Primary ciliary dyskinesia in a Staffordshire bull terrier

M De Scally[a] R G Lobetti[a*] and E Van Wilpe[b]

ABSTRACT

Primary ciliary dyskinesia (PCD) is a diverse group of inherited structural and functional abnormalities of the respiratory and other cilia, which results in recurrent respiratory tract infections. Primary ciliary dyskinesia was diagnosed in a 14-week old Staffordshire bull terrier that had a history of respiratory disease from 7 weeks of age. Pneumonia was diagnosed on thoracic radiographs and transtracheal aspirate. Transmission electron microscopy of the bronchi and trachea indicated the presence of both primary and secondary ciliary dyskinesia. The most prominent primary defects consisted of absent inner dyneim arms, absent radial spokes and absence of the central microtubules. These defects accounted for 62 % of the total number of cross-sections screened. Non-specific ciliary abnormalities encountered most often were compound cilia, swollen cilia, addition/deletion of peripheral doublets and disorganised axonemes (26 %). To the authors' knowledge, this is the first case of PCD described in the Staffordshire bull terrier and the first report of PCD in South Africa.

Key words: congenital, electron microscopy, immotile cilia, pneumonia.

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INTRODUCTION

Primary ciliary dyskinesia (PCD) is a diverse group of inherited structural and functional abnormalities of the respiratory and other cilia, which may cause a variety of clinical signs, including early onset, recurrent respiratory tract infections[2,9]. Structurally, cilia are thin, longitudinal extensions from the free surface of the cell. The core, or axoneme, has 2 central microtubules surrounded by 9 pairs of outer microtubules, referred to as the 9+2 microtubular arrangement. Attached to the outer tubules are inner and outer dyneim arms[2] (Fig. 1). The ciliary defect, which may either be immotile or dyskinetic cilia, results in impairment of mucociliary clearance, nasal discharge and intermittent sneezing and coughing. As the animal ages, this may progress to recurrent bacterial rhinosinusitis and bronchopneumonia[2].

Clearance of respiratory secretions is dependent on an intact mucociliary elevator, which if it fails, results in the accumulation of mucus in the lower airways with resultant airway blockage, atelectasis, and secondary bacterial infections[9]. Primary ciliary dyskinesia is a defect in the microtubule formation that affects cilia of the respiratory tract, urogenital tract, and auditory canal. Clinical defects include rhinitis, bronchiectasis, infertility, deafness, hydrocephalus, and renal tubule dilation[2,4]. Kartagener's syndrome is a subset of PCD and is characterised by PCD together with chronic sinusitis, bronchiectasis, and situs inversus[1,6].

Breeds that have been reported to be affected with PCD, include the English pointer, English springer spaniel, Cocker spaniel, Border collie, English setter, Dalmatian, Doberman pinscher, Chihuahua, Golden retriever, Old English sheepdog, Chow, Bichon frisé, Rottweiler, Shar Pei, Miniature poodle, Norwegian elkhound, Dachshund, and Newfoundland[3,6,9]. The speculated mode of inheritance of PCD is autosomal recessive, as affected puppies occur with unaffected parents. The disease occurs in pure breeds, in both sexes, and both normal and affected puppies can occur in a litter[2,4].

This paper describes the presence of PCD in the Staffordshire bull terrier and, to the authors' knowledge, the 1st report of PCD in South Africa.

CASE REPORT

Infectious tracheobronchitis was diagnosed in a 2-month-old male Staffordshire

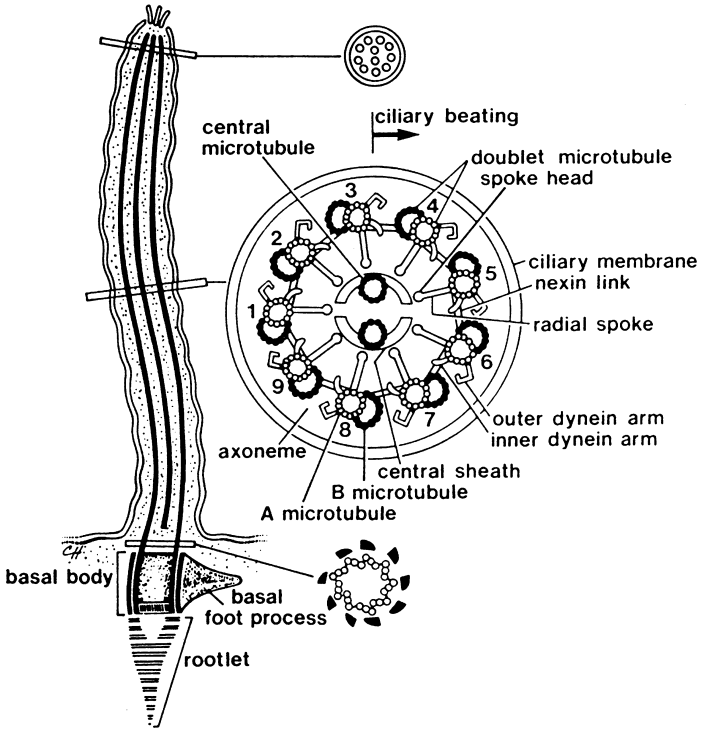

Fig. 1: **Schematic depiction of the ciliary ultrastructure in longitudinal and transverse sections.** (Reproduced with permission from Edwards D F, Patton C S, Kennedy J R 1992 Primary ciliary dyskinesia in the dog. *Problems in Veterinary Medicine* 4: 291–319.)

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bull terrier and treated with 50 mg Synulox® (Pfizer Laboratories, Rivonia Road, Sandton, South Africa) twice a day for 5 days. Despite treatment, the dog deteriorated in that the coughing had not resolved and the dog developed a mucoid-purulent ocular-nasal discharged. An inflammatory reaction was evident on peripheral blood smear evaluation and lung consolidation was present on survey thoracic radiographs. The dog was treated for bacterial pneumonia with fluid therapy and intravenous antibiotics. Although there was an improvement, the cough never resolved. At 11 weeks of age a culture taken from the nasal and pharyngeal areas yielded a non-resistant *Chryseobacterium luteola,* which is an opportunistic organism. As there was no resolution of the cough the patient was referred to Bryanston Veterinary Hospital for further evaluation at 13 weeks of age.

On clinical examination the dog was bright and alert, rectal temperature was normal, and had an irritable trachea, that evoked a cough response on palpation. Left shift neutrophilia and monocytosis was evident on haematology. Survey thoracic radiographs indicated a severe diffuse bronchopneumonia. On bronchoscopy the trachea and main-stem bronchi had a normal appearance but there was an accumulation of muco-purulent material in the distal trachea. Degenerative neutrophils, macrophages, and free and phagocytosed bacteria were present on transtracheal aspirate cytology, which is consistent for a bacterial infection. Transtracheal aspirate culture yielded resistant *Bordetella bronchiseptica* that was only sensitive to cefotaxime.

At this point the owners opted for euthanasia as the long-term prognosis was guarded. The owners consented to removal of a portion of the distal trachea and main-stem bronchi for electron microscopy.

The main-stem bronchi and a portion of the distal trachea were fixed in 10 % buffered formalin and processed for transmission electron microscopy by standard techniques using post-fixation in 1 % osmium tetroxide, dehydration through a graded ethanol series, and embedding in an epoxy resin. Ultra-thin sections were contrasted with uranyl acetate and lead citrate and examined in a Philips CM10 transmission electron microscope (FEI, Eindhoven, The Netherlands) operated at 80 kV.

Specimen areas containing transversely sectioned cilia were recorded, with the bronchial sections yielding the most cross-sectioned ciliary profiles. Normal as well as deviations from the 9+2 microtubular arrangement were recorded into

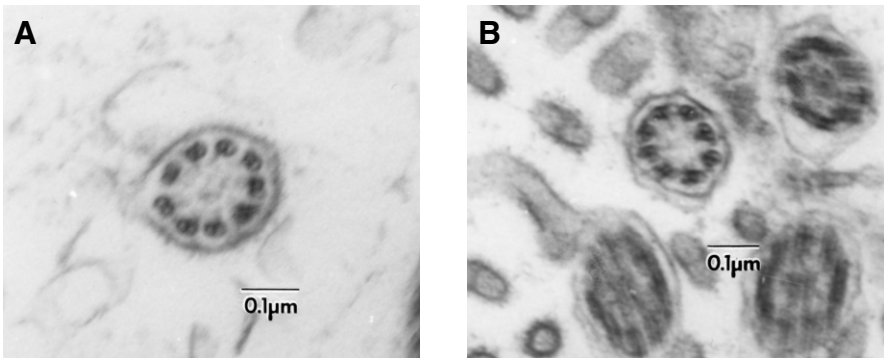

Fig 2: **EM micrographs of respiratory cilia indicating evidence of primary ciliary dyskinesia. Note the absence of the central pair, dynein arms and the radial spokes. Also note the deletion of a peripheral doublet in** B**.**

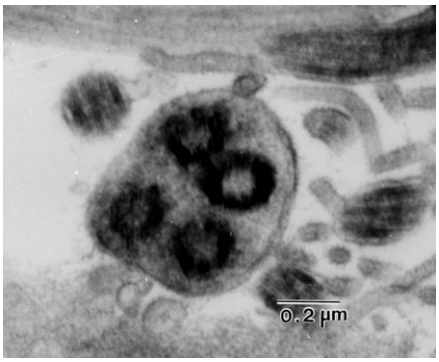

Fig. 3: **EM micrograph of respiratory cilia indicating a compound cilia containing many axonemes.**

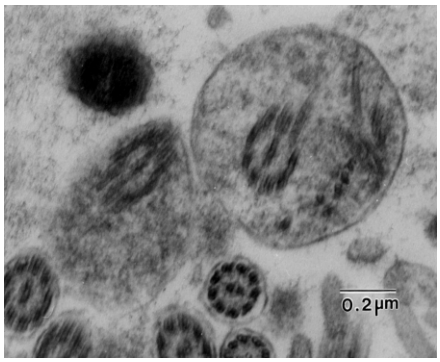

Fig. 4: **EM micrograph of respiratory cilia indicating swollen cilia.**

PCD or secondary ciliary dyskinesia according to the classification of Pizzi *et al.*[7] (Table 1). The most prominent primary defects consisted of absent inner dynein arms, absent radial spokes, and absence of the central microtubules (Figs 2). These defects accounted for 62 % of 401 cross-sections screened. The most frequently encountered non-specific ciliary abnormalities were compound cilia, swollen cilia (Figs 3, 4), addition/deletion of peripheral doublets, and disorganised axonemes (26 %).

DISCUSSION

Primary ciliary dyskinesia occurs in dogs, cats, pigs, and people[6], with the incidence in people being 1 per 16 000 births[8]. The disease usually manifests within the first few weeks of life; however, some animals have mild clinical signs that are not recognised until later in life (6 months to 10 years)[2]. Clinical signs include chronic muco-purulent nasal discharge, productive cough, exercise intolerance, and dyspnoea[4]. The dog described in this report showed early onset recurrent

Table 1: **Summary of cilia abnormalities seen on electron microscopy.**

	Cilia counted	% of total
Primary ciliary dyskinesia		
Absent/reduced inner and/or outer dynein arms	98	
Absent radial spokes	97	
Translocation of microtubular doublets	5	
Absent central pair	49	
Total	249	62
Secondary ciliary dyskinesia		
Addition/deletion of peripheral microtubules	82	
Disorganised axonemes	15	
Ciliary disorientation	6	
Blebs/discontinuity of axoneme membrane	3	
Total	106	26
Normal cilia	46	12
Compound cilia	Present	
Swollen cilia	Present	
Total number of cilia counted in cross-section	**401**	

upper and lower respiratory tract disease that was poorly responsive to antibiotic therapy. On clinical examination nasal discharge and tracheal sensitivity were evident, both of which have been reported in the literature[2,4,9]. As in the dogs in 1 report[9], this dog was bright and alert, despite the presence of severe respiratory disease and an inflammatory leukogram on haematology.

Reported radiographic findings in PCD include bronchitis, bronchiectasis, and consolidating pneumonia[4]. The dog in this report showed severe bronchopneumonia, without any obvious signs of bronchitis or bronchiectasis, which may have developed had the dog lived longer. On bronchoscopy it showed the accumulation of purulent material within the trachea, which was most likely due to failure in the mucociliary elevator. Tracheal culture also yielded only normal flora.

Further evaluation of a patient with PCD requires either tracheal or nasal scintigraphy or EM[2]. Although tracheal mucosal transit times measured by nuclear scintigraphy are suggestive of defective mucociliary clearance[4], a definitive diagnosis requires the electron microscopic evaluation of ciliary ultrastructure from nasal or respiratory biopsies, nasal cytobrush, or semen[2,4,9]. Typical findings in PCD include shortening or loss of dyneim arms, atypical microtubular orientation, and duplication or deletion of central or outer microtubule doublets[1,2,4]. The dog in the report showed 62 % abnormal cilia, with defects being absent inner dynein arms, absent radial spokes, and absence of the central microtubules. Normal animals may show structural abnormalities in 2–5 % of cilia[2].

Therapy for PCD is aimed at controlling infections and facilitating respiratory secretions, with cough suppressants being contra-indicated[4]. Reports of long-term survival of dogs with PCD are limited, with the majority of cases either dying or euthanased within 6 months of diagnosis[2]. Response to therapy in this dog was poor and it was euthanased because of the poor prognosis.

It is likely that PCD is more common than reported, because affected dogs may be misdiagnosed as having fading puppy syndrome, aspiration pneumonia, or infectious causes of pneumonia. This report illustrates that PCD should be considered in a young dog with recurrent respiratory signs.

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