



Acute eosinophilic pneumonia in the deployed military setting[☆]

Christy R. Sine^{a,b,*}, Paul D. Hiles^b, Stephanie L. Scoville^c, Ralph L. Haynes^a, Patrick F. Allan^a, Teri J. Franks^d, Michael J. Morris^b, Erik C. Osborn^e

^a Pulmonary/Critical Care Service, Landstuhl Regional Medical Center, Landstuhl, Germany

^b Pulmonary/Critical Care Service, San Antonio Military Medical Center, JBSA Fort Sam Houston, TX, United States

^c Army Public Health Center, Aberdeen Proving Grounds, MD, United States

^d Pulmonary & Mediastinal Pathology, The Joint Pathology Center, Silver Spring, MD, United States

^e Pulmonary Critical Care Sleep Medicine, Fort Belvoir Community Hospital, Fort Belvoir, VA, United States



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ABSTRACT

Rationale: Acute eosinophilic pneumonia (AEP) is a rare but important cause of severe respiratory failure most typically caused by cigarette smoking, but can also be caused by medications, illicit drugs, infections and environmental exposures. There is growing evidence that disease severity varies and not all patients require mechanical ventilation or even supplemental oxygen.

Objectives: To compare patients with AEP treated at Landstuhl Regional Medical Center (LRMC) to those in other published series, and to provide recommendations regarding diagnosis and treatment of AEP.

Methods: A retrospective chart review was completed on forty-three cases of AEP which were identified from March 2003 through March 2010 at LRMC, Germany.

Results: Tobacco smoking was reported by 91% of our patients. Only 33% of patients in our series had a fever (temperature > 100.4 °F) at presentation. Peripheral eosinophilia (> 5%) was present in 35% on initial CBC, but was seen in 72% of patients during their hospital course. Hypoxemia, as measured by PaO₂/FiO₂ ratio, seemed to be less severe in patients with higher levels of bronchoalveolar (BAL) eosinophilia percentage.

Conclusions: Based on our experience and literature review, we recommend adjustments to the diagnostic criteria which may increase consideration of this etiology for acute respiratory illnesses as well as provide clinical clues we have found particularly helpful. Similar to recent reports of initial peripheral eosinophilia correlating with less severe presentation we found that higher BAL eosinophilia correlated with less severe hypoxemia.

1. Introduction

Over 25 years have passed since acute eosinophilic pneumonia (AEP) was first described [1] as an acute febrile illness accompanied by severe hypoxemia, infiltrates on chest imaging and pulmonary eosinophilia on bronchoalveolar lavage (BAL). Following the diagnosis of AEP, the next step is identifying the underlying cause such as cigarette smoking, infections, medications and environmental exposures [2]. One consistent finding has been the connection of AEP to tobacco smoking, especially recent-onset smoking [3–12], and multiple case reports have demonstrated that repeat exposure to cigarette smoke may induce relapse [7,9–12]. Marijuana [13,14], electronic cigarettes [15], cocaine

[16,17], tobacco harvesting [18], environmental dust [8,19], and influenza vaccination [20] have also been implicated as causes of AEP in case reports.

There is growing evidence that disease severity varies and not all patients present in respiratory failure. There is support in the literature now for withholding corticosteroids in mild disease and rapidly tapering corticosteroids in patients without severe respiratory failure [21–23].

In 2004, Shorr et al. published the first series of 18 cases of AEP among United States military personnel deployed to Iraq and the surrounding area over a 13-month period [8]. The majority of patients were men, all used tobacco, and all but one reported exposure to

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* Corresponding author. CMR 402 Box 1042, APO, AE 09180, United States.

E-mail address: Christy.r.sine.mil@mail.mil (C.R. Sine).

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Table 1
AEP case characteristics of LRMC patients and other published series (> 20 patients).

Variable	Philit, 2002 [25]	Uchiyama, 2008 [4]	Rhee, 2013 [21]	Jhun, 2014 [29]	Jhun, 2015 [23]	Giacomi, 2017 [2]	LRMC	Totals	%
N	22	33	137	85	59	36	43	415	100%
Male	13	23	137	85	59	16	39	372	89.6%
Female	9	10	0	0	0	20	4	43	10.4%
Age	29	19.3	20	21	21	47	25.5	23.7	Years
Cigarette Smoking	8	32	135	84	57	12	39	367	88.4%
--Recent Increase	6	23	125	NR	NR	NR	33	187	79.6%
Days to Presentation	8.3	3.5	NR	3	NR	NR	NR	3.95	Days
Fever	22	31	120	66	54	NR	13	307	80.7%
Hypoxemia	22	33	80	71	51	22	43	323	77.6%
BAL Eosinophilia	54%	53%	40%	44%	48%	32%	37%	43%	
PaO ₂ /FiO ₂ Ratio	157	287	284	256	291	NR	182	260	
Chest Infiltrates	22	33	137	85	59	34	43	413	99.5%
Pleural Effusion	2	20	121	62	29	14	23	271	65.3%
Mechanical Ventilation	14	NR	3	2	14	9	29	97	25.4%
Corticosteroid Treatment	16	11	127	78	16	33	37	361	87%

NR = Not Reported; these studies were excluded from percentage calculations

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airborne dust. A comprehensive epidemiologic investigation did not reveal a common source exposure other than cigarette smoking. Mechanical ventilation was required in 67% of cases and two patients died. These patients were all treated at Landstuhl Regional Medical Center (LRMC) in Germany after evacuation from theater. Cases of AEP have continued to be seen at LRMC following this initial case series. The purpose of this study is to review the LRMC experience with AEP over a 7-year period to [1] compare our patients to those in other published series, and to [2] provide recommendations regarding diagnosis and treatment of AEP.

2. Methods

2.1. Study patients

The Army Public Health Center (APHC) has maintained a registry of AEP cases in the United States military occurring since March 2003 following a *MMWR* report in 2003 and a case series reported by Shorr [8,24]. Given that the APHC registry is a passive reporting system, we identified patients with symptom onset from March 2003 through March 2010 by reviewing a pre-existing database of LRMC admissions under an Institutional Review Board approved project on acute lung injury (C.2014.023d).

Cases were identified after clinical diagnosis by the pulmonary and/or intensive care unit (ICU) attending using diagnostic criteria proposed by Philit et al. [25] and the available literature at the time [26–28] as a guide. There were a total of 49 cases listed in the AEP registry including the 18 patients included in the original article by Shorr [8]. We excluded 6 of these patients, 5 from the original Shorr article, due to missing charts or inadequate data available for us to confirm the diagnosis. There were 30 new cases added to the case series. Cases without BAL performed were included if they met clinical criteria, had peripheral eosinophilia and demonstrated a clinical response to

corticosteroids. Nine of 13 patients without BAL data were from the original Shorr case series [8].

2.2. Data collection

Inpatient medical records were reviewed for patient demographics, presenting symptoms, smoking history, recent changes in smoking pattern, deployment location, ICU days, ventilator days, ventilator settings, arterial blood gases, vital signs, peripheral white blood cell counts including eosinophilia, BAL cell counts with differentials and cultures, radiographic studies and treatment with corticosteroids. Subjects included in the study had no traumatic injuries that complicated their lung injury such as blast injuries, bullet wounds, drowning or inhalation injuries related to burns. Whenever possible, clinical parameters were evaluated while in the combat theater, during air evacuation to LRMC, and during LRMC hospitalization.

2.3. Statistical analysis

Data is presented in absolute numbers and averages for our cases as well as compiled and compared to other large case series. If data for a particular variable was not available for one or more patients the number of patients (n) is specified within the table or results section. Mann-Whitney *U* test was used to compare data with continuous variables. Pearson's correlation coefficient was performed to evaluate BAL and peripheral eosinophilia in relation to ratios of arterial oxygen tension to fraction of inspired oxygen (PaO₂/FiO₂ ratio). A two-sided *p*-value of < 0.05 was considered statistically significant.

3. Results

Forty-three cases of AEP were identified from March 2003 through March 2010. The majority were deployed to Iraq (29/43; 67%)

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