AVIAN DISEASES 51:150–153, 2007

Case Report—

Chronic Pulmonary Interstitial Fibrosis in a Blue-Fronted Amazon Parrot (*Amazona aestiva aestiva*)

Olga Amann,[A] Marja J. L. Kik,[B] Maartje H. A. C. Passon-Vastenburg,[C] Ineke Westerhof,[A] Johannes T. Lumeij,[A] and Nico J. Schoemaker[A]

[A]Division of Avian and Exotic Animal Medicine, Department of Clinical Sciences of Companion Animals, Faculty of Veterinary Medicine, Universiteit Utrecht, Yalelaan 108, Utrecht 3584 CM, the Netherlands
[B]Department of Pathobiology, Division of Pathology, Faculty of Veterinary Medicine, Universiteit Utrecht, Yalelaan 1, Utrecht 3584 CI, the Netherlands
[C]Division of Diagnostic Imaging, Faculty of Veterinary Medicine, Universiteit Utrecht, Utrecht, the Netherlands

Received 20 August 2006; Accepted 6 November 2006

SUMMARY. A 30-yr-old blue-fronted Amazon parrot (*Amazon aestiva aestiva*) was presented to the clinic with a history of sneezing more often during the last 2 mo. Physical examination revealed only a mild nasal discharge. Complete hematologic and plasma biochemical examination showed no abnormalities. Computerized tomography (CT) of the complete bird showed generalized lung alterations consistent with lung fibrosis. Two lung biopsies were taken. The results of the histologic examination of the biopsies confirmed the tentative CT diagnosis of pulmonary interstitial fibrosis. To our knowledge this is the first reported case of chronic pulmonary interstitial fibrosis diagnosed by means of a lung biopsy in an avian species. The histologic characteristics are discussed and compared with those of human idiopathic pulmonary fibrosis.

RESUMEN. *Reporte de Caso*—Fibrosis pulmonar intersticial crónica en un papagayo de frente azul (*Amazona aestiva aestiva*). Un papagayo de frente azul (*Amazona aestiva aestiva*) de 30 años de edad se presentó a una clínica veterinaria con historia de estornudos que se hicieron más frecuentes durante los últimos dos meses. El examen físico sólo reveló una suave descarga nasal. El examen hematológico completo y el bioquímico del plasma no mostró anormalidades. La tomografía computarizada del ave mostró alteraciones generalizadas en el pulmón consistentes con fibrosis pulmonar. Se tomaron dos biopsias pulmonares. Los resultados del examen histopatológico de las biopsias confirmaron el diagnóstico tentativo de la tomografía computarizada de fibrosis intersticial pulmonar. Este es el primer caso de fibrosis intersticial pulmonar crónica diagnosticado por medio de la biopsia pulmonar en una especie aviar. Se discuten las características histológicas y se comparan con la fibrosis pulmonar idiopática del humano.

Key words: lung, fibrosis, Amazon parrot

Abbreviations: CPIF = chronic pulmonary interstitial fibrosis; CT = computerized tomography; H&E = hematoxylin and eosin; IIP = idiopathic interstitial pneumonia; ILD = interstitial lung disease; IPF = idiopathic pulmonary fibrosis

Chronic pulmonary interstitial fibrosis (CPIF) is a syndrome characterized by a chronic respiratory disease resulting in exercise intolerance (14). It was described for the first time in birds in a retrospective study conducted at the Department of Pathobiology, Diseases of Special Animals and Wildlife (Faculty of Veterinary Medicine, Universiteit Utrecht) by Zandvliet *et al.* (14). In their study, 25 Amazon parrots (*Amazona* spp.) submitted for necropsy had histologic lesions of chronic pulmonary interstitial fibrosis. The etiology of this syndrome was not identified, but it was suggested that toxic substances, bacterial and chemical toxins, allergy (5), or viral infections could play a role in the pathogenesis of CPIF in birds.

Interstitial lung diseases (ILDs) in veterinary medicine are poorly characterized. (11). In domestic animals, these diseases are usually called idiopathic pulmonary fibrosis (IPF). This terminology is confusing since they do not share the same histopathologic characteristics as described for IPF in humans (13). In animals, IPF was first described in West Highland white terriers, but other breeds can be affected. It has also been described on several occasions in cats (4). Furthermore, spontaneous feline idiopathic pulmonary fibrosis has recently been described (13) with the same characteristics as IPF in humans.

In humans IPF is a progressive and lethal pulmonary disease that belongs to the ILDs (10). Pulmonary fibrosis is a characteristic of more than 200 ILDs. ILDs are a group of lung diseases characterized by chronic inflammation and progressive fibrosis of the pulmonary interstitium (6). ILDs can be classified in the following categories: ILDs with a known etiology (occupational hazards, environmental hazards, drugs, hypersensitivity reactions, and infections), ILDs associated with systemic disorders (sarcoidosis and collagen vascular conditions), and rare miscellaneous conditions like idiopathic interstitial pneumonias (IIPs).

There are seven different types of IIPs designated by the American Thoracic Society and the European Respiratory Society (1). IPF is the most important of the IIPs and the only one unresponsive to treatment. The etiology of IPF is still unknown, but there are several conditions, and risk factors such as cigarette smoking, occupational hazards (dust from birds or heavy metals), and genetic predisposition have been associated with the disease (2,3,8).

The purpose of this article is to describe a case of chronic pulmonary interstitial fibrosis diagnosed in a blue-fronted Amazon parrot and to compare it with the actual knowledge of interstitial lung diseases in humans.

CASE REPORT

A 30-yr-old blue-fronted Amazon parrot (*Amazona aestiva aestiva*) was presented to the Division of Avian and Exotic Medicine of the Faculty of Veterinary Medicine (Universiteit Utrecht). The owner had noticed that the bird was sneezing more often in the last 2 mo. The bird has been in possession of the owner and has been fed

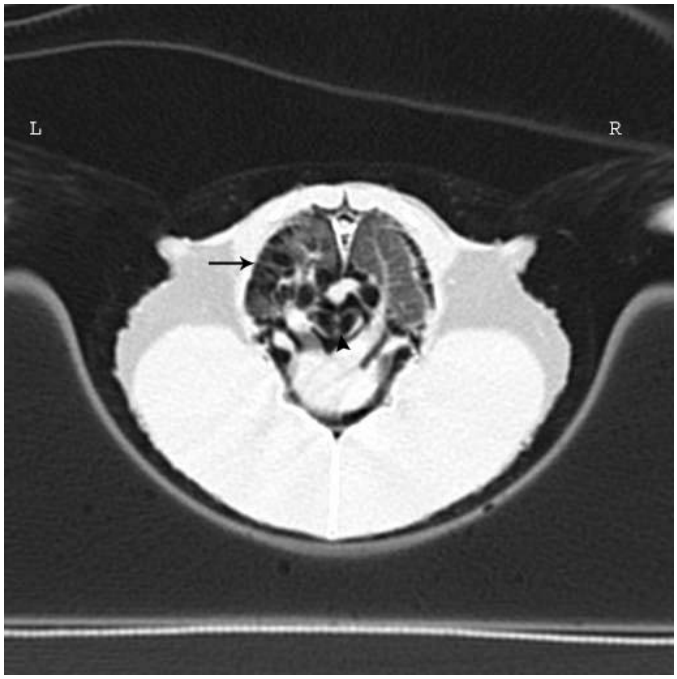

Fig. 1. Computerized tomography of cranial region of lungs and tracheal bifurcation into the primary bronchi (arrowhead). The left lung bronchi are very dilated (arrow).

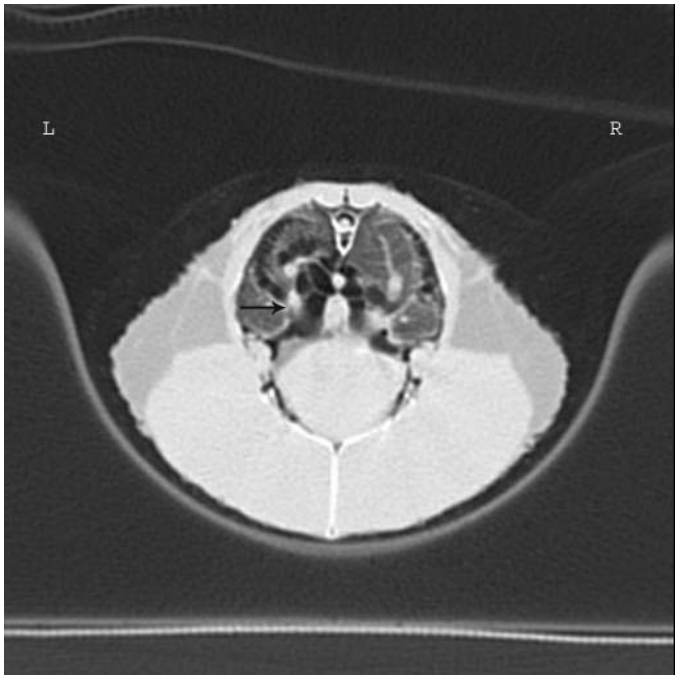

Fig. 2. Computerized tomography of region caudal to the tracheal bifurcation; enlargement of the bronchi with an increase in the density of their walls (arrow).

a seed-based diet for 30 yr. On physical examination the bird was in good condition, and nothing abnormal was observed apart from some clear fluid in the nares, which made the bird sneeze on several occasions during the examination. Furthermore, the bird presented no signs of respiratory distress, and auscultation of lungs and heart was uneventful.

Hematology and biochemistry revealed no abnormalities. Computerized tomography (CT) was performed to locate metaplastic alterations due to chronic hypovitaminosis A. In the cranial region of the lungs, the CT images showed a dilation of bronchi mainly in the left lung (Fig. 1). More caudally, several bronchi had thickened walls and an increased diameter compatible with bronchiectasis (Fig. 2). In the caudal region of both sides of the lung there was an increased tissue opacity (Fig. 3). These images were consistent with a generalized lung disease such as lung fibrosis or fungal, viral, or bacterial pneumonia.

In order to get a definitive diagnosis, lung biopsies were collected via the second intercostal space just above the processus uncinatus.

Previous to the surgery, the bird received carprofen (4 mg/kg i.m., Rymadil®, Pfizer Animal Health, the Netherlands) and subcutaneous fluids (20 ml s.c., Ringer Lactate®, B. Braun, the Netherlands). The bird was induced with isofluorane 4% and intubated. Monitoring was by means of a capnograph connected to the endotracheal tube, electrocardiography, and continuous cloacal temperature measurement. An incision in the skin was made on the left side in the second intercostal space. The intercostal muscles were bluntly dissected, and the lung was accessed. Two lung biopsies were taken, and a 2-mm piece of coagulation foam (Spongostan®, Johnson and Johnson Medical, Amersfoort, the Netherlands) was used to stop the bleeding. Muscles and skin were sutured with Monocryl® 4.0 (Poliglecaprone 25, Ethicon, Amersfoort, the Netherlands) in an interrupted pattern. The bird recovered from the anesthesia with no further complications and was maintained for 1 hr in a recovery incubator at 28 C with 2 liters/min oxygen. Several hours later the bird was sent home.

The two lung biopsies were sent for histopathologic examination to the Department of Pathobiology, Division Pathology (Faculty of Veterinary Medicine, Universiteit Utrecht). The biopsies were fixed in 4% phosphate-buffered formalin, embedded in paraffin, cut at 4-µm sections, and stained with hematoxylin and eosin (H&E) and van Gieson stain.

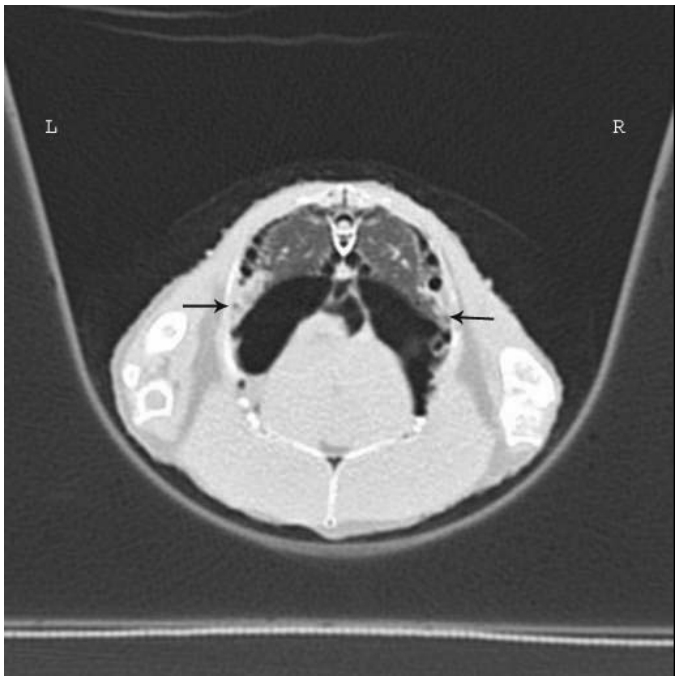

Fig. 3. Computerized tomography of caudal aspect of the lungs showing an increased opacity on the caudoventral region of both lungs (arrows).

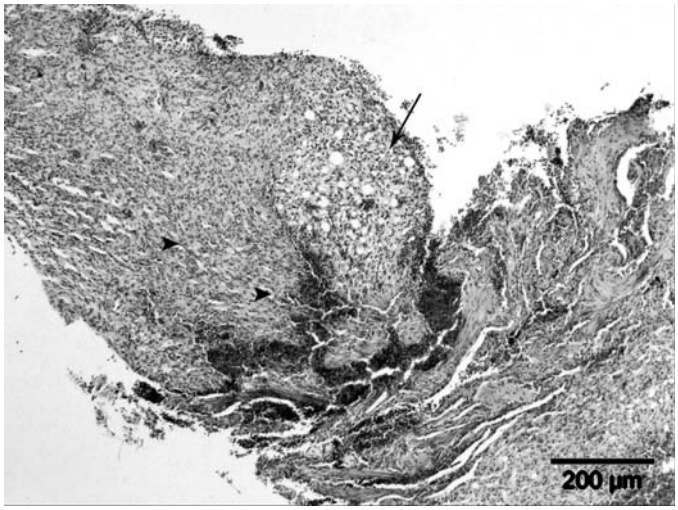

Fig. 4. Photomicrograph of the lung biopsy. Note the increase of interstitial fibrous tissue and the loss of respiratory tissue (arrowheads). Some functional respiratory tissue is still present in the top right side (arrow). H&E. Bar 200 µm.

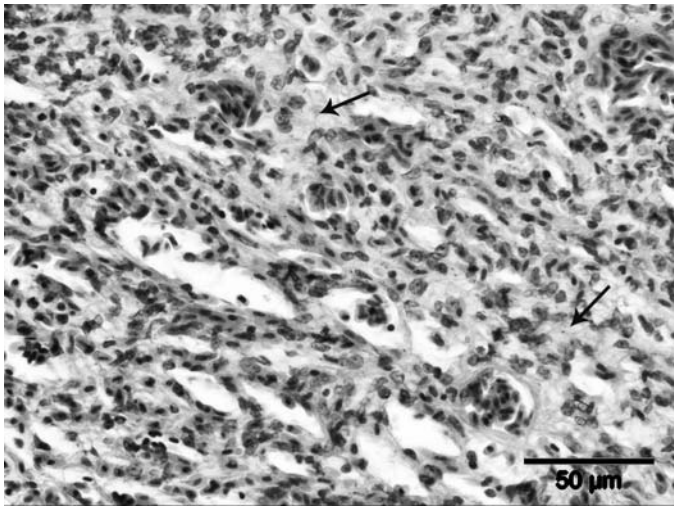

Fig. 5. Detail of the affected lung tissue. Note the obliteration of air capillaries (arrows). H&E. Bar 50 µm.

Histology showed lung tissue that no longer contained air with local loss of respiratory component, as well as fibrosis and diffuse increase of interstitial connective tissue suggestive of CPIF (Figs. 4 and 5). Perivascular fibrosis was evident around some of the present blood capillaries. The etiology of CPIF could not be determined. There were no signs of inflammation, fungal involvement, or bacterial involvement.

The bird was sent home without medication because the symptoms were very mild, and moreover no treatment has proved effective in human patients (10). After 1 yr the bird is still doing fine and the diet has been corrected.

DISCUSSION

CPIF in birds, first described by Zandvliet *et al.* (14), is a syndrome characterized by a chronic respiratory disease resulting in exercise intolerance. In their study the histologic lesions of CPIF consisted of loss of normal structure due to changes in the secondary bronchi and loss of functional respiratory tissue. The bronchial changes included thickening of the bronchiolar wall and an increase in the diameter of the bronchial lumen (due to smooth muscle and collagen fibers). The loss of respiratory tissue was characterized by local absence of air and by blood capillaries surrounding the parabronchi, leaving a fibrous network with blood vessels. This resulted in large air-filled caverns. The caudoventral areas of the lungs usually showed an extensive loss of functional pulmonary tissue. The remaining fibrous septa contained a small amount of lymphocytes and monocytes. Furthermore, there was a marked loss of air capillaries with congestion of blood capillaries. In some of these Amazon parrots there were also macroscopic findings of cardiac ventricular hypertrophy or right atrial dilation. These findings are frequently associated with primary or secondary pulmonary hypertension. In addition, congestion of vessels and organs, ascites, and hydropericardium were found. The microscopic changes found on these Amazon parrots resembled lesions found on IPF in humans.

In humans the criteria for the diagnosis of IPF have been reviewed by the American Thoracic Society and the European Respiratory Society (1). High-resolution CT scan has correctly diagnosed 80% of IPF of patients with biopsy-proved IPF (7,12). Changes that can be seen on the CT scan include reticular densities, traction bronchiectasis, honeycomb cysts, and septal thickening with a subpleural distribution mainly at the bases.

Lung biopsy is one of the best methods for the diagnosis of IPF, but it is not always definitive. The histologic features of IPF are called usual interstitial pneumonia and are as follows: temporary heterogeneity of lung remodeling, with the primary changes involved being interstitial fibrosis and ongoing fibroblast/myofibroblast proliferation; ''honeycomb'' change (enlarged air spaces lined by prominent variable epithelium); and in some cases inflammation (9). The distribution of the lesions is typically patchy, with normal areas of lung interspersed with adjacent foci of fibrosis and honeycomb change. This distribution is also important in the IPF diagnosis.

In our case, the CT images suggested the presence of a diffuse lung disease with dilation and increase in diameter of bronchiolar walls. There were also areas of increased density in the caudoventral lung. These findings were compatible with the macroscopic characteristics found on postmortem examination of Amazon parrots in the study by Zandvliet *et al.* (14) but not with the CT images of human IPF. The histology results of the lung biopsies taken in our patient showed lung tissue that no longer contained air with local loss of respiratory component, as well as fibrosis and diffuse increase of interstitial connective tissue suggestive of CPIF as described by Zandvliet *et al.* (14). These histologic lesions are compatible with the fibrotic lesions observed in human IIPs, but they differ from the histologic changes found in IPF. No evidence of inflammation or etiologic agent could be seen, although they cannot be excluded as a result of the reduced number of biopsies taken. The differences in anatomy and physiology between avian and mammal (human) lungs makes the CT imaging characteristics and the histopathologic identification of this lung disease difficult.

In conclusion, this is the first report of a psittacine species diagnosed antemortem with CPIF. The etiology of this syndrome was not found. More research is needed in order to describe this histopathologic condition of CPIF in birds and its possible etiology and treatment.

REFERENCES

1. American Thoracic Society/European Respiratory Society. International multidisciplinary consensus classification of the idiopathic interstitial pneumonias. Am. J. Respir. Crit. Care. Med. 165:277–304. 2002.

2. Baumgartner, K. B., J. M. Samet, D. B. Coultas, C. A. Stidley, W. C. Hunt, T. V. Colby, and J. A. Waldron. Occupational and environmental

risk factors for idiopathic pulmonary fibrosis: a multicenter case–control study. Collaborating centres. Am. J. Epidemiol. 152:307–315. 2000.

3. Baumgartner, K. B., J. M. Samet, C. A. Stidley, T. V. Colby, and J. A. Waldron. Cigarette smoking: a risk factor for idiopathic pulmonary fibrosis. Am. J. Respir. Crit. Care Med. 155:242–248. 1997.

4. Cohn, L. A., C. R. Norris, E. C. Hawkins, J. A. Dye, C. A. Johnson, and K. J. Williams. Identification and characterization of an idiopathic pulmonary fibrosis-like condition in cats. J. Vet. Intern. Med. 18(5):632–641. 2004.

5. Fudge, A. M., and D. R. Reavill. Pulmonary artery aneurysm and polycythemia with respiratory hypersensitivity in a blue and golden macaw. In: Proc. European Conference on Avian Medicine and Surgery, Utrecht, the Netherlands. pp. 382–387. 1993.

6. Green, F. H. Y. Overview of pulmonary fibrosis. Chest 122:334S–339S. 2002

7. Hunninghake, G. W., M. B. Zimerman, D. A. Schwartz, T. E. King, J. Lynch, R. Hegele, J. Waldron, T. Colby, N. Muller, D. Lynch, J. Galvin, B. Gross, J. Hogg, G. Toews, R. Helmers, J. A. Cooper Jr., R. Baughman, C. Strange, and M. Millard. Utility of a lung biopsy for the diagnosis of idiopathic pulmonary fibrosis. Am. J. Respir. Crit. Care Med. 164:193–196. 2001.

8. Iwai, K., T. Mori, N. Yamada, M. Yamaguchi, and Y. Hosoda. Idiopathic pulmonary fibrosis: epidemiological approaches to occupational exposure. Am. J. Respir. Crit. Care Med. 150:670–675. 1994.

9. Katzenstein, A. L., and J. L. Myers. Idiopathic pulmonary fibrosis: clinical relevance of pathologic classification. Am. J. Respir. Crit. Care Med. 157:1301–1315. 1998.

10. Khalil, N., and R. O'Connor. Idiopathic pulmonary fibrosis: current understanding of the pathogenesis and the status of treatment. Can. Med. Assoc. J. 171(2):153–160. 2004.

11. Nelson, O. L., and R. K. Sellon. Pulmonary parenchymal disease. In: Textbook of veterinary internal medicine, 6th ed. S. J. Ettinger and E. C. Feldman, eds. Elsevier Saunders, St. Louis, MO. pp. 1264–1265. 2005.

12. Raghu, G., Y. N. Mageto, D. Lockhart, R. A. Schmidt, D. E. Wood, and J. D. Godwin. The accuracy of the clinical diagnosis of new-onset idiopathic pulmonary fibrosis and other interstitial lung disease: a prospective study. Chest. 116:1168–1174. 1999.

13. Williams, K., D. Malarkey, L. Cohn, D. Patrick, J. Dye, and G. Toews. Identification of spontaneous feline idiopathic pulmonary fibrosis: morphology and ultrastructural evidence for a Type II pneumocyte defect. Chest. 125:2278–2288. 2004.

14. Zandvliet, M. M. J. M., G. M. Dorrestein, and M. van der Hage. Chronic pulmonary interstitial fibrosis in Amazon parrots. Avian Pathol. 30: 517–524. 2001.