

## THE MANY FACES OF PNEUMOMEDIASTINUM: AN OBSERVATIONAL STUDY

Narendra Kumar Narahari<sup>1</sup>, Anu Kapoor<sup>2</sup>, Mohammed Ismail Nizam<sup>3</sup>

<sup>1</sup>Assistant Professor, Department of Respiratory Medicine, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad.

<sup>2</sup>Associate Professor, Department of Radiology & Imaging, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad.

<sup>3</sup>Assistant Professor, Department of Emergency Medicine, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad.

### ABSTRACT

#### BACKGROUND

Pneumomediastinum is an uncommon condition which is defined by the presence of air in the mediastinum. It may result from a number of causes, but at times the underlying aetiology remains obscure. The present study aims to review the clinical and imaging features in patients who presented with pneumomediastinum alone or in association with other findings in order to establish the aetiological diagnosis. We report here, a series of cases with pneumomediastinum of various unusual aetiologies and also the clinical profile, predisposing factors and outcome of these patients along with the associated complications.

#### METHODS

We retrospectively reviewed the records of all patients who presented to the respiratory unit of our hospital with the diagnosis of pneumomediastinum over a period of 2 years from 2013-2015. The cases of pneumomediastinum resulting from trauma and iatrogenic causes were excluded from the study.

#### RESULTS

A total of six patients (4 males and 2 females) with pneumomediastinum were identified during the study period after applying the exclusion criteria. The most common presenting symptom in these cases was shortness of breath followed by dry cough, chest pain and fever. Subcutaneous emphysema and Hamman sign was identified in one patient each. Of the six cases, pre-existing lung disease was identified in 3 patients and these included connective tissue disease related interstitial lung disease in two cases and combined pulmonary fibrosis and emphysema in one case. In the remaining three cases, the causes of pneumomediastinum were *Pneumocystis carinii* pneumonia (PCP) in HIV positive patient, pulmonary tuberculosis in another and spontaneous oesophageal perforation in the third. Coexisting pneumothorax was present in 3 out of 6 cases. The mean duration of hospital stay in these six patients was 8 days. No recurrence of pneumomediastinum was seen in any of the six patients during six months of followup.

#### CONCLUSIONS

Pneumomediastinum is a condition with diverse aetiologies. It is important to identify the underlying cause of pneumomediastinum in order to manage these patients. Spontaneous pneumomediastinum needs to be differentiated from secondary pneumomediastinum as the latter is a more morbid condition and has to be managed promptly in order to avoid unfavourable outcome.

#### KEYWORDS

Pneumomediastinum, Spontaneous Pneumomediastinum, Connective Tissue Related Interstitial Lung Disease, Combined Pulmonary Fibrosis and Emphysema, Pneumothorax, Subcutaneous Emphysema, Hamman's Sign.

**HOW TO CITE THIS ARTICLE:** Narahari NK, Kapoor A, Nizami MI. The many faces of pneumomediastinum: An observational study. *J. Evid. Based Med. Healthc.* 2016; 3(51), 2598-2604. DOI: 10.18410/jebmh/2016/571

**INTRODUCTION:** Pneumomediastinum is an uncommon condition which is defined by the presence of air in the mediastinum.<sup>[1]</sup> It is further classified into spontaneous and secondary pneumomediastinum. Spontaneous pneumomediastinum (SPM) is defined as presence of free air in the mediastinum that is not preceded by trauma, surgery, or other medical procedures. It may occur with or without a concomitant pneumothorax.<sup>[2]</sup>

Secondary pneumomediastinum develops as a result of a specific injury or pathologic condition. Associated pneumothorax and mortality are more common with secondary pneumomediastinum.<sup>[3]</sup> Spontaneous pneumomediastinum which was originally described by Louis Hamman in 1939 is a benign condition, presenting in young adults exposed to a sudden pressure change within the intrathoracic cavity.<sup>[1]</sup> The pathophysiology of SPM was initially described by Macklin.<sup>[4]</sup> and is based on pressure gradient between the alveoli and the lung interstitium.

According to this sudden increase in intrathoracic pressure causes increase in intra-alveolar pressure. The increased alveolar pressure due to cough or over distension compared to decreased perivascular pressure in the interstitium creates a pressure gradient needed for terminal alveolar rupture.

*Financial or Other, Competing Interest: None.*

*Submission 28-05-2016, Peer Review 11-06-2016,*

*Acceptance 21-06-2016, Published 27-06-2016.*

*Corresponding Author:*

*Dr. Narendra Kumar Narahari,*

*Assistant Professor, Department of Respiratory Medicine,*

*Nizam's Institute of Medical Sciences, Punjagutta,*

*Hyderabad-500082, Telangana.*

*E-mail: drnarendrajipmer@gmail.com*

*DOI: 10.18410/jebmh/2016/571*

This leads to leakage of air into the interstitium along the broncho vascular sheaths and follows a centripetal course towards the hilum and mediastinum along a pressure gradient. The air may further track along the tissue planes causing surgical emphysema. The most common predisposing conditions in SPM were asthma, smoking, interstitial lung disease (ILD) and recent history of upper respiratory tract infection.<sup>[2,3,5]</sup> Emesis, cough, strenuous physical activity and drug abuse were the most common triggering factors.<sup>[2,3,5,6]</sup> However no triggering factor may be identified in a large number of cases as reported in the literature.<sup>[3,7,8]</sup>

Secondary pneumomediastinum develops as a consequence of a distinct underlying pathology or as a result of blunt thoracic trauma, high-pressure mechanical ventilation, pulmonary barotrauma in divers, intrathoracic infections, especially *Pneumocystis carinii* pneumonia (PCP), cavitary pulmonary disease, surgical procedures, and oesophageal or tracheobronchial disruptions.<sup>[9]</sup> It is essential to rule out a secondary pathologic event like major oesophageal or tracheobronchial disruption, which is a surgical emergency.<sup>[9]</sup>

The purpose of this study is to report our experience in the management of the patients with pneumomediastinum of varied and unusual aetiologies. The clinical presentation, diagnostic evaluation, radiologic findings, and outcome are analysed along with an extensive review of the existing literature.

**MATERIAL AND METHODS:** A manual search of all medical records maintained in the respiratory unit of our hospital was carried out to identify the cases of pneumomediastinum from January 2013 to December 2015. All patients with radiologically confirmed diagnosis of pneumomediastinum were included in the study and reviewed for the underlying aetiologies. Cases of pneumomediastinum following trauma, surgical or medical procedure related, and cardiopulmonary resuscitation were excluded.

The patient's demographic data, presenting symptoms and signs, precipitating events, pre-existing lung disease if any, length of hospital stay, treatment received and complications if any, were extracted from the case records. Any such activity or event preceding the clinical presentation, which were likely to have caused raised intrathoracic pressure were considered to be the most likely precipitating factor for pneumomediastinum.

**RESULTS:** The demographic data, clinical presentation, precipitating events, hospital course and management of patients presenting with pneumomediastinum are summarised in Table 1. A total of six patients (4 males and 2 females) were diagnosed with pneumomediastinum during the study period. Of the 637 patients admitted to the respiratory medicine unit during the study period, pneumomediastinum was diagnosed in 6 patients constituting 0.64%. The mean age at presentation was 31 years.

The most common presenting symptom was shortness of breath in 5 (83%) patients followed by cough in 4 (66%), chest pain in 3 (50%), fever in 3 (50%). Throat pain, dysphagia and haemoptysis was noted in one patient each. Subcutaneous emphysema and Hamman's sign was detected in one patient each constituting 16% of the total. Pre-existing lung disease was identified in 3 patients. Pneumomediastinum associated with underlying structural lung disease detected on imaging was classified as secondary spontaneous in our study. These causes included scleroderma, dermatomyositis related interstitial lung disease (ILD) and combined pulmonary fibrosis and emphysema (CPFE) in one patient each. Other causes of secondary pneumomediastinum included *Pneumocystis carinii* related interstitial pneumonia, tuberculosis and spontaneous oesophageal perforation.

The most common precipitating factors were intractable cough, strenuous physical activity, vomiting and respiratory infections. Chest radiograph revealed presence of pneumomediastinum in five of the six patients. Contrast enhanced CT of the thorax confirmed the presence of pneumomediastinum in all six cases and revealed a wide variety of underlying lung conditions as well as associated complications (Figures 1-6).

All patients received supplemental oxygen, analgesics, bronchodilators and supportive care. Antibiotics were administered in patients with mediastinitis followed by spontaneous oesophageal rupture and in the case of *Pneumocystis Jiroveci* Pneumonia (PCP). Antituberculous therapy was started in one patient whose sputum tested positive for AFB bacilli. Coexisting pneumothorax was found in 3 out of the 6 (50%) patients. One patient with CPFE had a large pneumothorax that required tube thoracostomy. Two patients, with scleroderma related ILD and tuberculosis presented with small pneumothoraces and improved with conservative management. One patient with mediastinitis required bilateral intercostal tube insertion for pleural effusions. This patient required intubation and vasopressor support in view of respiratory distress and septic shock. The mean length of hospital stay of these cases was 8 days. Patients with mediastinitis, PCP, CPFE had a higher median length of stay (14 days).

**DISCUSSION:** Pneumomediastinum is a rare clinical entity, diagnosed in 1 out of 44,500 accident and emergency attendances.<sup>[1]</sup> Others, report an incidence of 1 out of 25,000 in ages between 5-34 years.<sup>[1]</sup> However, many authors believe that the occurrence of pneumomediastinum is more frequent than initially believed due to underdiagnosis. The incidence of spontaneous pneumomediastinum (SPM) ranges from 0.001% to 0.01% of all adult inpatient admissions.<sup>[8]</sup> Most commonly seen in young males, it often goes unnoticed because of its benign, self-limiting nature and nonspecific symptoms.<sup>[5]</sup> Spontaneous pneumomediastinum is known to occur in patients with pre-existing lung diseases like asthma, emphysema, interstitial lung disease and bronchiectasis.<sup>[2,10]</sup>

It is an extremely rare complication and can mimic worsening of underlying lung condition. It seems controversial to address pneumomediastinum associated with pre-existing lung disease as 'Primary', since it can be attributed to the underlying structural lung changes. According to many authors,<sup>[7,8]</sup> it may be more appropriate to classify SPM occurring with such diseases as 'Secondary spontaneous', because underlying lung disease can affect the clinical course of SPM. In our study, we have classified the cases with spontaneous pneumomediastinum due to any underlying structural lung disease identified at imaging as 'Secondary spontaneous'.

The most common precipitating factors in our series were intractable cough followed by respiratory tract infection, strenuous physical activity, vomiting. The most common presenting symptoms reported in the literature were retrosternal chest pain with radiation to the back or neck and shortness of breath. Other less common symptoms include cough, dysphagia, dysphonia and odynophagia.<sup>[5,8]</sup> Unlike previous studies reporting chest pain as the most common symptom, the majority (83%) of our patients presented with dyspnoea. Cough is present in 66%, chest pain and fever were seen with equal frequency (50%). This disparity could be attributed to the high prevalence of underlying lung disease in our patients, as most presented with exacerbation of underlying lung disease and pneumothorax.

Subcutaneous emphysema is the most common reported sign, seen in majority of patients ranging from 40% -100% prevalence in many published series.<sup>[3,5,7,8]</sup> Hamman's sign, though classically reported in SPM is highly variable and is seen in 0- 18% of the patients as reported in the literature.<sup>[2,5,6]</sup> Subcutaneous emphysema and Hamman's sign were detected in one patient each in our series.

The clinical course of SPM is affected by pre-existing lung disease and may be complicated by concomitant pneumothorax. Interstitial lung disease (ILD) can be associated with spontaneous pneumomediastinum in 3%-18% of the cases as a predisposing condition.<sup>[2,3,10]</sup> Concomitant pneumothorax is seen in 8.6% of pneumomediastinum patients as observed in the literature.<sup>[8]</sup> and a very high prevalence is reported in patients with pre-existing lung disease.<sup>[2]</sup> Three of our patients had a coexisting pneumothorax. All of them had a pre-existing lung disease in the form of pulmonary fibrosis (ILD) in one patient along with co-existing emphysema in the other. One patient with cavitary form of pulmonary tuberculosis had associated pneumothorax.

Pneumomediastinum is a rare complication of ILD associated with connective tissue disorders (CTD). The common triggers identified are forced cough, spirometry and inflammatory pneumonitis.<sup>[11]</sup> Dermatomyositis (DM) is the most frequent CTD associated with pneumomediastinum.<sup>[11]</sup> In the largest published review, Golf et al<sup>[11]</sup> reported 62 patients of CTD associated with pneumomediastinum and 49 (79%) of these patients had DM while 3 others (4.8%) each

of rheumatoid arthritis, systemic lupus erythematosus and systemic sclerosis.

The overall mortality rate in these cases, when complicated by pneumomediastinum was reported as 34% in their series. In our series, two patients with ILD associated with CTD are reported, one with scleroderma and other with dermatomyositis. Only 3 cases of spontaneous pneumomediastinum associated with scleroderma are reported in the literature till now.<sup>[11]</sup> Our patient typically presented with both spontaneous pneumothorax and pneumomediastinum which was managed conservatively with 100% oxygen inhalation.

Spontaneous pneumomediastinum and pneumothorax present in this case can be attributed to the rupture of alveoli and subpleural cysts due to raised intrapulmonary pressure on coughing. Lung architecture distortion in ILD, rupture of alveoli and honeycomb cysts.<sup>[11,12]</sup> and also rupture of subpleural or paracardiac blebs.<sup>[11]</sup> with subsequent air leakage into the surrounding interstitium have been described as contributory in the aetiopathogenesis of SPM and pneumothorax in ILD. Weakening of lung interstitium by corticosteroids and necrosis of bronchial wall because of vasculitis are other alternative explanations for SPM in cases with dermatomyositis.<sup>[13]</sup>

One of our patient presented with mediastinitis and pneumomediastinum with bilateral pleural collections and septic shock. He was presumed to have a sealed oesophageal perforation following a severe bout of vomiting. He was managed conservatively with aggressive antibiotic therapy and mechanical ventilation with vasopressor support and did not require any surgical intervention. Though oesophageal perforation carries a high mortality and warrants surgical repair, Vogel et al<sup>[14]</sup> in their series report that an aggressive conservative treatment of sepsis and drainage of pleural collections by intercostal tube can avoid major surgery by allowing spontaneous healing of oesophagus as was seen in our case. This approach to management in such cases has proved to be successful with good survival rates as observed by many others in the literature.<sup>[15,16]</sup>

One of our patients with pneumomediastinum had combined pulmonary fibrosis and emphysema. CPFE is characterised by co-existence of emphysema in upper lobes and pulmonary fibrosis in lower lobes.<sup>[17]</sup> Seen predominantly in males and smokers with distinct physiological profile, it is characterised by relatively preserved lung volumes and markedly reduced diffusion capacity of the lungs. CPFE is unique with different natural history and prognosis when compared to emphysema or pulmonary fibrosis alone.<sup>[17]</sup> It is complicated by pulmonary hypertension, lung cancer and acute lung injury<sup>[17]</sup> but occurrence of pneumomediastinum and pneumothorax has never been reported before.

Pneumomediastinum in patients with CPFE may result from rupture of emphysematous bullae as this association has also been observed in patients with smoking related emphysema. However, an increased incidence of SPM in patients with CPFE has not been described in literature and

needs further validation. One patient in our series was HIV positive with very low CD4 counts and had PCP related interstitial pneumonia complicated by pneumomediastinum.

Pneumomediastinum is an uncommon complication of pneumocystis infection in HIV positive patients, and can occur any time in the clinical course of infection.<sup>[18]</sup> The air leak is thought to result from pneumatocoeles which are caused by release of proteases from the activated macrophages and ischemic necrosis of vessels due to infection.<sup>[19]</sup> Alveolar overdistension secondary to localised bronchiolar inflammation also can lead to pneumomediastinum in Pneumocystis infected patients.<sup>[20]</sup>

The diagnosis of pneumomediastinum is confirmed by radiographic examination. Plain chest radiograph may be sufficient to diagnose pneumothorax, but it may miss the diagnosis of pneumomediastinum in 30% of cases as observed by Kaneki.<sup>[21]</sup> However, careful observation of chest radiographs can reveal certain findings like subcutaneous emphysema, superior mediastinal streaks, double bronchial wall sign, continuous diaphragm sign and ring around the artery sign.<sup>[8,22]</sup> Pneumopericardium represents air within the pericardium, thus surrounding the heart. Plain chest radiographs and CT appearances are characteristic, the heart being partially or completely surrounded by air, with the pericardium sharply outlined by air density on either side.

Underlying causes include direct injury to the pericardium, pericardial fluid drainage, barotrauma and infectious pericarditis with gas producing organisms. However, pneumopericardium can be differentiated from pneumomediastinum in the chest imaging by the following signs. Air within the pericardium unlike pneumomediastinum remains below the level of great vessels. And also in decubitus position, air in the pericardial sac will shift immediately, while air in the mediastinum will not shift in a short interval between films.

Computed tomography (CT) of the chest is the gold standard in diagnosis of SPM. CT chest can detect even small amounts of air in the mediastinum in case of diagnostic uncertainty,<sup>[3]</sup> and also can reveal the associated lung abnormality and complications if any. Chest CT can also demonstrate linear collections of air contiguous to the bronchovascular sheaths, also known as Macklin effect.<sup>[23]</sup> A Macklin effect seen on CT differentiates respiratory from other aetiologies of pneumomediastinum.<sup>[23]</sup>

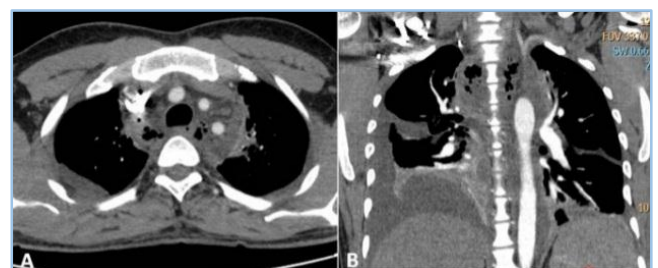
Clinical differential diagnosis of pneumomediastinum include acute coronary syndrome, pericarditis, pulmonary embolism, pneumonia and reflux disease.<sup>[7,8]</sup> Treatment options recommended for patients with SPM include close observation, hospitalisation, analgesics, cough suppressants and inhalation of 100% oxygen.<sup>[5]</sup> With 100% oxygen inhalation, nitrogen is washed out of blood thus creating a pressure gradient for diffusion of gas in to the tissues.<sup>[24]</sup> Antibiotics are usually not indicated, except in cases of viscus perforation leading to mediastinitis.<sup>[25]</sup> Although spontaneous resolution of pneumomediastinum is a possibility and is described in literature.<sup>[8]</sup> We attribute the

speedy recovery of pneumothorax and pneumomediastinum in our cases to inhalation of 100% oxygen.

SPM is usually self-limiting without any complications in majority of the cases.<sup>[6,8]</sup> But occasional life threatening complications have been reported in literature and therefore one should be vigilant in management of these cases.<sup>[26]</sup> Unable to decompress the pressure within the mediastinum with potential rise in intra-mediastinal pressure can cause rupture of mediastinal parietal pleura leading to pneumothorax,<sup>[8]</sup> tension pneumomediastinum and tension pneumothorax.<sup>[25]</sup> Emergency chest tube placement and surgical decompression is needed if such complications arise.<sup>[5]</sup>

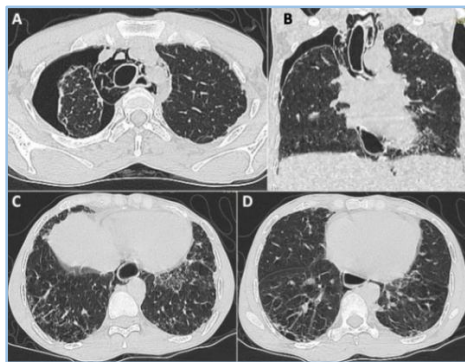
One should be aware of spontaneous pneumomediastinum and pneumothorax occurring in patients of ILD associated with CTD as these cases may present with new onset or sudden worsening of dyspnoea. The situation can mimic worsening of underlying lung condition. Systemic sclerosis, DM and CPFE should be considered in differential diagnosis of spontaneously occurring pneumomediastinum. SPM may be the presenting manifestation in CPFE and many of the CTD associated ILD. Initial misdiagnosis and lack of understanding of pathophysiology can often lead to unnecessary diagnostic and therapeutic interventions.

In most cases, SPM usually resolves over a period of one week and requires only conservative management with close observation.<sup>[8,25]</sup> Complications like pneumothorax and respiratory distress can occur in some patients and should be managed promptly. Secondary pneumomediastinum is a morbid condition and therefore a high index of clinical suspicion should be maintained in order not to miss any secondary pathology and associated complications. Secondary pneumomediastinum may have unfavourable outcomes if not diagnosed timely and managed promptly.



**Fig. 1**

**Fig. 1: Axial (A) and coronal (B) CT images in mediastinal window showing features of mediastinitis with air pockets within the mediastinum, Also note the presence of right sided pleural effusion.**

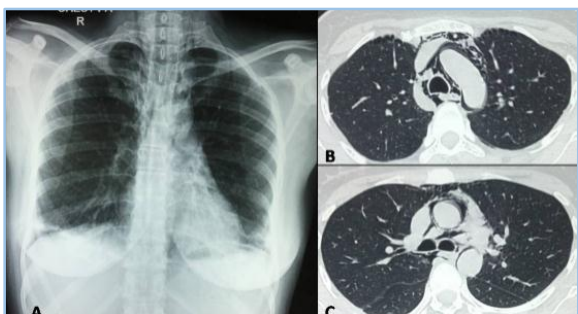


**Fig. 2**

**Fig. 2: A.** HRCT images in lung window depicting right-sided pneumothorax with partial collapse of the right lung. Pneumomediastinum is visible as air around the mediastinal vessels, trachea and oesophagus.

**B.** Coronal HRCT image in lung window showing right-sided pneumothorax and pneumomediastinum, air filled dilated thoracic oesophagus and bilateral subpleural interstitial thickening with apicobasal gradient and minimal basal honeycombing (UIP pattern).

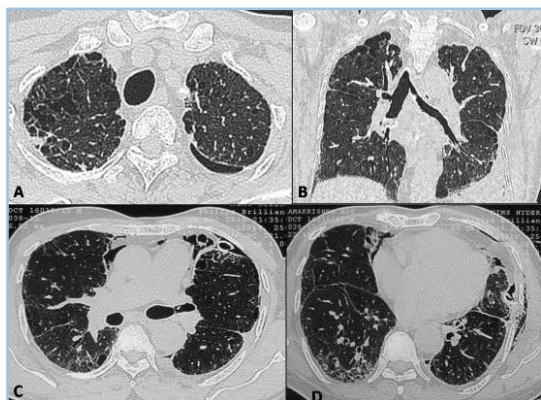
**C & D.** HRCT sections through the lower lung fields show interstitial thickening in both lungs in subpleural location with evidence of fibrosis, bronchiolectasis and minimal subpleural honeycombing. Pneumomediastinum is visible as air around the dilated distal oesophagus.



**Fig. 3**

**Fig. 3: A.** Chest radiograph shows presence of air in the mediastinum tracking into the soft tissues of neck.

**B & C.** Axial CT images in lung window shows pneumomediastinum with presence of air around the mediastinal vascular structures and trachea.



**Fig. 4**

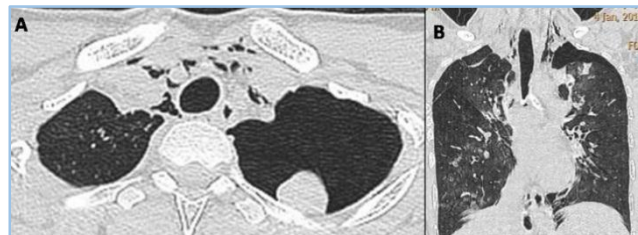
**Fig. 4: A & B & C & D.** Axial and coronal CT images in lung window showing centrilobular and paraseptal emphysema with a small left-sided pneumothorax with ICD tube in situ and small air pockets in the mediastinum.

HRCT sections of the lung fields show bilateral sub pleural interstitial thickening with evidence of fibrosis, bronchiolectasis and minimal basal honeycombing.



**Fig. 5**

**Fig. 5:** Axial CT images in lung window showing extensive ground glass attenuation of both lungs fields suggestive of pneumocystis infection along with pneumomediastinum seen as air in retrosternal location and around the mediastinal vascular structures.



**Fig. 6**

**Fig. 6: A & B.** Axial and coronal CT images in lung window showing left-sided pneumothorax with pneumomediastinum. Left upper lobe consolidation with breakdown is also noted suggesting the underlying tubercular infection.

Sl. No.	Age & Sex	Clinical Features	Signs	Predisposing Factors	Pre-existing Lung Disease	Concomitant pneumothorax	Management	Length of Hospital Stay
1	25/ M	Fever, throat pain, chest pain, SOB, dysphagia	HS	vomiting induced esophageal rupture	-	-	ICT insertion for bilateral pleural effusion, intubation and vasopressor support, antibiotics in view of septic shock, mediastinitis and respiratory distress.	10 days
2	30/F	Chest pain, SOB, dry cough		Respiratory tract infection, intractable cough	Scleroderma related interstitial lung disease	Yes	Conservative management	3 days
3	34/F	Dry cough, fever, progressive SOB		Respiratory tract infection, intractable cough	Dermatomyositis with interstitial lung disease	-	Conservative management	3 days
4	60/ M	Chest pain, SOB	SE	Strenuous physical activity, Smoking	Combined pulmonary fibrosis and emphysema	Yes	ICT insertion	14 days
5	12/ M	SOB, cough, fever		PCP related interstitial pneumonia, AIDS	-	-	Conservative management, Antiretroviral therapy and antimicrobial therapy	14 days
6	25/ M	Cough, Haemoptysis		Cavitating pneumonia of tuberculous aetiology	-	Yes	Conservative management, Anti-tubercular therapy	7 days

**Table 1: The Demographic Data, Clinical Presentation, Precipitating Events, Hospital Course and Management of Patients Presenting with Pneumomediastinum**

SOB: Shortness of breath, HS: Hamman's Sign.

SE: Subcutaneous Emphysema.

PCP: Pneumocystis Jiroveci Pneumonia.

AIDS: Acquired Immunodeficiency Syndrome.

ICT: Intercostal Tube Insertion.

**CONCLUSIONS:** Pneumomediastinum is a rare condition and is generally benign. The authors consider it appropriate to classify pneumomediastinum on the same lines as pneumothorax into spontaneous (primary and secondary) or traumatic (iatrogenic or accidental) to avoid confusion and to develop a uniform terminology. Most cases that are reported as 'spontaneous' have associated underlying lung conditions that present for the first time with pneumomediastinum. Chest radiography is insensitive in detection of small quantities of air in the mediastinum as well as subtle lung changes resulting from coexisting interstitial lung disease or small air cysts and bullae which require CT for confirmation.

It is only appropriate to label such cases as having 'Secondary' and not 'Primary' pneumomediastinum under the spontaneous category. Most of these patients although recover spontaneously with conservative management, should be closely monitored for any complications. Treatment consists of removing the trigger, rest and administration of oxygen. Antibiotic administration or chest tube placement is reserved for specific aetiologies and complications.

**LIMITATIONS:** This is a single departmental study with retrospective analysis of a small group of patients. Therefore, this data might not be representative of the larger population group.

#### REFERENCES

1. Kouritas VK, Papagiannopoulos K, Lazaridis G, et al. Pneumomediastinum. J Thorac Dis 2015;7(1):S44-49. DOI: 10.3978/j.issn.2072-1439.2015.01.11.
2. Iyer VN, Joshi AY, Ryu JH. Spontaneous pneumomediastinum: analysis of 62 consecutive adult patients. Mayo Clin Proc 2009;84(5):417-421.
3. Caceres M, Ali SZ, Braud R, et al. Spontaneous pneumomediastinum: a comparative study and review of the literature. Ann Thorac Surg 2008;86(3):962-966.
4. Macklin MT, Macklin CC. Malignant interstitial emphysema of the lungs and mediastinum as an important occult complication in many respiratory diseases and other conditions: interpretation of the clinical literature in the light of laboratory experiment. Medicine 1944;23(4):281-358.
5. Sahni S, Verma S, Grullon J, et al. Spontaneous pneumomediastinum: time for consensus. N Am J Med Sci 2013;5(8):460-464.

6. Takada K, Matsumoto S, Hiramatsu T, et al. Management of spontaneous pneumomediastinum based on clinical experience of 25 cases. *Respir Med* 2008;102(9):1329-1334.
7. Macia I, Moya J, Ramos R, et al. Spontaneous pneumomediastinum: 41 cases. *Eur J Cardiothorac Surg* 2007;31(6):1110-1114.
8. Takada K, Matsumoto S, Hiramatsu T, et al. Spontaneous pneumomediastinum: an algorithm for diagnosis and management. *Ther Adv Respir Dis* 2009;3(6):301-307.
9. Caceres M, Braud RL, Maekawa R, et al. Secondary pneumomediastinum: a retrospective comparative analysis. *Lung* 2009;187(5):341-346.
10. Dajer-Fadel WL, Argüero-Sánchez R, Ibarra-Pérez C, et al. Systematic review of spontaneous pneumomediastinum: a survey of 22 years data. *Asian Cardiovasc Thorac Ann* 2014;22(8):997-1002.
11. Goff LB, Chérin P, Cantagrel A, et al. Pneumomediastinum in interstitial lung disease associated with dermatomyositis and polymyositis. *Arthritis Rheum* 2009;61(1):108-118.
12. Fujiwara T. Pneumomediastinum in pulmonary fibrosis. Detection by computed tomography. *Chest* 1993;104(1):44-46.
13. Kono H, Inokuma S, Nakayama H, et al. Pneumomediastinum in dermatomyositis: association with cutaneous vasculopathy. *Ann Rheum Dis* 2000;59(5):372-376.
14. Vogel SB, Rout WR, Martin TD, et al. oesophageal perforation in adults: aggressive, conservative treatment lowers morbidity and mortality. *Ann Surg* 2005;241(6):1016-1021.
15. Cameron JL, Kieffer RF, Hendrix TR, et al. Selective nonoperative management of contained intrathoracic oesophageal disruptions. *Ann Thorac Surg* 1979;27(5):404-408.
16. Martinez L, Rivas S, Hernandez F, et al. Aggressive conservative treatment of oesophageal perforations in children. *J Pediatr Surg* 2003;38(5):685-689.
17. Jankowich MD, Rounds SIS. Combined pulmonary fibrosis and emphysema syndrome: a review. *Chest* 2012;141(1):222-231.
18. Cheng WL, Ko WC, Lee NY, et al. Pneumomediastinum in patients with AIDS: a case report and literature review. *Int J Infect Dis* 2014;22:31-34.
19. Moss S, Carey PB, Hind CR. Pneumocystis carinii pneumonia presenting with pneumomediastinum in an HIV-positive patient. *Postgrad Med J* 1995;71(832):96-97.
20. Mina NM, Soubani AO. Complication of pneumocystis jiroveci pneumonia. *Respiration* 2011;82(3):288-289.
21. Kaneki T, Kubo K, Kawashima A, et al. Spontaneous pneumomediastinum in 33 patients: yield of chest computed tomography for the diagnosis of the mild type. *Respiration* 2000;67(4):408-411.
22. Zylak CM, Standen JR, Barnes GR, et al. Pneumomediastinum revisited. *Radiographics* 2000;20(4):1043-1057.
23. Murayama S, Gibo S. Spontaneous pneumomediastinum and Macklin effect: overview and appearance on computed tomography. *World J Radiol* 2014;6(11):850-854.
24. Fine J, Frehling S, Starr A. Experimental observations on the effect of 95% oxygen on the absorption on air from the body tissues. *J Thorac Surg* 1935;4:635-642.
25. Newcomb AE, Clarke CP. Spontaneous pneumomediastinum: a benign curiosity or a significant problem? *Chest* 2005;128(5):3298-3302.
26. Bhardwaj H, Bhardwaj B, Carlile PV. Recurrent pneumomediastinum in a patient with rheumatoid arthritis. *Monaldi Arch Chest Dis* 2013;79(3-4):136-139.