Neurologic manifestations in anaphylaxis due to subcutaneous allergy immunotherapy

A case report

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Abstract

Rationale: Life-threatening anaphylactic shock is a rare (1 in 1 million) but documented occurrence in response to subcutaneous immunotherapy. Immediate administration of Epinephrine (Epi) is critical to save lives in these situations. The current protocol for systemic reactions in immunotherapy is for the prescribing physician to reassess the dosing and schedule as well as the risk-benefit assessment for the therapy and determine whether or not to proceed.

Patient concerns: The patient revealed concerns regarding the neurologic sequela sustained after undergoing life-threatening anaphylactic shock.

Diagnosis: The patient was diagnosed with anaphylactic shock and treated appropriately.

Interventions: The patient experienced shortness of breath and was promptly administered 2 shots of 0.3mg Epi followed by a loss of consciousness (LOC) and a series of 4 consecutive seizures accompanied with LOC and urinary incontinence. Seizures as a manifestation of anaphylaxis are rare with 1 study claiming 13% of cases of anaphylaxis having LOC and only 1.5% cases with loss of bladder or bowel control.

Outcomes: This case is one of continued subcutaneous immunotherapy after the patient had an initial systemic reaction suspicious for anaphylaxis 6 months before the life-threatening anaphylaxis, both induced by immunotherapy. In both instances, there was a significant amount of neurologic involvement. Neurologic sequela included a transient tremor and permanent deficits in vision, fine motor coordination evidenced by a change in handwriting.

Lessons: The current protocol was followed in this patient but still ended up almost ending her life. This protocol seems to be inadequate with regards to potential fatality. Even though a very small number, some patients face life-threatening adverse effects after apparently very low-risk immunotherapies. Therefore, reevaluating the treatment protocol with addition of a longer post-shot observation step and discontinuing treatment in the case of adverse events may help minimize the overall risk of any fatal outcome.

Abbreviations: Epi = epinephrine, LOC = loss of consciousness, ACE = angiotensin-converting enzyme, CT = computed tomography, ED = emergency department, EEG = electroencephalogram, EMS = Emergency Medical Services, FEV1 = forced expiratory volume in 1 second, FVC = forced vital capacity, GCS = Glasgow Coma Scale, MRI = magnetic resonance imaging, PFTs = pulmonary function tests, RAST = radioallergosorbent test, SOB = shortness of breath.

Keywords: anaphylactic shock, desensitization, neurologic, seizure, subcutaneous immunotherapy

1. Introduction

Subcutaneous immunotherapy is a common practice for those with unrelenting allergies (especially environmental allergies). This kind of immunotherapy carries a low risk of anaphylaxis approximately 1 in 1 million injection visits.[1] Certain groups are at a higher risk for adverse systemic reactions in response to immunotherapy including those with severe/labile asthma, and those patients on beta blockers or angiotensin-converting enzyme (ACE) inhibitors.[2] The case presented here is one of a patient with a 10-year history of asthma but no other high-risk variables. More interesting is the neurologic manifestation with escalation of the responses that are very rare in anaphylactic reactions,[3,4] with 1 study reporting a loss of consciousness (LOC) in only 13% of anaphylactic reactions and loss of bladder/bowel control in only 1.5% of anaphylactic reactions.[1,5] This patient had both LOC and urine incontinence as well as other lasting neurologic sequela including change in vision and handwriting, which arguably may be the result of hypoxic injury sustained in anaphylactic shock.

2. Case report

The patient is a 51-year-old female who started allergy shots on a conventional schedule beginning in May 2007. Before starting this therapy, a radioallergosorbent test (RAST) was
performed and pulmonary function tests (PFTs) were done to determine the makeup of the therapeutic shots and establish a baseline lung function (Fig. 1). Throughout therapy, PFTs were done to assess progress (Fig. 2). The patient’s RAST results guided the constituents of the shots, which included trees (American Elm, Arizona Ash, Black Willow, Mesquite, Mountain Cedar, Mulberry, Oak, Pecan and Sycamore), grasses (Bermuda, Johnson, Meadow Fescue, Perennial Rye, Redtop and Timothy), weeds (Careless, Cocklebur, Lamb’s Quarter, Marsh Elder, Pigweed, Russian Thistle, and Sagebrush), ragweeds (Franseria, Short Ragweed, Tall Ragweed, and Western Ragweed), molds (Alternaria, and Epicoccum), and environmental (Cat Dander, and Dog Dander) allergens. These allergens were used at a frequency of 1 to 3 times a week with an initial dose of 1:2,000,000 dilution with a target maintenance dose of 1:2000. The target dilution could not be reached due to cessation of treatment due to anaphylaxis incidences.

| RAST rating | IgE level (kU/l) | comment |
|-------------|------------------|---------|
| 0           | < 0.35           | ABSENT OR UNDETECTABLE ALLERGEN SPECIFIC IgE |
| 1           | 0.35 – 0.69      | LOW LEVEL OF ALLERGEN SPECIFIC IgE         |
| 2           | 0.70 – 3.49      | MODERATE LEVEL OF ALLERGEN SPECIFIC IgE    |
| 3           | 3.50 – 17.49     | HIGH LEVEL OF ALLERGEN SPECIFIC IgE        |
| 4           | 17.50 – 49.99    | VERY HIGH LEVEL OF ALLERGEN SPECIFIC IgE   |
| 5           | 50.00 – 100.00   | ULTRA HIGH LEVEL OF ALLERGEN SPECIFIC IgE  |
| 6           | > 100.00         | EXTREMELY HIGH LEVEL OF ALLERGEN SPECIFIC IgE |

Figure 1. Radioallergosorbent test (RAST) from baseline demonstrating patient’s very high level of allergies to ragweed and grasses corresponding to approximately 17.5–49.99 IgE levels.
After a couple of months of therapy, the patient had a systemic reaction that entailed shortness of breath (SOB), loss of visual acuity, tremors, and LOC. She managed to take 100mg of diphenhydramine and a puff of albuterol inhaler (180 µg) before LOC. At this point, the patient was given options for cessation of treatment or taking the injections at lower doses with smaller increments than before. The patient chose to continue the therapy at the lower dose increments. It is important to note at this point that the patient was prescribed an Epi-pen.

Approximately 6 months after this event and the change to the immunotherapy regimen, the patient went in for her immunotherapy shots per schedule and immediately developed severe SOB. At this point, the patient was placed on 4L of oxygen delivered via nasal cannula and 2 shots of 0.3mg Epi were given. The patient continued to have severe breathing difficulties, which were managed by increasing the oxygen flow to 6L and administering another 2 shots of 0.3mg Epi. The patient was discharged on a regimen of 2 shots of 0.3mg Epi every 24 hours.

Figure 2. Baseline pulmonary function test (PFT) top left. Sequential PFTs showing improvement in lung function until November with a slight decline in forced expiratory volume in 1s (FEV1) and forced vital capacity (FVC) from July but an overall improvement from baseline.
administered. Shortly thereafter, the patient became unresponsive and medical staff began resuscitation efforts. The patient then had a series of 4 consecutive seizures in rapid succession, which were presumably induced from severe hypotension. These seizures had associated urinary incontinence and tongue lacerations noted in the emergency department (ED). Emergency Medical Services (EMS) arrived and tried unsuccessfully to intubate the patient at which point the patient was transferred to the ED. The patient was intubated in the ED after approximately 20 minutes of being bagged and resuscitated by EMS. Physical examination revealed LOC, dilated pupils, unresponsive with a Glasgow Coma Scale (GCS) of 3. Subsequently, the patient gradually improved and was extubated the following day. Although the patient remained a little shaky, her neurologic functions were remarkably otherwise intact. Computed tomography (CT) and magnetic resonance imaging (MRI) were done and were unremarkable. These images served to rule out severe hypoperfusion injury and the possibility of causative brain pathology (i.e., tumor, hematoma, hemorrhage) (Fig. 3). An electroencephalogram (EEG) was also done to rule out the possibility of an underlying seizure disorder and was found to be negative. Patient’s reported home medications were Albuterol, Clarinex, Claritin, Progensa, Testosterone, Endosis, and Singulair.

3. Long-term sequelae

After the second incident, the patient noticed her handwriting to be tremulous for approximately 8 months post event. After the tremors abated (which was presumably a side effect from high-dose steroids), her handwriting had significantly changed and had become smaller and subjectively harder to read. Not only were the effects evident in the patient’s handwriting but also in her vision. The patient stated post event her distance vision had decreased, along with her depth perception to the point where she now needed progressive lenses versus the reading glasses she previously wore. In addition, there were several instances wherein while driving at night the patient noticed halos around the lights that impaired her ability to safely drive. The patient did have ophthalmologic evaluation during this time, as she required a new prescription for glasses after the event. It is possible that there was an underlying eye issue that was either exacerbated or accentuated in light of the events that occurred.

The patient also had some short-term memory issues noticeable to her but not significant enough to dip below the sensitivity threshold on the neurologic examinations administered. The patient was able to return to work after 6 weeks.

4. Discussion

These 2 episodes of anaphylaxis in response to immunotherapy in this 51-year-old female were the end of her encounter with this possible therapeutic method, which could improve her quality of life by alleviating everyday sufferings from various allergic episodes. It is rare to have such an overwhelming neurologic response to anaphylaxis. More common are the effects readily associated with a systemic histamine release causing itching, erythema, warmth, hypotension, and swelling with airway compromise. Although these common manifestations were present as well, the rapid decline in visual acuity in the first episode was novel. Also novel was the presentation of her anaphylactic reaction including multiple seizures without regaining consciousness. Not only this but also the tremulous nature of the reaction and both episodes of LOC is another novel presentation, which may be explained by significant global hypoxic injury to the brain.

The lasting sequelae of visual and fine motor skill deficits may very well be a result of hypoxic injury to the brain. Although CT and MRI were unremarkable, one may argue that it is reasonable to infer that the imaging sensitivity for milder hypoxic injuries may fall below the sensitivity of current imaging modalities and thus go unrecognized. These long-term sequelae and residual deficits are not reported in any other case of anaphylaxis. It is important to note that the patient had no pre-existing neurologic conditions nor symptoms of such.

The decision to continue with therapy after the first event was a joint decision, but begs the question whether there are more definitive approaches or criteria to decide who needs to unequivocally stop therapy. Should this case be a guide to clinicians to err on the side of caution, or should we continue as is and let that be a joint discussion and decision being made.
arbitrarily? If patients decide to accept the risks for the benefit much as they do with any other treatment, then it will be up to the physician to ensure it is done in the safest way possible.

It is important to note that this treatment is considered very low risk. However, cases such as this may actually prove fatal and end a patient’s life. Therefore, modifying the protocol with a prolonged post-treatment observation period should be seriously considered.

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