High prevalence of Primary Ciliary Dyskinesia in a British Asian population

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ABSTRACT

Determining the prevalence of primary ciliary dyskinesia (PCD) in different populations has proved difficult with estimates varying between 1 in 4,000 to 1 in 40,000. The aim of this study was to determine the incidence of PCD in a well defined highly consanguineous Asian population in the UK.

Over a fifteen year period all patients suspected of PCD in the Asian population of Bradford, UK, were tested by measurement of ciliary beat pattern, frequency and electron microscopy.

The prevalence of primary ciliary dyskinesia in the population studied was 1 in 2265. 52% of the patients' parents were first cousins. All patients had a history of chronic cough and nasal symptoms from the first year of life. 73% had a history of neonatal respiratory distress.

Clinical suspicion of PCD should be high in populations where it is possible that high levels of consanguinity may result in an increase in those with PCD. In these communities the combination of chronic cough and nasal symptoms should prompt early diagnostic testing.

INTRODUCTION

Primary ciliary dyskinesia (PCD) is usually inherited in an autosomal recessive fashion. It is a serious condition where impaired mucociliary clearance is associated with recurrent chest infections, leading to bronchiectasis. Almost all patients have nasal symptoms, with either a runny or blocked nose. Patients are frequently diagnosed after many years of chronic respiratory symptoms with established and frequently significant lung disease.[1, 2]

PCD has an estimated prevalence of 1:15,000-1:30,000 live births although it is acknowledged that this may be an underestimate.[1] It is likely that due to lack of clinical suspicion and a lack of appropriate diagnostic facilities many patients remain undiagnosed.

The aim of this study was to determine the incidence of primary ciliary dyskinesia in the Asian, mainly Pakistani, population of Bradford, UK where a higher than expected number of patients were diagnosed with PCD. The ultrastructural phenotypes responsible for these defects are also described.

METHODS

Over a 15 year period patients suspected on clinical grounds of primary ciliary dyskinesia were referred for diagnostic testing to the PCD diagnostic centre in Leicester, UK. Basic demographics and age at diagnosis were recorded. Details of when the diagnosis was first suspected were not available.

The nasal brush biopsies were performed as previously described.[3] Ciliated edges greater than 50μm in length were observed at 37°C using an oil immersion x100 objective lens. They were recorded using a digital high-speed video camera (Kodak-Ektapro-Motion-Analyser, CA, USA) at a rate of 400 frames per second. The ciliary beat frequency and ciliary beat pattern could then be determined directly.[3] Brushings were fixed and prepared for transmission electron microscopy as previously described.[3] The microtubular and dynein arms of individual cilia from a minimum of 15 cells (370 individual cilia) were examined. The percentage of cilia with microtubular or dynein arm defects was then calculated. The criterion for a positive diagnosis was based on positive electron microscopy findings.

Information on the number of South Asian patients in the Bradford area was obtained from the Bradford and Airedale PCT and was based on analysis of patients registered with Bradford general practitioners.

RESULTS

The total number of children with primary ciliary dyskinesia from Asian families living in Bradford, 14 years or younger, was 19. In total there are 43,049 children of Asian origin of 14 years or under in the Bradford area (females = 20,449; males = 22,600). This gives a prevalence of primary ciliary dyskinesia in this community of 1 in 2265. Ten of the patients' parents were known to be first cousins; one patient's parents were second cousins. Eighteen of the patients' parents were from Pakistan and one of the patient's parents was from Bangladesh. No children were from ethnically mixed families.

The defects causing PCD included combined inner and outer dynein arm defects (n=13), central microtubular defects (n=3), inner dynein arm defects (n=1), radial spoke defects (n=1) and outer dynein arm defects (n=1). Fourteen patients had a history of respiratory distress in the neonatal period and all had a chronic cough and nasal symptoms from their first year of life. Two patients had been diagnosed as asthmatic. The average age at diagnosis was 5.8 years (range: 1-12 years). In this study 10 out of the 19 patients with PCD had situs inversus.

DISCUSSION

The prevalence of primary ciliary dyskinesia in the Asian population of Bradford was high at 1 in 2,265 and higher than any previous incidence of PCD reported. Of interest only three children in the same Asian population have been diagnosed with cystic fibrosis compared to 19 with PCD. The vast majority of the Asian population in Bradford are of Pakistani origin and approximately 55% of marriages in this population are between first cousins[4]. As inheritance of PCD is predominantly autosomal recessive, this is most likely due to the high incidence of consanguineous marriages in this population. Unfortunately we did not have a full data set to analyse the incidence of PCD in Caucasian patients from the same population.

It is likely that despite high local awareness of paediatricians to the presentation of PCD, a number of patients remain undiagnosed. Although 50% of patients with PCD are thought to have situs inversus, we have noted that only 40% of patients diagnosed in our centre with PCD have situs inversus. This may be explained by the maintenance of normal nodal ciliary function in the developing embryo in patients with PCD secondary to central microtubular abnormalities. Unlike respiratory cilia, motile nodal cilia lack a central microtubular pair and beat in a circular fashion. Disruption of this beat pattern occurs in most forms of PCD and appears to result in a 50% chance of situs inversus. Although the cilia of PCD patients with central microtubular defects have a circular beat pattern resulting in ineffective movement of mucus, these defects do not affect the movement of nodal cilia during embryogenesis and normal situs solitus is maintained.[5] In this study, 10 of our 19 patients had situs inversus, suggesting there may be an under diagnosis of PCD in the population.

Early diagnosis is considered important, allowing appropriate respiratory management to hopefully prevent or at least to reduce the recurrent respiratory infections and subsequent bronchiectasis that is commonly seen in this condition.[2, 6] Worryingly, Noone and colleagues, from the USA, reported that 61% of children and 98% of adults with PCD had bronchiectasis and 27% of their adult patients had severe disease with an FEV_1 less than or equal to 40% predicted.

In summary, the prevalence of PCD was found to be high in a predominantly Pakistani population with a high incidence of consanguinity. Clinical suspicion of PCD should be high in such populations. In these communities, chronic cough and nasal symptoms should prompt early diagnostic testing, especially if there is a history of neonatal cough.

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