

## Session #2557

### Interesting Cases I – Saturday, March 14, 2020

#### Case Report #3

**Author** Benjamin D. St. Clair, DO; Karla Davis, MD; Bruce McClenathan, MD

**Training Program** Tripler Army Medical Center Pediatric Residency Program

#### Case Title

Cutaneous Mastocytosis Presenting as Anaphylaxis to Multiple Immunizations

#### Summary

The patient is a 19 month male with hyper-pigmented skin patches clinically diagnosed as café-au-lait macules who experienced adverse symptoms to vaccinations including fever, flushing, rash, pruritus, facial swelling, and conjunctival injection for several days following multiple different vaccines in combination and in series. No clear association between vaccines or excipients and adverse symptoms were identified. Evaluation for a mast cell disorder was pursued to include serum tryptase and skin biopsy of the hyperpigmented skin patches. The serum tryptase level was normal on serial blood draws and skin biopsy demonstrated increased dermal mast cells without significant mucin, consistent with cutaneous mastocytosis.

#### Patient Presentation

The patient is a 19 month Caucasian male with a past medical history remarkable for mild atopic dermatitis and a few hyperpigmented skin patches clinically diagnosed as café-au-lait macules. The patient had experienced adverse symptoms in temporal relation to vaccinations including fever, flushing, rash, pruritus, facial swelling, and conjunctival injection. Symptoms lasted for several days and followed multiple different vaccines in combination and in series.

The patient had no adverse reaction after receiving the Hepatitis B vaccine in the newborn period or after receiving Diphtheria, Tetanus, and acellular Pertussis (DTaP), Haemophilus influenzae type-b (Hib), Inactivated polio virus (IPV), Protein-conjugated pneumococcal vaccine (PCV-13), and Rotavirus vaccines at 2 months of life. At 4 months of life he received DTaP, Hib, IPV, PCV-13, and Rotavirus vaccines and approximately 24 hours later developed a fever of 100.5°F, a pruritic rash on his legs and torso that persisted for 5 days. At 7 months he received the DTaP vaccine in isolation and within 12 hours developed fever of 102°F and a pruritic erythematous rash on his legs and torso that persisted for 5 days. At 9 months he received PCV-13 and within 12 hours developed fever of 103.5°F with full body rash for 3 days. At 13 months he received PCV-13 and Varicella vaccine and within 3 hours developed facial swelling, conjunctival injection, a diffuse rash of his torso and legs, and fever.

He had no accompanying dyspnea, stridor, coughing, vomiting, or diarrhea with any of the above-described episodes.

On review of vaccine components, there was no clear association between a specific vaccine antigen or excipient and adverse reactions. The patient is known to tolerate eggs, soy, yeast, and gelatin. In the absence of a common antigen explaining the patient's multiple systemic reactions to vaccinations, evaluation was pursued for an underlying etiology. Prior to our evaluation hyperpigmented skin patches

were clinically diagnosed as café-au-lait macules. Dermatology felt that the lesions were most consistent with café-au-lait macules but could not definitively rule out mastocytomas or Urticaria Pigmentosa. An initial serum tryptase level was obtained and was 2.2µg/L (reference range 2.2- 13.2µg/L). Approximately three months after initial presentation, the patient's previously-noted hyperpigmented skin patches began to develop flushing and induration in response to various stimuli such as touch, friction, increase in ambient temperature, and systemic illness. Suspicion for mast cell disease increased.

### **Diagnosis**

Cutaneous mastocytosis is common in pediatric patients, while systemic mastocytosis is more common in adults. Cutaneous mastocytosis is a clinical diagnosis that can be made with the presence of macular lesions and appearance of erythema, wheals, or vesicles when lesions are stroked, referred to as a positive Darier's sign. A tryptase level of < 20µg/L with no signs of systemic involvement argues against systemic disease, which was the case for our patient. A few months after initial presentation, lesions responded in a way anticipated with cutaneous mastocytosis. Biopsy secured the patient's diagnosis.

### **Testing**

Serial serum tryptase levels were obtained in temporal relation to skin flares and ranged from 1.0µg/L to 2.2µg/L. After Mother noted a hyperpigmented patch becoming indurated and erythematous after light stroking, Dermatology re-evaluation was requested with a working diagnosis of cutaneous mastocytosis. Skin biopsy of the hyperpigmented skin patches was performed. The pathology results demonstrated increased dermal mast cells without significant dermal mucin. Giemsa and CD 117 staining highlighted increased mast cell burden.

### **Treatment**

Recurrent episodes of flushing, pruritus and rash associated with mast cell mediator release prompted prescription of a daily second generation antihistamine. Given history of anaphylactic symptoms auto-injectable epinephrine was prescribed.

### **Patient Outcomes**

The patient continues to be followed in the Allergy/Immunology and Dermatology clinics. Discussion is ongoing with the patient's parents regarding future administration of immunizations. A proposed plan to administer immunizations under controlled circumstances, in series, with premedication, and careful clinical observation has been discussed with the patient's parents.

### **Lessons Learned**

Local reactions and fever after vaccinations is common but anaphylactic reactions to vaccines occur at a rate of 1 per million doses(1). In a study of 72 children with mastocytosis the rate of adverse reactions to vaccinations is rare (4 cases per 431 vaccine doses) but more common than in the general population (2.3 cases per 10,000 doses). These reactions occurred in all subtypes of mastocytosis and occurred most commonly with a hexavalent vaccine administered at 3 months of life(2). It is important for clinicians to consider a mast cell disorder when a patient presents with anaphylaxis to multiple different vaccines.

In our patient on initial exam, skin lesions seemed most consistent with café-au-lait macules with a negative Darier's sign. A positive Darier's sign is very specific but not 100% sensitive suggesting these

lesions evolve over time(3). Serial exams, caregiver education, and vigilance over the subsequent months aided in making the diagnosis.

Once the etiology of the adverse reactions was identified discussion regarding the risks and benefits of future vaccine administration with the family became a priority. It was felt that the benefit of protection from routine vaccinations, administered in a controlled and closely monitored environment, outweigh the risk of future reactions prompting our recommendation to the parents to proceed with immunizations.

References:

(1) Kelso JM, Greenhawt MJ, Li JT, Nicklas RA, Bernstein DI, Blessing-Moore J, et al. Adverse reactions to vaccines practice parameter 2012 update. *J Allergy Clin Immunol* 2012 Jul;130(1):25-43.

(2) Carter MC, Metcalfe DD, Matito A, Escribano L, Butterfield JH, Schwartz LB, et al. Adverse reactions to drugs and biologics in patients with clonal mast cell disorders: A Work Group Report of the Mast Cells Disorder Committee, American Academy of Allergy, Asthma & Immunology. *J Allergy Clin Immunol* 2019 Mar;143(3):880-893.

(3) Kiszewski AE, Duran-Mckinster C, Orozco-Covarrubias L, Gutierrez-Castrellon P, Ruiz-Maldonado R. Cutaneous mastocytosis in children: a clinical analysis of 71 cases. *J Eur Acad Dermatol Venereol* 2004 May;18(3):285-290.



