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

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Introduction

First reported by Hamman in 1939, spontaneous pneumomediastinum (SPM) refers to the presence of extraluminal air in the mediastinum when chest trauma, oesophageal rupture, hollow viscus 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 build-up 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,

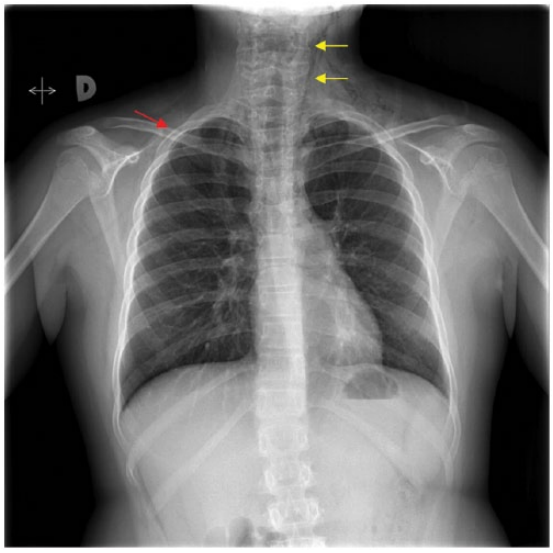

Figure 1. Pneumomediastinum (red arrow) with subcutaneous emphysema in supraclavicular and left neck regions (yellow arrows).

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 O_2 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, pCO_2 51.6 mmHg, pO_2 18.1 mmHg, HCO_3 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 $\times$ 10^9/l; neutrophil count 77.3%; platelet count 303 $\times$ 10^9/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 a substantially reduced amount of gas in the neck and mediastinum. The patient was discharged at day 4; prescribed therapy at discharge included budesonide 200 µg twice daily with AeroChamber, and she was advised not to perform extreme physical activity to avoid pneumothorax development due to potential bullae.

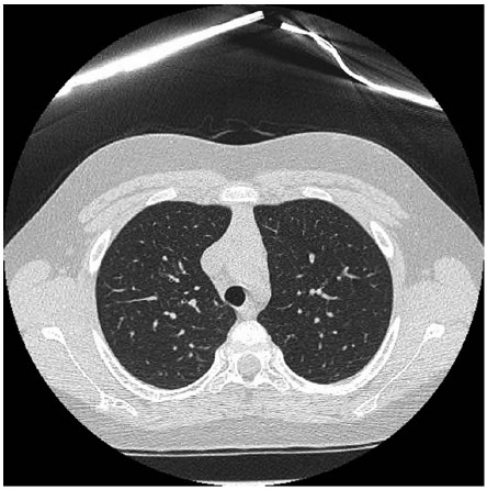

Figure 2. Chest computerized tomography: no subpleural bullae are observed.

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 (FEV_1): 3.12 (105%), FEV_1/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] OR '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 recurrent pneumomediastinum ($n = 3$)	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	–			chest X-rays	–	–	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: 106–107.

Dajer-Fadel, W., Arguero-Sanchez, R., Ibarra-Perez, C. and Navarro-Reynoso, 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. *Eur 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.

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

Fitzwater, J., Silva, N., Knight, C., Malvezzi, L., Ramos-Irizarry, 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 pneumorrachis. *Am J Respir Crit Care Med* 189: e69.

Giri, P., Roy, S., Bhattyacharya, 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 (Madr)* 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.

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.

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.