ORIGINAL CONTRIBUTION

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Rhinosinusitis, symptomatology & absence of polyposis in children with primary ciliary dyskinesia*

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SUMMARY

Introduction: *Primary Ciliary Dyskinesia (PCD) describes a group of inherited disorders which result in functional ciliary defects leading to mucous stasis. Clinical manifestations include otitis media with effusion and chronic rhinosinusitis. Nasal polyposis has previously been thought to be linked to PCD, and current theories of 'polypogenesis' suggest that early and severe polyp formation could be expected among sufferers of this condition.*

Methods: *Cross-sectional observational review of all children attending the multi-disciplinary clinic at a national tertiary-referral centre for PCD across a 3-month period. Careful examination was undertaken, and the SNOT-20 questionnaire administered.*

Results: *Thirty patients were included. No nasal polyps were found, despite children clearly suffering rhinosinusitis and being debilitated by their symptoms. The rhinologically orientated questions of the SNOT-20 produced the most positive responses; however some other questions were found not to be useful in a paediatric population.*

Conclusions: *Nasal polyps do not occur in children with PCD, despite the presence of rhinosinusitis. Given that many current theories of polyp pathogenesis hinge on prolongation of pro-inflammatory stimuli, further investigations are needed into why this should not occur in the situation of chronic mucous stasis which is the hallmark of PCD.*

Key words: Rhinosinusitis, nasal polyposis, Primary Ciliary Dyskinesia, Kartagener Syndrome

INTRODUCTION

Primary ciliary dyskinesia (PCD) describes a group of inherited disorders of ciliary structure or function. Clinical manifestations include neonatal respiratory distress, otitis media with effusion, rhinosinusitis and subfertility. Fifty percent of those with PCD may also demonstrate *situs inversus*, in which case the term used is Kartagener's Syndrome (the triad described by Kartagener in 1933 [1] was that of *situs inversus*, bronchiectasis and chronic sinusitis; it is now considered a subtype of PCD). Several ciliary ultrastructural defects have been identified to date, and in some cases specific genetic loci have been identified [2,3]. The great majority of cases are inherited as an autosomal recessive condition [3-5].

The incidence is approximately one in 15000, and there are estimated to be 3000 affected individuals in the UK, with approximately 70 new cases each year, although the condition is generally accepted to be somewhat under-diagnosed [3,5-7]. Diagnosis is via a cascade of investigations, culminating in mucosal biopsy for ciliary examination [2,3,5,7].

Chronic rhinosinusitis, the most common chronic disease, is an inflammatory disorder of the upper airways with a multifactorial and incompletely understood causation. It exists along a spectrum of severity, and in its more severe forms is noted to be a significantly debilitating condition, with adult patients demonstrating poorer "quality of life" scores than sufferers of many other chronic cardiorespiratory diseases such as angina or congestive cardiac failure [8]. Nasal polyps are benign protrusions of chronically-inflamed and oedematous nasal mucosa into the upper airway. Originally thought to be a separate clinical entity, this condition is now considered, by some, to represent part of the continuum of chronic rhinosinusitis [9-13].

The prevalence of chronic rhinosinusitis has been estimated as 14% of the (USA-based) population [14]. Other studies have estimated the prevalence of polypoid rhinosinusitis as lying between 0.2 and 4.3% of the general population [12], and much higher in the immunosuppressed [14].

There is a well-documented link between polypoid rhinosinusitis and host-defence disorders such as cystic fibrosis

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[10,12,15]. Decreased mucociliary clearance has also been demonstrated in studies of otherwise-healthy adults with chronic rhinosinusitis [8,16].

The consensus view now points towards a strictly localised inflammatory process as being responsible for the genesis of polypoid rhinosinusitis [9,12,17,20,21]. Current theories regarding this inflammatory state [9,11,13,15,17,18,22-24] universally rely on a spectrum of mediators released in response to an initial inflammatory stimulus [9,11-15,17,18,22-26].

It follows that a state of permanent mucous stasis would result in persistence of initial pro-inflammatory stimuli, supporting and accelerating general progress towards a state of chronic inflammation. Logically, this implies that patients with primary ciliary dyskinesia could be expected to show signs of chronic rhinosinusitis, leading to early and marked polyp formation.

Correspondingly, chronic rhinosinusitis is an accepted manifestation of PCD, appearing on most lists of childhood signs & symptoms suggestive of the condition [2,4,7,27], and whilst polypoid disease has been considered to be similarly linked [7,28,29], the prevalence has not been reported.

The 20-question Sino-Nasal Outcome Test (SNOT-20), which arose as a modification of the 31-question Rhinosinusitis Outcome Measure (RSOM-31), is a validated patient-reported subjective measure of symptomatology in sino-nasal disorders[30], which has also recently begun to gain popularity as a research tool [30,31]. 20 factors related to nasal function (and its impact on overall function) are subjectively scored from 0 to 5 depending on the impact each has on the subject's daily life (Table 1). Results can be given as a mean score (0 to 5) or a total (0 to 100). The SNOT-20 has not been validated for use with paediatric patients.

Table 1. The SNOT-20 scoring system.

Question	
1	Need to blow nose
2	Sneezing
3	Runny nose
4	Cough
5	Postnasal drip
6	Thick nasal discharge
7	Ear fullness
8	Dizziness
9	Ear pain
10	Facial pain / pressure
11	Difficulty falling asleep
12	Waking up in the night
13	Lack of a good night's sleep
14	Waking up tired
15	Fatigue
16	Reduced productivity
17	Reduced concentration
18	Frustration / restlessness / irritability
19	Sadness
20	Embarrassment

METHODS

Setting

The Royal Brompton Hospital multidisciplinary paediatric PCD clinic (an internationally-recognised centre for this condition). The baseline entry criterion for the study was an existing firm diagnosis of PCD, made following observation of a functional ciliary defect on light microscopy of nasal brushings, with or without a structural ciliary defect demonstrated on Transmission Electron Microscopy. A cross-sectional observational review of all such children attending the clinic was performed across a three-month period, from mid-July to mid-September 2007.

Examination

Careful bilateral examination of the nasal cavity was performed without anaesthesia by a single senior clinician, using either a 5mm or 3mm endoscope. Detailed examination was made of the lateral nasal wall, middle and superior meati. Tympanic membranes were also carefully examined.

Questionnaire

The SNOT-20 questionnaire was administered to the attending parent, with age-appropriate input from the child, in order to determine symptom load. One question was modified from the official SNOT-20 in order to be more relevant to a paediatric population: "reduced productivity" was changed to "difficulty with schoolwork". Details of demographics, diagnosis and specialist investigations were obtained from the notes.

RESULTS

Thirty patients were included in the study. Twelve had ciliary dyskinesia with situs inversus, two had ciliary dyskinesia with dextrocardia, and 16 had ciliary dyskinesia alone.

Seventeen patients were male, 13 were female, and in the case of both Kartagener's Syndrome and simple PCD, the distribution of male and female patients was broadly equal. Patients' ages ranged from 1 to 14 years, the mean age of PCD patients (9 years) being slightly higher in this sample than the mean age of Kartagener's Syndrome patients (6 years).

Two patients regularly used nasal steroid inhalers (one fluticasone, one mometasone), and in addition one of these patients used Stérimar daily. Nineteen patients took oral antibiotics regularly; 11 patients used an oral steroid inhaler daily; and 8 used an oral salbutamol inhaler daily. None of the patients had recently been prescribed oral steroids, and none had had any form of nasal or sinus surgery.

No nasal polyps were found on examination in any of the patients. Two patients (identical twins aged 6 years) were suffering with acute upper respiratory tract infections at the time of examination, and were noted to have congested nasal

mucosa and mucopus. Moderate to severe rhinitis without polyposis was noted in two patients (aged 8 and 12 years) and bilateral hypertrophy of the inferior turbinates in one (aged 4). Eight patients (27%) were found to have mild to moderate rhinitis with significant buildup of secretions; 16 patients (53%) were mildly rhinitic with pooling of secretions (Figure 1). No correlation was found between clinical findings and age.

Eighteen patients were found to have healed chronic otitis media, and 10 showed evidence of otitis media with effusion. One patient had bilateral perforations, and another was suffering with wax impaction which precluded examination of the membrane (Figure 2). Age was correlated negatively with severity of clinical findings, in line with previous work [32] ($R = 0.392$; $R2 = 0.153$; $t = -2.257$; $p = 0.032$). Across the cohort as a whole, no correlation was found between these findings and those on nasal examination.

Mean total SNOT score was 14.7 (SD 9.37, range 0-44). Scores of zero in every patient were recorded for questions 16 (difficulty with schoolwork) and 19 (sadness related to symptomatology).

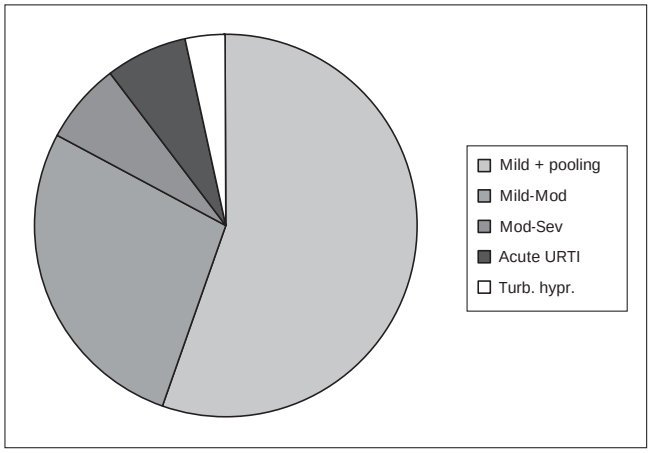

Figure 1. Rhinological symptoms.

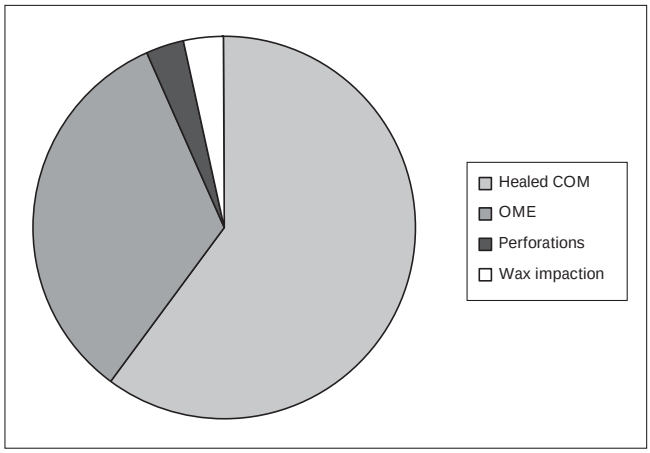

Figure 2. Otological symptoms.

Table 2. Highest-scoring responses to the SNOT-20 questions.

Question	Mean score
Need to blow nose	3.07
Thick nasal discharge	2.13
Cough	2.07
Watery nasal discharge	1.73
Waking up feeling tired	1.13
Post-nasal discharge	0.8
Lack of a good night's sleep	0.77
Fatigue	0.63
Waking up in the night	0.53
Difficulty falling asleep	0.37

The results of two questions correlated negatively with age: questions 12 (waking in the night, $R = 0.437$; $R^2 = 0.191$; $t = -2.572$; $p = 0.015$) and 15 (feeling tired in the day, $R = 0.421$; $R^2 = 0.177$; $t = -2.458$; $p = 0.020$). Responses to all other questions did not show a relationship to age.

Questions producing the highest response scores in this cohort tended to be rhinological in nature, with three of the highest four scores relating to nasal symptoms. The next-highest-scoring group tended towards sleep function (Table 2).

Only the highest-scoring five questions of the 20 showed a mean score above 1.0. Overall mean score per question was 0.735 (SD 0.0468).

DISCUSSION

These results show that, whilst polypoid rhinosinusitis is considered to be amongst the sequelae of PCD [7,28,29], the true prevalence may be far lower than previously thought. Indeed, in our sample, no evidence of nasal polyposis was seen in any patient.

This occurred despite the fact that clinical signs consistent with some degree of rhinitis were noted in virtually all patients in this cohort. Nasal symptoms clearly trouble these patients: symptoms attributable to rhinitis formed the mainstay of the positive SNOT responses, and symptoms which were scored as significantly impacting on patients' lives were exclusively rhinological in nature.

Current theories of polyp pathogenesis hinge on prolongation of an initial pro-inflammatory stimulus; and invite the conclusion that relative mucous stasis within the upper airway should lead to persistence of such a stimulus, and relative perpetuation of upper airway inflammation. It follows that patients with PCD should show signs both of significant rhinosinusitis, and of early (possibly extensive) polyp formation. This group of patients, however, despite clearly suffering from a chronic rhinitic process, universally showed no sign of polyp formation.

This suggests that part of the pathophysiological process of polyp formation is not explicable by current theories.

No symptom-scoring system was available that had been validated for use with children. The SNOT-20 has been validated for use in adults, and was therefore chosen as an evidence-based alternative, in the knowledge that it would be unlikely to provide a perfect solution. This assumption was confirmed, and it is also acknowledged that use of a control group for the SNOT questionnaire might have enhanced the reliability of this symptom-scoring data. The use of a subjective symptom scale with a young child is naturally coloured by the fact that the majority of the responses are given by a parent or carer. Certain questions in the SNOT-20 are highly age-dependent: questions 10 (facial pain/pressure), 12 (waking in the night) and 15 (daytime tiredness) are examples. No child or parent admitted to any sadness related to their symptoms.

These findings suggest that, contrary to the popular general perception, nasal polyposis does not occur in children with PCD. Further work is needed in order to arrive at a full understanding of the pathophysiology of polyp formation in the upper airways. We suggest that the SNOT-20 should be used with great caution in a paediatric population, and the development of a new instrument should be considered.

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