



Positive Response of Vitamin D Therapy in Conjunction with Conventional Treatments of Reactive Airways Dysfunction Syndrome (RADS)

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Authors' contributions

Conceived and designed the experiments: authors RI, YWID, AG, MZ analysed the data, authors RI, YWID, TC, OM, AG, MZ wrote the first draft of the manuscript: Authors RI, YWID, AG, OM, MZ corrected spelling mistakes and editing authors TC, OM, YWID jointly developed the structure and arguments author RI, YWID, TC, OM, AG, MZ made critical revisions and approved final version authors RI, YWID, TC, OM, AG, MZ. All authors reviewed and approved of the final manuscript.

Others Article

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ABSTRACT

Reactive Airways Dysfunction Syndrome (RADS) is an understudied condition resulting from extensive injury to the respiratory system from the inhalation of corrosive gas, vapor, or fumes. Our study focuses on a 51-year-old African female with exposure to a significant volume of chloride bleach in which RADS symptoms developed. The patient was admitted with a long treatment history; however was unresponsive to usual methods of treatment. Therefore, we report upon the initiation of a Vitamin D regimen incorporated with typical treatment methods a progressive decline in bronchodilators and steroid requirements. Interestingly, the patient was a vitamin D-deficient female able to discontinue all her medications after the complete alleviation of her symptoms subsequent to maintenance of therapeutic Vitamin D level.

Keywords: RADS; Vitamin D; Resistant asthma.

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1. INTRODUCTION

RADS was first described and diagnosed among industrial workers and World War I combatants in the early part of the 20th century [1,2]. RADS is a respiratory syndrome most accurately classified by its bronchial symptoms, such as chronic cough and intense wheezing. RADS symptoms were able to become more clearly defined and diagnosed following a chlorine spill in 1969 which left those exposed with severe symptoms of respiratory distress [3,4]. Härkönen and colleagues were able to document persistent airway hyperresponsiveness in five of seven subjects who were exposed to pyrite dust, an airway irritant associated with miners and steel workers [5]. Studies were conducted including firefighters, and residents living in the neighbourhood of the World Trade Centers' collapse site in September 2001 [6], whom have inhaled corrosive particles to evaluate disease course.

The American College of Chest Physicians diagnostic criteria for RADS are:

- Absence of preceding respiratory complaint.
- Occurrence following a single exposure event.
- High concentration of irritant gas, smoke, vapors.
- Development of symptoms within 24 hours after exposure with symptoms for 3 months or more.
- Asthma like symptoms.
- Obstructive picture on pulmonary function with nonspecific airway hyper-activity
- Exclusion of all other pulmonary diseases [7].

Although RADS presents similar to bronchial asthma it typically does not respond adequately to bronchial asthma protocols. However, in the acute phase of RADS, several studies found limited positive results with the use of corticosteroids. RADS is a complex asthma-like syndrome resulting from a high level of exposure to a corrosive inhalant, such as pyrite or chlorine gas as was previously described [8]. Determining the acute phase is not always feasible as the magnitude and duration of exposure at the time of inhalation must be known, which is not always available. The reported positive results of corticosteroids are rarely applicable to the sufficient treatment for RADS [9].

Extensive inflammation associated with short-term exposure alters receptors' thresholds in the respiratory zone. This leads to the persistence of airway hyper-excitability and direct damage to the bronchial mucosa, as well as the unregulated release of inflammatory mediators [10,11]. As more is documented and discovered about the cellular physiology of RADS, more effective treatments can be administered. For that reason, we report a case describing a patient with RADS with a possible response to vitamin D following an exposure to a substantial amount of spilled bleach.

2. CASE SUMMARY

A 51-year-old African female with medical history of cervical intraepithelial hyperplasia, ovarian cystectomy, osteoporosis, and three caesarian sections was exposed to a large spill of chlorine bleach at her home. Exposure of the irritant was estimated to be approximately 60 minutes consequential to cleaning the spill without respiratory protection. She noted shortly afterwards development of symptoms including; cough, shortness of breath, and the burning of her nasal mucosa. Immediately once the symptoms were presented she was

referred to our emergency room for treatment. Upon admission, we administered intravenous corticosteroids, methylprednisolone, bronchodilator therapy, ipratropium bromide, and albuterol to our patient. Shortly afterwards she was discharged from the emergency department with an improvement of symptoms and was prescribed a tapering dose of oral steroids. Results of laboratory studies for our patient prior to release were within normal range in regard to complete cell count and basal metabolic profile but refused an arterial blood gas at that time. Several weeks after her release, she traveled overseas for several months before returning to the United States.

Upon her return she developed severe shortness of breath and wheezing coupled with a dry cough prompting her to come to our emergency department again. She received oxygen therapy via nasal cannula at 3L/minute. She was furthered treated with bronchodilators and intravenous steroid regimens; however her symptoms did not improve compare to her previous admission. We further attempted treatments including inhaled mast cell stabilizers, high doses of pulsed methylprednisolone and broad spectrum anti-bacterial, anti-viral and anti-fungal medications. Results of a CT of the chest revealed a ground glass appearance of the lungs. Pulmonary function tests were consistent with airway obstruction, evidence data of airway resistance at 168% of predicted, with less small airway indices. Lung volumes and gas transfer measurements were within normal limits. A histamine challenge test was given yielding positive results, methacholine-provoking concentration for a 20% fall (PC₂₀) of 7.3 mg/mL. Supportive treatments used included Ibuprofen (600 mg) every eight hours as needed for pain. Additionally, she was administered Tramadol for chest wall pain as well as proton pump inhibitor in the form of omeprazole for acid suppression.

Vitamin D levels (19nmol/L) were obtained due to the patient's history of osteoporosis which had an unclear etiology, as it was neglected due to a lack of medical insurance. An oral vitamin D therapy (ergocalciferol) of 50,000 units once per week for 8 weeks, followed by 50,000 units every 4 weeks thereafter was initiated with regular scheduled follow ups. Our patient's symptoms began to gradually improve and she was able to decrease her medication dosage requirements. Furthermore, after four months during a follow up, her vitamin D serum 25(OH) D levels (110nmol/L) were measured in our lab using a 25-OH Vitamin D ELISA assay kit. Vitamin D₄ serum 25(OH) D levels were collected four months after the complete resolution of symptoms and termination of medication regimens. It was at this time her Vitamin D serum 25(OH) D levels were recorded to be 200 nmol/L.

3. DISCUSSION

The pathology of RADS shows nonspecific inflammation, mainly with a cellular infiltrate. The initial chemical assault leads to lymphocytic infiltration, epithelial desquamation, and hyper-responsiveness. This occurrence resulted in an inflamed lower airway mucosa [12]. Massive inflammation and epithelial sloughing consequentially reduces receptor thresholds to amplify a bronchial reactivity response. The majority of documented cases show a minimal improvement of symptoms with time and persisting chronic asthma-like symptoms. The traditional treatment of RADS is similar to that of asthma; however, RADS is less responsive to β_2 agonists or the conventional treatment strategies of airway hyper-excitability syndromes [13].

Vitamin D is a fat-soluble responsible for intestinal absorption of calcium and phosphate. Recently, it has been discovered to be a major immunoregulatory hormone. Vitamin D is a steroid sensitizer and an inhibition mediator for various inflammatory processes. It has subtle effects on cytokines, CD4+ T cells, interleukin-2, interferon-gamma, and macrophages [14].

Our patient had a complete recovery following the use of a vitamin D regimen parallel to conventional treatments despite the diagnosis of severe unremitting symptoms of RADS following bleach exposure. A similar case was reported in 2011 in a thirty-six-year-old nurse exposed to ammonia following a spill. She later developed RADS and responded to high dose vitamin D therapy similar to our case study[15],. .To sum up, the use of vitamin D as a standard disease regimen needs to be investigated due to numerous studies proposing its benefits in medical use.

Two other extraneous variables may have accelerated recovery of the patient. Firstly, the patient was taking over the counter multivitamins which contained Vitamin D without reporting to the physician. Secondly, the patient's travel to South America made her prone to adequate sun exposure due to the tropical climate which could have possibly increased endogenous Vitamin D production.

4. CONCLUSION

Our case demonstrates a relatively fast improvement of RADS with the initiation of vitamin D supplements parallel to bronchodilators and steroid treatments. Due to the rarity of this disease or perhaps it's under diagnosis, repeating such procedures will be difficult. However the potential is endless, and therefore proper diagnosis is necessary to enhance our understanding of the anti-inflammatory effects of vitamin D regimens. We propose that any patients presenting with symptoms of RADS have their vitamin D levels monitored periodically. Moreover, RADS patients with normal lab levels of vitamin D might still benefit from supratherapeutic levels of the vitamin. In conclusion, future research should examine the possible role of Vitamin D as an immune buffer or desensitizer as well as its additional anti-inflammatory properties for better treatment outcomes to enhance the quality of life.

DISCLOSURES AND ETHICS

As a requirement of publication the authors have confirmed that this article is unique and not under consideration or published in any other publication, and that they have permission from rights holders to reproduce any copyrighted material. The external blind peer reviewers report no conflicts of interest. Verbal consent was obtained from the patient for publication of this case report as patient had a hand injury and was unable to sign at the time of consent and thereafter died few months later of unrelated cause and no family could be reached.

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.”

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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