

Neither iatrogenic nor hereditary cause; A rare case of anaphylaxis to low sorb tubing used for infusions

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Abstract

Presented is an interesting case of a patient with diagnosis of central nervous system (CNS) malignancy and Hashimoto thyroiditis, who developed anaphylaxis to low sorb tubing which was used for chemotherapy and supportive care medication. The patient had no known drug allergies and an unremarkable work up for hereditary angioedema, rheumatological and immunodeficiency disorders. This hypersensitivity reaction (HSR) has not been previously reported in literature and delayed the patient's cancer related treatment, which has the potential of impacting patient outcomes. We report this rare case, discuss differential diagnosis for HSR in patients with negative allergy history, and provide management guidelines.

Introduction

Hypersensitivity reaction to medications is not an uncommon phenomenon in cancer patients, but anaphylaxis to commonly used infusion lines, particularly low sorb tubing has not been previously reported in the literature. The possibility of adverse effects from interaction between blood and plastic tubing created some concern in the early days of medical care. The mechanisms responsible for most of these reactions are unknown, and these reactions may be immunologic or non-immunologic. The clinical presentation of these reactions can vary from mild cutaneous reactions to severe life-threatening reactions. These life-threatening anaphylactic reactions can limit the use of front-line chemotherapeutic agents making it imperative to accurately find the inciting factor so that appropriate chemotherapy can continue. Here we present a unique case of a child with brain cancer and Hashimoto thyroiditis, who developed an allergic reaction to the IV tubing system.

Case Description

A previously healthy four-year-old female with a new diagnosis of grade IV primitive neuroectodermal (PNET) brain tumor underwent surgical resection and came to our institution for chemo-radiation as standard of care. The patient was scheduled to receive vincristine during radiation therapy. During her initial infusion of vincristine she developed an anaphylactic reaction with facial flushing, cough, lip swelling and oxygen desaturation to 87% at room air within 3 minutes of starting the infusion. The infusion was stopped and the patient was given a dose of diphenhydramine and hydrocortisone, which abated her symptoms.

An extensive root cause analysis was done to determine the cause of the allergic reaction, since anaphylaxis to vincristine is rare. In the following 2 weeks the patient had similar anaphylactic reactions while receiving IV pentamidine and premedication with IV hydrocortisone, proving that anaphylaxis was not due to vincristine. The patient did not experience any reaction to saline flushes, chlorhexidine or alcohol wipes.

Our work up for multiple allergic reactions included complement levels, antibodies for rheumatologic and autoimmune diseases and thyroid function tests. Thyroid stimulating hormone (TSH) was elevated at 7.3 mcunit/mL (normal reference 0.27 - 4.20). No eosinophilia or immunodeficiency was detected in the work up and immunoglobulin levels were unremarkable. The patient was referred to endocrinology and a complete work up showed elevated prolactin 50.1 ng/mL (4.8 - 23.3 ng/mL) which was secondary to TSH elevation. The patient also had clear rhinorrhea for which an upper respiratory viral panel was sent and this was negative. She was diagnosed as having allergic rhinitis, a common co-existing condition with Hashimoto's thyroiditis, for which cetirizine was started with moderate improvement of her symptoms.

Further work up by endocrine team revealed elevated thyroid peroxidase antibodies at 29.8 IU/mL (reference range: 0.2 - 8.9 IU/mL) with subsequent normalization of TSH and Free T4 which was consistent with the diagnosis of Hashimoto thyroiditis.

The consistency found between all the allergic reactions was the IV tubing set used. When we changed from low sorb tubing to regular tubing, the patient did not experience any further allergic reactions to chemotherapeutic and non-chemotherapeutic agents, without the use of premedication. She was able to successfully receive additional doses of vincristine and proceed with maintenance chemotherapy as standard of care for PNET. The patient was referred to allergy and immunology for further work up but there were no significant findings.

Discussion

Hypersensitivity Reaction (HSR) is common in cancer patients. Although this can potentially happen with any therapeutic agent, such reactions are common with platinum compounds, L-asparaginase, epipodophyllotoxins, methotrexate, procarbazine and taxanes at a rate of approximately 6% of infusions. (1,2) HSR to plasticizing agents like phthalates and triphenyl phosphite that are used in combination with polyvinyl chloride (PVC) have also been well studied in the past. Phthalates specifically have been found to be a triggering factor for asthma and contact dermatitis. (3) Additionally, triphenyl phosphite has been reported to cause HSR in a case series involving 5 patients with reactions varying from urticarial, angioedema to anaphylaxis. (4) Direct allergic reactions to PVC are rare but several studies have suggested allergic reactions to different components of PVC. (5-6) Because of this reported hypersensitivity to PVC, many hospitals have now switched to PVC free tubing systems. As in our case, the low sorb tubing system was used, which is PVC free and has a polyethylene lining which provides an inert surface to most chemicals and helps prevent absorption of drugs into the matrix of the tubing material. Polyethylene compounds such as Polyethylene glycol has been reported previously to cause HSR as part of the PEGylated L-asparaginase or oral agents used for bowel regimen. (7-9)

The HSR rate and severity depends on the administration route of allergen. For example, pooled HSR rates using PEG-asparaginase in children with acute lymphoblastic leukemia were between 23.5% and 8.7% for IV and intramuscular (IM) administration, respectively (10). However, Burke et al reported higher rates of PEG asparaginase associated HSR with IM route (11).

Although HSR in pediatric cancer patients is not rare, for patients with negative allergy history, the HSR differential diagnosis should include autoimmune/rheumatologic disorders, hereditary angioedema, some immunodeficiency disorders and mast cell disorders. As in our patient, she was diagnosed with Hashimoto Thyroiditis during her work up. High concordance of allergic disorders with Hashimoto disease (up to 23%) has previously been reported, which could be an added factor for the severe reaction in our patient. (12) HSR management options include use of an alternative drug, giving the same drug with premedication, or performing desensitization. Switching agents, especially chemotherapy can have a negative impact on patients' outcome when the culprit agent is essential or is the best treatment option.

Skin tests can be used in the evaluation of IgE-mediated drug reactions, but standardized testing dose for testing is only available for a few drugs. The unclear mechanisms responsible for reactions to certain drugs, and possible toxicity of testing reagents restrict the use of this testing approach.

Furthermore, referral to allergist/immunologist is warranted for patients with negative allergy history and multiple and/or severe HSR.

Up to date, no HSR to low sorb tubing has been reported in the published literature. This case highlights the importance of targeted work up and referral to an allergist in cancer patients with negative allergy history, as switching cancer specific management may affect patient outcomes.

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TABLE 1: Types of allergic reactions

Type of allergic reaction		Type of allergic reaction	
Immune related (Allergic or immune)		Non-immune related (Non Immune)	
Sub type	Characteristics	Sub type	Characteristic
Type I	IgE antibody related (Anaphylaxis)	Anaphylactoid	Similar to Type I HSR (Direct mast cell degranulation)
Type II	Antibody mediated cytotoxicity reaction (Same as in Blood transfusions)	Idiosyncratic reaction	Uncommon, unpredictable and unrelated to and are not related to drugs' pharmacologic activity
Type III	Immune complex mediated HSR (Similar to vasculitis)		
Type IV	Delayed T cell response (contact dermatitis)		

HSR (hypersensitivity reaction), Ig (Immunoglobulin)

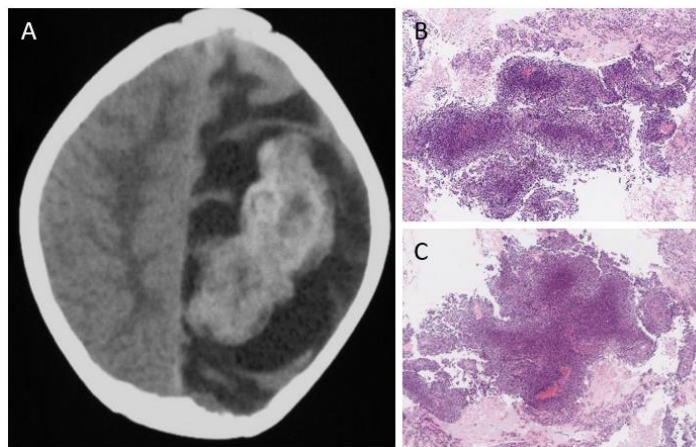


Fig. 1: (A) CT brain axial section showing tumor in the left cerebral hemisphere. (B&C) Hematoxylin & eosin (H&E) staining of brain biopsy showing sheets of small tumor cells