Spontaneous pneumomediastinum and subcutaneous emphysema as a complication of asthma in children: case report and literature review

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Abstract
Background: Spontaneous pneumomediastinum (SPM) is an uncommon disorder. It is rarely reported in paediatric patients and may be accompanied by subcutaneous emphysema. It is usually benign and self-limiting, with only supportive therapy being needed, but severe cases may require invasive measures. Asthma exacerbations have classically been described as a cause of SPM. However, detailed descriptions in asthmatic children are scarce. We aimed at improving the current understanding of the features of SPM and subcutaneous emphysema, and outcomes, by means of a case report and a systematic review.

Methods: For the systematic review a literature search was performed in PubMed to identify reported cases of SPM in asthmatic children.

Results: The case a 10-year-old asthmatic girl with SPM is reported. The patient received an inhaled corticosteroid and long-acting beta2 agonist, in addition to sublingual immunotherapy (SLIT) with eventual control of asthma symptoms. Review: A total of 114 published cases were found since 1995, most of them in teenagers; no sex differences were observed. Clinical presentation was associated with an asthma exacerbation in a number of cases. Other presenting features were chest pain, dyspnoea, cough, and particularly acute swelling of the face, neck, and upper chest. Subcutaneous emphysema was present in most patients. Overall, three cases of pneumothorax and two cases of pneumorrhachis were reported. Therapy was mainly based on supportive care, rest, oxygen therapy, analgesics, steroids, and bronchodilators. All patients recovered spontaneously, in spite of a small initial increase in SPM in a few cases.

Conclusions: Early identification of patients at risk of SPM would avoid the high number of under-diagnosed cases. Patients should be treated not only with supportive therapy but also with measures to achieve control of the underlying cause (such as poorly controlled asthma).

Keywords: asthma, case report, children, spontaneous pneumomediastinum, subcutaneous emphysema, systematic review

Introduction
First reported by Hamman in 1939, spontaneous pneumomediastinum (SPM) refers to the presence of extraluminal air in the mediastinalum when chest trauma, oesophageal rupture, hollow viscous rupture, barotrauma, underlying lung disease, and other disorders have been excluded [Hamman, 1939; Crespo Marcos et al. 2006]. SPM is an uncommon disorder with an incidence of 0.0025% among emergency room visits [McMahon, 1976; Fitzwater et al. 2015]. SPM is rare in paediatric patients; however, occasional cases are reported to result from forced Valsalva’s manoeuvre due to cough, emesis, a first attack of wheeze, or asthma exacerbations [Bullaro and Bartoletti, 2007]. The first paediatric series was
reported by Thaler and colleagues in 1964 [Thaler et al. 1964]. In spite of being rare, SPM is probably under-diagnosed in children. Two incidence peaks have been reported; one of them in children under 7 years of age, probably due to lower airways infections, and the other in adolescents, due to asthmatic exacerbations and high airways infections [Lee et al. 2010; Reed et al. 2013].

Several studies have found a number of triggering factors for SPM [Cicak et al. 2009; Lee et al. 2010; Maithani et al. 2012]. As shown by Lee and colleagues, the most common ones are: lower airways infection (43.2%), asthma (21%), oesophageal rupture (5.4%), foreign body aspiration (2.7%), and diabetic ketoacidosis (2.7%), with a cause not being found in about 35.1% of patients (idiopathic SPM) [Lee et al. 2010]. In recent literature, some cases have been reported due to repeated scuba diving [Donoso Fuentes et al. 2009], spontaneous bronchial rupture [Maithani et al. 2012], high-frequency oscillatory ventilation [Hughes et al. 2012], influenza A (H1N1) virus infection [Ozdemir et al. 2010; Patra et al. 2011], drug rash with eosinophilia and systemic symptoms (DRESS) syndrome [Giri et al. 2011], hyperventilation due to anxiety states [Crespo Marcos et al. 2006], and inhaled drugs such as cocaine, cannabis, or ecstasy [Crespo Marcos et al. 2006].

As a clinical syndrome, pneumomediastinum was first reported in 1819 by Laennec, and its pathophysiology was described in 1939 by Macklin [Macklin, 1939]. A sudden increase in intra-alveolar pressure can cause alveolar rupture and a leak of air resulting in interstitial emphysema. Air may then reach the hilium and cause pneumomediastinum/pneumothorax, or may reach the lung periphery resulting in subpleural bullae (ruptured bullae may also cause pneumothorax). If leaked air spreads into subcutaneous tissues in chest wall and neck, through fascial planes, subcutaneous emphysema occurs. Extension into the rachis resulting in pneumorrhachis is rare but has also been reported in SPM [Eesa et al. 2006; Girard et al. 2014; Murayama and Gibo, 2014].

Clinical presentation includes the following triad: acute substernal chest pain (90%), subcutaneous emphysema (90%), and variably severe dyspnoea (30%) [Crespo Marcos et al. 2006]. Other reported symptoms are neck pain (20%) and low-to-moderate pain on swallowing (20%), whereas torticollis, dorsally-radiating pain, dysphonia, loss of lung dullness, and paradoxical pulse are very rare. Cyanosis, haemodynamic compromise, and even an associated pneumopericardium have been reported in most severe cases [Kucukosmanoglu et al. 2001].

Subcutaneous emphysema refers to air being present within subcutaneous tissue. Massive buildup of air can even be life-threatening due to chest compression, resulting in progressive hypoxemia and hypercapnia. Substernal crackles synchronous with heart systole (Hamman’s sign) are common (40–80%) [Donoso Fuentes et al. 2009]. Differential diagnoses include pneumomediastinum (though association is common), oesophageal perforation (Boerhaave syndrome if spontaneously developed), pneumothorax, hollow viscus rupture, chest trauma, foreign body aspiration, and acute coronary syndrome and pulmonary thromboembolism, both very rare findings in paediatric patients [Cicak et al. 2009; Donoso Fuentes et al. 2009; Reed et al. 2013]. In clinical practice, diagnosis should be confirmed by chest X-ray, including a lateral view to show extraluminal air [Donoso Fuentes et al. 2009]. When the diagnosis is uncertain, chest computerized tomography (CT) allows small amounts of air in the mediastinum and tracheal injuries to be detected [Donoso Fuentes et al. 2009; Cremaschini et al. 2012]. If an oesophageal rupture is suspected, an oesophagogram should be obtained [Crespo Marcos et al. 2006; Cicak et al. 2009].

SPM is usually benign and self-limiting, with only supporting therapy being needed; rest for 1–4 days, analgesia, oxygen, and clinical monitoring [Crespo Marcos et al. 2006; Donoso Fuentes et al. 2009; Cremaschini et al. 2012]. Underlying disorders should be treated, if possible [Cicak et al. 2009]. SPM usually resolves spontaneously within 2–7 days [Donoso Fuentes et al. 2009]. Severe cases, such as tension pneumomediastinum or tension pneumothorax may require invasive measures (e.g. subcutaneous drains) [Cicak et al. 2009].

Asthma exacerbations have classically been described as a cause of SPM [Hashim et al. 2013]. An increased airway pressure due to a chronic inflammatory disorder appears to reduce airway lumen. In children, SPM can appear with the first asthma exacerbation or can appear later as a complication of asthma [Versteegh and Broeders, 1991; Bullaro and Bartoletti, 2007]. However,
reported frequency of SPM in asthmatic patients is low [Lee et al. 2010]. In a series of 12,000 asthmatic children seen at a paediatric emergency department, SPM was observed in only 0.3% of patients [Stack and Caputo, 1996]. In a series of 479 patients aged 1–20 years hospitalized with asthma, SPM incidence was 5% [Eggleston et al. 1974]. Follow up of patients with SPM has shown subclinical or clinical asthma in some cases [Dekel et al. 1996], and asthma has been reported in 50% of SPM patients in a Taiwan series [Chiu et al. 2005].

Recently, a large systematic review of 600 patients with SPM, mostly young adults, was published [Dajer-Fadel et al. 2014]. Previous asthma was found in 13.7%; however, no specific data on asthmatic or paediatric patients were provided. Furthermore, very recently, a large series of SPM in paediatric patients has also been reported [Fitzwater et al. 2015]. In this retrospective review, 96 children with 99 episodes were identified and their characteristics and management were described; 38.4% were asthmatic. This will be a landmark study in the field and includes some specific data on management and outcomes in asthmatic children as a group, although no specific description of such patients is reported. Taking into account that detailed descriptions of SPM in asthmatic children are scarce, we aimed at improving current understanding of their features and outcomes regarding both SPM and underlying asthma, by means of a systematic review and a report of a typical case.

Case report
A 10-year-old asthmatic girl attended the emergency department with a persistent dry cough, dyspnoea and severe chest/neck pain, after having been exposed to environmental smoke and ash after a recent fire. Family history: father with asthma associated with sensitization to house dust mites (HDM); two brothers (aged 17 and 13) with allergic asthma associated with sensitization to HDM, olive, and Parietaria pollen, respectively. Personal history: preterm birth (36 weeks) and small for dates (2175 g). Hyperreactive airways after bronchiolitis at age 9.

Clinical examination: no fever, 40 breaths/min, 135 beats/min, sat O₂ 97%, blood pressure 105/50 mmHg, sallow skin, bags under the eyes, and normal peripheral perfusion. Chest: inspiratory substernal retraction; reduced vesicular breath sound and widespread persistent inspiratory/expiratory wheezing in left hemithorax. Centrally-located trachea, and heart sounds neither distant nor shifted. Palpable subcutaneous emphysema resulting in crepitus over lateral left neck area, left supraclavicular pit and first ipsilateral rib. Asthma attack was classified as severe based on a Wood–Downes–Ferres scoring of 8 [Wood et al. 1972; Ferres, 1988]. Laboratory tests: arterial blood gases: pH 7.33, pCO₂ 51.6 mmHg, pO₂ 18.1 mmHg, HCO₃ 27 mmol/l, base excess + 0.6 mmol/l. Biochemistry: C reactive protein 20.2 mg/l; normal renal function tests and electrolyte levels. Haematology: haemoglobin 14.7 g/dl; white blood cell count 12.7 × 10⁹/l; neutrophil count 77.3%; platelet count 303 × 10⁹/l. Imaging: chest X-ray showed pneumomediastinum with subcutaneous emphysema in supraclavicular and left neck area with no pneumothorax (Figure 1).

The patient was admitted and received noninvasive monitoring, analgesia, oxygen (5 l/min), inhaled bronchodilators (salbutamol and ipratropium), intravenous steroids, and omeprazole as a prophylaxis for ulcus. After 72 hours, a chest X-ray showed pneumomediastinum with subcutaneous emphysema in supraclavicular and left neck area with no pneumothorax (Figure 1).
Therapeutic Advances in Respiratory Disease

Prick tests for usual inhalants were performed. Based on European Academy of Allergy and Clinical Immunology recommendations, a positive test was defined as a 3 mm diameter papule 15 minutes after the test [European Academy of Allergy and Clinical Immunology, 1993; Bousquet et al. 2012]. Prick tests were positive for HDM: *Dermatophagoides pteronyssinus* (++++), *Dermatophagoides farinae* (+++), and for dog (+) and cat epithelia (++). Pulmonary function tests: forced vital capacity (FVC) 3.47 (104%), forced expiratory volume in 1 second (FEV1): 3.12 (105%), FEV1/FVC: 102%, forced expiratory flow (FEF 25–75%): of 99% of predicted by age, improving to 115% after bronchodilator administration peak expiratory flow. Bronchodilator test was positive and fractional exhaled nitric oxide (FeNO) using Mini Wright was 37.1 ppb NO (normal < 30 NO). A nonenhanced chest CT excluded bullae (Figure 2).

Clinical course: A diagnosis of severe persistent allergic asthma (allergy to HDM) was established. Asthma control was not adequate with an inhaled corticosteroid and long-acting beta2 agonist. Sublingual immunotherapy (SLIT) with STALORAL® 300 IR, containing a mix of HDM, was added, which proved highly efficient, with eventual control of asthma symptoms.

**Literature review method**
A systematic review was carried out in PubMed to identify reported cases of SPM in asthmatic children. Search terms were ‘spontaneous pneumomediastinum’ and ‘asthma’. Only English-language articles published after 1 Jan 1995 were included. The search string was: (spontaneous[All Fields] AND (‘mediastinal emphysema’[MeSH Terms] OR (‘mediastinal’[All Fields] AND ‘emphysema’[All Fields]) OR ‘mediastinal emphysema’[All Fields]) AND (‘pneumomediastinum’[All Fields]) AND (‘asthma’[MeSH Terms] OR ‘asthma’[All Fields]) AND English[lang] AND (’1995/01/01’[PDAT]: ’3000/12/31’[PDAT]). Full articles were retrieved for those references that included asthmatic patients <18 years of age based on a review of titles and abstracts. A manual search for additional references in selected articles (snowball method) was also performed. Articles providing a description of one or several asthmatic patients <18 years of age with SPM were selected. Data from reported cases were abstracted and tabulated.

**Results**
Overall, 63 references were identified. A total of 35 were selected for full article retrieval and of these, 17 articles complying with the inclusion criteria were found. A total of 114 cases were identified and tabulated (Table 1). Cases had been reported from Europe, Asia, and the Americas. The age range was 1–18 years, but most patients were teenagers, with a similar number of cases having been reported in boys and girls.

Clinical presentation was associated with an asthma exacerbation in a number of cases. However, in four patients, SPM was a sign of their first asthma exacerbation or first time wheezing. Other presenting features were chest pain, dyspnoea, cough, and particularly acute swelling of the face, neck, and upper chest. Subcutaneous emphysema was present in most patients.

Diagnosis was most commonly achieved by means of chest X-ray in older reports (sensitivity 89.1% in a reported series) and CT in most recent ones. Lateral neck radiographs appear to be very useful in doubtful cases. Most patients had no complications, although three cases of pneumothorax and two cases of pneumorrhachis were reported.

Therapy was mainly based on supportive care, rest, oxygen therapy, analgesics, steroids, and...
Table 1. Reported cases of SPM in asthmatic children.

| Reference | Year  | Country | N    | Mean age (or individual age) | Sex | Presentation | Diagnostic imaging | Complications | Therapy | Course | Length of hospital stay (days) |
|-----------|-------|---------|------|-------------------------------|-----|---------------|-------------------|---------------|---------|--------|-------------------------------|
| [Fitzwater et al. 2015] | 2015 USA | 38      | 10.3 | –                            | –   | –             | –                 | –             | –       | resolution | no difference from nonasthmatics |
| [Firinci et al. 2014] | 2014 Turkey | 1      | 12   | M                            | chronic coughing | CT | no | inhaled steroids, analgesics | resolution | a few days |
| [Girard et al. 2014] | 2014 France | 1      | 18   | F                            | acute swelling of the face, neck, and upper chest | CT | pneumorrhachis | rest, bronchodilators, corticosteroids | resolution | 7 |
| [Wong et al. 2013] | 2013 Taiwan | 15     | n = 2 under 6 years, n = 13 over 6 years | acute exacerbation | chest X-ray [sensitivity, 89.1%, lateral neck radiographs] | no | – | – | resolution | 5.8 (over 6 years), 11.4 (under 6 years) |
| [Ojima et al. 2012] | 2012 Japan | 2      | 15–17 | neck and chest pain, dyspnoea and discomfort in the chest | chest and neck X-rays | no | – | – | resolution | 4 or 5 |
| [Lee et al. 2010] | 2010 Taiwan | 4      | 15.8 | 2 M 2 F | – | associated pneumothorax [n = 3] | analgesics, rest, oxygen therapy | resolution | 4.2 |
| [Romero and Trujillo, 2010] | 2010 Venezuela | 1      | 17   | F | severe asthma exacerbation | chest X-rays | no | oxygen therapy, parenteral steroids, bronchodilators | resolution | 2 |
| [Chen et al. 2010] | 2009 Taiwan | 6      | –    | – | – | – | – | – | resolution | 4.8 (significantly longer than in nonasthmatics) |
| [Lee et al. 2009] | 2009 Taiwan | 2      | <10 | 2 F | wheezing, first attack of asthma | – | no | bronchodilators | resolution | – |
| [Bullaro and Bartoletti, 2007] | 2007 USA | 1      | 4    | F | first-time wheezing | chest X-ray [spinnaker sail sign and continuous diaphragm sign] | no | supportive care | resolution | – |
| [Eesa et al. 2006] | 2006 India | 1      | 18   | M | swelling over the neck and upper chest after a mild episode of bronchospasm | CT | pneumorrhachis | – | resolution | – |
| [Ameh et al. 2006] | 2006 United Kingdom | 1      | 1    | M | cough, dyspnoea, first attack of asthma | chest X-ray | no | salbutamol, steroids, antibiotics, oxygen therapy | resolution | 7 |
| [Chiu et al. 2005] | 2005 Taiwan | 8      | 9.6  | – | asthma exacerbations | chest X-rays | – | – | resolution | 3.3 |
| [Kucukosmanoglu et al. 2001] | 2001 Turkey | 1      | 4    | F | dyspnoea, chest pain, palpitation and cough | chest X-rays | no | salbutamol, budesonide, oxygen therapy | resolution | 10 |
| [Ba-Ssalamah et al. 1999] | 1999 Austria | 1      | 18   | M | severe respiratory compromise | chest X-rays | no | medical treatment for status asthmaticus | resolution | 12 |
| [Caramella et al. 1997] | 1997 Italy | 1      | 13   | M | coughing during an asthmatic attack | CT | fever | steroids, bronchodilators, antibiotics | resolution | 8 |
| [Stack and Caputo, 1996] | 1996 USA | 30     | 11.8 | 16 M 14 F | chest pain was reported in 27% subcutaneous emphysema was detected in 73% | X-rays | no | – | small increase of SPM [n = 3] | resolution | – |

CT, computerized tomography; F, female; M, male; SPM, spontaneous pneumomediastinum.
bronchodilators. All patients recovered spontaneously, in spite of a small initial increase in SPM in a few cases. However, in the largest reported series, three cases of recurrent SPM were found during a prolonged follow up. All patients were discharged after 2–12 days, and a series comparing asthmatic versus nonasthmatic SPM patients showed no difference in length of stay.

**Discussion**
SPM is an uncommon disease that usually has a benign course. It should be treated conservatively unless a complication requires using invasive procedures. Although few cases of SPM have been fully described in asthmatic children, our review confirms that asthma, and asthma exacerbation, appears to be one of the most prominent risk factors for SPM (Table 1). SPM has been reported both as a consequence of an asthma exacerbation and as a sign of a first asthma attack in children. SPM may be associated with poorly-controlled asthma. A majority of cases appear to occur in teenagers and no obvious differences in incidence have been reported between the sexes. Chest X-ray is increasingly being replaced by CT to confirm diagnosis, whereas pneumomediastinum has recently been reported as a sonographic mimic of pneumothorax [Saracino and Tessaro, 2015]. Clinical course in reported cases has been generally favourable with spontaneous recovery being achieved after hospital admission and supportive care. Very recently, unusual cases of SPM have also been reported in nonasthmatic children with exercise-induced bronchoconstriction [Anantasit et al. 2015], a syndrome causing transient narrowing of lower airway either in the presence or the absence of clinical asthma [Weiler et al. 2010]. The usual course of SPM is spontaneous resolution after a few days, if supporting therapy is provided to the patient and good asthma control is achieved. Recurrent SPM may occur in asthmatic children, thus, from our point of view, careful control of asthma appears to be particularly important in such patients. Alpha1-antitrypsin deficiency screening has been recently recommended in patients with asthma and was performed in our patient for differential diagnosis purposes [Siri et al. 2013; Craig, 2015]. In our patient, SPM and subcutaneous emphysema were associated with severe asthma. Control of asthma symptoms proved particularly difficult to achieve. To our knowledge, this is the first patient reported with asthma-associated SPM that has been treated with SLIT. Our case suggested SLIT could change asthma course in children and may avoid potential complications such as SPM.

In conclusion, it is important to stress the importance of an early identification of patients at risk of SPM, which would avoid the high number of under-diagnosed cases. Moreover, patients should be treated not only with supportive therapy but also with measures to achieve control of the underlying cause of SPM (such as poorly-controlled asthma).

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**References**
Ameh, V., Jenner, R., Jilani, N. and Bradbury, A. (2006) Spontaneous pneumopericardium, pneumomediastinum and subcutaneous emphysema: unusual complications of asthma in a 2-year-old boy. *Emerg Med J* 23: 466–467.

Anantasit, N., Manuyakorn, W., Anantasit, N., Choong, K. and Preuthipan, A. (2015) Spontaneous pneumomediastinum in non-asthmatic children with exercise-induced bronchoconstriction. *Am J Case Rep* 16: 648–651.

Ba-Ssalamah, A., Schima, W., Umek, W. and Herold, C. (1999) Spontaneous pneumomediastinum. *Eur Radiol* 9: 724–727.

Bousquet, J., Heinzerling, L., Bachert, C., Papadopoulos, N., Bousquet, P., Burney, P. *et al.* (2012) Practical guide to skin prick tests in allergy to aeroallergens. *Allergy* 67: 18–24.

Bullaro, F. and Bartoletti, S. (2007) Spontaneous pneumomediastinum in children: a literature review. *Pediatr Emerg Care* 23: 28–30.

Caramella, D., Bulleri, A., Battolla, L., Pifferi, M., Baldini, G. and Bartolozzi, C. (1997) Spontaneous epidural emphysema and pneumomediastinum during an asthmatic attack in a child. *Pediatr Radiol* 27: 929–931.

Chen, I., Tseng, C., Hsu, J., Wu, J. and Dai, Z. (2010) Spontaneous pneumomediastinum in adolescents and children. *Kaohsiung J Med Sci* 26: 84–88.
Chiu, C., Wong, K., Yao, T. and Huang, J. (2005) Asthmatic versus non-asthmatic spontaneous pneumomediastinum in children. *Asian Pac J Allergy Immunol* 23: 19–22.

Cicak, B., Verona, E., Mihatov-Stefanovic, I. and Vrsalovic, R. (2009) Spontaneous pneumomediastinum in a healthy adolescent. *Acta Clin Croat* 48: 461–467.

Craig, T. (2015) Suspecting and testing for alpha-1 antitrypsin deficiency – an allergist’s and/or immunologist’s perspective. *J Allergy Clin Immunol Pract.* 3: 506–511.

Cremaschini, G., Sassi, G., Tedoldi, S., Corna, A., Vaccaro, T., Cipolletta, E. et al. (2012) [An unusual pneumomediastinum case in a child caused by spontaneous bronchial rupture]. *Minerva Pediatr* 64: 243–249.

Crespo Marcos, D., Iglesias Fernandez, C., Marquez De La Plata, L., Panadero Carlavilla, E. and Vazquez Lopez, P. (2006) [Spontaneous idiopathic pneumomediastinum: apropos of a case]. *An Pediatr (Barc)* 64: 106–111.

Dajer-Fadel, W., Arguero-Sanchez, R., Ibarra-Perez, C. and Navarro-Reyno, F. (2014) Systematic review of spontaneous pneumomediastinum: a survey of 22 years’ data. *Asian Cardiovasc Thorac Ann* 22: 997–1002.

Dekel, B., Paret, G., Szeinberg, A., Vardi, A. and Barzilay, Z. (1996) Spontaneous pneumomediastinum in children: clinical and natural history. *Europ J Pediatr* 155: 695–697.

Donoso Fuentes, A., Cruces, P. and Bertran Salinas, K. (2009) [Immersion-induced spontaneous pneumomediastinum]. *An Pediatr (Barc)* 70: 95–97.

Eesa, M., Kandpal, H., Sharma, R. and Misra, A. (2006) Spontaneous pneumorrhachis in bronchial asthma. *Acta Radiol* 47: 672–674.

Eggleton, P., Ward, B., Pierson, W. and Bierman, C. (1974) Radiographic abnormalities in acute asthma in children. *Pediatrics* 54: 442–449.

European Academy of Allergy and Clinical Immunology (EAACI) (1993) Position paper: allergen standardization and skin tests. *Allergy* 48: 48–82.

Ferres, J. (1988) Comparison of two nebulized treatments in wheezing infants. *Eur Respir J* 1: 306.

Firinci, F., Ozguler, F., Dogan, M., Kocyigit, A. and Mete, E. (2014) Spontaneous pneumomediastinum in childhood: report of an adolescent case diognose with asthma. *Tuberk Toraks* 62: 253–254.

Fitzwater, J., Silva, N., Knight, C., Malvezzi, L., Ramos-Frizarry, C. and Burnweit, C. (2015) Management of spontaneous pneumomediastinum in children. *J Pediatr Surg* 50: 983–986.

Girard, C., Khouatra, C., Cordier, J. and Cottin, V. (2014) Spontaneous pneumomediastinum associated with pneumorrhachis. *Am J Respir Crit Care Med* 189: e69.

Giri, P., Roy, S., Bhattacharyya, S., Pal, P. and Dhar, S. (2011) Dress syndrome with sepsis, acute respiratory distress syndrome and pneumomediastinum. *Indian J Dermatol* 56: 763–765.

Hamman, L. (1939) Spontaneous mediastinal emphysema. *Bull Johns Hopkins Hosp* 64: 1–21.

Hashim, T., Chaudry, A., Ahmad, K., Imhoff, J. and Khouzam, R. (2013) Pneumomediastinum from a severe asthma attack. *JAAPA* 26: 29–32.

Hughes, D., Judge, T. and Spigland, N. (2012) Tension pneumoperitoneum in a child resulting from high-frequency oscillatory ventilation: a case report and review of the literature. *J Pediatr Surg* 47: 397–399.

Kucukosmanoglu, O., Karakoc, G., Yilmaz, M., Altintas, D. and Guneser Kendirli, S. (2001) Pneumomediastinum and pneumopericardium: unusual and rare complications of asthma in a 4 years old girl. *Allergol Immunopathol (Madrid)* 29: 28–30.

Lee, C., Wu, C. and Lin, C. (2009) Etiologies of spontaneous pneumomediastinum in children of different ages. *Pediatr Neonatol* 50: 190–195.

Lee, C., Wu, C. and Lin, C. (2010) Etiologies of spontaneous pneumomediastinum in children in middle Taiwan. *Pediatr Pulmonol* 45: 869–873.

Macklin, C. (1939) Transport of air along sheaths of pulmonic blood vessels from alveoli to mediastinum: clinical implications. *Arch Intern Med* 64: 913–926.

Maithani, T., Dey, D. and Sharma, C. (2012) Spontaneous cervicofacial subcutaneous emphysema secondary to pneumomediastinum in an otherwise asymptomatic child. *Ear Nose Throat J* 91: e9–e11.

McMahon, D. (1976) Spontaneous pneumomediastinum. *Am J Surg* 131: 550–551.

Murayama, S. and Gibo, S. (2014) Spontaneous pneumomediastinum and Macklin effect: overview and appearance on computed tomography. *World J Radiol* 6: 850–854.

Ojima, H., Fukai, Y., Soda, M. and Kuwano, H. (2012) Asymptomatic spontaneous cervical and mediastinal emphysema. *BMJ Case Rep* 2012. doi:10.1136/bcr-2012-006248

Ozdemir, H., Kendirli, T., Dincaslan, H., Ciftci, E. and Ince, E. (2010) Spontaneous pneumomediastinum in a child due to 2009 pandemic influenza A (H1N1) virus. *Turk J Pediatr* 52: 648–651.
Thaler, M., Krieger, E., McKee, J. and Fearon, B. (1964) Treatment of mediastinal and subcutaneous emphysema complicating asthma in children: report of a case. *J Pediatr* 65: 75–80.

Versteegh, F. and Broeders, I. (1991) Spontaneous pneumomediastinum in children. *Eur J Pediatr* 150: 304–307.

Weiler, J., Anderson, S., Randolph, C., Bonini, S., Craig, T., Pearlman, D. *et al.* (2010) Pathogenesis, prevalence, diagnosis, and management of exercise-induced bronchoconstriction: a practice parameter. *Ann Allergy Asthma Immunol* 105: s1–s47.

Wong, K., Wu, H., Lai, S. and Chiu, C. (2013) Spontaneous pneumomediastinum: analysis of 87 pediatric patients. *Pediatr Emerg Care* 29: 988–991.

Wood, D., Downes, J. and Lecks, H. (1972) A clinical scoring system for the diagnosis of respiratory failure. Preliminary report on childhood status asthmaticus. *Am J Dis Child* 123: 227–228.

Patra, P., Nayak, U. and Sushma, T. (2011) Spontaneous pneumomediastinum in H1N1 infection. *Indian Pediatr* 48: 976–977.

Reed, J., Larson, K. and Hsu, B. (2013) Spontaneous pneumomediastinum with subcutaneous emphysema: report of two pediatric cases. *S D Med* 66: 89, 91–93.

Romero, K. and Trujillo, M. (2010) Spontaneous pneumomediastinum and subcutaneous emphysema in asthma exacerbation: the Macklin effect. *Heart Lung* 39: 444–447.

Saracino, C. and Tessaro, M. (2015) Pneumomediastinum as a sonographic mimic of pneumothorax. *J Ultrasound Med* 34: 1521–1522.

Siri, D., Farah, H. and Hogarth, D. (2013) Distinguishing alpha1-antitrypsin deficiency from asthma. *Ann Allergy Asthma Immunol* 111: 458–464.

Stack, A. and Caputo, G. (1996) Pneumomediastinum in childhood asthma. *Pediatr Emerg Care* 12: 98–101.