

Gastro-oesophageal Reflux in Children with Severe Respiratory Symptoms – Clinical Spectrum and Management

M Z Norzila, MMed*, B H O Azizi, FRCP**, C T Deng**, MMed, A Zulfikar, MMed***, P Devadass, MMed***, Amin Tai, FRCS****, * Jabatan Pediatrik, Institut Pediatrik, Hospital Kuala Lumpur, ** Jabatan Pediatrik, *** Jabatan Radiologi, **** Jabatan Operasi Kanak-Kanak, Universiti Kebangsaan Malaysia, 50300 Kuala Lumpur

Summary

Respiratory symptoms in children may be associated with underlying gastro-oesophageal reflux (GOR). We reviewed the case notes of 20 children who presented to us from June 1993 to June 1994 with respiratory symptoms and GOR.

The patients consisted of 16 Malays, two Chinese and two Indians with equal number of males and females. Their age at diagnosis was less than one year in 17 patients. The earliest age at presentation was at the third day of life. All patients had major respiratory manifestations i.e. recurrent wheezing, recurrent cough and pneumonia. In addition, three patients had stridor and six patients had apparent life threatening episodes (ALTE). Fourteen patients required ventilation because of respiratory failure.

Diagnosis of GOR was based on clinical grounds supported by barium oesophagogram in seven patients and ultrasound examination in 11 patients. Eight patients were fundoplicated because of ALTE and recurrent severe bronchospasm. On follow up, 14 patients had hyperactive airways requiring inhaled bronchodilator and steroid therapy.

Key Words: Gastro-oesophageal reflux, Respiratory symptoms, Fundoplication

Introduction

Gastro-oesophageal reflux is a common condition observed in children¹. The exact pathology is not known. However episodes of reflux are associated with three groups of disorder of the lower oesophageal sphincter i.e. low basal sphincter pressure, inappropriate sphincter relaxation and increase in the intraabdominal pressure². The relationship between gastro-oesophageal reflux and respiratory disease is now well known. Respiratory symptoms that have been described include aspiration pneumonia, wheezing, stridor and ALTE³. These respiratory symptoms may be associated with

significant morbidity and mortality. The diagnosis and treatment of GOR in such patients are important.

We reviewed 20 patients with severe respiratory symptoms who had been managed at our unit for the past one year in whom the diagnosis of gastro-oesophageal reflux was also made. Three cases with different clinical presentations are presented to illustrate the spectrum of disease.

Methods

We reviewed 20 cases of gastro-oesophageal reflux with

respiratory manifestations who presented to us from June 1993 to June 1994. These were cases referred to the respiratory team of Universiti Kebangsaan Malaysia at the Paediatric Institute, Hospital Kuala Lumpur. Demographic data, clinical presentations, method of diagnosis and management of patients were reviewed.

All patients were referred for recurrent or chronic respiratory problems. The diagnosis of GOR was based on history and physical examination. This was supported by radiological investigations. Gastro-oesophageal reflux was suspected when there was history of recurrent vomiting, cough, choking, apnoea or ALTE especially after feeding. ALTE is defined as one or more episodes characterised by some combination of cyanosis, marked pallor, apnoea, bradycardia and hypertonica or hypotonia. Other special features were recurrent admissions for pneumonia which suggested recurrent aspiration.

On physical examination all the patients had increase respiratory rate, subcostal and intercostal recessions with crepitations or rhonchi on auscultation.

The radiological investigations done were chest radiographs, barium oesophagogram and ultrasonography. No milk scans were performed on these patients. In the chest radiographs there were radiological findings of consolidation and collapse particularly involving the right upper and middle lobes. Gastro-oesophageal reflux was present on barium oesophagogram when there was reflux of barium during intermittent screening for a period of five minutes. The reflux could be at the level of proximal, distal oesophagus or at the level of carina. Ultrasonography for diagnosis of gastro-oesophageal reflux was performed by giving milk feeds during the procedure⁹. Reflux was said to be present when there was three to five episodes of reflux detected during five to ten minutes of scanning.

Results

There were 16 Malays, two Chinese and two Indians with equal number of males and females. Five of the patients were born premature. In 17 patients gastro-oesophageal reflux was diagnosed between one to 11 months old. Two children were diagnosed at one and

a half years old while the third child was diagnosed at two and a half years old.

All children were referred to the respiratory team for severe respiratory manifestations. The respiratory symptoms were recurrent cough (75%), wheezing (100%), recurrent pneumonia (45%), apparent life threatening episodes (30%) and stridor (15%). Other associated features were failure to thrive (50%), vomiting after feeds (35%) and irritability (5%), the latter manifestations occurring in neonates. Fourteen patients were ventilated for respiratory failure. Table I summarises the relevant information of the 20 patients.

An association with congenital heart disease was noted in four children; ventricular septal defect (2), patent ductus arteriosus (1), and transposition of great vessels (1). One child had cerebral palsy and another child was operated for congenital lobar emphysema.

Clinical diagnosis of reflux was supported by barium oesophagogram in seven patients and by ultrasound in 11 patients. In two patients we were unable to demonstrate the reflux by ultrasound or by barium oesophagogram. However with antireflux therapy, both patients had remarkable clinical improvement.

All patients were initially treated medically with oral metoclopramide 0.1 mg/kg/dose six hourly alternating with oral cisapride 0.1-0.2 mg/kg/day six hourly given half hour before each feeds. Since we did not perform endoscopy routinely to determine oesophagitis, oral cimetidine 5 mg/kg/dose six hourly were added as well on very ill patients with severe bronchospasm which would be tapered off after six weeks.

Nissen's fundoplication was performed when there was no clinical improvement i.e. when the patients continued to have recurrent wheeze after feeds, unresolved pneumonia or ALTE. Based on these indications eight children underwent fundoplication. Five of them continued to have respiratory symptoms but with reduced frequency and severity.

The patients had been followed-up from six months

to a year. All 20 patients gained weight and six of the patients had no residual respiratory symptoms. The remaining 14 patients had persistent respiratory symptoms which required inhalational bronchodilator and steroid to control their symptoms.

We illustrate this review by discussing three children with gastro-oesophageal reflux who presented with three different respiratory manifestations.

Case 1

A two and a half month old baby boy, born full term with a birth weight of 3.0 kg, was discharged well after 24 hours. At one month old he developed a sudden episode of cyanosis and apnoea following feeding. On arrival to the hospital he was tachypnoeic and cyanosed with reduced air entry on auscultation. He was ventilated in the intensive care for 24 hours. Post extubation he developed noisy breathing, cyanosis and cough after feeds requiring supplemental oxygen.

On examination, he was pink in head box oxygen of 10 l/min. He had suprasternal, subcostal and intercostal recession. There was audible wheeze. Other systems were normal. In view of the sudden episode of apnoea, cyanosis and recurrent wheeze following feeding, gastro-oesophageal reflux was suspected. This was confirmed by ultrasonography which documented six episodes of reflux in five minutes. He was started on oral cisapride 1 mg 6 hourly alternating with oral metoclopramide 0.5 mg 6 hourly taken half an hour before feeds. He was nebulised with a bronchodilator for the bronchospasm. Although he was on medical therapy for two weeks he continued to have respiratory distress particularly after feeding with evidence of airway obstruction. Nissen's fundoplication was performed. Post fundoplication the respiratory symptoms resolved and he did not require any respiratory or anti reflux therapy.

Case 2

A six-month-old baby boy who was born full term normal delivery with a birth weight of 2.8 kg was discharged well at day two of life. He was noted to have stridor on the third day of life. Echocardiography

and bronchoscopy were normal. Following that he was admitted four times for bronchopneumonia. On all four admissions, mother gave a history of sudden onset of breathlessness and cyanosis after feeding. The stridor was worsened by these episodes. There was also a history of choking after feeds. On his fourth admission he had severe bronchospasm.

On admission he was tachypnoeic, cyanosed with subcostal and intercostal recessions. Chest radiographs showed hyperinflation with hazy lung fields. He was treated as having severe bronchopneumonia and was ventilated in the intensive care unit for three days. Post extubation, he had sudden episodes of bronchospasm particularly after feeds which required reinstatement of ventilatory support. An ultrasound examination was performed and this documented 5 episodes of reflux in 10 minutes. He was managed with oral cisapride alternating with oral metoclopramide taken half an hour before feeds. In view of recurrent episodes of ALTE Nissen's fundoplication was performed.

Post fundoplication he was successfully weaned off from the ventilator. His stridor resolved and there was no episode of severe bronchospasm. His airway remained hyperactive which was controlled with intermittent inhaled bronchodilator and regular inhaled steroid. On follow-up he had gained weight and no longer required antireflux therapy.

Case 3

A one and a half year old Malay boy was referred to us for recurrent episodes of severe exacerbation of asthma. He was born full term normal delivery with a birth weight of 3.0 kg. His antenatal and immediate postnatal period was uneventful. He was diagnosed as an asthmatic at the age of one year when he presented with recurrent episodes of cough, breathlessness and wheezing which was treated symptomatically with oral bronchodilator. He had two to three episodes of wheezing in a month. Three days prior to admission he had developed fever, cough and wheezing. On admission he was tachypnoeic and cyanosed with marked subcostal and intercostal recessions. Auscultation showed reduced air entry with diffused rhonchi bilaterally. Despite continuous nebulised bronchodilator, subcutaneous terbutaline, intravenous hydrocortisone and aminophylline infusion he showed

Table 1
Characteristics of 20 patients with respiratory illness associated with gastro-oesophageal reflux

No.	Sex	Age at diagnosis (months)	Onset (months)	GOR symptom	Resp. symptom	Method of diagnosis	Associated abnormality	Treatment	Respiratory symptoms persists
1.	F	9.5	8.0	vomit, failure to thrive	stridor, cough, wheeze	ultra-sound	VSD	medical	yes
2.	M	3.5	3 days	nil	stridor wheeze, pneumo	ultra-sound	nil	fundo	yes
3.	M	1	1	nil	pneumo	barium	PDA	medical	no
4.	M	11	2	vomit, failure to thrive	wheeze, cough, pneumo	clinical	nil	medical	yes
5.	F	2	1	irritable	ALTE	ultra-sound	nil	fundo	no
6.	F	3	2	failure to thrive	cough, wheeze, pneumo	ultra-sound	TGA R Hemi	medical	yes
7.	M	6	6	vomit	cough, wheeze	barium	nil	medical	yes
8.	F	7	7	vomit	wheeze, pneumo	barium	cerebral palsy	medical	yes
9.	M	5	9 days	vomit, failure to thrive	ALTE	barium	nil	fundo	yes
10.	M	5	2	vomit	cough, wheeze, pneumo	clinical	VSD	medical	yes
11.	F	7	0.5	failure to thrive	cough, wheeze, pneumo	barium	eventra of diaphra	fundo	no
12.	M	3	1	failure to thrive	stridor, wheeze, ALTE	ultra-sound	nil	fundo	yes
13.	M	5	3	vomit	cough, wheeze, pneumo	ultra-sound	nil	medical	yes
14.	F	3	0.5	vomit, failure to thrive	cough wheeze	ultra-sound	nil	medical	no
15.	F	9	4	failure to thrive	cough, wheeze, ALTE	ultra-sound	nil	medical	no
16.	F	29	12	nil	cough, wheeze, ALTE	ultra-sound	nil	medical	yes
17.	F	2.5	5	failure to thrive	cough, pneumo, ALTE	barium	nil	medical	yes
18.	M	4	4	nil	pneumo, wheeze	ultra-sound	CLE	fundo	no
19.	M	11	11	failure to thrive	cough, stridor	barium	nil	fundo	yes
20.	M	3.5	36	vomit	pneumo, wheeze	ultra-sound	nil	fundo	no

Abbreviations: ALTE-apparent life threatening episode, CLE-congenital lobar emphysema, pneumo-pneumonia, fundo-fundoplication, event of diaph-eventration of diaphragm, R. Hemi-Right Hemidiaphragm, TGA-Transposition of Great Vessels, VSD-Ventricular septal defect, PDA-Patent ductus arteriosus

minimal improvement. He required ventilatory support for 24 hours.

Post extubation he improved and was discharged with inhaled bronchodilator and steroid. Two days later he was readmitted for severe bronchospasm. In addition to the inhaled therapy he required regular subcutaneous terbutaline for 24 hours and oral steroid 2 mg/kg per day. He was on 5 liter/min of oxygen via facemask to maintain saturation of 95%. He was investigated for other possible causes of his refractory asthma. The titres for *Respiratory Syncytial Virus*, *Adenovirus*, *Parainfluenza*, *Influenza* viruses and *Mycoplasma Pneumoniae* were low. The sweat electrolytes were normal. The barium oesophagogram did not show any vascular ring, tracheal oesophageal fistula or gastro-oesophageal reflux. However the ultrasonography documented three episodes of reflux in ten minutes.

He was started on oral metoclopramide six hourly alternating with oral cisapride six hourly as well as oral cimetidine. However he continued to have episodes of bronchospasm in the ward requiring reventilation for four days. In view of this Nissen's fundoplication was performed.

Post fundoplication he had no severe episodes of bronchospasm but he continued to have wheezing which required 4-6 hourly regular inhaled bronchodilator and high dose inhaled steroid 1600 microgram/day as well as low dose steroid 5 mg on alternate days. His chest radiographs initially showed air trapping with peribronchial thickening and areas of consolidation. Subsequent chest radiographs showed evidence of bronchiectasis. A computed tomogram showed areas of air trapping with hyperlucency with peribronchial thickening which was consistent with bronchiolitis obliterans. Both basal lung fields showed areas of bronchiectasis. He stayed in the ward for three months before we were able to stabilize his hyperactive airways. He was discharged with inhaled steroid 1200 microgram/day and low dose prednisolone 2.5 mg on alternate days. His anti-reflux therapy was continued. Subsequently he had three admissions for episodes of bronchospasm which were not severe secondary to respiratory tract infections. However in between episodes he was doing well. His oxygen saturation was 95% in air. We were able to reduce the inhaled steroid

to 800 microgram/day and the oral steroid and anti reflux therapy were stopped.

In retrospect this child's early symptoms were erroneously attributed to asthma. It was more probable that he had been having a chronic aspiration syndrome consequent to GOR which had resulted in bronchiolitis obliterans.

Discussion

A relationship between gastro-oesophageal reflux and respiratory symptoms was well known and for decades pulmonary symptoms were thought to be due to pulmonary aspiration⁴. More recently additional proposed mechanisms include reflex bronchospasm, reflex bradycardia, reflex laryngospasm and reflex central apnoea⁵.

Gastro-oesophageal reflux may be responsible for the pulmonary dysfunction and vice versa, or both may apply. Gastro-oesophageal reflux should be considered in children with persistent respiratory symptoms such as recurrent pneumonia⁶ and in those with poorly controlled asthma or unexplained severe exacerbations. A small group of patients present in infancy with ALTE⁷ in which the infants present with recurrent apnoeas which can be potentially fatal. Some children may present with stridor⁸.

The most recent method of diagnosis is a 24 hour ambulatory pH oesophageal monitoring⁹. It records the number of reflux episodes of different specified durations, the time taken to clear reflux acid and the proportion of time during which the pH is abnormally low. It is a sensitive and specific tool to diagnose gastro-oesophageal reflux and it is non invasive. The only disadvantage is its inability to detect an alkaline reflux. Other methods of diagnosis are barium oesophagogram and ultrasound. Barium studies can demonstrate the disturbed oesophageal activity but gastro-oesophageal reflux can be missed in 40% of patients compared to pH study. Ultrasonography¹⁰ is a convenient and non invasive method of diagnosing gastro-oesophageal reflux. It can demonstrate the presence of reflux post-prandial. However it is time consuming (as the radiologist has to wait to detect the presence of reflux) and it is operator dependent.

It is useful when the child is ventilated or too ill to be moved. In our situation GOR remains a clinical diagnosis with ultrasound and barium oesophagogram are tools used to aid in the diagnosis¹¹.

The management of gastro-oesophageal reflux can be medical or surgical. Cisapride is a prokinetic agent which acts selectively on the gut mainly through facilitation of the acetylcholine release from the myenteric plexus. This will produce a significant increase in the lower oesophageal sphincter as well as in the peristaltic amplitude and duration. It offers promise as an effective agent in the treatment of gastro-oesophageal diseases¹². Metoclopramide and domperidone have been used to augment gastric emptying. In patients with documented esophagitis H2 blocker is used. However we do not perform endoscopy in all our patients. Treatment such as positioning, thickening of feeds may be used although it might not be useful when the reflux is severe causing marked respiratory symptoms.

Fundoplication is the most reliable way to prevent

reflux¹³. It is reserved for patients who are resistant to medical therapy after maximum antireflux therapy and patients with ALTE. In our series, eight patients required fundoplication due to their severe respiratory symptoms. They developed severe frequent bronchospasms requiring ventilation and six of these patients had recurrent ALTE. The high rate of fundoplication indicates that medical therapy are less successful in severe cases. In a paediatric unit with extensive experience with fundoplication, symptomatic relief is achieved in 95% of patients¹⁴. Post fundoplication five of our patients continued to wheeze. This is not due to failed fundoplication but residual lung damage secondary to chronic aspiration not treated earlier.

The cases we have illustrate the varied presentations and various causes of gastro-oesophageal reflux with respiratory manifestations. Prompt diagnosis and management could result in dramatic improvement in symptoms and even in the prevention of death. On the other hand, as we have illustrated in case 3, severe lung damage may result from frequent aspirations.

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