recent history of receiving a typical agent that is known to be associated with serum sickness syndrome is usually evident in most cases.

Diagnostic Workup for Pediatric Serum Sickness

Laboratory investigations are helpful in the evaluation of the child with suspected serum sickness. A **complete blood count** might show leukocytosis with eosinophilia. Thrombocytopenia, which is usually mild, can also be seen.

Non-specific markers of inflammation, such as the erythrocyte sedimentation rate and c-reactive protein levels, might be elevated in some patients with serum sickness. Due to the involvement of the kidneys, proteinuria, hematuria and the presence of hyaline casts can be demonstrated in patients with serum sickness syndrome.

Blood urea nitrogen and serum creatinine levels can be mildly elevated. Because of the nature of the immunologic response in serum sickness syndrome, complement factors C3 and C4 can be slightly decreased due to increased consumption.

Treatment of Pediatric Serum Sickness

Like other immune-mediated drug reactions seen in children, the first step in the management of serum sickness is to **discontinue the offending agent**. The use of typical heterologous proteins, such as antitoxins, can be easily identified as the cause of the syndrome and should be stopped.

After the discontinuation of the causative agent, most patients show a significant improvement and all they need is supportive care. Patients who develop severe joint pain should **receive non-steroidal anti-inflammatory drugs** only if they do not have renal involvement.

Sedating antihistamines are recommended for the treatment of the intense pruritic rash seen in children with serum sickness. Children who develop serum sickness due to the administration of antitoxins, antivenoms or AGT should also receive oral steroids.

Patients with severe serum sickness, who do not respond to systemic steroids, should undergo **plasma exchange therapy**.

Patients who develop serum sickness as a reaction to a certain triggering agent should be instructed to avoid future exposure to the same offending agent in the future because recurrent serum sickness is usually more severe and carry a significant mortality and morbidity risk.

Finally, those who develop chronic vasculitis or arthritis should be referred to a rheumatologist for a specialized opinion and to formulate an individualized treatment plan.

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