The Value of Flexible Bronchoscopy in Childhood Pulmonary Tuberculosis

Jacques de Blic, M.D.;† Inès Azevedo, M.D.;‡ Christine P. Burren, M.B., B.S.;† Muriel Le Bourgeois, M.D.;† Denys Lallemand, M.D.;§ and Pierre Scheinmann, M.D.†

The value of 121 flexible bronchoscopy (FB) procedures was evaluated in 54 children, aged three months to 14 years, suspected of having pulmonary tuberculosis. Specimens from FB were culture-positive for Mycobacterium tuberculosis in seven of the 13 bacteriologically confirmed cases. Bronchial abnormalities consistent with the diagnosis were found in 31 of 54 cases. Separate or coexistent findings at initial FB included airway compression (20 cases), granulation tissue (ten cases), and obstructive cæsure (four cases). Chest roentgenograms underestimated bronchial involvement in 14 children. Further FB monitoring documented disease evolution. The FB was important in the management of patients, as it (1) guided the use of prednisone therapy, especially in the children with a chest roentgenogram not suggestive of bronchial involvement; (2) indicated a need for resection of granulation tissue by rigid bronchoscopy (three cases); and (3) guided the surgical decision (two children with persistent bronchial obstruction). Thus, FB is a safe and valuable procedure in the management of childhood pulmonary tuberculosis.

(Chest 1991; 100:688-92)

The incidence of tuberculosis in developed countries has declined over the last several decades; however, in recent years, there has been an increase in reported cases, especially in urban areas.¹ In Paris and its surrounding region, the incidence of tuberculosis was 33/100,000 in 1989, which is increased in comparison to 1988 figures.² Acquired immunodeficiency syndrome is probably one of the factors responsible.³ Due to the increased incidence of tuberculosis among the general population, childhood tuberculosis will inevitably remain an important health problem. Diagnosis of childhood tuberculosis is classically based on epidemiologic factors, clinical features, tuberculin skin test results, and chest roentgenograms.⁴ ⁵ ⁶ ⁷ Bacterial confirmation of childhood tuberculosis is difficult to achieve. The recent development of small flexible bronchoscopes has enabled the collection of further specimens for bacteriologic culture. Moreover, due to marked mediastinal lymph node disease, bronchial involvement is frequent. The presence of marked nodal enlargement is a suggestive chest roentgenographic finding, especially when associated with atelectasis or hyperaeration; however, bronchial disease may be present without these abnormalities.⁸ ⁹ Flexible bronchoscopy (FB) allows direct visualization of airways and hence provides a more accurate assessment than chest roentgenography.

This retrospective study considers the role of FB in the management of childhood pulmonary tuberculosis.

MATERIALS AND METHODS

The clinical records were reviewed in 54 suspected cases of childhood tuberculosis in which FB was performed at the Hôpital des Enfants Malades, Paris, from January 1987 to December 1989. During the same period, 44 children with tuberculous infection without pulmonary disease were observed. Flexible bronchoscopy is routinely performed in our institution when there are abnormalities on chest roentgenograms (enlarged hilar, parahilar, and paratracheal lymph nodes; parenchymal consolidation; or miliary hyperinflation). These abnormalities were present in 49 cases. In five cases with normal roentgenograms, FB was performed on the basis of a clinical suspicion of bronchial involvement. Chest roentgenograms were read blindly by the same pediatric radiologist (D.L.).

Tuberculin skin test results were considered in conjunction with symptoms, a history of close contact with active tuberculosis, and roentgenographic findings. Tuberculin skin test results were interpreted according to the recommendations of the American Thoracic Society and the Centers for Disease Control.¹² Adequate criteria for a strong suspicion of tuberculosis were fulfilled in all children.

The evaluation and management of the 54 children involved 121 FBs. All FBs were performed in the operating room after premedication with atropine, with the addition of midazolam in children aged over six months, as previously reported.¹³ Topical anesthetics were induced with lidocaine at a dose not exceeding 5 mg/kg; 2 percent lidocaine was applied in proximal airway passages, and 0.5 percent lidocaine was used in passages distal to the glottis. Transnasal FB was performed (using either the Olympus BF 3C20 or BF P20D or Pentax FB 10 H). Activated alkaline glutaraldehyde was used to disinfect the bronchoscope.¹⁴ Bronchial washings were obtained in 45 children by the instillation and aspiration of 5 to 10 ml of physiologic saline. Bronchoalveolar lavage, which was performed in the remaining nine children, involved the instillation of physiologic saline to a maximum of 10 percent of functional residual capacity with the bronchoscope wedged in the right lower lobe, unless another abnormal and accessible region had been identified on radiologic examination. Postbronchoscopic gastric aspirates were collected in 24 patients on three consecutive days. In 29 children, early morning samples of pre-FB gastric aspirates were obtained on...
three consecutive days. Sputum samples were collected in five older children.

Specimens were screened for acid-fast bacilli with both rhodamine-aurantine and Ziehl-Neelsen techniques and cultured in Löwenstein-Jensen medium.

Standard treatment involved two months of quadritherapy (isoniazid, rifampin [rifampicin], ethambutol, and pyrazinamide), followed by four months of isoniazid and rifampin.19 Granulation tissue, obstructive caseum, or bronchial compression greater than 50 percent found at the initial FB was an indication for prednisone therapy (1 to 2 mg/kg/24 h). The duration of prednisone therapy was at least four weeks and was modified according to FB findings.

For the purpose of analysis, patients were divided into those younger and those older than two years. Data were analyzed by Fisher's exact test. A p value of less than 0.05 was accepted as significant.

RESULTS

Features of Population

The sex distribution of the studied population was 30 female and 24 male subjects. The mean age at presentation was four years (range, three months to 14 years). Eighteen of the children were less than two years old. Twenty-four children (44 percent) were symptomatic, the most frequent symptom being cough. The proportion of symptomatic cases was identical in the group aged less than two years. Twenty-eight (52 percent) of the 54 patients had previously received BCG vaccination. A history of close infectious contact with active tuberculosis was elucidated in 35 of the 54 cases. Forty-two of the cases (78 percent) occurred in minority population groups: 19 were central African, nine were north African, five were Asian, and three were Portuguese. The central African children were tested for human immunodeficiency virus infection, and all were seronegative.

Roentgenographic Findings

Chest roentgenograms performed prior to FB demonstrated abnormalities on 49 of 54 occasions. Abnormalities were predominantly right-sided. Hilar or tracheal adenopathy was present in a total of 25 cases. Lymphadenopathy was isolated (seven cases) or accompanied by atelectasis (six cases), obstructive hyperinflation (three cases), or areas of consolidation (nine cases). When there was no roentgenographically evident mediastinal lymphadenopathy, abnormalities included consolidation (20 cases), pleural effusion (three cases), and miliary tuberculosis (one case).

Bacteriologic Findings

Mycobacterium tuberculosis was identified in 13 (24 percent) of the 54 cases. Overall bacteriologic yield of FB was 13 percent (seven cases). If we considered only the 24 children in whom a post-FB gastric aspirate was also obtained, the yield rose to 29 percent (7/24). Comparison between pre-FB and post-FB specimens was not possible, as the number of cases in which

Disease was multifocal in 14 cases and more frequently...
affected the upper lobes.
Abnormalities were found in 13 (72 percent) of the 18 children younger than two years and in 18 (50 percent) of the 36 older children. There was no statistically significant difference between the two age groups (p>0.1).

Indications and Timing of Subsequent FBs

Indications for further FBs were based on macroscopic findings at the first FB: (1) compression causing lumen reduction greater than 30 percent (18 of 20 cases); (2) marked formation of granulation tissue (eight cases, four of which also warranted FB due to compression); and (3) obstructive caseum (four cases). A child with a normal initial FB warranted endoscopic reassessment due to clinical and roentgenographic progression of disease.

Four cases were lost to follow-up, as they were subsequently managed at other centers. A second FB (23 children) was performed from day 9 to day 84 after the initial FB. The range of timing of a third FB (18 children) was from day 16 to day 167 and for the fourth FB (11 children) was day 37 to day 161. Seven patients were submitted to five or more FB examinations. This wide range occurred because the severity of the disease influenced timing and frequency of FB. The FB procedure was performed at closer intervals in infants with tracheal compression or children with nearly complete occlusion of bronchial lumen. All FBs were well tolerated, and no major complications occurred.

Evolution of Extrinsic Compression

The evolution and time course for restoration of normal airway diameter varied between cases (Fig 3). Aggravation of compression was seen in one case at the second FB. Airway compression became apparent subsequently, without major changes in chest roentgenograms, in an additional three children being monitored due to initial granulation tissue. Compression resolved in less than 100 days (14 to 98 days) in all but nine cases. Five of these children were monitored up to 170 days until improvement was noted. Four children with both initial severe compression and marked inflammation showed the long-term sequelae of bronchial stenosis. One of them (four months old) underwent decompressive lymphadenectomy for persistent severe bronchial airway narrowing. In another one, the severity of the stenosis led to right middle and lower lobe resection. Initial bronchoscopic findings were not predictive of the need for subsequent surgery.

Evolution of Granulation Tissue

In eight cases with marked granulation tissue observed at the initial FB, six resolved between three and ten weeks. The remaining two patients underwent rigid bronchoscopy for granuloma resection. There were an additional eight patients with initial extrinsic compression in whom granulation tissue was evident only at subsequent FBs. One of these patients ultimately required rigid bronchoscopy for resection of granulation tissue.

Evolution of Obstructive Caseum

Resolution of obstructive caseum occurred between six weeks and four months in three cases. In a further two patients, FB documented delayed appearance of caseum (after five months of therapy in one case).

Discussion

The flexible bronchoscope has proven to be a useful investigative tool in many pediatric respiratory diseases.12-13 Its use in children with suspected pulmonary tuberculosis has already been advocated.14-15 In adults, FB is especially used in sputum-negative pulmonary tuberculosis, in an attempt to isolate M tuberculosis;16-20 however, other authors have emphasized its use in the identification and survey of endobronchial tuberculosis.5,6,21 Both aspects were analyzed in our pediatric population.

Our data showed 24 percent bacteriologically proven tuberculosis cases (all specimens combined). This correlates with figures of 25 to 26.5 percent reported in other pediatric populations.\(^1\)\(^2\) More recently, Starke et al\(^7\) obtained bacteriologic confirmation of disease in 39 percent of the cases of pulmonary tuberculosis, using both standard medium and the Bactec radiometric system for culture of gastric aspirates. Bacteriologic yields obtained in adults are even higher, but methods of specimen collection differ. Bronchial brushings and transbronchial biopsy, which are reported to provide a higher bacteriologic yield,\(^1\)\(^6\)\(^7\) cannot be performed with the smaller pediatric flexible bronchoscope due to the inadequate diameter of the operating channel. In our study, FB did contribute significantly for \textit{M tuberculosis} identification, as FB specimens confirmed disease in five of the 13 positive cases; however, the overall culture yield of FB was low (13 percent), and so routine FB cannot be justified on the basis of obtaining a culture. Flexible bronchoscopy is probably indicated when drug resistance is suspected or the source case is not known, as all attempts to culture \textit{M tuberculosis} should be made in such circumstances.\(^3\)\(^5\)\(^7\) All specimens were smear-negative, and initial antibiotic treatment was therefore not guided by bacteriologic studies. This may be changed with the development of newer methods of \textit{M tuberculosis} identification (enzyme-linked immunosorbent assay, DNA hybridization) in conjunction with rapid isolation by Bactec.\(^19\)\(^14\)\(^25\)

In contrast to bacteriologic results, macroscopic features immediately reinforced the clinical diagnosis of tuberculosis in 57 percent of the cases. Leigh et al\(^15\) also found bronchial abnormalities in 63 percent of 16 children less than five years of age. These high figures of bronchial involvement, compared to reported results of 10 to 18 percent in adults,\(^5\)\(^7\) reinforce the importance of direct visualization by FB in children. Although infants tend to have a more severe progression of clinical disease than older children, in our study, bronchial abnormalities were of a similar frequency and severity in both age groups.

Furthermore, FB verifies the underlying cause of atelectasis or hyperaeration seen on the roentgenogram by establishing the presence of bronchial compression, granulation tissue, caseum after rupture of nodal disease into the bronchus, or stenosis. Most important, significant bronchial disease may be present in the absence of enlarged hilar or mediastinal lymph nodes, as was demonstrated in 14 children when first observed. Underestimation of bronchial disease when assessed by chest roentgenograms has been previously emphasized in pediatric studies involving rigid bronchoscopy.\(^7\) We could not correlate all radiologic and endoscopic evolution of disease, because follow-up chest roentgenograms had not been systematically read by the same radiologist and in most cases were not available for review. Endobronchial abnormalities have been observed to respond favorably to prednisone therapy in the double-blind randomized study of Nemir et al.\(^7\)\(^8\) More recently, Toppet et al\(^9\) confirmed a beneficial effect of steroids in bronchial compression when added to a drug regimen comprising isoniazid, rifampin, and ethambutol. Also, FB evaluated the need for resection of granulation tissue using rigid bronchoscopy and influenced the decision to undertake surgery in cases of persistent bronchial obstruction.

Information gained by subsequent FBs documented improvement of bronchial lesions and response to therapy. Further progression of bronchial disease during the initial stages of antituberculous therapy is not uncommon, and hence surveillance is important.\(^7\)\(^7\) This is demonstrated by the development of airway compression in three children and granulation tissue in a further eight children. Therefore, the indication for further medical or surgical therapy may occasionally become evident only at follow-up FBs.

In conclusion, FB is useful in the initial investigation of pediatric cases of tuberculosis when chest roentgenograms are abnormal. Subsequent FBs are indicated when severe compression, granulation tissue, or caseum is found at the first FB or whenever there is clinical or radiologic aggravation of disease; FB allows documentation of disease evolution and provides information as to the need for steroid therapy or surgery (or both). Provided FB is performed by an experienced bronchoscopist, it is a safe and well-tolerated procedure which is to be advocated in the management of childhood pulmonary tuberculosis.

REFERENCES

6 Ip MSM, So SY, Lam WK, Mok CK. Endobronchial tuberculosis revisited. Chest 1986; 80:727-30
Diagnostic Ultrasound: Principles and Instruments

This course will be held November 11-15 sponsored by and at the Center for Medical Ultrasound, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina. For information, contact the Registrar, 300 South Hawthorne Road, Winston-Salem, NC 27103 (919:748-4504 or 1-800-277-7654).