Review

DOI: 10.5582/irdr.2024.01020

Spontaneous pneumomediastinum: A comprehensive review of diagnosis and management

Ankoor Talwar[1], Athira Rajeev[2], Shasank Rachapudi[2], Sara Khan[2], Vijay Singh[3], Arunabh Talwar[2]

[1] Department of General Surgery, MedStar Georgetown University Hospital-Washington Hospital Center, Washington, DC, USA;
[2] Division of Pulmonary, Critical Care and Sleep Medicine, Northwell Health, New Hyde Park, NY, USA;
[3] Department of Cardiovascular and Thoracic Surgery, Northwell Health, Bayshore, NY, USA.

SUMMARY Pneumomediastinum is a rare condition defined by the presence of air in the mediastinum. In the absence of traumatic injury, iatrogenic injury, or clear etiology, it is called spontaneous pneumomediastinum (SPM). Spontaneous pneumomediastinum most commonly occurs in younger individuals and has a self-limiting course with a good outcome. The purpose of the present manuscript is to systematically review the existing literature on SPM evaluation and management for updated clinical understanding of this condition. A literature search was conducted of publications about SPM on MEDLINE/PubMed and Google Scholar by identifying all the articles with key search terms "pneumomediastinum" and "spontaneous pneumomediastinum". Inclusion criteria were case series published in English between 1980 and 2023. In total, 24 case series were selected and reviewed to determine presenting symptoms, clinical signs and predisposing factors associated with spontaneous pneumomediastinum. Most patients were male; the average age at diagnosis was 26.3 years. The most common presenting symptoms were chest pain and dyspnea. The most common exam finding was subcutaneous emphysema, in 35.4% of patients. Only 5.9% had the classic Hamman's sign. Risk factors include history of asthma, history of smoking, and recent physical activity. This manuscript presents an extensive review of relevant literature highlighting the diagnosis and essential management of spontaneous pneumomediastinum.

Keywords spontaneous pneumomediastinum, mediastinal emphysema, chest pain, subcutaneous emphysema, systematic review

1. Introduction

Pneumomediastinum (PM), or mediastinal emphysema, was first described in 1819 and is defined as the presence of air within the mediastinal cavity (*1*). PM often occurs in the setting of trauma, blunt or penetrating, or conditions causing changes in intrathoracic pressure, lung disease, childbirth, physical activity, *etc*. Spontaneous pneumomediastinum (SPM) is the presence of air in the mediastinum without a clear etiology. The most common presenting symptoms are dyspnea and chest pain. SPM may be associated with subcutaneous emphysema on physical exam and Hamman's sign on cardiac auscultation (*2*). While previous studies enumerate the presenting clinical characteristics of SPM, there is a paucity of work describing the various triggering events or predisposing risk factors of this interesting clinical entity. In addition, although SPM has been reviewed by many authors, over the last few years there has been a greater appreciation for atraumatic SPM, particularly from viral infection (*e.g*. COVID-19) and underlying collagen vascular disorders (*3*).

Thus, the purpose of the present manuscript is to systematically review the existing literature on SPM evaluation and management to create an up-to-date understanding of this condition, as well as a schema for clinical use.

2. Literature search strategy

We systemically searched clinical literature databases, including MEDLINE/PubMed and Google Scholar, for case series on SPM published in English between 1980 and 2023 following PRISMA guidelines (Figure 1). Key search terms included "spontaneous pneumomediastinum" and "pneumomediastinum". Single case reports and manuscripts reporting on less than 10 patients were not considered. Abstracts of all these

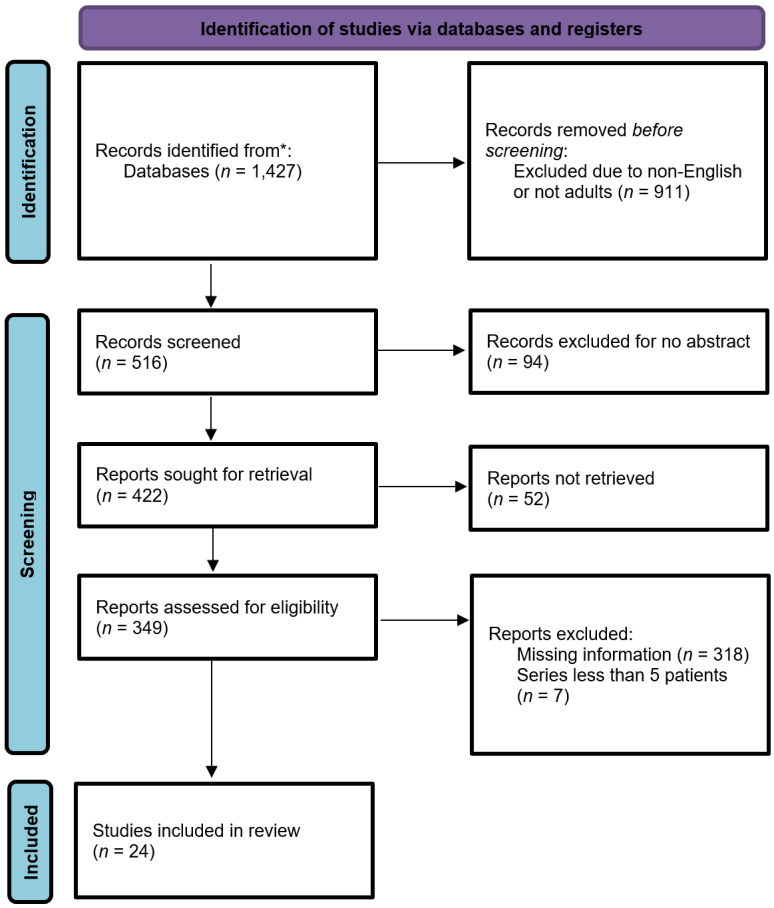

Figure 1. PRISMA flow diagram.

articles were independently screened by two authors (SR, SK) to assess eligibility, with discrepancies resolved by senior author (AT). Full texts of selected articles were then reviewed, and reference list were examined for additional relevant studies.

All data was accessed between August to September 2023. Extracted Information included demographic population, symptoms, clinical findings, triggering events, comorbidities and management strategies for each included patient. Data (means age and range for variable studied) were calculated using Microsoft Excel.

3. Results

The abstracts of 1,427 publications were screened for inclusion criteria eligibility (Figure 1). After selecting for case series published in the English language reporting at least 10 cases of SPM in the adult population, we found 24 articles for full text review. These case series included a total of 1,134 patients who had an eventual diagnosis of spontaneous pneumomediastinum (*4-27*). Clinicodemographic information for these patients was outlined in Table 1. The mean age, of this cohort was determined to 26.33 years, with an age range spanning from 2 to 87. Notably, most cases, 73% (n = 828) were male patients, while 27% (306) were female patients.

3.1. Features of presentation

Of the 24-case series reviewed, the most common presenting symptom was chest pain, occurring in 59% of patients (n = 674) (Table 2). The occurrence of chest pain as a presentation varied from 100% (*14*) in some cases to 16% (*16,27*) in others across different series. Other common symptoms included dyspnea, reported in 31% (n = 352), cough in 10% (n = 112), neck pain in 23% (n = 259), and dysphagia in 10% (n = 118). There were also sporadic complaints of throat pain, odynophagia, dysphonia, lightheadedness, hoarseness, weakness, fever, nausea, back pain, nasally sounding voice (rhinolalia), shoulder pain, swelling of the face, swollen neck, throat discomfort, asthenia and central abdominal pain.

Clinical examination revealed the presence of subcutaneous emphysema in 35.4% (n = 402) of the patients. Various authors have reported the presence of subcutaneous emphysema ranging from 100% (*14,26*) to 3% of the cases (*9*). However, the presence of Hamman's sign, a crunching or bubbling sound over the mediastinum synchronous with the heartbeat was identified in only 5.9% (n = 67) of the patients (*1,28,29*). Associated pneumothorax (*24*) was present in 5.2% (n = 60). Other less commonly reported findings were vomiting, pneumopericardium, pulsus paradoxus,

Table 1. Demographic data on patients diagnosed with spontaneous pneumomediastinum

Ref.	Sample (*n*)	Mean age (Range) (years)	Male/Female	Length of stay (days)	Follow up (months)	Recurrence
Potz *et al.* (*4*)	249	38.7 (17-81)	151/98	2.8	0.46	0
Al-Mufarrej *et al.* (*5*)	17	25.5 (19-39)	11/6		6.72	0
Bakhos *et al.* (*6*)	49	19	26/23	1.8	24-84	1
Dionisio *et al.* (*7*)	18	35.4 (18-87)	12/6	10.5	1-76	0
Yamairi *et al.* (*8*)	71	19.3 (7-48)	53/18	6.3		2
Yu *et al.* (*9*)	237	23.4	222/15	7.5	48.6	11
Freixinet *et al.* (*10*)	32	21.4	25/7	3.2	12-228	0
De Giacomi *et al.* (*11*)	25	(18-82)	10/15			0
Iyer *et al.* (*12*)	62	(20-69)	41/21			1
Okada *et al.* (*13*)	20	22 (13-41)	19/1	7		0
Mondello *et al.* (*14*)	18	25 (5-34)	10/8	6	1	0
Abolnik *et al.* (*15*)	25	18.8 (8-31)	21/4	6.3	87.4	2
Newcomb *et al.* (*16*)	18	(11-58)	14/4			0
Koullias *et al.* (*17*)	24	17.5 (15-26)	18/6	2	36-120	0
Kobashi *et al.* (*18*)	17	19.5	12/5			
Halperin *et al.* (*19*)	10	21.2 (2-56	7/3			
Jougon *et al.* (*20*)	12	25 (16-46)	11/1	4	19	0
Song *et al.* (*21*)	45	18.96	35/10	3.93		0
Weiss *et al.* (*22*)	14	22.5 (18-30)	9/5	2.2		
Macia *et al.* (*23*)	41	21.3 (14-35)	34/7	5		1
Caceres *et al.* (*24*)	28	27 (3-71)	16/12	3	12-120	0
Kaneki *et al.* (*25*)	33	17.6 (13-27)	26/7			0
Perna *et al.* (*26*)	47	27.3 (16-42)	33/14	3.5		
Weissberg *et al.* (*27*)	22	(15-37)	12/10	3.5	12	0
Total	1134	26.33	828/306	4.76		18

Percentages are given in parentheses. Blank cells indicate this information was omitted from the reference.

Table 2. Chief complaints at the time of diagnosis of spontaneous pneumomediastinum

Ref.	Chest pain	Dyspnea	Neck pain	Dysphagia	Cough	Throat pain	Odynophagia	Dysphonia
Potz *et al.* (*4*)								
Al-Mufarrej *et al.* (*5*)	10 (59)	7 (41)	2 (12)				3 (18)	
Bakhos *et al.* (*6*)	32 (65)	25 (51)	14 (29)	4 (8)				
Dionisio *et al.* (*7*)	14 (78)	15 (83)	10 (56)	5 (28)	10 (56)		3 (17)	
Yamairi *et al.* (*8*)	51 (72)	23 (32)	31 (44)	29 (41)		31 (44)		
Yu *et al.* (*9*)	211 (89)	78 (33)	123 (52)					
Freixinet *et al.* (*10*)	25 (78)	13 (41)		2 (6)	3 (9)			
De Giacomi *et al.* (*11*)	7 (28)	11 (44)			3 (12)			
Iyer *et al.* (*12*)	39 (63)	27 (44)	11 (18)	3 (5)	28 (45)			3 (5)
Okada *et al.* (*13*)	15 (75)	8 (40)	2 (10)	10 (50)	1 (5)	5 (25)		
Mondello *et al.* (*14*)	18 (100)	16 (88)	8 (44)	4 (22)	14 (77)			12 (66)
Abolnik *et al.* (*15*)	22 (88)	15 (60)	12 (48)	10 (40)				
Newcomb *et al.* (*16*)	16 (89)	12 (67)	2 (11)	3 (17)				1 (6)
Koullias *et al.* (*17*)	16 (67)	2 (8)		2 (8)	10 (42)	6 (25)		
Kobashi *et al.* (*18*)	14 (82)			1 (6)				
Halperin *et al.* (*19*)	5 (50)	6 (60)						
Jougon *et al.* (*20*)	6 (50)		3 (25)				1 (8)	
Song *et al.* (*21*)	33 (41)	15 (19)		1 (1)	1 (1)	31 (38)		
Weiss *et al.* (*22*)	11 (79)	8 (57)					5 (36)	
Macia *et al.* (*23*)	35 (85)	20 (49)	18 (44)	5 (12)	10 (24)		15 (37)	5 (12)
Caceres *et al.* (*24*)	15 (54)	11 (39)			9 (32)		1 (4)	
Kaneki *et al.* (*25*)	33 (100)	19 (58)	23 (70)	13 (39)				
Perna *et al.* (*26*)	28 (60)	11 (26)		18 (38)	15 (33)			
Weissberg *et al.* (*27*)	18 (16)	10 (9)		8 (7)	8 (7)			
Total	674 (59)	352 (31)	259 (23)	118 (10)	112 (10)	73 (6)	28 (2)	21 (2)

Percentages are given in parentheses. Blank cells indicate no information was given regarding that chief complaint. The less common complaints were Fever (1%), Lightheadedness (1%), Weakness (1%), Back pain (1%), Nausea/Emesis (0.4%), Hoarseness (0.4%), Abdominal pain (0.1%), Shoulder pain (0.1%), Swollen neck (0.1%), Rhinolalia (0.1%), Asthenia (0.07%).

hemoptysis, neck swelling (*i.e.* cervical emphysema), pneumorrhachis and pneumoperitoneum (Table 3).

3.2. Predisposing factors

Of the 24-case series reviewed, the most common triggering event or predisposing risk factor identified was a history of asthma, present in 21.9% (n = 248) of the patients (*5-8*), with reported prevalence ranging from 42% (*9*) to 2% (*21*) (Table 4). A history of smoking or tobacco use was identified in 16% (n = 182) of the patients. Physical activity or sports-related

pneumomediastinum was reported in 14.5% (n = 164) cases. A detailed analysis revealed that emesis occurred in 8% (n = 93) of patients, and bouts of cough in 15% (n = 172) of patients. A recent history of respiratory infection was present in 9% patients (n = 102). 53 patients (4.7%) had a history of interstitial lung disease (ILD), and a history of COPD was identified in 1.7% of the patients (n = 19).

Table 3. Clinical findings in spontaneous pneumomediastinum patients

Ref.	Subcutaneous emphysema	Hamman's sign	Pneumothorax	Crepitus	Pleural effusion	Esophageal perforation
Portz *et al.* (*4*)	39 (16)				27 (11)	24 (10)
Al-Mufarrej *et al.* (*5*)	7 (41)					
Bakhos *et al.* (*6*)	7 (16)		5 (11)	15 (30)		
Dionisio *et al.* (*7*)	15 (83)	1 (6)				
Yamairi *et al.* (*8*)	26 (37)	4 (6)				
Yu *et al.* (*9*)	6 (3)		9 (4)			
Freixinet *et al.* (*10*)	25 (78)		2 (6)			
De Giacomi *et al.* (*11*)	15 (68)		4 (18)	4 (16)		
Iyer *et al.* (*12*)	28 (45)		20 (32)			
Okada *et al.* (*13*)	9 (45)	2 (10)				
Mondello *et al.* (*14*)	18 (100)	8 (44)				
Abolnik *et al.* (*15*)	15 (60)	10 (40)				
Newcomb *et al.* (*16*)	14 (78)	4 (22)				
Koullias *et al.* (*17*)	12 (50)		2 (8)			
Kobashi *et al.* (*18*)	8 (47)	6 (35.3)				
Halperin *et al.* (*19*)	5 (50)	5 (50)	1 (10)			
Jougon *et al.* (*20*)	11 (92)					
Song *et al.* (*21*)	17 (38)		2 (4)			
Weiss *et al.* (22)				8 (57)		
Macia *et al.* (*23*)	29 (71)	5 (12)				
Caceres *et al.* (*24*)	11 (40)		2 (7)			
Kaneki *et al.* (*25*)	26 (79)	17 (52)				
Perna *et al.* (*26*)	47 (100)		7 (15)			
Weissberg et al.(27)	12 (11)	5 (4)	6 (5)			
Total	402 (35)	67 (6)	60 (5)	27 (2)	27 (2)	24 (2)

Percentages are given in parentheses. Blank cells indicate no information was given about patients presenting with that clinical finding. Less commonly reported findings were Hematemesis (1%), Pneumopericardium (1%), Pulsus paradoxus (1%), Hemoptysis (0.5%), Neck swelling (0.4%), Pneumorachis (0.08%), Decreased heart sounds (0.08%), and Pneumoperitoneum (0.08%).

Table 4. Triggering events and risk factors for spontaneous pneumomediastinum

Ref.	Asthma	Smoking/ Tobacco	Cough	Physical activity	Respiratory Infection	Vomiting/ Retching	Illicit drug use
Portz *et al.* (*4*)	32 (13)						
Al-Mufarrej *et al.* (*5*)	4 (24)			2 (12)		4 (24)	1 (6)
Bakhos *et al.* (*6*)	20 (41)	11 (22)	14 (29)	3 (6)		8 (16)	12 (24)
Dionisio *et al.* (*7*)	5 (28)	12 (67)	9 (50)	1 (6)	8 (44)	2 (11)	2 (11)
Yamairi *et al.* (*8*)	13 (18)		3 (4)	18 (25)		2 (3)	
Yu *et al.* (*9*)	99 (42)	92 (39)	72 (30)	56 (24)	66 (28)	34 (14)	
Freixinet *et al.* (*10*)	9 (28)	9 (28)		11 (34)			3 (9)
De Giacomi *et al.* (*11*)		9 (36)	4 (16)			2 (8)	
Iyer *et al.* (*12*)	9 (15)		5 (8)	2 (3)	5 (8)	4 (6)	6 (10)
Okada *et al.* (*13*)	4 (20)		3 (15)	8 (40)		2 (10)	
Mondello *et al.* (*14*)	8 (22)		12 (66)	6 (33)			
Abolnik *et al.* (*15*)	6 (24)	6 (24)	2 (8)	6 (24)	3 (12)		
Newcomb *et al.* (*16*)	7 (39)	6 (33)	3 (17)	3 (17)		2 (11)	4 (22)
Koullias *et al.* (*17*)	4 (17)		4 (17)	6 (25)	4 (17)	2 (8)	6 (25)
Kobashi *et al.* (*18*)			6 (35)				
Halperin *et al.* (*19*)	2 (20)		2 (20)	1 (10)	3 (30)	2 (20)	
Jougon *et al.* (*20*)	1 (8)			4 (33)			
Song *et al.* (*21*)	1 (2)		4 (9)	3 (7)		2 (4)	
Weiss *et al.* (*22*)	1 (7)	2 (14)	6 (43)		4 (29)	8 (57)	14 (100)
Macia *et al.* (*23*)	9 (22)	14 (41)	3 (7)	5 (12)	3 (7)	4 (10)	4 (10)
Caceres *et al.* (*24*)	6 (21)	8 (29)	2 (7)	1 (4)		10 (36)	
Kaneki *et al.* (*25*)			6 (18)	21 (61)			
Perna *et al.* (*26*)	8 (17)	13 (26)	4 (7)	7 (12)	6 (12)	3 (7)	26 (55)
Weissberg *et al.* (*27*)			8 (36)			2 (2)	
Total	248 (22)	182 (16)	172 (15)	164 (14)	102 (9)	93 (8)	78 (7)

Table 4. Triggering events and risk factors for spontaneous pneumomediastinum (continued)

Ref.	Invasive Procedures	Trauma	Vocal exercise	Thoracic Surgery	Interstitial lung disease	COPD
Portz *et al.* (*4*)						
Al-Mufarrej *et al.* (*5*)						
Bakhos *et al.* (*6*)						
Dionisio *et al.* (*7*)					2 (11)	
Yamairi *et al.* (*8*)			11 (15)			
Yu *et al.* (*9*)						
Freixinet *et al.* (*10*)						
De Giacomi *et al.* (*11*)					23 (92)	
Iyer *et al.* (*12*)					11 (18)	5 (8)
Okada *et al.* (*13*)			3 (15)			
Mondello *et al.* (*14*)						
Abolnik *et al.* (*15*)						
Newcomb *et al.* (*16*)					1 (6)	
Koullias *et al.* (*17*)					1 (4)	
Kobashi *et al.* (*18*)			3 (18)			
Halperin *et al.* (*19*)						1 (10)
Jougon *et al.* (*20*)						2 (17)
Song *et al.* (*21*)						
Weiss *et al.* (*22*)						
Macia *et al.* (*23*)						2 (17)
Caceres *et al.* (*24*)					2 (7)	1 (4)
Kaneki *et al.* (*25*)						
Perna *et al.* (*26*)						4 (7)
Weissberg *et al.* (*27*)	36 (32)	34 (30)	7 (6)	19 (17)		
Total	36 (3)	34 (3)	24 (2)	19 (2)	40 (3)	13 (1)

Percentages are given in parentheses. Blank cells indicate no information was given about patients presenting with that clinical finding. Less commonly reported findings were Hematemesis (1%), Pneumopericardium (1%), Pulsus paradoxus (1%), Hemoptysis (0.5%), Neck swelling (0.4%), Pneumorachis (0.08%), Decreased heart sounds (0.08%), and Pneumoperitoneum (0.08%).

4. Discussion

Spontaneous pneumomediastinum is a complex clinical entity with a reported incidence of less than 1:44,000 (*23*). It occurs most commonly in young males and generally has a benign course (*30*). The pathogenesis of SPM (termed the "Macklin Effect") involves alveolar rupture leading to air dissection along bronchovascular sheaths with eventual spread into the mediastinum (*31,32*). This process explains the occurrence of SPM in patients with a sudden increase in intrathoracic pressure (*12,24,25,33,34*). The absence of a discernable etiological factor in SPM presents a diagnostic challenge and opportunity for heightened comprehension. The present study is the most comprehensive review of SPM to date and reports a unique diagnostic framework for this condition. We have reviewed 24 published studies which included 1,134 patients with spontaneous pneumomediastinum (*4-27*) (Figure 1). To the best of our knowledge, our review comprises of the largest number of reported spontaneous pneumomediastinum cases. In doing so, this work beckons a broader discourse on the need for standardized diagnostic criteria, prognostic indicators, and therapeutic modalities tailored to the distinctive etiologies of SPM.

In our review, SPM most often presented as chest pain and dyspnea. Neck pain was also a prevalent symptom, which is under appreciated in existing reviews of SPM (Table 5). Common physical exam findings were subcutaneous emphysema, Hamman's sign, and associated pneumothorax, which is consistent with previous reports (Table 5). Given the nonspecific nature of SPM symptoms, the differential diagnosis for patients presenting with this condition tends to be broad, and may lead to delayed diagnosis (*25*). Once confirmed, effort should be made to investigate potential predisposing factors. In the present analysis, the common factors included asthma, history of smoking, cough, and sudden change in intrathoracic pressure (related to physical activity/sports) (Table 5).

Table 5. Most common clinical signs, symptoms and predisposing events reported in literature

	Highest- Lowest %
Subcutaneous emphysema (402/1134) (35.4)	100-2.5
Hamman's sign (67/1134) (5.9)	52-4.4
Pneumothorax (60/1134) (5.2)	32.2-3.8
Chest Pain (674/1134) (59.4)	100-15.8
Dyspnea (352/1134) (31.04)	88-8.3
Neck Pain (259/1134) (22.8)	70-10
Asthma (248/1134) (21.9)	41.7-7.1
Smoking/ tobacco (182/1134) (16)	100-22
Cough (172/1134) (15.2)	42.9-4.2
Sudden change in intrathoracic pressure (*i.e.* physical activity/ sports related) (164/1134) (14.5)	58.3-3.2

Percentages are given in parentheses.

The most salient result of our study was a

Table 6. Risk factors for pneumomediastinum

SMOKING AND SUBSTANCE USE ASCOIATED WITH SPONTANEOUS PNEUMOMEDIASTINUM
Smoking or tobacco use (*26*)
Vaping (*44*)
Other inhalational substance use (*e.g.*: Hookah smoking (*45*), Cocaine (*35*), Methamphetamine (*46*), Marijuana (*47*), Heroin (*48*))
INTRINSIC LUNG DISEASES AND AIRWAY CAUSES
Asthma (*49*)
Chronic obstructive pulmonary disease (*26*)
Interstitial lung disease (*e.g.*: Dermatomyositis (*50*), SLE (*51*))
Cystic fibrosis (*52*)
Lung cancer (*53*)
Foreign body in the airway (*54*)
Metastatic cancers (*55*)
Thoracic endometriosis (*56*)
Mounier-Kuhn syndrome (*57*)
INFECTIOUS CAUSES
Bacterial (*e.g.*: Pertussis (*58*), Tuberculosis (*59*), Mycoplasma pneumoniae (*60*))
Viral pneumonias (*e.g.*: COVID-19 (*3*), Influenza (H5N6) (*36*), HIV infected pneumonia) (*61*)
Fungal (*e.g.*: Pneumocystis jirovecii) (*62*)
CONDITIONS CAUSING CHANGES IN THE INTRATHORACIC PRESSURE
Valsalva maneuver (*e.g.*: Coughing (*63*), Forceful sneezing/inhalation (*64*), Shouting (*65*), Persistent yelling (*66*), Inflation of party balloons (*67*), Forceful blowing into a bottle (*68*))
Pregnancy and labor (*69*)
Vomiting (*e.g.*: Anorexia Nervosa (*70*), Boerhaave syndrome (*71*), Cannabinoid hyperemesis syndrome (*72*), Hyperemesis gravidarum (*73*))
Strenuous physical activities (*e.g.*, Weightlifting (*74*), sports, sex (*75*), pushup exercise (*76*))
Playing musical instruments/Vocal training (*e.g.*, Baritone Practice (*77*))
Pulmonary function testing (*78*)
High flow nasal canula (*79*)
Scuba diving (*80*)
Air travel (*81*)
Mechanical Ventilation (*82*)
IATROGENIC
Drug related (*e.g.*: Bleomycin induced interstitial pneumonitis (*83*))
Procedures (*e.g.*: Bronchoscopy (*84*), Endoscopy Procedures (*85*))
Head and neck surgeries (*e.g.*: Dental (*86*), Adenotonsillectomy (*87*))
Thoracic surgeries (*e.g.*: Esophageal surgery (*88*))
Infra diaphragmatic surgeries (*e.g.*: Laparoscopic surgeries (*89*), Whipple surgery (*90*))
Graft Vs Host disease (*91*)
Tracheobronchial injury (*92*)
OTHER RARE CAUSES
Inflammatory bowel disease (*93*)
Intestinal perforation (*94*)
Dress syndrome (*95*)
Poisonings (*e.g.*: Paraquat (*96*))
Ecstasy ingestion (*97*)

comprehensive review of the conditions associated with SPM. We confirm several well-known associations such as smoking, tobacco use, asthma, and chronic obstructive pulmonary disease (Table 6). Sudden changes in intrathoracic pressure (playing wind instrument, physical activity, Valsalva maneuver, pregnancy/labor induced) also remain an important cause and should be considered. However, other associations which have been reported more recently in the literature are much less appreciated in clinical practice. These include inhalation substance abuse (*35*), collagen vascular disorders (*e.g.* dermatomyositis), and viral infections (*e.g.* COVID-19 (*3*), Influenza (*36*)). We hope these important findings serve as a primer for physicians when faced with a case of SPM and helps guide workup/treatment strategies.

Our study is limited by its design as a systematic review of the literature. A more thorough understanding of SPM will likely require retrospective evaluation of several hospitals' EMRs, as it is a rare condition. In addition, our search did not encompass single case studies. With time, and especially with the onset of COVID-19, our analysis may underrepresent the population of SPM due to viral illness.

A definitive diagnosis of SPM is made with imaging evidence of air in the mediastinum. Chest radiography is the imaging modality of choice and can identify up to 70% of cases (*33*). In cases where additional workup is necessary, CT chest is diagnostic

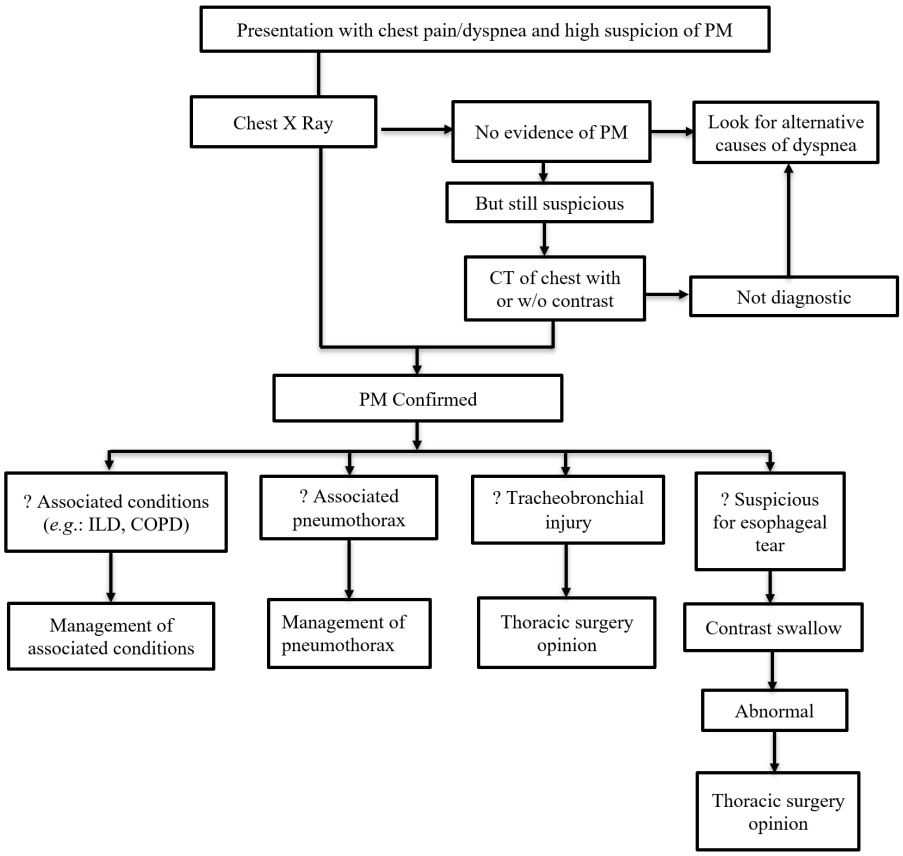

Figure 2. Evaluation and management of pneumomediastinum (PM).

(*37*). The CT scan not only helps confirm the diagnosis but also provides information about the extent of pneumomediastinum as well as evaluation of associated conditions (*e.g.* mediastinal compartment of air, presence of subdiaphragmatic air, presence of subcutaneous air, presence of pleural effusion, presence of acute pulmonary airspace opacification or infiltrate, presence of pulmonary interstitial emphysema, and presence of pneumothorax) (*38*). Those suspected with esophageal injury may require esophagogram.

The goals of SPM treatment are to *i*) promote resorption of free air and *ii*) prevent progression of free air. The most common management strategy is conservative including analgesia, rest, and cough control. Supplemental oxygen has been recommended in many previous reports (*39*) as it provides relief by increasing the diffusion pressure of nitrogen in the interstitium and promoting absorption of free air in the mediastinum. Additional treatment is directed and based on associated conditions. For example, patients with asthma and COPD may benefit from bronchodilators. Patients with associated pneumothorax may necessitate a chest tube placement. If there is tracheobronchial injury or evidence of esophageal injury on esophagogram, surgical consultation is appropriate. However, in the majority of patients, SPM has a benign course and most patients can be discharged for outpatient follow up after 24 to 48 hours of observation in the hospital (*17,30*). Symptomatic relief is typically observed within 24 hours, but complete radiological resolution may take up to 3 weeks (*40*). The authors of this paper recommend documenting complete resolution of the process with a follow up chest x-ray around 2-3 weeks in patients with SPM. A simple, clinically relevant algorithm for workup and management is provided in Figure 2.

Complications of SPM that clinicians should be aware of include progressive respiratory distress, extension of air into the retropharyngeal/retroperitoneal spaces, extension of air into the spinal canal (pneumorhachis), or tension pneumomediastinum (accumulation of air causing tracheal obstruction, compression of the great vessels, or decreased venous return) (*41-43*). SPM related mortality is rare but if it does occur, it is related to underlying associated conditions (pneumonia, COVID-19 (*3*)).

In conclusion, SPM is a unique clinical diagnosis with several associated conditions. SPM typically has a benign course and generally resolves with conservative management. The breadth of associated predisposing conditions is important to understand as they may guide additional treatment.

Funding: None.

Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Roguin A. Rene Theophile Hyacinthe Laennec (1781-1826): The man behind the stethoscope. Clin Med Res. 2006; 4:230-235.
2. Alexandre AR, Marto NF, Raimundo P. Hamman's crunch: A forgotten clue to the diagnosis of spontaneous pneumomediastinum. BMJ Case Rep. 2018. 2018:bcr2018225099.
3. Chowdhary A, Nirwan L, Abi-Ghanem AS, Arif U, Lahori S, Kassab MB, Karout S, Itani RM, Abdalla R, Naffaa L, Karout L. Spontaneous pneumomediastinum in patients diagnosed with COVID-19: A case series with review of literature. Acad Radiol. 2021; 28:1586-1598.
4. Potz BA, Chao LH, Ng TT, Okereke IC. Clinical significance of spontaneous pneumomediastinum. Ann Thorac Surg. 2017; 104:431-435.
5. Al-Mufarrej F, Badar J, Gharagozloo F, Tempesta B, Strother E, Margolis M. Spontaneous pneumomediastinum: Diagnostic and therapeutic interventions. J Cardiothorac Surg. 2008; 3:59.
6. Bakhos CT, Pupovac SS, Ata A, Fantauzzi JP, Fabian T. Spontaneous pneumomediastinum: An extensive workup is not required. J Am Coll Surg. 2014; 219:713-717.
7. Dionisio P, Martins L, Moreira S, Manique A, Macedo R, Caeiro F, Boal L, Bárbara C. Spontaneous pneumomediastinum: Experience in 18 patients during the last 12 years. J Bras Pneumol. 2017; 43:101-105
8. Yamairi K, Yoshimatsu Y, Shimazu H, Kakuno S, Sawa N, Mizukubo Y, Nishijima M, Otani K, Kamimori T, Fujiwara H. Clinical analysis of 71 spontaneous pneumomediastinum cases: An observational study from a tertiary care hospital in Japan. Respir Investig. 2021; 59:530-534.
9. Yu MH, Kim JK, Kim T, Lee HS, Kim DK. Primary spontaneous pneumomediastinum: 237 cases in a single-center experience over a 10-year period and assessment of factors related with recurrence. PLoS One. 2023; 18:e0289225.
10. Freixinet J, Garcia F, Rodriguez PM, Santana NB, Quintero CO, Hussein M. Spontaneous pneumomediastinum long-term follow-up. Respir Med. 2005; 99:1160-1163.
11. De Giacomi F, Baqir M, Cox CW, Moua T, Matteson EL, Ryu JH. Spontaneous pneumomediastinum in connective tissue diseases. J Clin Rheumatol. 2019; 25:239-245.
12. Iyer VN, Joshi AY, Ryu JH. Spontaneous pneumomediastinum: Analysis of 62 consecutive adult patients. Mayo Clin Proc. 2009; 84:417-421.
13. Okada M, Adachi H, Shibuya Y, Ishikawa S, Hamabe Y. Diagnosis and treatment of patients with spontaneous pneumomediastinum. Respir Investig. 2014; 52:36-40.
14. Mondello B, Pavia R, Ruggeri P, Barone M, Barresi P, Monaco M. Spontaneous pneumomediastinum: Experience in 18 adult patients. Lung. 2007; 185:9-14.
15. Abolnik I, Lossos IS, Breuer R. Spontaneous pneumomediastinum. A report of 25 cases. Chest. 1991; 100:93-95.
16. Newcomb AE, Clarke CP. Spontaneous pneumomediastinum: A benign curiosity or a significant problem? Chest. 2005; 128:3298-3302.
17. Koullias GJ, Korkolis DP, Wang XJ, Hammond GL. Current assessment and management of spontaneous pneumomediastinum: Experience in 24 adult patients. Eur J Cardiothorac Surg. 2004; 25:852-855.
18. Kobashi Y, Okimoto N, Matsushima T, Soejima R. Comparative study of mediastinal emphysema as determined by etiology. Intern Med. 2002; 41:277-282.
19. Halperin AK, Deichmann RE. Spontaneous pneumomediastinum: A report of 10 cases and review of the literature. N C Med J. 1985; 46:21-23.
20. Jougon JB, Ballester M, Delcambre F, Mac Bride T, Dromer CE, Velly JF. Assessment of spontaneous pneumomediastinum: experience with 12 patients. Ann Thorac Surg. 2003; 75:1711-1714.
21. Song IH, Lee SY, Lee SJ, Choi WS. Diagnosis and treatment of spontaneous pneumomediastinum: Experience at a single institution for 10 years. Gen Thorac Cardiovasc Surg. 2017; 65:280-284.
22. Weiss ZF, Gore S, Foderaro A. Pneumomediastinum in marijuana users: Aretrospective review of 14 cases. BMJ Open Respir Res. 2019; 6:e000391.
23. Macia I, Moya J, Ramos R, Morera R, Escobar I, Saumench J, Perna V, Rivas F. Spontaneous pneumomediastinum: 41 cases. Eur J Cardiothorac Surg. 2007; 31:1110-4.
24. Caceres M, Ali SZ, Braud R, Weiman D, Garrett HE Jr. Spontaneous pneumomediastinum: A comparative study and review of the literature. Ann Thorac Surg. 2008; 86:962-966.
25. Kaneki T, Kubo K, Kawashima A, Koizumi T, Sekiguchi M, Sone S. Spontaneous pneumomediastinum in 33 patients: Yield of chest computed tomography for the diagnosis of the mild type. Respiration 2000; 67:408-411.
26. Perna V, Vila E, Guelbenzu JJ, Amat I. Pneumomediastinum: Is this really a benign entity? When it can be considered as spontaneous? Our experience in 47 adult patients. Eur J Cardiothorac Surg. 2010; 37:573-575.
27. Weissberg D, Weissberg D. Spontaneous mediastinal emphysema. Eur J Cardiothorac Surg. 2004; 26:885-888.
28. Fraser R, Pare J, Fraser R, Pare P. The normal chest. Synopsis of Diseases of the Chest. 2nd edition. Saunders. 1994; pp.1-116.
29. Laënnec R. De l'Auscultation Médiate, ou Traité du Diagnostic des Maladies des Poumons et du Coeur 1819; 1st ed. Paris: Brosson & Chaude.
30. Takada K, Matsumoto S, Hiramatsu T, Kojima E, Watanabe H, Sizu M, Okachi S, Ninomiya K. Management of spontaneous pneumomediastinum based on clinical experience of 25 cases. Respir Med. 2008; 102:1329-1334.
31. Macklin M, Macklin C. Malignant interstitial emphysema of the lungs and mediastinum as an important occult complication in many respiratory diseases and other conditions: an interpretation of the clinical literature in the light of laboratory experiment. Medicine (Baltimore). 1944; 23:281-358.
32. Macklin C. Transport of air along sheaths of pulmonic blood vessels from alveoli to mediastinum: Clinical implications. Arch Intern Med. 1939; 64:913-926.
33. Duffy BL. Post partum pneumomediastinum. Anaesth Intensive Care. 2004; 32:117-119.
34. Dechambre S, d'Odemont JP, Cornelis JP, Fastrez J. Spontaneous pneumomediastinum after sneezing. Ann Thorac Surg. 1995; 60:1457.
35. Blasco V, Nafati C, Reydellet L, Harti-Souab K, Albanese J. Spontaneous pneumomediastinum secondary to inhalation of crack. Ann Fr Anesth Reanim. 2014; 33:282-283. (in French)
36. Zhang X, Wang J, Zeng Q, Wu X, Jiang S, Shen J. Spontaneous pneumomediastinum and subcutaneous emphysema in avian influenza A (H5N6) human

pneumonia. Clin Case Rep. 2019; 7:2594-2595.
37. Rogers LF, Puig AW, Dooley BN, Cuello L. Diagnostic considerations in mediastinal emphysema: A pathophysiologic-roentgenologic approach to Boerhaave's syndrome and spontaneous pneumomediastinum. Am J Roentgenol Radium Ther Nucl Med. 1972; 115:495-511.
38. Ho AS, Ahmed A, Huang JS, Menias CO, Bhalla S. Multidetector computed tomography of spontaneous versus secondary pneumomediastinum in 89 patients: Can multidetector computed tomography be used to reliably distinguish between the 2 entities? J Thorac Imaging. 2012; 27:85-92.
39. Kim KS, Jeon HW, Moon Y, Kim YD, Ahn MI, Park JK, Jo KH. Clinical experience of spontaneous pneumomediastinum: Diagnosis and treatment. J Thorac Dis. 2015; 7:1817-1824.
40. Esayag Y, Furer V, Izbicki G. Spontaneous pneumomediastinum: is a chest X-ray enough? A single-center case series. Isr Med Assoc J. 2008; 10:575-578.
41. Steffey WR, Cohn AM. Spontaneous subcutaneous emphysema of the head, neck, and mediastinum. Arch Otolaryngol. 1974; 100:32-35.
42. Al-Mufarrej F, Gharagozloo F, Tempesta B, Margolis M. Spontaneous cervicothoracolumbar pneumorrhachis, pneumomediastinum and pneumoperitoneum. Clin Respir J. 2009; 3:239-243.
43. Nene RV, Hryniewicki AT, Roderick E, Chicotka S, Vazquez MH, Thistlewaite PA, Coffey C, Odish MF. Tension pneumomediastinum from opioid inhalation. Am J Emerg Med. 2022; 53:281.e5-281.e8.
44. Adhikari R, Manduva D, Malayala SV, Singh R, Jain NK, Deepika K, Koritala T. A rare case of vaping-induced spontaneous pneumomediastinum. Cureus. 2021; 13:e17166.
45. Alaska YA. Spontaneous pneumomediastinum secondary to hookah smoking. Am J Case Rep. 2019; 20:651-654.
46. Agustin M, David G, Kang JY, Teerasukjinda O. Spontaneous pneumomediastinum and diffuse subcutaneous emphysema after methamphetamine inhalation. Case Rep Pulmonol. 2020; 2020:7538748.
47. Jain A, Ashiq A, Ahmed R, Rane RP, Hussain KM. A case of pneumothorax secondary to marijuana use disorder. Cureus. 2022; 14:e26634.
48. Ali S, Colaco LB, Trikkur S, Kumar G. Silent dyspnea: Spontaneous pneumomediastinum in a heroin user. Cureus. 2021; 13:e20496.
49. Tortajada-Girbes M, Moreno-Prat M, Ainsa-Laguna D, Mas S. Spontaneous pneumomediastinum and subcutaneous emphysema as a complication of asthma in children: case report and literature review. Ther Adv Respir Dis. 2016; 10:402-409.
50. Le Goff B, Cherin P, Cantagrel A, Gayraud M, Hachulla E, Laborde F, Papo T, Sibilia J, Zabraniecki L, Ravaud P, Puéchal X. Pneumomediastinum in interstitial lung disease associated with dermatomyositis and polymyositis. Arthritis Rheum. 2009; 61:108-118.
51. Ahmed AH, Awouda EA. Spontaneous pneumomediastinum and subcutaneous emphysema in systemic lupus erythematosus. BMJ Case Rep. 2010; 2010:bcr0220102765.
52. Zsiboras C, Adonyi M, Stankovics J, Farkas A, Vajda P, Rozsai B. Severe spontaneous pneumomediastinum in a girl with cystic fibrosis. European J Pediatr Surg Rep. 2021; 9:e65-e67.
53. Libeer C, Verbeken E, De Wever W, Vansteenkiste J, Nackaerts K. Mediastinal emphysema and small cell lung cancer (SCLC): A case-report. Lung Cancer. 2005; 47:139-142.
54. Velecharla MS, Shah KD, Bradoo RA, Subramaniasami GS, Joshi AA. "AIR LEAK SYNDROME": An unusual presentation of foreign body in the airway. Indian J Otolaryngol Head Neck Surg. 2019; 71(Suppl 1):693-695.
55. Park SI, Choi E, Lee HB, Rhee YK, Chung MJ, Lee YC. Spontaneous pneumomediastinum and hemopneumothoraces secondary to cystic lung metastasis. Respiration. 2003; 70:211-213.
56. Haga T, Kataoka H, Ebana H, Otsuji M, Seyama K, Tatsumi K, Kurihara M. Thoracic endometriosis-related pneumothorax distinguished from primary spontaneous pneumothorax in females. Lung. 2014; 192:583-587.
57. Naciri S, Zahraoui R, Soualhi M, Bourkadi JE. An unusual cause of spontaneous pneumomediastinum: The Mounier-Kuhn syndrome. Case Rep Pulmonol. 2019; 2019:5359309.
58. Ideno S, Miyazawa N, Ishikawa S, Wakamiya R, Shinto A, Mikasa H, Yamamoto S. Anesthetic management of a patient with severe subcutaneous and mediastinal emphysema due to pertussis infection. Masui. 2014; 63:671-674. (in Japanese)
59. Goussard P, Andronikou S, Morrison J, van Wyk L, Mfingwana L, Janson JT. Management of children with tuberculous broncho-esophageal fistulae. Pediatr Pulmonol. 2020; 55:1681-1689.
60. Fearon D, Hesketh EL, Mitchell AE, Grimwood K. Mycoplasma pneumoniae infection complicated by pneumomediastinum and severe mucositis. J Paediatr Child Health. 2007; 43:403-405.
61. Li JC, Nie G, Dai HF. A case of spontaneous mediastinal and subcutaneous emphysema in a patient with HIV-infected pneumonia. Curr HIV Res. 2022; 20:479-484.
62. Park YK, Jung HC, Kim SY, Kim MY, Jo K, Kim SY, Kang B, Woo G, Choi HJ, Wie SH. Spontaneous pneumomediastinum, pneumopericardium, and pneumothorax with respiratory failure in a patient with AIDS and pneumocystis jirovecii pneumonia. Infect Chemother. 2014; 46:204-208.
63. Fiorelli A, Messina G, Capaccio D, Santini M. Recurrent spontaneous pneumomediastinum: a rare but possible event! J Thorac Dis. 2012; 4:431-433.
64. Zachariah S, Gharahbaghian L, Perera P, Joshi N. Spontaneous pneumomediastinum on bedside ultrasound: Case report and review of the literature. West J Emerg Med. 2015; 16:321-324.
65. Al-Hurani M. A rare case of spontaneous pneumomediastinum in a female after shouting: A literature review. Cureus. 2022; 14:e30894.
66. Talmy T, Izhaki Z, Gendler S, Aviram E. Spontaneous pneumomediastinum resulting from passionate cheering at a soccer match. Mil Med. 2023; 188:e2823-e2825.
67. Mumford AD, Ashkan K, Elborn S. Clinically significant pulmonary barotrauma after inflation of party balloons. BMJ. 1996; 313:1619.
68. Swe T, Naing AT, Lixon A, Quist J. Spontaneous pneumomediastinum, pneumoretroperitoneum, and cervicofacial subcutaneous emphysema after repeatedly and forcefully blowing into a bottle. J Community Hosp Intern Med Perspect. 2016; 6:33361.
69. Kouki S, Fares AA. Postpartum spontaneous pneumomediastinum 'Hamman's syndrome'. BMJ Case Rep. 2013. 2013:bcr2013010354.

70. Hochlehnert A, Lowe B, Bludau HB, Borst M, Zipfel S, Herzog W. Spontaneous pneumomediastinum in anorexia nervosa: A case report and review of the literature on pneumomediastinum and pneumothorax. Eur Eat Disord Rev. 2010; 18:107-115.
71. van der Weg G, Wikkeling M, van Leeuwen M, Ter Avest E. A rare case of oesophageal rupture: Boerhaave's syndrome. Int J Emerg Med. 2014; 7:27.
72. Hernandez Garcia LR, Kemper S, Chillag SA. Pneumomediastinum and pneumorrhachis aAssociated with cannabinoid hyperemesis syndrome. Cureus. 2022; 14:e32380.
73. Russell CR 3rd, Benjamin G, Salabei JK, Okonoboh P, Sun L. Pneumopericardium, epidural pneumatosis, and muscular emphysema: Rare complications of spontaneous pneumomediastinum due to refractory hyperemesis Gravidarum. Cureus. 2022; 14:e23800.
74. Bolvardi E, Pishbin E, Ebrahimi M, Mahmoudi Gharaee A, Bagherian F. Spontaneous pneumomediastinum with a rare presentation. Case Rep Emerg Med. 2014; 2014:451407.
75. Flatman S, Morrison E, Elahi M. Spontaneous pneumomediastinum associated with sex. J Radiol Case Rep. 2010; 4:25-29.
76. Tsay CY, Chen YL, Chen CS, Lin PC, Wu MY. Pediatric spontaneous pneumomediastinum after a push-up exercise: An uncommon complication of a common exercise. Children (Basel). 2020; 7:287.
77. Meloy P, Bhambri A, Emeli IM. A case report of spontaneous pneumomediastinum from an unusual cause: Baritone practice. Cureus. 2023; 15:e47289.
78. Nemet D, Suchard JR, DiBernardo LM, Mukai DS, Cooper DM. Pneumomediastinum and subcutaneous emphysema after pulmonary function tests in a young healthy woman. Eur J Emerg Med. 2004; 11:105-107.
79. Baudin F, Gagnon S, Crulli B, Proulx F, Jouvet P, Emeriaud G. Modalities and complications associated with the use of high-flow nasal cannula: Experience in a pediatric ICU. Respir Care. 2016; 61:1305-1310.
80. Cheung HY, Law S, Wong KH, Kwok KF, Wong J. Spontaneous pneumomediastinum in a scuba diver. Hong Kong Med J. 2006; 12:152-153.
81. El Haj Chehade A, Debal G, Mansour W, Avula A, Chalhoub M. Pneumopericardium, pneumomediastinum and air travel: A case report in a patient with Gardner syndrome. Respir Med Case Rep. 2020; 31:101271.
82. Diaz R, Heller D. Barotrauma and mechanical ventilation. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
83. Frusch N, Servais S, De Prijck B, Corhay JL, Beguin Y, Louis R, Duysinx B. Spontaneous pneumomediastinum caused by bleomycin-induced pneumonitis. Acta Clin Belg. 2012; 67:370-371.
84. Fidkowski CW, Zheng H, Firth PG. The anesthetic considerations of tracheobronchial foreign bodies in children: A literature review of 12,979 cases. Anesth Analg. 2010; 111:1016-1025.
85. Widana Pathirana P, Liyanage C. Pneumoperitoneum post esophageal stent insertion managed with paracentesis. J Med Cases. 2022; 13:178-182.
86. Tomasetti P, Kuttenberger J, Bassetti R. Distinct subcutaneous emphysema following surgical wisdom tooth extraction in a patient suffering from 'Gilles de la Tourette syndrome'. J Surg Case Rep. 2015; 2015:rjv068.
87. Randrup TS, Rokkjaer MS. Subcutaneous emphysema after adenotonsillectomy. Ugeskr Laeger. 2012; 174:1904-1905.
88. Rodrigues C, Cabral D, Mota L, Bettencourt A. Bilateral recurrent spontaneous pneumothorax as a late consequence of oesophageal surgery: Case report. Rev Port Cir Cardiotorac Vasc. 2017; 24:142.
89. Vetter MH, Mutscheller C, Cardenas-Goicoechea J. Iatrogenic lower extremity subcutaneous emphysema after prolonged robotic-assisted hysterectomy. Case Rep Obstet Gynecol. 2015; 2015:860719.
90. Vrakopoulou GZ, Michalopoulou V, Kormentza CE, Matiatou M, Zografos KG, Toutouzas KG. Pneumomediastinum and pneumopericardium 11 days after Whipple procedure. A case report and review if the literature. Int J Surg Case Rep. 2020; 71:27-29.
91. Moon MH, Sa YJ, Cho KD, Jo KH, Lee SH, Sim SB. Thoracic air-leak syndromes in hematopoietic stem cell transplant recipients with graft-versus-host disease: A possible sign for poor response to treatment and poor prognosis. J Korean Med Sci. 2010; 25:658-662.
92. Kitami A. Tracheobronchial Injury. Kyobu Geka. 2022; 75:841-845. (in Japanese)
93. Mihatov N, Fenves AZ. Pneumomediastinum in inflammatory bowel disease. Proc (Bayl Univ Med Cent). 2015; 28:347-349.
94. Farah R, Makhoul N. Pneumomediastinum as a presenting symptom of perforated sigmoid cancer: A case report. Cases J. 2009; 2:7356.
95. Giri PP, Roy S, Bhattyacharya S, Pal P, Dhar S. Dress syndrome with sepsis, acute respiratory distress syndrome and pneumomediastinum. Indian J Dermatol. 2011; 56:763-765.
96. James N, Bakshi R, Rudresh SS, Kaushik K, Ghumaan KS, Pannu AK. Pneumoperitoneum from pneumomediastinum in paraquat poisoning. Trop Doct. 2021; 51:241-242.
97. Moorchilot R, Orr PK, Prescott RW. Spontaneous pneumomediastinum after oral ingestion of ecstasy. Acute Med. 2008; 7:37-38.

Received April 30, 2024; Revised July 9, 2024; Accepted July 25, 2024.

*Address correspondence to:
Arunabh Talwar, Division of Pulmonary, Critical Care and Sleep Medicine, Northwell Health, 410 Lakeville Rd. New Hyde Park, NY 11040, USA.
E-mail: arunabh@northwell.edu

Released online in J-STAGE as advance publication August 7, 2024.