



Letters

Allergic disease in patients with common variable immunodeficiency at a tertiary care referral center



Common variable immunodeficiency (CVID) represents a group of immunodeficiencies characterized by impaired immunoglobulin production.¹ CVID is the most common symptomatic primary immunodeficiency in adult and pediatric populations.^{2,3}

The hallmark of CVID is dysfunctional antibody production.⁴ Serum levels of IgE have not been well described in CVID, although they are often decreased or undetectable, likely because of poor formation of specific antibodies. Little has been published on the presence of allergy in this population, although studies have found a low incidence of positive allergen test results in patients with upper and lower respiratory tract symptoms.^{5,6}

To our knowledge, no study has yet to examine demographic or laboratory characteristics of patients with CVID with positive allergen test results. We sought to explore the prevalence of allergic disease in patients with CVID at our institution. In addition, we hoped to identify characteristics to allow for easier identification of individuals more likely to have IgE-mediated comorbid disease.

We performed a retrospective medical record review of patients seen during the last 10 years with a diagnosis of CVID in their electronic medical record (EMR). Institutional review board approval was obtained. Patients were eligible for inclusion by fulfilling the European Society for Immunodeficiencies/Pan-American Group for Immunodeficiency diagnostic criteria for CVID, which includes marked decrease in serum IgG and a marked decrease in serum IgA or IgM, with onset of immunodeficiency at older than 2 years, poor response to vaccines, and exclusion of secondary causes of hypogammaglobulinemia.¹

Of reviewed EMRs, 160 patients met the study criteria. Data were extracted from the EMR on multiple topics, including asthma, rhinitis, drug allergy, and food allergy. Not all patients had complete data. Serum immunoglobulin levels were recorded as zero if below the lower detectable limit. Categorical variables were compared using the Pearson χ^2 test, and continuous variables were compared using Wilcoxon rank sum test.

The median age of our population was 57 years at the time of our study, with a female predominance (58%). All but 7 patients had a positive or negative history of asthma symptoms documented in their EMR. A history consistent with asthma was reported in 60 patients or 37.5% of patients with CVID. Fifty-seven of these patients were prescribed a controller medication. Six patients with a history of asthma had evidence of sensitization to inhalant allergens with cutaneous testing (Table 1).

Eighty-nine patients reported symptoms consistent with perennial or episodic rhinitis. Unfortunately, for 43 patients no rhinitis history was documented; therefore, these patients were assumed to have a history negative for rhinitis. Seventy-six patients were prescribed medication for rhinosinusitis, most commonly intranasal steroids (63%).

Thirty-seven patients with rhinitis underwent immediate hypersensitivity skin testing to environmental allergens. Ten had recorded positive reactions, defined as a wheal of 3 mm greater than the negative control. Remarkable reactions to perennial and seasonal allergens were observed. One additional patient had elevated serum IgE levels to environmental allergens (Table 1).

Thirty-four patients had documented penicillin allergy. Of these, 11 underwent immediate hypersensitivity skin testing with penicillin G and benzylpenicilloyl polylysine (ALK-Abello, Round Rock, Texas). No positive test results were documented, and all 9 patients who underwent subsequent oral challenge to amoxicillin tolerated testing without difficulty. Two patients underwent cephalosporin skin testing with negative results. One of 2 patients skin tested to latex had a remarkable wheal-flare reaction (Table 1).

Eighteen patients with CVID had a food allergen documented in their EMR; 9 of these patients underwent skin testing. Two tested positive, one each to shellfish and peanut, although neither underwent a diagnostic food challenge to confirm allergy (Table 1).

Patients with positive test results to environmental, drug, or food allergens were analyzed, with characteristics compared with those with negative test results. The median serum IgE level in patients with positive test results (3.8 kU/L) was significantly higher than patients with negative test results (0 kU/L) ($P = .02$). No difference was found in evaluation of patient age, age of CVID diagnosis, sex, or serum levels of other immunoglobulin classes.

In our cohort of patients with CVID, we found evidence of IgE-mediated disease as it relates to allergic asthma, rhinitis, food allergy, and drug allergy. An allergic cause was confirmed by detection of specific IgE via cutaneous or in vitro testing to aeroallergens in only 11% of patients with CVID and rhinitis, and only 10% of patients with CVID and asthma were found to have an allergic trigger, although testing was limited. It is unclear whether patient characteristics prompted testing for allergic concerns vs symptomatic management alone or if the relatively low rate of skin testing in patients with respiratory concerns results from lack of recognition of potential for IgE-mediated disease in patients with CVID.

Two patients had positive reactions to food allergen testing. Prevalence of food allergy in primary immunodeficiency was reported using data from the US Immunodeficiency Network, but the publication did not reveal the outcome of objective evaluation of

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Table 1
Characteristics of Patients With Positive Allergen Test Results^a

Patient No.	Age, y	Sex	Age at CVID diagnosis, y	Allergen(s) tested	Positive results	Diagnosis of asthma	Serum IgE, kU/L ^b	Serum IgG, mg/dL ^b	Serum IgA, mg/dL ^b	Serum IgM, mg/dL ^b	Serum IgG1, mg/dL ^b	Serum IgG2, mg/dL ^b	Serum IgG3, mg/dL ^b	Serum IgG4, mg/dL ^b
1	64	Female	58	Environmental	Mold Weed	Yes	27	391	7	302	217	104	49	14
2	75	Male	65	Food (fish) Environmental	<i>Dermatophagoides farinae</i> , <i>Dermatophagoides pteronyssinus</i>	Yes	4	483	15	22	207	215	35	3
3	73	Male	60	Drug (latex, penicillin)	Latex	No	0	416	9	67	U	U	U	U
4	72	Male	68	Environmental	<i>D farinae</i> , <i>D pteronyssinus</i>	No	0	279	0	27	U	U	U	U
5	57	Male	38	Food (peanut) Environmental	Peanut	Yes	13	509	40	23	329	123	34	24
6	60	Male	56	Environmental	Dog, horse ^c	No	47	470	108	108	343	98	17	12
7	60	Male	58	Environmental	Grass	Yes	28	346	187	220	U	U	U	U
8	58	Female	55	Food (shellfish) Drug (penicillin)	Shellfish	No	239	427	4	21	301	75	40	19
9	72	Male	63	Environmental	<i>D pteronyssinus</i>	No	3	263	18.3	125	163	52	20	52
10	27	Male	22	Environmental	Cat, <i>D farinae</i> , <i>D pteronyssinus</i> , trees grass	No	U	550	4	8	U	U	U	U
11	13	Female	7	Environmental	Dog, ^c mold, ^c weed ^c	No	12	80	0	0	64	15	12	0
12	60	Male	51	Environmental	<i>D pteronyssinus</i>	Yes	3	400	52	38	U	U	U	U
13	33	Female	30	Environmental	Cat	Yes	0	69	0	0	0	0	0	0

Abbreviations: CVID, common variable immunodeficiency; U, unknown.

^aOur panel assesses for sensitivity to cat, dog epithelia, cockroach, *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, *Alternaria tenuis*, *Aspergillus fumigatus*, *Cladosporium sphaerospermum*, *Epicoccum nigrum*, *Fusarium solari*, *Bipolaris sorokiniana*, penicillium mix, ash, beech, birch, maple, cottonwood, elm, hickory, mulberry, black oak, American sycamore, black walnut, willow, Bermuda grass, Kentucky bluegrass, Timothy grass, meadow fescue, Johnson grass, orchard grass, perennial ryegrass, cocklebur, sheep sorrel, English plantain, lamb's quarter, marsh elder, pigweed, and ragweed mix.

^bAt diagnosis or earliest value available in the electronic medical record.

^cIn vitro only.

reported food allergens.⁷ Similar to the experience of the authors of a recent publication,⁸ penicillin allergy evaluation was negative in all patients who underwent testing, which is noteworthy given the previously described morbidity associated with the use of second-line antimicrobials.⁹

Comparing patients with positive and negative test results revealed significantly higher median serum IgE levels in those with objective evidence of sensitization. We note positive test results in 3 patients with serum IgE of less than 0.35 kU/L, the lower detectable limit in our laboratory.

Our study was limited by its retrospective nature and that the analysis was contingent on documentation by treating physicians. Not all patients underwent cutaneous or in vitro testing.

We provide evidence of IgE-mediated disease in patients with CVID evaluated at our referral center. These data are illustrative of the morbidity associated with the presence of allergy in a high-risk population. In patients with CVID, testing should be considered in all patients with a history suggestive of allergic disease given the lack of identifiable features to assist in predicting those with an intact immediate hypersensitivity response.

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Acute generalized exanthematous pustulosis with multisystem manifestations

Pinpoint pustules and purulent lakes

Affecting 2% of hospitalized patients, severe cutaneous adverse reactions (SCARs) are associated with high health care cost, morbidity, and mortality.¹ SCARs are a class of life-threatening reactions that typically include Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) or drug hypersensitivity induced syndrome, and acute generalized exanthematous pustulosis (AGEP).²

AGEP is a rare adverse reaction (estimated to occur in 1 in 5 million cases annually) and is characterized by numerous, nonfollicular, sterile pustules on an erythematous and edematous base.³ Topographical distribution includes the face, limbs, and trunk, with a propensity toward intertriginous areas.³ Cutaneous manifestations are accompanied by fever and neutrophilia, with progression to a confluence of pustules (purulent lakes) and eventual resolution through desquamation of the affected areas.⁴ After this typical progression, the diagnosis of AGEP can be made clinically, but biopsy is often performed. The presence of eosinophilia on a biopsy,⁵ as well as a historical correlation with recent antibiotic use and previous or active psoriasis or arthritis, can be used to distinguish AGEP from pustular psoriasis. AGEP responds well to topical or oral corticosteroids within a few weeks, and prompt removal or abating of the causative agent is paramount (eg, anti-

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biotics, calcium channel blockers, carbamazepine, paracetamol, infections, spider bites, UV radiation).^{3,6}

Atypical presentations of AGEP have been known to cause organ dysfunction beyond the dermis. Prior reports have noted hypotension, acute renal failure, abnormal hepatic function, acute respiratory distress, and severe lactic acidosis.⁷ Because of overlapping features in their initial presentations, differentiation among different SCARs can be challenging. AGEP has been reported to occasionally display features of other SCARs.^{8,9} For example, AGEP may display facial edema or mucosal involvement suggestive of SJS or TEN. Herein, we describe a patient who experienced atypical AGEP in response to piperacillin-tazobactam.

A 66-year-old white woman presented to the emergency department from a nursing home for treatment of left leg cellulitis, manifested primarily by an area of painful and warm erythema on the medial aspect of her thigh. She had concurrent morbid obesity, paraplegia secondary to a remote spinal abscess, hypertension, diabetes, congestive heart failure, and obstructive sleep apnea, for which she was using continuous positive airway pressure. Considering her diabetic history, the patient was admitted to the hospital and prescribed a course of piperacillin-tazobactam and vancomycin. With an appropriate response to broad-spectrum treatment in 72 hours, her antibiotics were changed to amoxicillin-clavulanate on her day of discharge. On return to her nursing home and before her ingestion of amoxicillin-clavulanate, the nursing staff observed a diffuse cutaneous erythema. She returned to the emergency department within 12 hours of discharge. Initial assessment de-