SHORT REPORT

Bronchoscopy following diagnosis with cystic fibrosis

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We recently changed our practice to perform bronchoscopy following diagnosis with cystic fibrosis. On a retrospective review of 25 children, *Pseudomonas aeruginosa* was detected in bronchoalveolar lavage for the first time in five children (20%) and *Staphylococcus aureus* in four (16%). Lavage culture was positive in eight of 18 children without respiratory symptoms. This highlights the potential of bronchoscopy following diagnosis, even in asymptomatic children.

Cystic fibrosis (CF) is characterised by infection with specific bacterial organisms, pulmonary inflammation and subsequent chronic lung disease.[1] Infection and inflammation are known to occur even in early infancy, and there can be abnormalities in pulmonary function tests in the absence of clinical symptoms.[2] Infection would appear to initiate and sustain airway inflammation.[3] First isolation of *Pseudomonas aeruginosa* commonly occurs in infancy and infection with this organism is associated with significantly increased morbidity.[1] Early detection of infection is therefore vital to maximise the chance of eradication and prevent chronic infection. However, young children with CF do not usually produce sputum. Oropharyngeal culture, which may be the only available alternative, has a significantly lower sensitivity and negative predictive value for the presence of infection compared with bronchoalveolar lavage (BAL) or sputum.[4] We therefore felt that there was a need to intensify our search for occult infection in newly diagnosed children, and changed our clinical practice in 2003 to routinely perform bronchoscopy following diagnosis.

METHODS

We performed a retrospective review of all children who underwent flexible bronchoscopy following a diagnosis of CF over a period of 27 months between March 2003 and May 2005 in a paediatric specialist CF centre with a clinic population of 350 children. Data were collected from case notes and computerised microbiology records by a single investigator (SS). We recorded all positive cultures before bronchoscopy, culture results of BAL, changes to therapy following bronchoscopy and culture results following bronchoscopy up to the time of data collection. Cases were defined as having respiratory symptoms at the time of bronchoscopy if any of the following were documented in the case notes: increased cough, tachypnoea, increased work of breathing or dyspnoea.

Bronchoscopy was performed under general anaesthesia. BAL was performed in a single lobe, usually the right middle lobe, unless the clinical or radiological picture dictated otherwise. Semi-quantitative microbiology was performed using media appropriate for CF pathogens.

Ethical approval was given by the Royal Brompton & Harefield NHS Trust and National Heart and Lung Institute Ethics Committee. Parents gave written consent for this study and as part of a larger study investigating airway remodelling in CF.

RESULTS

Twenty five children underwent flexible bronchoscopy at a median age of 12 months (table 1). The median age at diagnosis of CF had been 5 months and bronchoscopy was performed a median of 3 months later. No case had been identified through routine neonatal screening. Fourteen cases were ΔF508 homozygotes (56%), nine were ΔF508 heterozygotes and two cases had two other mutations.

Ten children had previous positive microbiological cultures at any time prior to bronchoscopy; all these children had been given appropriate antibiotic therapy in response to isolation of these organisms. Twenty children were on prophylactic oral antibiotics at the time of bronchoscopy, three were on nebulised colistin and four were on intravenous antibiotics.

Bronchoscopy was performed via the nose in 24 children and via an endotracheal tube in one child. BAL culture was positive in 12 cases (table 1). Four out of the eight cases with *S aureus* were new isolations (16% of children) and all five of the cases with *P aeruginosa* were new isolations (20% of children). In all, eight children had *P aeruginosa* or *S aureus* identified for the first time. Eight of the 18 children who had no respiratory symptoms at the time of bronchoscopy had a positive culture (44%), and four out of the seven who had symptoms had a positive culture (57%). Of the four cases on intravenous antibiotics, three had positive cultures on BAL (MRSA in one, *P aeruginosa* in one, and both *S aureus* and *P aeruginosa* in the other). Nine of the 20 children who were on prophylactic oral antibiotics had positive cultures on BAL, compared to three out of five children who were not. Two children had respiratory complications after bronchoscopy with increased cough, but for less than 24 h. Twelve children (48%) had a change in antibiotic therapy following bronchoscopy.

The median follow-up time after bronchoscopy was 18.2 months. *S aureus* and *P aeruginosa* were subsequently isolated from non-invasive cultures in two and 12 children, respectively. First isolation of *P aeruginosa* occurred subsequent to bronchoscopy in eight children, after a median of 14.4 months (range 3.5–30 months).

DISCUSSION

We have shown that performing bronchoscopy in children newly diagnosed with CF reveals a significant prevalence of previously undetected infection. *P aeruginosa* was found in 20% and *S aureus* in 16% of children in BAL for the first time. In addition, eight of the 18 children who had no respiratory symptoms at the time of bronchoscopy had a positive culture on BAL, so that the clinical picture cannot be relied upon to prompt invasive investigation in these children.

This study has a number of limitations. It involves a relatively small number of children in a single centre and we have no outcome data on whether our interventions were beneficial. The study group was too small for a randomised trial, and in any case we felt it would be unethical to randomise children to treatment or observation if we had discovered a treatable infection. We had no control group to establish whether oropharyngeal cultures

Abbreviations: BAL, bronchoalveolar lavage; CF, cystic fibrosis

Table 1 Demographic details, culture results and change in antibiotic therapy following bronchoscopy in all 25 cases

Case	Age diagnosed, years	Age at FOB, years	Respiratory symptoms at FOB	Microbiology pre-FOB	Microbiology on BAL	Change in antibiotic treatment?	Subsequent microbiology	Follow-up, years
1	0.0	0.5	None	Negative	*Moraxella catarrhalis*	PO	Negative	1.9
2	10.8	11.3	None	Negative	Negative	No	Negative	2.2
3	0.1	0.5	Tachypnoea and increased WOB	Negative	Negative	No	Negative	0.7
4	0.0	1.7	None	Negative	*P aeruginosa*	PO and neb	Negative	0.6
5	0.8	1.1	None	*S aureus* and coliforms	Negative	No	*S aureus* and *H influenzae*	1.2
6	2.2	3.2	None	*P aeruginosa*	Negative	No	Negative	0.9
7	0.0	0.2	None	Negative	Negative	No	*P aeruginosa*	1.5
8	0.0	0.4	None	Negative	Negative	No	*H influenzae*	1.8
9	0.4	0.5	Increased WOB	*S aureus*	MRSA	Changed IV	*P aeruginosa*	2.8
10	0.0	0.2	None	*P aeruginosa*	Negative	No	*P aeruginosa*	1.5
11	3.4	3.4	None	Negative	*P aeruginosa*	IV and neb	*P aeruginosa*	2.6
12	0.0	0.4	None	Negative	Negative	No	Negative	1.1
13	5.8	5.8	None	Negative	*S aureus*	PO	Negative	0.6
14	1.4	1.5	None	Negative	*S aureus*	IV	*P aeruginosa* and *H influenzae*	2.7
15	1.2	1.4	None	Negative	Negative	No	*P aeruginosa*	2.7
16	1.2	1.4	Increased cough	*S aureus*	*S aureus*	PO	*P aeruginosa* and *S aureus*	2.7
17	0.3	0.4	None	Negative	Negative	No	*P aeruginosa*	2.5
18	0.3	0.4	Tachypnoea, cough	Negative	*P aeruginosa*	Changed IV and neb	Negative	2.2
19	8.2	8.6	None	Negative	*S aureus*	PO	*P aeruginosa*	1.2
20	0.0	0.3	None	Coliforms	Negative	No	Coliforms	1.3
21	0.4	0.4	Tachypnoea and increased WOB	MRSA	*P aeruginosa* and *S aureus*	Changed IV and neb	*P aeruginosa*	1.4
22	7.7	8.1	None	Negative	*P aeruginosa* and *S aureus*	PO and neb	Negative	0.6
23	9.2	9.2	Increased cough	*S aureus*	Negative	No	*P aeruginosa*	2.8
24	0.7	1.0	None	*P aeruginosa* and *S aureus*	*S aureus*	PO	*P aeruginosa*	0.6
25	0.0*	0.3	Tachypnoea and increased WOB	MRSA	Negative	No	Negative	1.9

*Prenatal diagnosis.
BAL, bronchoalveolar lavage; FOB, fibre-optic bronchoscopy; *H influenzae, Haemophilus influenzae;* IV, intravenous; MRSA, methicillin resistant *S aureus;* neb, nebulised; PO, oral antibiotics; *S aureus, Staphylococcus aureus;* WOB, work of breathing.

would have subsequently become positive, and over what time course. BAL was performed in only one lobe, and there may be regional variation in the microbiology of the lung. In addition, bronchoscopy was performed at a single point in time following diagnosis, so this does not obviate the need for further regular non-invasive microbiological screening to detect subsequent infection or establish clearance of previously identified organisms. Indeed, positive cultures on non-invasive specimens, particularly *P aeruginosa*, occurred following bronchoscopy in a significant number of children, although after a median time of over 1 year. The earlier detection of organisms on BAL and their subsequent treatment may have provided temporary eradication, or at least a reduction in bacterial load; however, we cannot provide any evidence on whether this had any effect on subsequent appearance of the organism.

Our group of children was unscreened, with several late diagnoses. Our data may therefore be less applicable to a younger, screened population who may have started appropriate therapy at an earlier age. However, bronchoscopy on a screened population, albeit primarily for research reasons, still reveals lower airway infection in young children.[3] Whether routine bronchoscopy at diagnosis, with or without subsequent elective bronchoscopy, improves outcome requires a large prospective randomised controlled trial, such as that currently ongoing in Australasia. In addition, bronchoscopy is an invasive investigation requiring general anaesthesia in children, and has a small but additional risk of a major complication and the potential for deterioration in a child's clinical status.

In conclusion, the identification of previously unrecognised respiratory pathogens in this study highlights the potential of bronchoscopy following diagnosis of CF, even in apparently well children.

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