

[CASE REPORT]

Hypersensitivity Pneumonitis Caused by Exposure to a Gray Parrot (*Psittacus erithacus*)

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Abstract:

A 73-year-old woman complaining of cough and dyspnea was admitted to our hospital. High-resolution computed tomography chest revealed patchy ground-glass attenuation in the upper lung field. The patient suffered an asthma attack and was diagnosed with allergic pneumonitis; prednisolone was administered for treatment. Bird-related hypersensitivity pneumonitis was suspected, as she had a gray parrot (*Psittacus erithacus*) and a budgerigar (*Melopsittacus undulatus*) at home. An immunoblotting analysis with the patient's serum demonstrated IgG-binding fractions to the gray parrot's feathers only; no binding was noted with the budgerigar antigens. The patient was conclusively diagnosed with hypersensitivity pneumonitis related to exposure to a gray parrot.

Key words: hypersensitivity pneumonitis, gray parrot, immunoblotting

(Intern Med 61: 2197-2202, 2022)

(DOI: 10.2169/internalmedicine.8679-21)

Introduction

Hypersensitivity pneumonitis (HP) is an immunologically mediated interstitial lung disease caused by the repeated inhalation of certain antigens. Several causative agents have been recognized in occupational dusts or mists, but most new cases arise from residential exposure (1). Ultrasonic humidifiers, heated swimming pools, and composting waste at home have also been described as causes of HP (2-4). Notably, bird-related HP has emerged as more common than other forms of HP worldwide (5).

Avoidance of the causative antigen is the most important prophylaxis for HP. However, in several cases, identification of the antigen is difficult, although it can be inferred from the time of the onset and through environmental studies.

We herein report a case of HP caused by a gray parrot in a home environment that was confirmed by an immunoblot analysis using the bird's feathers. To our knowledge, this is

the first case of HP associated with exposure to a gray parrot.

Case Report

A 73-year-old woman presented to our hospital complaining of gradually progressive dry cough and dyspnea for over 2 years. She had been diagnosed with myasthenia gravis eight years earlier. In addition, she had a 24-year history of asthma, for which she was being treated with inhaled corticosteroids, long-acting beta agonists, and short-acting beta agonists (SABAs) by a general practitioner.

She had a 15 pack-year smoking history but had quit smoking 1 month earlier. She denied any alcohol or recreational drug use, contact with sick individuals, recent travel history, and occupational exposure to dust. She had lived in a reinforced concrete house for 50 years. There was no mold in her house. Her daughter had asthma and an allergy to crustaceans. The medications in her possession at home

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Received: September 16, 2021; Accepted: November 16, 2021; Advance Publication by J-STAGE: December 28, 2021

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Figure 1. (A) Gray parrot (*Psittacus erithacus*). (B) Budgerigar (*Melopsittacus undulatus*).

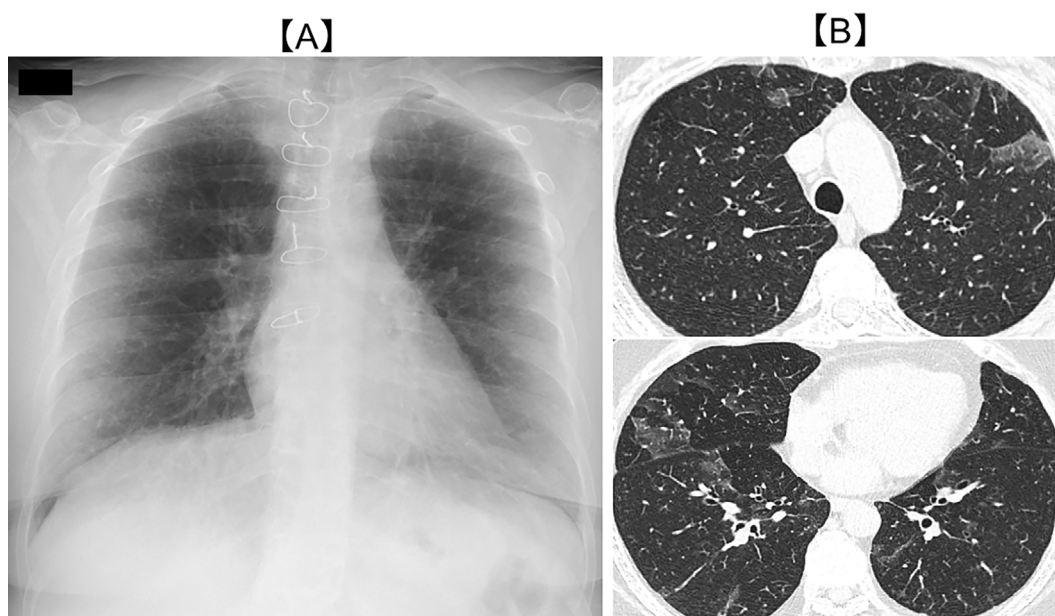


Figure 2. (A) Chest radiography shows diffuse bilateral nodular shadowing. (B) Chest plain CT shows diffuse bilateral ground-glass opacities in both upper lobes, indicating interstitial pneumonia. CT: computed tomography

were montelukast, theophylline, lysedron, olopatadine, lansoprazole, pyridostigmine, tiotropium, budesonide, formoterol fumarate dihydrate, procaterol, and prednisolone (8 mg).

The patient had two pet birds in her home: a gray parrot (Fig. 1A) that she had had for two years and a budgerigar (Fig. 1B) that she had had for three years. As the seasons changed, she experienced annual exacerbation of her asthma, which responded to SABAs and oral corticosteroids (OCS). In addition, she noted that the frequency of cough, sputum, and dyspnea had increased after her gray parrot started breeding and that the symptoms were more resistant to treat-

ment than before.

A physical examination on admission revealed desaturation of 93% with 2 L/min of oxygen and precordial wheezes. Chest radiography revealed diffuse bilateral nodular shadowing (Fig. 2A). High-resolution computed tomography (HRCT) of the chest revealed diffuse bilateral ground-glass opacities (Fig. 2B). The white blood cell count and C-reactive protein levels were $16.7 \times 10^3/\mu\text{L}$ (89% neutrophils) and 2.56 mg/L, respectively (Table 1). Immunological investigations, including estimation of antinuclear antibodies and antineutrophil cytoplasmic antibodies, were negative. The total IgE concentration was 93.6 IU/mL. All microbio-

Table 1. Laboratory Data on Admission.

Peripheral blood		Immunoserology	
WBC	16.7×10 ³ /μL	ANA	<40
Neutrophil	89.1 %	PR3-ANCA	<1.0
Lymphocyte	5.8 %	MPO-ANCA	<1.0
Eosinophil	1.6 %	Anti-CCP	(-)
Monocyte	2.7 %	Anti-Scl-70	(-)
Basophil	0.2 %	Anti-ARS	(-)
Hb	15.2 g/dL	SS-A	(-)
Ht	49.4 %	SS-B	(-)
Plt	27.7 /μL		
Blood chemistry		Allergy	
Total Bil	0.5 mg/dL	IgE	93.6 IU/mL
AST	25 IU/L	Japanese cedar	(-)
ALT	34 IU/L	Ragweed	(-)
LDH	201 IU/L	Hinoki cypress	(-)
BUN	7 mg/dL	Aspergillus	(-)
Cr	0.64 mg/dL	Alternaria	(-)
Na	142 mmol/L	Cadida	(-)
K	3.8 mmol/L	Penicillium	(-)
Cl	102 mmol/L	Dog	(-)
CK	250 IU/L	Budgerigar feather	(-)
Glu	260 mg/dL	Budgerigar dropping	(-)
CRP	2.56 mg/dL	Housedust	(-)
KL-6	274 IU/mL	Sarcoptes scabiei	(2+)
SP-D	24.1 ng/mL	Acanthopanax sciadophylloides	(2+)
Artery Blood Gas			
pH	7.489		
pO ₂	65.6 mmHg		
pCO ₂	32.8 mmHg		
HCO ₃	24.7 mmol/L		
BE	2.5 mmol/L		

Table 2. Respiratory Function Test.

	6 month before admission	1 month after admission
VC	2.65 L	2.44 L
%VC	87.5 %	80.5 %
FVC	2.47 L	2.21 L
FEV _{1.0}	1.99 L	1.79 L
%FEV _{1.0}	83.4 %	75.4 %
FEV _{1.0} %	80.2 %	81.0 %
V50 /V25	3.43	3.88

logical tests were negative.

She was diagnosed with asthma based on her history and responsiveness to SABAs. Since she had an asthma attack, bronchoscopy was not performed. However, HP due to exposure to her pet birds was suspected, and she was treated with 500 mg methylprednisolone for 4 days. The clinical symptoms and abnormal findings on chest computed tomography (CT) improved dramatically within five days of admission (Supplemental material 1). Three days later, the patient was discharged with a prescription for an oral corticosteroid (prednisolone, 30 mg). Further questioning re-

vealed that the parrot's molting period had started one month before her hospital admission. At the time of discharge, we advised her to clean her room and the birds' cage more frequently. Her respiratory symptoms did not reappear after discharge. The results of respiratory function tests performed six months before her admission and on Day 7 of admission, including the decrease in her percent vital capacity (%VC) and increase in her V₅₀/V₂₅ ratio over time, are shown in Table 2.

Subsequently, an immunoblotting analysis was performed to confirm the diagnosis.

The immunoblot analysis

The feathers and droppings of the gray parrot and budgerigar were provided by the patient. Each sample (approximately 0.2 g) was mixed with distilled water (10 mL), soaked at room temperature (25°C) overnight, and squeezed with quadruple gauze to obtain protein extract. The extract was then diluted with distilled water to obtain approximately the same concentration.

The sample proteins (approximately 6 μg protein/lane) were separated by sodium dodecyl sulfate-polyacrylamide

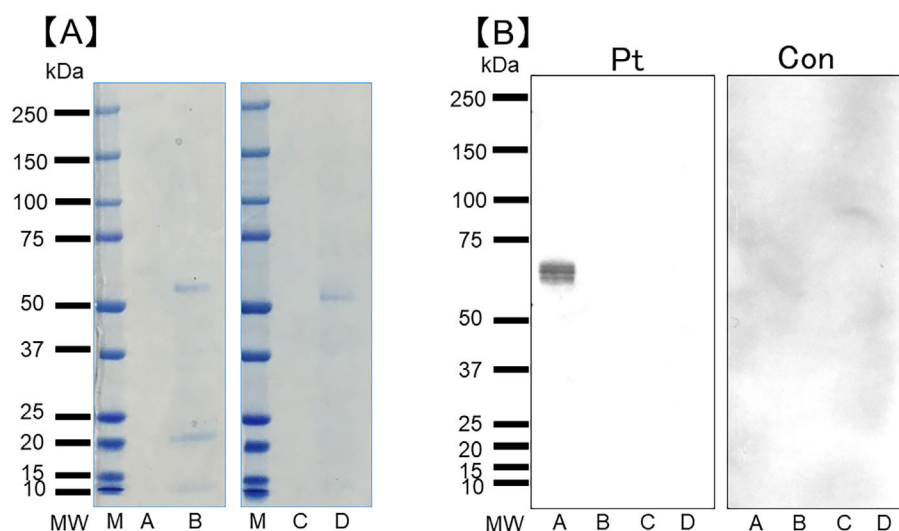


Figure 3. (A) Coomassie Brilliant Blue staining of the bird samples. Coomassie Brilliant Blue-stained SDS-PAGE gel of the samples. Lane A: Gray parrot's feather extract, B: Gray parrot's dropping extract, C: Budgerigar's feather extract, D: Budgerigar's dropping extract. The marker (M) and molecular weight (MW; kDa) are indicated on the left. (B) IgG-binding bands in bird samples by immunoblotting. Lanes: Pt (Patient), representing serum from the patient, containing multiple protein bands around 70 kDa; Con (Control), representing a negative control of serum from two non-atopic volunteers. MW: molecular weight marker (kDa). A: Gray parrot's feather extract, B: Gray parrot's dropping extract, C: Budgerigar's feather extract, D: Budgerigar's dropping extract. Con: control, M: marker, MW: molecular weight, Pt: patient, SDS-PAGE: sodium dodecyl sulfate-polyacrylamide gel electrophoresis

gel electrophoresis (SDS-PAGE). Proteins on the gel were stained with Coomassie Brilliant Blue R-350 (GE Healthcare, Chicago, USA) to detect the total protein (Fig. 3A). An immunoblot analysis was conducted using a semi-dry method, by transferring the SDS-PAGE gel onto an Immobilon™-P PVDF membrane (Merck Millipore, Burlington, USA) (6). The membrane was incubated in 10 mM phosphate-buffered saline containing 0.1% tween-20 (PBS-T) (pH 7.5) and 5% skim milk for blocking and then incubated overnight at 4°C in diluted serum (20-fold) in the same blocking buffer. After washing the membranes 4 times with PBS-T for 10 minute, the bound primary antibodies were detected using a 5,000-fold horseradish peroxidase (HRP)-conjugated goat anti-human IgG mouse-monoclonal antibody (Bethyl Laboratories, Montgomery, USA) and an electrochemiluminescence Western blotting detection reagent (GE Healthcare, Boston, USA). After washing the membranes 4 times with PBS-T for 10 minutes, the resultant chemiluminescent signals were detected on an X-ray film (Hyperfilm MP; GE Healthcare). Sera from non-atopic healthy volunteers were used as negative controls.

Fig. 3B shows the binding of specific IgG in the patient and non-atopic healthy volunteer sera on the blotted PVDF membrane. Several IgG-binding bands were observed in the gray parrot's feather sample with the patient's sera. The 60-kDa band was recognized as the main band exclusive to the patient's sera and was not detected in the control sera. There were no specific bands observed in the gray parrot's drop-

ping, budgerigar's feathers, or budgerigar's dropping with the sera of the patient.

Discussion

HP is a lung disease that develops after the inhalation of environmental antigens in sensitized individuals. Bird fanciers' lung (BFL) is the most common form of HP, with an estimated prevalence of 0.5-7.5% (7). BFL is a severe disease that may progress to respiratory failure due to chronic pulmonary fibrosis. It is caused by exposure to avian antigens located in droppings, feathers, and bloom (white powder that coats the feathers) (8). The diagnosis of HP is made by a combination of clinical, radiological, physiological, pathological, and immunological criteria. In general, a patient's environmental history provides clues to a possible etiologic agent. Avoidance of the offending antigen is the most important treatment for HP. In fact, it has been reported that the prognosis of patients with HP is better when the causative antigen is identified than when it is not identified (9). In the "Diagnosis of Hypersensitivity Pneumonitis in Adults" guidelines, jointly published by the three societies of ATS/JRS/ALAT in 2020, specific serum IgG testing is recommended to identify the causative antigen (10).

Based on her history of asthma, responsiveness to SABAs, and her physical examination findings, our patient was diagnosed with asthma on admission. Her blood investigations revealed no eosinophilia or elevated IgE levels. The

findings of respiratory function tests performed at six months before admission and on Day 7 of admission were within normal limits; however, given her asthma, the estimations were not accurate. She also showed an increase in her V_{50}/V_{25} ratio and a drop in her %VC. These findings were suggestive of the progression of peripheral airway obstruction due to HP.

In the present case, episodes of cough and dyspnea were typical of allergic alveolitis. Chest radiography showed a ground-glass-like appearance, and CT showed interstitial pneumonia. In allergic alveolitis, it is often difficult to differentiate between HP and eosinophilic pneumonia (EP) (11). Typical symptoms of EP include a fever, non-productive cough, dyspnea, myalgia, and malaise. In this case, the low peripheral eosinophil count was not consistent with EP. According to Prazma et al., an inverse association between amount of oral corticosteroid and peripheral eosinophil count is common among patients with eosinophilic asthma (12). In patients with severe asthma, oral corticosteroids reduce the eosinophil count by eosinophil apoptosis (13). In the present case, long-term oral corticotherapy may have caused the low peripheral eosinophil count.

Furthermore, bronchoalveolar lavage was not performed because of her asthma attack. Therefore, it was difficult to estimate the eosinophil count in the alveoli. Low serum IgE levels did not support the diagnosis of EP. In addition, exposure to avian antigens for two years was not compatible with EP. In contrast, according to the guidelines for HP (10), the clinical certainty of HP in this case was “compatible” despite no bronchoscopy results. However, specific IgG antibodies to the gray parrot feathers were detected in the patient’s serum, which supports the diagnosis of HP.

Depending on disease duration, HP can be acute, sub-acute, or chronic (10). We suspected acute exacerbation of chronic HP in this case. After the gray parrot started breeding, the frequency of cough, sputum, and dyspnea increased in our patient. This suggested that chronic HP developed slowly and went unnoticed after the breeding of the parrot. Regarding the cause of the exacerbation, it is possible that the increase in antigen levels from the bird’s molting period led to exacerbation of the HP. We were unable to conclude whether or not a reduction in the steroid dose was a direct cause of exacerbation of HP (Supplementary material 2).

African gray parrots (*Psittacus erithacus*) are often kept in private homes as pets. These animals are sociable and can imitate human speech (14). Bird-related HP can be caused by a variety of bird species, although it is particularly associated with the Psittaciforme bird family (parrots), most likely due to the structure and components of their plumage. All plumage of pigeons and parrots are coated with very fine particles, similar to talcum powder. Most of this powder is produced by special feathers called pulviplumes (powder down). Parrots and pigeons have the largest number of pulviplumes among all bird species, while chickens, singing birds, ducks, and geese have fewer (15).

Our patient was diagnosed with HP caused by a pet gray

parrot (*P. erithacus*). Although HP caused by other birds has been described, there are no reports dealing specifically with gray parrot-induced HP. The specific sources and characteristics of the gray parrot antigens are unknown.

In this study, feathers and droppings from two bird species were used as samples. IgG immunoblotting of these samples demonstrated specific IgG-binding components only in the gray parrot’s feathers. The presence of a serum-specific IgG antibody to the gray parrot provides additional support for the diagnosis of HP and suggests it was indeed the causative agent.

In conclusion, this is the first case of HP caused by a gray parrot. This case report emphasizes the need to perform an immunoblot analysis to diagnose HP.

Informed consent was obtained from the patient.

The authors state that they have no Conflict of Interest (COI).

References

- Patel AM, Ryu JH, Reed CE. Hypersensitivity pneumonitis: current concepts and future questions. *J Allergy Clin Immunol* **108**: 661-670, 2001.
- Alvarez-Fernández JA, Quirce S, Calleja JL, Cuevas M, Losada E. Hypersensitivity pneumonitis due to an ultrasonic humidifier. *Allergy* **53**: 210-212, 1998.
- Moreno-Ancillo A, Vicente J, Gomez L, et al. Hypersensitivity pneumonitis related to a covered and heated swimming pool environment. *Int Arch Allergy Immunol* **114**: 205-206, 1997.
- Brown JE, Masood D, Couser JI, Patterson R. Hypersensitivity pneumonitis from residential composting: residential composter’s lung. *Ann Allergy Asthma Immunol* **74**: 45-47, 1995.
- Morell F, Roger À, Reyes L, Cruz MJ, Murio C, Muñoz X. Bird fancier’s lung: a series of 86 patients. *Medicine (Baltimore)* **87**: 110-130, 2008.
- Kyhse-Andersen J. Electroblotting of multiple gels: a simple apparatus without buffer tank for rapid transfer of proteins from polyacrylamide to nitrocellulose. *J Biochem Biophys Methods* **10**: 203-209, 1984.
- Stauffer-Ettlin M, Pache JC, Rebevey F, Hanquinet-Ginter S, Guinand S, Argiroffo CB. Bird breeder’s disease: a rare diagnosis in young children. *Eur J Pediatr* **165**: 55-61, 2006.
- McSharry C, Anderson K, Boyd G. A review of antigen diversity causing lung disease among pigeon breeders. *Clin Exp Allergy* **30**: 1221-1229, 2000.
- Fernández-Pérez ER, Swigris JJ, Forssén AV, et al. Identifying an inciting antigen is associated with improved survival in patients with chronic hypersensitivity pneumonitis. *Chest* **144**: 1644-1651, 2013.
- Raghu G, Remy-Jardin M, Ryerson CJ, et al. Diagnosis of hypersensitivity pneumonitis in adults. An official ATS/JRS/ALAT clinical practice guideline. *Am J Respir Crit Care Med* **202**: e36-e69, 2020.
- Sommerfeld CG, Weiner DJ, Nowalk A, Larkin A. Hypersensitivity pneumonitis and acute respiratory distress syndrome from e-cigarette use. *Pediatrics* **141**: e20163927, 2018.
- Prazma CM, Bel EH, Price RG, Bradford ES, Albers FC, Yancey SW. Oral corticosteroid dose changes and impact on peripheral blood eosinophil counts in patients with severe eosinophilic asthma: a post hoc analysis. *Respir Res* **20**: 83, 2019.
- Ilmarinen P, Kankaanranta H. Eosinophil apoptosis as a therapeutic

- tic target in allergic asthma. *Basic Clin Pharmacol Toxicol* **114**: 109-117, 2014.
14. Costa P, Macchi E, Valle E, et al. An association between feather damaging behavior and corticosterone metabolite excretion in captive African gray parrots (*Psittacus erithacus*). *PeerJ* **4**: e2462, 2016.
15. Tauer-Reich I, Fruhmann G, Czuppon AB, Baur X. Allergens

causing bird fancier's asthma. *Allergy* **49**: 448-453, 1994.

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Intern Med 61: 2197-2202, 2022