Journal of Paediatric Respirology and Critical Care

A boy with adenoviral type 7 pneumonia complicated by organising pneumonia and heavy proteinuria

Chin-Pang WONG 黃展鵬[1] and Kwok-Chun WONG 黃國俊[2]

[1]Department of Paediatrics and [2]Department of Radiology, Kwong Wah Hospital, Hong Kong

Introduction

Respiratory failure is rather uncommon in children who present with pneumonia in the absence of complications. Organising pneumonia after viral pneumonia is one such complication. We presented here a case of adenoviral type 7 pneumonia, complicated by organising pneumonia and heavy proteinuria.

Case

A 1-year-old boy with good past health presented with cough and fever to a private doctor in late March 2011. He was admitted to a private hospital in Hong Kong initially and diagnosed to have adenoviral (subtype B) pneumonia by real-time PCR (RT-PCR) from nasopharyngeal aspirate (NPA) and chest X-ray (CXR). He was transferred to our unit because of increasing respiratory distress in early April 2011.

Upon arrival (Day 10 of disease), his general condition was satisfactory. He was in mild respiratory distress with respiratory rate 48/min and saturation by pulse oximetry (SpO_2) 88% in room air. There was no sign of meningitis or encephalitis. His heart rate, rhythm and blood pressure were normal. CXR showed patchy ill-defined consolidation over right middle zone, right lower zone and left lower zone. Ill-defined nodular opacities are seen over right upper zone (Figure 1). He was given oxygen supplement at 1 L/min via nasal cannula and put on IV cefotaxime and oral clarithromycin.

He developed increasing tachypnoea and higher oxygen dependency over the next few days after admission and fever persisted. Continuous positive airway pressure (CPAP) at 6 cm H_2O and FiO_2 30% was commenced since day 11 of disease. Non-invasive ventilation (NIV) with pressure support (PS) was started at 12/6 cm H_2O and FiO_2 40% to support his ventilation since day 13 of disease. In the same afternoon, he further deteriorated and required intubation and was ventilated with pressure-regulated volume-controlled (PRVC) mode at rate= 30/min, tidal volume= 60 ml and PEEP= 6 cmH_2O. Repeated CXR (Figure 2) showed progression of the airspace consolidation changes in right middle zone. IV vancomycin was added to cover drug-resistant

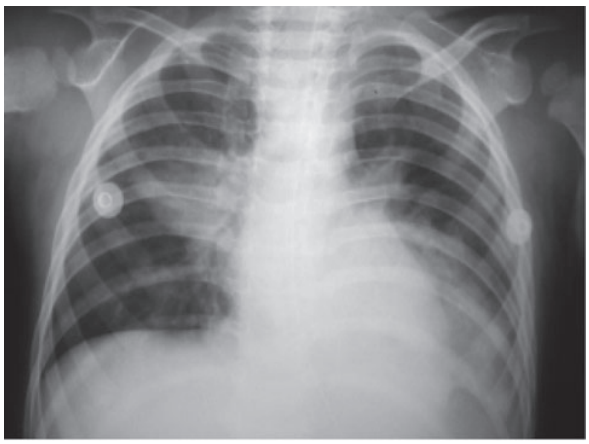

Figure 1. Day 10 CXR (on admission to our unit). Airspace consolidations over bilateral lower lobes.

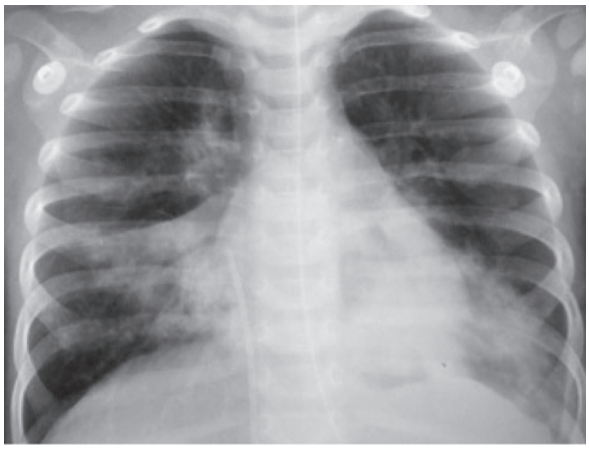

Figure 2. Day 12 CXR. Consolidations extended to right middle lobe.

Email: jeffcpwong@gmail.com

pneumococcus and community acquired methicillin-resistant Staphylococcus aureus (CA-MRSA). Computer Tomography (CT) thorax with contrast was performed on day 13 of disease (Figure 3). It showed multiple areas of consolidation with air-bronchogram over both lungs. Ground-glass opacities and sub-centimeter nodules with peribronchial distribution are noted over right middle lobe and posterior segment of right upper lobe. These findings are compatible with the typical features of organising pneumonia as discussed below. There was no sign of lung abscess.

Apart from adenoviral infection with evolving organising pneumonia, other differential diagnoses e.g. pneumonia caused by drug resistant bacteria, other concomitant viral or atypical bacterial infections were entertained. Mantoux test was negative. Early morning gastric lavage was negative for acid-fast bacilli. Blood culture was negative for bacterial growth. NPA showed negative immuno-fluorescence (IF) for Influenza A & B; Parainfluenza 1,2,3; RSV and negative PCR for Chlamydia trachomatis, metapneumovirus and Mycoplasma pneumoniae. Modified BAL showed pus cells on microscopy but negative gram stain and negative bacterial culture. Urine was negative for pneumococcal antigen and bacterial culture.

Based on the compatible radiological features and clinical context, he was managed as secondary organising pneumonia due to adenoviral infection with IV methylprednisolone at 1 mg/kg/dose Q12H since Day 12 evening. Lung biopsy was not performed for histological diagnosis as the parents refused consent. He responded well to methylprednisolone with resolution of fever within 24 hours after its commencement (Figure 4). He also showed improved lung mechanics and his ventilatory support could be weaned gradually. He could be extubated to CPAP support since Day 16 and became oxygen and ventilatory support independent since Day 19. The areas of consolidation over both lungs are partially resolved on Day 14 chest radiograph (Figure 5) and largely resolved on Day 23 chest radiograph (Figure 6).

He remained haemodynamically stable throughout the stay in hospital. His initial liver enzymes (AST and ALT) were raised to four times of the upper limits. They returned to normal before discharge. Clotting profile was normal. Complete blood picture (CBP) was unremarkable. C-reactive protein (CRP) was raised. The highest CRP was 43 mg/L upon admission and it reduced to normal gradually before discharge. His urinary output, renal function and electrolytes remained normal all along. However, he was also found to have heavy proteinuria (spot urine protein to creatinine ratio= 518 mg/mmol) after admission. It was complicated by hypoalbuminaemia requiring albumin infusion once. Autoimmune markers were negative and there was no hyperlipidaemia detected. The proteinuria responded to methylprednisolone treatment (Figure 7).

He was finally discharged on Day 23 of disease. His saturation was normal in room air. Physical examination revealed no signs of respiratory distress. But there were persistent crepitation over bilateral lower lobes. Adenovirus type 7 was later isolated from his previous NPA sample.

Discussion

Organising pneumonia (OP) is defined pathologically by the presence of buds of granulation tissue in distal air spaces (i.e. the alveoli, alveolar ducts, and possibly bronchioles).[1] The granulation tissue consists of fibroblasts and myofibroblasts embedded in a loose connective matrix.[2] This process is usually patchy with all lesions of the same age. It is regarded as a form of inflammatory process resulting from lung injury. However, this pathological pattern is not specific for any cause or disorder.

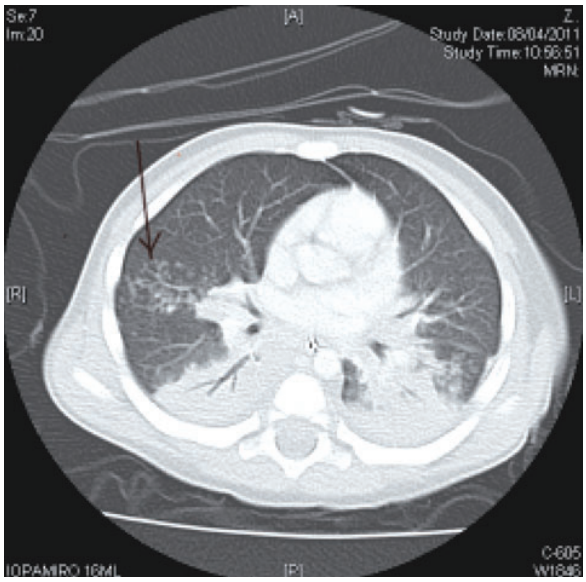

Figure 3. Day 13 CT. Thorax with contrast. Bilateral lower lobes airspace consolidation with air bronchogram. Centrilobular nodules were observed on right side (arrow).

Causes of OP could be classified into three categories according to its cause:[1] 1) OP of determined cause; 2) OP of undetermined cause but occurring in a specific context; and 3) cryptogenic (idiopathic) organising pneumonia (COP). For the first category, infection is a common cause of OP. In fact, this condition was once thought to be a failure of the usual resolution of infectious pneumonia. OP was found to be associated with mainly bacterial, but also in viral, parasitic and fungal infections (Table 1). Apart from infections, some of the drugs (Table 2) were also found to be associated with OP. For OP of undetermined cause but in a specific context, it was found to be associated with connective tissue disorders e.g. polymyositis and rheumatoid arthritis; bone marrow transplantation and haematological malignancies e.g. myelodysplasia and leukaemia.[1] For the third category

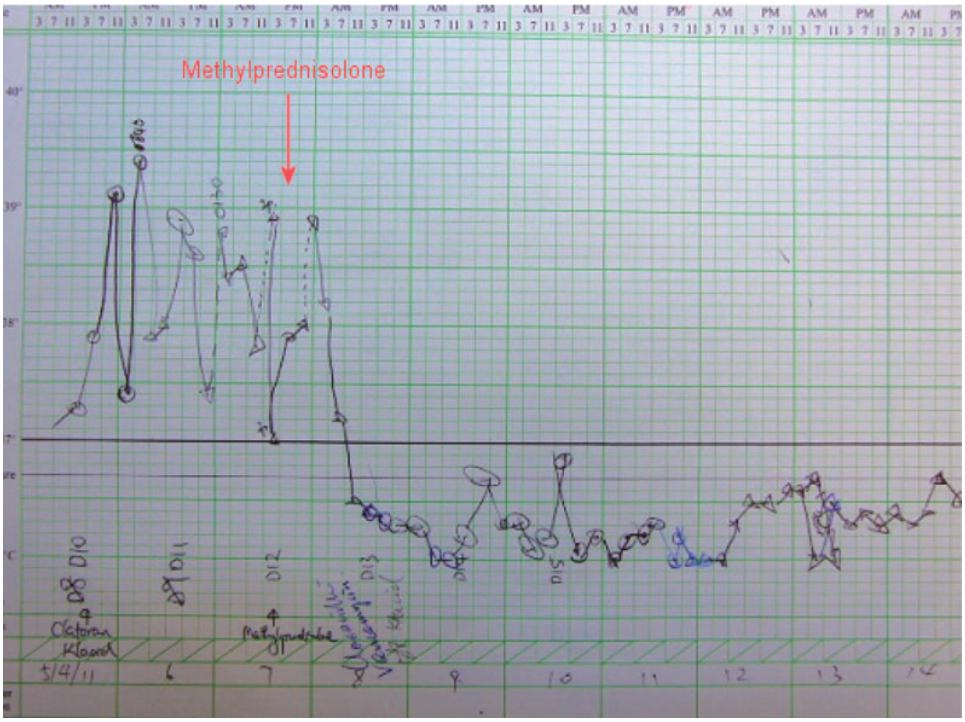

Figure 4. Temperature chart. Fever resolved within 24 hours after commencement of IV Methylprednisolone.

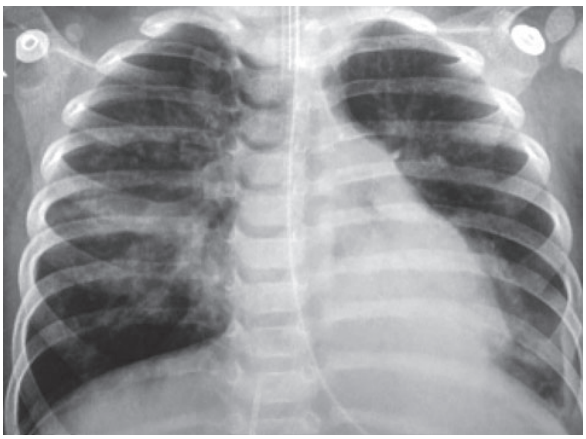

Figure 5. Day 14 CXR. Dramatic resolution of consolidation after Methylprednisolone.

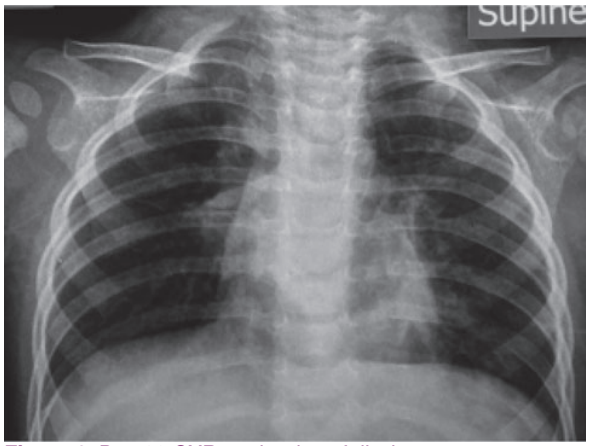

Figure 6. Day 23 CXR on the day of discharge.

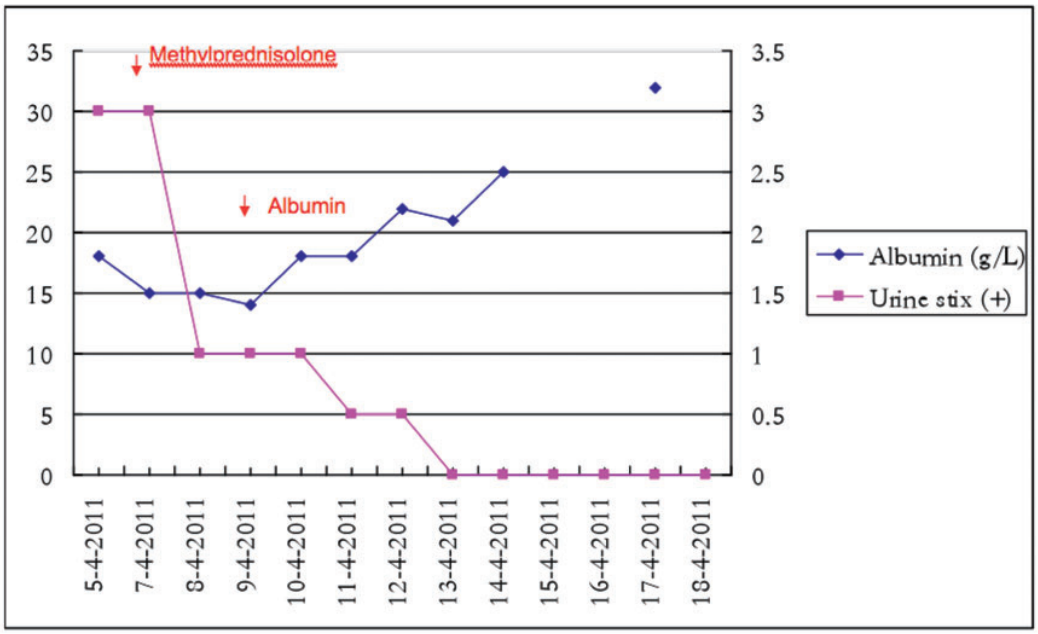

Figure 7. Progress of proteinuria and hypoalbuminaemia.

Table 1. Infectious causes of OP.

Bacteria	Chlamydia pneumoniae
	Coxiella burnetii
	Legionella pneumophila
	Mycoplasma pneumoniae
	Nocardia asteroides
	Pseudomonas aeruginosa
	Serratia marcescens
	Staphylococcus aureus
	Group B Streptococcus
	Streptococcus pneumoniae
Viral	Herpes virus
	Human immunodeficiency virus
	Influenza virus
	Parainfluenza virus
Parasites	Plasmodium vivax
Fungi	Cryptococcus neoformans
	Penicillium janthinellum
	Pneumocystis carinii

Adapted from Cordier JF. Organising pneumonia. Thorax 2000;55:318-28.[1]

Table 2. Drugs causing OP.

5-aminosalicylic acid
Acebutolol
Acramin FWN
Amiodarone
Amphotericin
Bleomycin
Busulphan
Carbamazepine
Cephalosporin
Cocaine
Gold salts
Hexamethonium
Interferon alpha
L-tryptophan
Mesalazine
Minocycline
Nilutamide
Paraquat
Phenytoin
Sotalol
Sulfasalazine
Tacrolimus
Ticlopidine
Vinabarbital-aprobarbital

Adapted from Cordier JF. Organising pneumonia. Thorax 2000;55:318-28.[1]

i.e. COP, previously known as idiopathic bronchiolitis obliterans organising pneumonia (BOOP), it is a distinct clinico-pathological entity that remains cryptogenic in many cases. Patients are usually aged 50-60 years with subacute onset of symptoms e.g. fever, non-productive cough, malaise, anorexia and weight loss. Symptoms usually develop over a few weeks after a viral like illness.

Although OP is a pathological diagnosis, some characteristic radiological features help with its diagnosis before lung biopsy as in our case. In terms of chest radiograph, though bilateral patchy areas of consolidation are not specific for organising pneumonia, the feature is the most common radiographic finding of organising pneumonia in CXR.[3,4] For typical CT features, OP commonly presents with predominant bilateral areas of consolidation involving subpleural region, with the lower and middle lobes affected more than the upper lobes.[5,6] Ground-glass opacities and nodules are also common findings in OP, which are usually randomly distributed.[6]

The most important characteristic of OP is its responsiveness to corticosteroids. Although the ideal dose and duration for complete healing are less certain, corticosteroid is the current standard treatment for OP. Clinical improvement usually takes place within 48 hours of commencement of corticosteroids. Radiographic improvement may take a longer period of time (i.e. several weeks). Recommended starting dose ranges from prednisolone 0.75 mg/kg/day to 1-1.5 mg/kg/day for 1-3 months. Relapses could occur but the final outcome is not significantly affected by the presence of relapses.

OP is a rare but important respiratory disease which is amenable to treatment. In the literature, only various case series were published. Its prevalence and incidence remained undetermined in adults.[7] Information of the condition is also scarce in children. It could be related to the difficulty of obtaining a lung biopsy in children. According to our review, only two patients with biopsy confirmed idiopathic bronchiolitis obliterans organising pneumonia (BOOP) were reported.[8]

In our case, the most important challenge was to make the presumptive diagnosis of OP based on clinical and radiological information while lung biopsy was not performed in such an unstable young child. We succeeded by recognising the clinical picture of treatment failure despite multiple antibiotics and supportive care to a "usual" community acquired pneumonia and more importantly, compatible CT findings as described earlier. Another interesting phenomenon observed in this case was the low serum albumin and heavy proteinuria on admission. The hypoalbuminaemia could be related to heavy proteinuria together with the on-going process of organising pneumonia which had formed a protein-rich matrix in the distal air spaces. There was not much mentioning of this phenomenon in our literature search. They responded very well to corticosteroids too.

Conclusion

We reported a 1-year-old patient with possible organising pneumonia secondary to adenoviral type 7 pneumonia responded to corticosteroids dramatically well clinically and radiologically.

References

1. Cordier JF. Organising pneumonia. Thorax 2000;55:318-28.
2. Cordier JF. Cryptogenic organizing pneumonia. Clin Chest Med 2004;25(4):727-38.
3. Montesinos JJ, Laguna MA. Thoracic case of the day case 1 cryptogenic organizing pneumonia. AJR Am J Roentgenol. 1998;171(3):835, 838-9.
4. Haddock JA, Hansell DM. The radiology and terminology of cryptogenic organizing pneumonia. Br J Radiol 1992;65(776): 674-80.
5. Preidler KW, Szolar DM, Moelleken S, Tripp R, Schreyer H. Distribution pattern of computed tomography findings in patients with bronchiolitis obliterans organizing pneumonia. Invest Radiol 1996;31(5):251-5.
6. Lee KS, Kullnig P, Hartman TE, Muller NL. Cryptogenic organizing pneumonia: CT findings in 43 patients. AJR Am J Roentgenol 1994;162(3):543-6.
7. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. This joint statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was adopted by the ATS board of directors, June 2001 and by the ERS Executive Committee, June 2001. Am J Respir Crit Care Med 2002;165(2):277-304
8. Inoue T, Toyoshima K, Kikui M. Idiopathic Bronchiolitis Obliterans Organizing Pneumonia (Idiopathic BOOP) in Childhood. Pediatr Pulmonol 1996;22(1):67-72.