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Case 1: A long history of cough and dyspnea

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Case 1: A long history of cough and dyspnea

A 10-year-old girl presented with a nine-year history of six to eight upper and lower respiratory tract infections annually, each with a duration of three to six weeks in spite of antibiotic treatment, accompanied with cough, dyspnea and occasional wheezing. She also reported these symptoms during physical exercise, independent of infections. Until now, three pneumonias and multiple bronchitic episodes had been verified. At five years of age, she was diagnosed with bronchial asthma. For two years, treatment consisted of intermittent courses of short-acting beta-agonists and inhaled corticosteroids, before she was switched to a daily combination treatment with long-acting beta-agonists and inhaled corticosteroids (budesonide-formoterol 160 µg/4.5 µg twice daily) plus montelukast 5 mg orally without any breakthrough. A sweat test performed at four years of age was normal, as was a skin prick test to common aeroallergens and measurements of exhaled nitric oxide. Previous lung function tests were reported as a bronchial obstruction with no or only partial bronchodilator response. On presentation, the child was afebrile with normal vital signs, including an oxygen saturation of 97% on room air. A physical examination was unremarkable except for a prolonged expiration on auscultation. A complete blood count was normal and the erythrocyte sedimentation rate was 18 mm/h (0 mm/h to 10 mm/h). Further workup revealed the diagnosis.

Case 2: A persistent fever

A 3.5-month-old Asian girl presented to the emergency department (ED) with a two-week history of intermittent fever. Fifteen days before arrival, the patient began to have fevers as high as 41.1°C axillary. Her primary care physician (PCP) saw her on day 3 of her illness. The mother reported fever and increased fussiness, which responded to antipyretic medication. The baby had no other symptoms or sick contacts, good oral intake, and normal urination and bowel movements. In the office, she had a 39.6°C rectal temperature. A physical examination and urinalysis were normal. She was diagnosed with a viral illness and asked to return in 24 h. The next day, the mother reported no fever overnight, the physical examination remained normal and the urine culture was negative. The PCP instructed the family to come back if the fever returned.

The patient was seen on day 15 for a health maintenance examination. Through an interpreter, the PCP found out that the patient had persistent intermittent fevers at night with fussiness and decreased appetite, but no daytime symptoms. The PCP found a slightly fussy but consolable baby with a normal physical examination. The patient was sent to the ED for evaluation of fever without a source.

In the ED, the patient's temperature was 39°C. She was alert and smiling. Once again, the physical examination was normal. Influenza A and B antigen tests were negative, with a clear urinalysis. A complete blood count showed leukocytosis (35.5×10^9/L with 70.4% granulocytes and 20.1% lymphocytes by automatic differential) and thrombocytosis (1192×10^9/L). The erythrocyte sedimentation rate was 89 mm/h. Chest x-ray was normal. Cerebrospinal fluid (CSF) was sent for cell count and biochemistry analysis, and to culture for bacteria, fungus and tuberculosis. CSF studies showed pleocytosis (white blood cell count 0.453×10^9/L; red blood cell count 0.015×10^9/L) with a neutrophil predominance (77% neutrophils, 14% lymphocytes, 9% monocytes). CSF glucose was 1.28 mmol/L, protein was 2.15 g/L and Gram stain showed no organisms.

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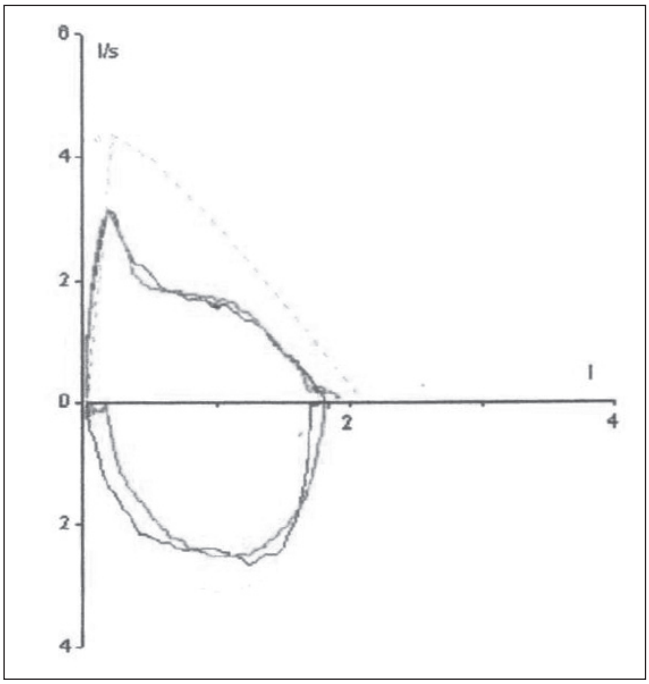

Figure 1) *Spirometry shows a nonreversible mid-expiratory flow limitation*

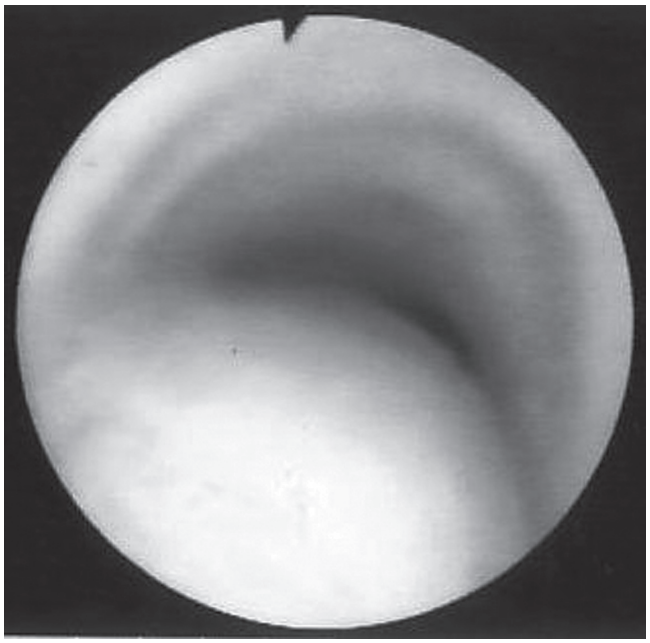

Figure 2) *Flexible bronchoscopy shows a reduced anterior-posterior diameter of distal trachea due to a prolapse of the distal part of the membranous trachea during expiration*

CASE 1 DIAGNOSIS: DISTAL TRACHEOMALACIA AND STENOSIS AT THE ORIGIN OF THE RIGHT MIDDLE LOBE BRONCHUS

While the chest x-ray and another sweat test were unremarkable, spirometry showed a mid-expiratory flow limitation on the flow-volume loops, unresponsive to bronchodilator challenge (Figure 1). This is suggestive of an intrathoracic airway stenosis. Exercise-induced bronchoconstriction could not be demonstrated (standardized 8 min exercise challenge using a treadmill). These results were suggestive of a partial central airway obstruction. Flexible bronchoscopy under general anesthesia with spontaneous ventilation confirmed a distal tracheomalacia with partial narrowing of the airway lumen due to a prolapse of the membranous trachea (Figure 2), and revealed a stenosis of the right middle lobe bronchus at its origin. The asthma medications were discontinued, and the girl and her family were taught home chest physiotherapy exercises including the use of portable positive expiratory pressure and flutter devices for the event of lower respiratory infections. Follow-up visits after more than one year were unremarkable except for two short-lived upper respiratory tract infections. The girl became physically active and her quality of life improved dramatically.

Tracheomalacia results from missing, hypoplastic or unusually soft tracheal cartilage. In the majority of cases, such as in the present case, the intrathoracic part and especially the lower one-third of the trachea is affected. The reduced cartilage support may lead to variable extensive collapse of the affected part of the trachea, notably when the intrathoracic pressure exceeds the intratracheal pressure as with forced expiration, eg, due to coughing or crying. Tracheomalacia may be primary (congenital) or secondary due to an external compression (eg, from vascular abnormalities such as a vascular ring due to a double aortic arch or an aberrant innominate artery), can be acquired (eg, as a consequence of long-term mechanical ventilation), or may be associated with a tracheoesophageal fistula or a connective tissue disorder. While long-lasting external compression (such as from vascular abnormalities) locally disturbs the development of the tracheal cartilage, tracheomalacia secondary to long-term intubation or tracheostomy with or without mechanical ventilation is most likely due to a chronic perichondritis resulting from pressure and local inflammatory processes (1).

Clinical symptoms include stridor, barking cough, wheezing, dyspnea, feeding problems, and recurrent and prolonged respiratory infections. Therefore, as in our case, the condition might be mistaken for other disorders, such as bronchial asthma (2). Tracheomalacia is predominantly symptomatic in infants and is one of the main causes of stridor in this age group. It is usually benign and self-limiting, with major improvement or resolution of symptoms within the first year of life, chiefly because of an increase in smooth muscle tone and rigidity of the cartilage. In more severe cases, tracheomalacia may be associated with significant morbidity and mortality. In all children with evidence of airway obstruction unresponsive to bronchodilators, the differential diagnoses need to be carefully explored.

Although invasive, flexible bronchoscopy with maintained spontaneous ventilation is considered the investigation of choice. On chest x-ray, an invisible carina or distal trachea can be suggestive. Fluoroscopy and computed tomography (CT) scanning can also be diagnostic, but require exposure to radiation. However, if a secondary tracheomalacia from an external

compression is suspected, further imaging with CT or magnetic resonance imaging is needed. In older children, a spirometry with flow-volume loops is useful and, as in the present patient with intrathoracic tracheomalacia, typically shows an expiratory flow limitation with a flow plateau.

Because tracheomalacia in the majority of cases is self-limited, a conservative approach should be attempted if clinically possible. In severe cases, continuous positive airway pressure, or if not sufficient or not feasible, surgical procedures such as aortopexy might be needed. Tracheostomy and long-term mechanical ventilation have been more readily used in the past, but are nowadays, due to the various associated problems, reserved for otherwise unmanageable cases. Beta$_2$-agonists should be used very cautiously in affected infants, because they could potentially worsen symptoms by reducing smooth muscle tone and thus increasing tracheal collapsibility (3).

CLINICAL PEARLS

- Tracheomalacia, even though a rare cause for persistent cough, wheezing and dyspnea on exertion, should be considered in all patients with asthma-like symptoms and bronchial obstruction without proper response to beta-agonists and inhaled steroids, especially when accompanied by frequent and prolonged respiratory tract infections. Other differential diagnoses to consider include, among others, gastroesophageal reflux, infections such as pertussis and *Mycoplasma pneumoniae*, cystic fibrosis, primary ciliary dyskinesia, immunodeficiencies, vocal cord dysfunction and habitual cough.
- While spirometry can be suggestive, a flexible bronchoscopy is indicated to confirm the diagnosis. Imaging studies, such as CT scans or magnetic resonance imaging, are required when a secondary tracheomalacia from external compression is suspected.
- Because the majority of cases are self-limited, a conservative approach should be attempted if clinically possible. For severe cases, other therapeutical options include continuous positive airway pressure, aortopexy, or, rarely, tracheal stents or tracheostomy. Beta$_2$-agonists in infants should be used with caution because they could potentially aggravate symptoms.

CONFLICT OF INTEREST: The authors have no conflicts of interest.

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CASE 2 DIAGNOSIS: MENINGITIS

The patient was diagnosed with presumed bacterial meningitis and started on intravenous (IV) antibiotics, including ceftriaxone and vancomycin. IV steroids were not given to this patient. A computed tomography of the head was ordered after admission to rule out a parameningeal focus of infection (Figure 3). Appearance was suggestive of a chronic hematoma, abscess or hygroma. On the same day, preliminary CSF culture showed group B streptococcus (GBS). Blood cultures remained negative. Given the patient's computed tomography findings and positive CSF culture, a decision was made to transfer the patient to a nearby paediatric intensive care unit. She remained on ceftriaxone and vancomycin. Repeat blood and urine cultures and purified protein derivative testing were negative. She was taken to the operating room. A burr hole was performed, fluid drained and a subdural drain placed. Cultures sent at the time of surgery revealed white blood cell (WBC) count 0.149×10^9/L (85 neutrophils, 64 monocytes); red blood cell count 25.45×10^9/L; glucose 4.72 mmol/L; and negative bacterial, acid-fast bacteria and fungal cultures. After obtaining susceptibility testing of the GBS organism, which grew from the initial lumbar puncture, antibiotics were switched from vancomycin and ceftriaxone to ampicillin and gentamicin. Repeat lumbar puncture showed a decrease in WBC count to 0.125×10^9/L, glucose of 1.72 mmol/L, and protein of 1.25 g/L. As per the infectious disease specialist, synergistic gentamicin was discontinued due to the improvement in the WBC count in the CSF. The plan was to continue ampicillin (300 mg/kg/day divided every 6 h) for 21 days.

The subdural collection in this case was presumed to be secondary to the GBS bacterial meningitis. Late-onset GBS typically presents at seven to 89 days of age. Sixty per cent of cases present as bacteremia without a source, but 35% of cases occur as meningitis and the remaining 5% as other focal infections (1). The incidence of late-onset GBS disease has remained relatively stable from 1990 to 2004 at 0.35 per 1000 live births for 1996 to 2004 (2), and is unchanged by peripartum antibiotic therapy. Treatment of meningitis in the neonate or young infant is focused on eradication of the offending organism. Initial empirical antibiotic treatment focuses on coverage of the typical organisms including GBS and other streptococci, Gram-negative enterics, staphylococci and *Listeria*. A typical antibiotic regimen includes third-generation cephalosporins and vancomycin. Once antibiotic susceptibility is available, treatment is narrowed. GBS generally is susceptible to penicillin G, ampicillin, vancomycin, and first- and

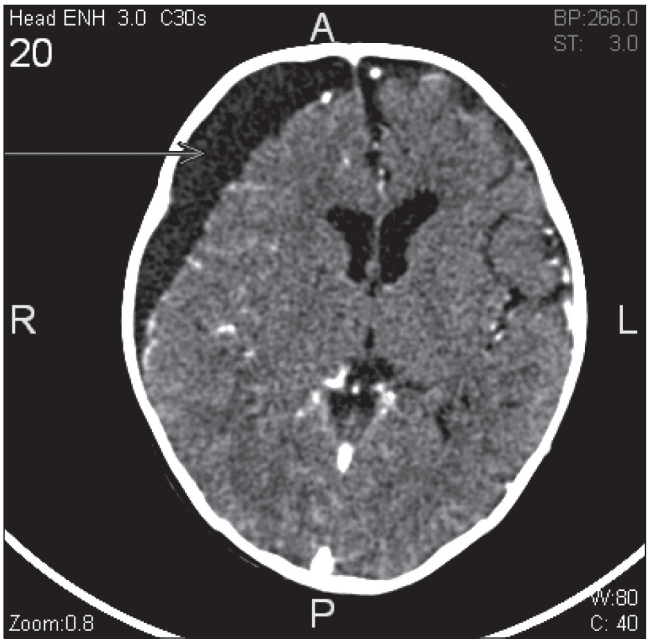

Figure 3) *A computed tomography scan of the head showing a 1.2 cm extra-axial fluid collection with a 6 mm leftward midline shift*

second- generation cephalosporins. Total duration of therapy should be 10 days for sepsis and 14 to 21 days for meningitis (1).

The differential diagnosis of isolated chronic subdural fluid collections in infants includes bacterial meningitis, head trauma (including nonaccidental and subdural hygromas) and, rarely, arachnoid cysts. Considering the fact that GBS grew from the CSF fluid of this child, it is likely the subdural fluid collection was a complication of the bacterial meningitis. A known documented neurological complication of meningitis includes subdural effusion, which may occur in approximately 10% to 20% of children with acute bacterial meningitis. While a bulging fontanel may be a sign of this complication, most children with a subdural effusion produce few symptoms and require no treatment. Subdural effusions rarely produce increased intracranial pressure and a shift of intracranial structures. They are rarely seen in adults with meningitis.

One part of the present case that is still a puzzle is how the child remained so well despite having fevers for two weeks before GBS meningitis was confirmed. One theory is that the initial fevers and symptoms may have been due to a viral illness, and later in the course of this illness, the child developed meningitis. However, the actual reason this child was clinically stable remains unknown.

CLINICAL PEARLS

- Late-onset GBS disease needs to be considered even in three- to four-month-old infants presenting with fever.
- Subdural fluid collections are a complication of bacterial meningitis.
- Child abuse should be on the differential of subdural hematomas, especially in the absence of other diagnostic findings.

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