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Pediatric Serum-Like Sickness: A Multicenter Analysis

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Background

- Serum sickness-like reaction (SSLR) is an acute inflammatory reaction that presents 5-21 days following infections, vaccines, drugs, and most notably antibiotics.
- The pathogenesis of SSLR is not well understood but thought to be caused by drug-specific immune complexes.
- SSLR is a diagnosis of exclusion and has been reported to be associated with nonspecific symptoms including fever, rash, and joint involvement. However, there is no clearly defined clinical or diagnostic criteria, nor are there guidelines for management.

Study Aim

To describe the drugs implicated, clinical presentation, resource utilization, and treatment strategies for children diagnosed with SSLR.

Methods/Design

- A retrospective study across 2 freestanding children's hospitals at Children's Mercy in Kansas City, MO and Riley Children's Hospital in Indianapolis, IN evaluated in the emergency department or admitted to the hospital from January 1, 2015 – December 31, 2021.
- Patients were selected through ICD-9/10 codes [T80.69XA, 999.59], SNOMED codes [1782626019, 3293325014], and by pharmacovigilance program review dedicated to evaluating documented adverse drug reactions. Eligible patients included children 0-21 years of age. Patients with reactions to biologics, vaccines, and chemotherapy were excluded.
- Data was manually extracted to identify demographic characteristics, pertinent medical history, drug exposure, and clinical course including labs and treatment.
- Data was compared between patients who were evaluated in the emergency department (ED) to those who were admitted to the hospital.
- Analyses of descriptive statistics were conducted for continuous and categorical variables.

Results

Table 1. Demographics of patients with suspected SSLR, implicated drugs, implicated drug indication, and presenting symptoms.

	Total Cohort N=201, n (%)
Demographic characteristics, n (%)	
Gender, male	113 (56)
Age at diagnosis, mean ± SD (range)	4.1 ± 4.07 (0.33-18)
Ethnic origin	
White	162 (80.5)
African American	12 (6)
Hispanic	7 (3.5)
Asian	2 (1)
Other	4(2)
Multiracial	6 (3)
Unknown	8 (4)
Drugs, n (%)	
Amoxicillin + Amoxicillin/Clavulanate	161 (80)
Cefdinir	18 (9)
Trimethoprim / Sulfamethoxazole	7 (3.5)
Cephalexin	4 (2)
Oxcarbazepine	1 (0.5)
Other	10 (5)
Indications, n (%)	
Acute otitis media	121 (60)
Strep pharyngitis	26 (13)
Pneumonia	7 (3.5)
Dental	3 (1.5)
Skin infections	6 (3)
Acne	4 (2)
Urinary tract infection	3 (1.5)
Viral illness	8 (4)
Seizures	1 (0.5)
Multiple diagnoses	7 (3.5)
Other	9 (4.5)
Unknown	6 (3)
Symptoms, n (%)	
Rash	199 (99)
Joint symptoms	161 (80)
Joint edema	148 (73.6)
Joint pain	107 (53.2)
Joint stiffness	7 (3.5)
Joint erythema	26 (12.9)
Fever	78 (38.8)
Mobility limited	65 (32.3)
Facial edema	58 (28.9)
GI symptoms	56 (27.9)
Malaise	13 (6.5)
Myalgias	12 (6)
Conjunctivitis	8 (4)
Mucosal involvement	8 (4)
Headache	7 (3.5)
Lymphadenopathy	4 (2)

Results

Table 2. Laboratory values obtained for patients with suspected SSLR

	ED N = 115 Mean ± SD (range)	Inpatient N=68 Mean ± SD (range)
WBC x 10^6	13.80 ± 5.86 (2.98-35.76)	14.36 ± 5.64 (3.2-35.76)
C Reactive Protein (mg/dl)	3.26 ± 5.27 (0-30)	5.55 ± 6.73 (0-37.9)
Erythromycin Sedimentation Rate (mm/hr)	13.61 ± 8.69 (1.2-38)	20.21 ± 14.14 (2-48)
Labs obtained n (%)	53 (46)	75 (87.0)
Basic Metabolic Profile	44 (83.02)	67 (89.33)
Liver Function Tests	77 (77.36)	58 (77.33)
Complement Levels	3 (0.06)	8 (10.67)

Figure 1. Consulting services utilized in patients with suspected SSLR.

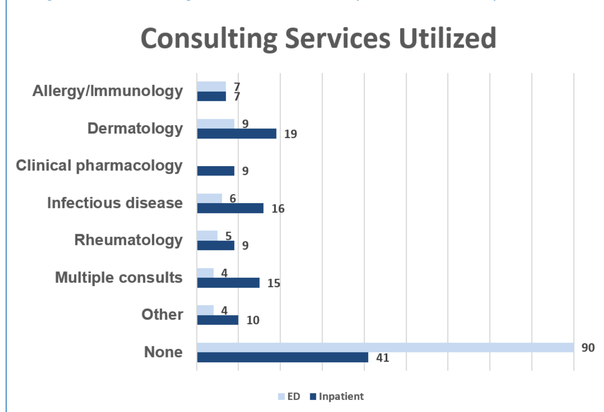

Table 3. Management of suspected SSLR in the ED and inpatient settings.

	Total Cohort N=201, n (%)	ED N=115, n (%)	Inpatient N=86, n (%)
Antihistamines	186 (92)	105 (91.3)	81 (94)
1st generation	168 (83.6)	93 (80.1)	75 (87)
2nd generation	18 (8)	12 (10.4)	6 (7)
Acetaminophen	119 (4.5)	53 (26.4)	66 (76.7)
NSAIDs			
Ibuprofen		87 (43.2)	68 (79)
Ketorolac		5 (2.5)	19 (22)
Other pain medications	6 (3)		6 (7)
Steroids	105 (52.2)	54 (47)	51 (59)
Epinephrine	9 (4.5)	2 (0.1)	7 (8)
Acid reducer	42 (20.9)	22 (10.1)	20 (23)

Results

- Patients experienced on average 1.9 healthcare visits due to symptoms until SSLR was on the differential. Forty-three percent of patients were hospitalized.
- Amoxicillin/amoxicillin-clavulanate was the most common implicated antibiotic. Antibiotics were most often prescribed for acute otitis media.
- Suspected SSLR often presented with rash (99%), joint involvement (80%), and documented fever (38.3%). Unable to further characterize the rash due to poor descriptions. Joint involvement included edema, pain, stiffness, and erythema. GI symptoms including abdominal pain, nausea, and vomiting occurred 27.9% of the time.
- Medical consultation occurred in 35% of cases of which multiple consulting services were involved 27% of the time.
- Treatment centered around supportive care including antihistamines, acetaminophen and ibuprofen.
- Variability in treatment remains controversial. Half of the patients were treated with systemic steroids in this cohort. Additional treatments included acid reducer (21%), and epinephrine (4.5%).

Conclusions

- To our knowledge, this is the largest study describing suspected pediatric SSLR.
- Patients most commonly presented with rash, joint, and surprisingly GI symptoms. Only 40% of patients presented with a documented fever.
- Diagnosis is difficult and often required several consulting services input as well as multiple encounters prior to SSLR being on the differential.
- Treatment is focused on supportive care and there is not a general consensus of steroid utilization in SSLR management. This may be due to uncertainty of diagnosis versus no standardization of treatment. Future research is needed to evaluate optimal management.
- Antibiotic stewardship is key to avoiding unnecessary antibiotics that may result in unintended consequences such as SSLR.

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