

Bronchiolitis obliterans in children – A report of six cases

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Summary

Six children who survived severe acute bronchiolitis in infancy and early childhood continued to have persistent symptoms of breathlessness, cough and wheeze resistant to bronchodilator therapy. Hyperinflation of the chest, widespread crepitations and rhonchi were persistent clinical features. Failure to thrive was a problem in most. At presentation clinical measles was diagnosed in one child and adenovirus titres were raised in another; the aetiological agents in the others were not known. Lung biopsy from the child with measles showed features of severe bronchiolitis. The clinical and radiological features and course of the illness were consistent with those of bronchiolitis obliterans. Although illness was prolonged the long term prognosis was satisfactory with the majority of children showing improved chest signs, growth and general health after four to eight years of follow up.

Key words: Bronchiolitis, bronchiolitis obliterans.

Introduction

Acute viral bronchiolitis affects young children and is most common among children below six months. The respiratory syncytial virus (RSV) is responsible for most cases but adenovirus types 3, 7 and 21, rhinovirus, parainfluenza virus types 1 and 3, mumps, influenza and measles viruses may also cause the illness.^{1,2,3} *Mycoplasma pneumoniae* may cause bronchiolitis in infants.¹ Most children recover within two to three weeks of the onset of illness and mortality is low in developed countries. However, long term sequelae of acute bronchiolitis may be associated with a high degree of morbidity. A large proportion of children may develop recurrent wheezing associated with bronchial hyperreactivity.^{4,5} In one study 56% of children hospitalised for acute bronchiolitis responded positively to methacholine challenged nine to ten years later.⁶ This association between acute bronchiolitis and bronchial hyperreactivity and asthma is a major area of investigation of risk factors for respiratory illness in children. A less common complication of acute bronchiolitis is bronchiolitis obliterans, which is characterised by chronic respiratory obstruction not responsive to bronchodilator therapy. The incidence of bronchiolitis obliterans is unknown and it is not generally due to RSV, adenovirus being the most commonly implicated organism.^{2,7-9}

In the past eight years we have seen several children with severe persistent respiratory obstruction following acute bronchiolitis. The clinical course of these children was similar to that of children with bronchiolitis obliterans following acute bronchiolitis reported in other series.⁷ The purpose of this paper is to describe the clinical features and course of six such children who have been managed at our unit.

Patients and method

We reviewed the case notes of six children who were admitted to the Paediatric Unit of the Universiti Kebangsaan Malaysia at the Kuala Lumpur General Hospital in the past eight years with initial episodes of acute bronchiolitis that were followed by persistent respiratory obstruction. Their ages at the last follow up ranged from four to eight years. They were all male, two Malays, two Chinese and two Indians. One of the Indian children had Down's Syndrome. The first patient presented in 1981 and the last in 1986.

Acute bronchiolitis was diagnosed clinically in children who presented with a history of coryzal symptoms, cough, rapid respiration with respiratory distress and wheezing, and whose physical findings included hyperinflation of the chest and fine inspiratory crepitations and/or rhonchi. Radiological features of hyperinflation of the chest and peribronchial thickening were supportive of the diagnosis in all cases.⁸ Symptoms of acute bronchiolitis normally disappear by the end of three weeks. In this report, persistent respiratory obstruction is defined as cough, rapid respiration (>60 /minute), wheezing, hyperinflation of the chest, widespread crepitations and rhonchi that failed to resolve completely either spontaneously or after the administration of bronchodilators and/or corticosteroids and continued to be present months or years after the initial acute episodes. Children who fully recovered after the initial acute episodes and subsequently presented with recurrent wheezing or asthma are not included in this report.

At the initial presentation investigations were performed to establish the aetiology of acute bronchiolitis. Serological investigations were performed on all six children except the first to identify respiratory viruses including RSV, influenza and parainfluenza viruses, adenoviruses, measles virus as well as *Mycoplasma pneumoniae*. A four-fold increase in titres or a single very high titre (1:128 or more) were accepted as indicative of infection. Blood and tracheal aspirate cultures and chest radiographs were done in all children.

When symptoms persisted, further investigations included serum immunoglobulins G, A and M, serum alpha-1-antitrypsin, the sweat test, the Mantoux test and oesophageograms. The first child (LSS) underwent bronchoscopy and open lung biopsy but the subsequent cases were not subjected to these procedures.

Results

Mode of presentation: The main characteristics of the children are summarised in Table 1.

The ages of the children at the time of the initial presentation ranged from six weeks to 14 months (mean 6.8 months). All were previously well except for one child who had hyaline membrane disease in the early neonatal period. The major findings during their initial acute illness were tachypnoea (respiratory rate >60 /minute), hyperinflation of the chest and widespread crepitations. Rhonchi were also noted in all children. The liver was easily palpable up to 3 cm below the costal margin in each child, giving an impression of enlargement when in fact

Table I
Characteristics of six children with persistent respiratory obstruction
following acute bronchiolitis
 (— = absent, + = present, NA = not available, * = lost to follow up)

	Patients					
	LSS	WCS	MS	P	M	AA
Birth weight (kg)	3.5	3.0	NA	0.9	3.0	NA
Neonatal respiratory illness	—	—	—	+	—	—
Family history of asthma/allergy	+	—	—	—	—	+
Age at presentation (months)	10	1.5	3.5	6.0	6.0	14
Duration of symptoms at presentation (days)	10	3	4	3	2	15
Complications at presentation:						
Respiratory failure	+	+	—	—	—	—
Pneumothorax	+	—	—	—	—	—
Oxygen dependence	—	—	—	—	—	+
Total no. of admissions	3	4	7	6	2	1*
Average duration of stay per admission (days)	34	65	17	25	23	NA*
Duration of follow up (years)	8	6	6	6	4	NA*

it was a result of hyperinflation of the chest. Two children (LSS and WCS) were treated in the Intensive Care Unit for respiratory failure characterised by carbon dioxide retention, while another (AA) was cyanosed without oxygen. The remaining children were treated with oxygen initially but needed no further support several days after admission.

Subsequent progress: The respiratory symptoms and signs of these children persisted beyond the normal expected recovery period for acute bronchiolitis and were still present at the last follow up.

The mean duration of their initial hospital stay was 22 days. One child (AA) was lost to follow up after being discharged, and no further information on his progress was available. However, he was still oxygen dependent at the time of discharge. The remaining five children needed repeated hospitalisations, most of which were prolonged. The longest periods of hospital stay ranged from 35 days in one child (M) to 180 days in another (MS). Most of these hospitalisations were due to exacerbations of their chronic problems associated with superimposed chest infection. The first two years of their illness were the most eventful. Growth was retarded in four children whose weight and height were below the third centile. Subsequently, hospitalisation became unusual and a general improvement in health was noted.

Investigations: Only one child (AA) had significantly increased titres of adenovirus (1:8 to 1:128). Serological tests for other viruses and mycoplasma, were negative. Bacteriological cultures of blood and tracheal aspirates were negative.

Chest radiographs taken at presentation were typical of those of acute bronchiolitis showing hyperinflation, increased peribronchial thickening and small patchy areas of atelectasis and consolidation. Hyperinflation remained as the major finding in subsequent radiographs.

Serum immunoglobulins G, A and M, serum alpha-1-antitrypsin, the sweat test, the Mantoux test, and oesophageograms were normal in all children.

The first child (LSS) underwent bronchoscopy and an open lung biopsy. The bronchoscopic findings were normal and the lung biopsy was reported as consistent with bronchiolitis. The subsequent cases did not undergo either of these procedures.

Treatment and outcome: During the earlier phases of their illness the mainstay of treatment was oxygen therapy during exacerbations. Antibiotics were used when secondary infections were suspected. Physiotherapy was prescribed for all cases. Although there has been no objective indication that bronchodilators are useful, we have used them in all these children. Though none experienced a reversal of the airway obstruction it did appear that some alleviation of symptoms was achieved in WS. Corticosteroids were used on three of these children (LSS, WCS and MS) at one time or another but these failed to reverse respiratory obstruction.

Five of these children are still being followed up. All five have shown significant improvement in their tachypnoea, crepitations and rhonchi, although all still have hyperinflated lungs. Four of these have mild symptoms and signs, while the fifth (LSS) still has severe hyperinflation of the chest and exhibited crepitations and rhonchi of moderate severity. None has clubbing of fingers and all are now growing satisfactorily.

Three of these patients are described briefly.

Case 1: LSS, a Chinese boy, was admitted in July 1981 at the age of ten months. He had been born normally at term with a birthweight of 3.5 kg. After contracting measles from an elder sibling, he was admitted to our unit with fever and acute respiratory difficulty, associated with hyperinflation and widespread crepitations. In the ward he developed a pneumothorax and respiratory failure and needed respiratory support for five days. Clinical and radiological features indicated respiratory obstruction. Investigations proved unhelpful and after a prolonged hospital stay, an open lung biopsy was performed. This was reported: "appearances are those of bronchiolitis and atelectasis, possibly a sequel of previous measles."

During the initial period of illness he was treated with bronchodilators and steroids in alternate days doses. He is still on bronchodilator therapy. He is now eight years old and has severe hyperinflation with persistent and widespread crepitations and rhonchi. However, he is quite active and growing satisfactorily, attending school and has not needed hospitalisation in the past five years.

Case 2: MS was first admitted in June 1983 at the age of three and a half months. He had been an inmate of an orphanage since the age of one month. The initial admission was due to acute bronchiolitis. However, persistence of respiratory symptoms required extensive investigations. Clinical and radiological features were consistent with respiratory obstruction. His chest was hyperinflated and there were widespread crepitations and rhonchi. He also failed to thrive and was slow in both motor and mental development, but this could be attributable partially to his life in the orphanage. He required repeated hospital admissions for exacerbations of his persistent respiratory obstruction, often precipitated by chest infection. On one of these hospitalisations he developed respiratory failure, with severe hypercarbia. He survived the episode. He demonstrated partial response to bronchodilators and steroid and this probably indicated that he had bronchial hyperreactivity in addition to persistent respiratory obstruction. For this particular hospitalisation he stayed for 160 days. Presently, his respiratory symptoms are much

improved and crepitations and rhonchi are much less. His height and weight have increased from below the 3rd centile to the 50th centile of the Standard Wellcome charts.

Case 3: AA was referred to us when he was one year two months old. He had earlier presented to another hospital with a nonresolving respiratory illness which was initially treated as tuberculosis. When he developed cyanosis he was sent for a cardiac assessment. No cardiac lesion was found. He was ill and cyanosed without oxygen when first seen by us. His chest was hyperinflated and had widespread crepitations. His viral serological studies showed a more than four fold increase in titres of adenovirus antibodies (1:8 to 1:128). Investigations for tuberculosis and other disorders were negative. He was still oxygen dependent when he was sent home. His subsequent progress is unknown.

Discussion

We have described six children with bronchiolitis obliterans.^{2,7} These children had developed persistent respiratory obstruction characterised by hyperinflation of the chest, tachypnoea, widespread crepitations and rhonchi consequent to initial episodes of acute bronchiolitis. Bronchiolitis obliterans, although uncommon, results in prolonged severe illness that may result in growth impairment. Affected children need careful follow up and timely interventions of respiratory infection. The management of our patients were in line with the practices of Hodges et al.⁷

Adenovirus has been implicated in most reports of bronchiolitis obliterans.^{2,8,9} However, in our study, adenovirus infection was shown in only one case. Our observation was similar to that of another study in which only two of the reported 13 cases could be attributed to adenovirus infection while another to *Mycoplasma pneumoniae*.⁷

The place of bronchodilators and corticosteroids in this condition is controversial⁷ but occasional bronchodilator responsiveness has been observed in some patients in one report.¹⁰ Although we have used bronchodilators in all and corticosteroids occasionally in several of these children there was no evidence that these helped relieve respiratory obstruction apart from a subjective impression that one child experienced some benefit. Since bronchial hyperreactivity is a common consequence of acute bronchiolitis⁶ it is reasonable to postulate that children who develop bronchiolitis obliterans may also exhibit bronchial hyperreactivity and thus bronchodilators and/or steroid may have a place in the management of some of them.

The long term progress of our patients has been encouraging. This is consistent with the observations of Hodges et al.⁷ Lung growth with age is the most likely explanation for the slow improvement over time.⁷ This promising outlook should alleviate parental anxiety over the long term prognosis of their children.

It is likely that the incidence of this illness in Malaysian children is higher than it is realised. An awareness of its occurrence and clinical course will allow a rational and successful approach to its management.

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