Original Article

One hundred cases of primary spontaneous pneumomediastinum: leukocytosis is common, pleural effusions and age over 40 are rare

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Background: Primary spontaneous pneumomediastinum (PSPM) is a benign condition, but it can be difficult to discriminate from Boerhaave syndrome. The diagnostic difficulty is attributable to a shared constellation of history, signs, and symptoms combined with a poor understanding of the basic vital signs, labs, and diagnostic findings characterizing PSPM. These challenges likely contribute to high resource utilization for diagnosis and management of a benign process.

Methods: Patients aged 18 years or older with PSPM were identified from our radiology department's database. A retrospective chart review was performed.

Results: Exactly 100 patients with PSPM were identified between March 2001 and November 2019. Demographics and histories correlated well with prior studies: mean age (25 years); male predominance (70%); association with cough (34%), asthma (27%), retching or emesis (24%), tobacco abuse (11%), and physical activity (11%); acute chest pain (75%), and dyspnea (57%) as the first and second most frequent symptoms and subcutaneous emphysema (33%) as the most common sign. We provide the first robust data on presenting vital signs and laboratory values of PSPM, showing that tachycardia (31%) and leukocytosis (30%) were common. No pleural effusion was found in the 66 patients who underwent computed tomography (CT) of the chest. We provide the first data on inter-hospital transfer rates (27%). 79% of transfers were due to concern for esophageal perforation. Most patients were admitted (57%), with an average length of stay (LOS) of 2.3 days, and 25% received antibiotics.

Conclusions: PSPM patients frequently present in their twenties with chest pain, subcutaneous emphysema, tachycardia, and leukocytosis. Approximately 25% have a history of retching or emesis and it is this population that must be discriminated from those with Boerhaave syndrome. An esophagram is rarely indicated and observation alone is appropriate in patients under age 40 with a known precipitating event or risk factors for PSPM (e.g., asthma, smoking) if they have no history of retching or emesis. Fever, pleural effusion, and age over 40 are rare in PSPM and should raise concern for esophageal perforation in a patient with a history of retching, emesis, or both.

Keywords: Pneumomediastinum; esophageal perforation; Boerhaave syndrome

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Introduction

Primary spontaneous pneumomediastinum (PSPM) is a benign condition that is problematic because it can be confused with Boerhaave syndrome (esophageal rupture). Hamman first described PSPM in 1939 (1). Macklin and Macklin elucidated the pathophysiologic mechanism, showing that sudden intrathoracic pressure changes can cause alveolar rupture and subsequent air tracking in the broncho-vascular tissue plane (2). Consistent with this mechanism, PSPM patients often have a history of cough, asthma, retching, emesis, smoking, or strenuous physical activity (3). The patients are typically young (in their twenties), healthy, and most frequently present with chest pain or dyspnea (4). They may have subcutaneous emphysema and/or a "Hamman sign", an auscultatory finding of mediastinal crunching synchronous with cardiac contraction (5-13). They may have a history of forced Valsalva events, such as childbirth or cannabinoid hyperemesis syndrome (14,15). However, some present with no identifiable predisposing history or inciting event (8,16).

Why are PSPM patients so difficult to discriminate from patients with esophageal perforation? One important reason is that both conditions frequently share a common constellation of history, symptoms, and signs: chest pain, subcutaneous emphysema, and a recent history of retching or emesis. Additionally, there is a very limited understanding of the vital signs and laboratory values of patients presenting with PSPM. For example, only 3 of 19 spontaneous pneumomediastinum case series commented on the presence of tachycardia (8,9,17). Finally, aside from rare cases where a perforation can be clearly identified on computed tomography (CT), no chest radiographic (CXR or CT) findings are known that can definitively discriminate PSPM from Boerhaave syndrome. We suspected that these factors drive frequent inter-hospital transfers to facilitate access to thoracic surgery consultation or urgent esophagrams. Our aims were to improve our understanding of the clinical presentation, diagnostic evaluation, and management of patients with a descriptive study of PSPM by evaluating a large case series treated within our hospital system. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-1136/rc).

Highlight box

Key findings

- Tachycardia and leukocytosis are common in primary spontaneous pneumomediastinum.
- Pleural effusions and age over 40 years are rare in primary spontaneous pneumomediastinum.

What is known and what is new?

- Primary spontaneous pneumomediastinum is a benign condition that can be difficult to discriminate from Boerhaave syndrome due to a shared constellation of history, signs, and symptoms combined with a poor understanding of basic vital signs, labs, and diagnostic findings.
- We provide robust data on vital signs, laboratory values and imaging findings of primary spontaneous pneumomediastinum in 100 patients.

What is the implication, and what should change now?

- Esophagram is not indicated in patients under age 40 without a history of retching or emesis if they have risk factors or history consistent with primary spontaneous pneumomediastinum (e.g., asthma, smoking, Valsalva).
- Fever, pleural effusion, age over 40 and a history of retching or emesis raise concern for esophageal perforation.

Methods

This retrospective case series utilized our Radiology Department's database to generate a list of all CXR and CT chest studies reporting on "pneumomediastinum" in patients 18 years of age or older between March 2001 and November 2019 at University of Wisconsin (UW) Health. Data were from UW Hospital (a 505-bed regional referral center), UW Health East Madison Hospital (a 55-bed community based hospital and Emergency Department), and Unity Point Health-Meriter (a-448 bed community based hospital) with approximately 70,000 annual inpatient admissions and 200,000 Emergency Department visits. Our project was part of a quality improvement initiative for PSPM patient management at our institution. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Institutional Review Board (IRB) approval was deemed unnecessary by institutional review board of the University of Wisconsin Health and consent was waived for this retrospective analysis. The initial search generated 13,286 reports. The vast majority of these commented on the absence of pneumomediastinum. For example, phrases such as "no pneumomediastinum" and "no pneumothorax or pneumomediastinum" were common. Other reports had a positive finding of pneumomediastinum clearly attributable to a specific cause (e.g., postoperative, traumatic, etc.). We selected cases where the etiology of

Table 1 Demographics, histories, symptoms, and signs

Demographics	Values
Age, range (years)	18–66
Age, mean ± SD (years)	25.03±8.5
Male, %	70
History, %	
Cough	34
Asthma	27
Retching or emesis	24
Smoking	11
Exertional physical activity	11
Symptoms, %	
Chest pain	76
Dyspnea	57
Neck pain	47
Signs, %	
Subcutaneous emphysema	33
Hamman sign	10
Pneumothorax	1
Pseudo-pneumothorax	4

SD, standard deviation.

pneumomediastinum was specified as spontaneous or was unclear from the reports. Detailed chart reviews were performed (CTM and EEL), resulting in the identification of 100 cases of PSPM. Predetermined clinical variables were selected from our recent review of nineteen PSPM case series and included demographics, histories, symptoms, clinical signs, and vital signs (3). Vital sign definitions were as follows: fever [defined as a temperature of 38 degrees Celsius (℃) or higher], tachycardia [defined as a heart rate of 100 beats per minute (bpm) or greater], hypotension (defined as systolic blood pressure of less than 90 mmHg), tachypnea (defined as a respiratory rate over 20 per minute), and hypoxia [defined as an oxygen saturation (SpO_2) of less than 90%]. Additional clinical variables included laboratory values: white blood cell count (WBC, cells per 10^9/L), leukocytosis (defined as WBC greater than 11×10^9/L), hemoglobin (Hgb, grams per deciliter), platelet count (PLT, cells per 10^9/L), and serum creatinine (Cr, milligram per deciliter). Finally, we evaluated diagnostic studies, management, and treatment approaches, thoracostomy tube placement, hospital admission, length of stay (LOS), and antibiotic use.

Statistical analysis

Descriptive statistical analysis was performed in Excel.

Results

Demographics

Exactly 100 patients with PSPM were identified between March 2001 and November 2019. Patients ages ranged 18–66 years old (*Table 1*). The mean age was 25 years. Only three patients were over the age of 50, and only five were over the age of 40 (*Figure 1A*). There was a male predominance (n=70, 70%) (*Table 1*). The annual average number of PSPM cases in our system was 5.3, range, 1–18 (*Figure 1B*).

Histories

We evaluated histories reported by the patients. A recent cough (34%) was reported most frequently (*Table 1*). 27% of the patients reported a history of asthma. Retching or emesis were noted in 24% of the patients. A history of smoking was reported in 11% of the patients. Recent strenuous (e.g., sports) physical activity was reported in 11%. Consistent with a reported recurrence rate of 0.98%, one patient (1%) had a prior PSPM (3). We also found some less common past medical histories (e.g., hyperemesis gravidarum, seizure, diabetic ketoacidosis, overdose on methylphenidate). Many of these have been reported previously but were not common enough to be included in our pre-determined variables.

Symptoms and signs

We next evaluated symptoms and signs reported by our patients. Chest pain (76%) was the most common symptom (*Table 1*). Dyspnea (57%) was the second most common symptom (*Table 1*). Finally, neck pain was reported in 47% (*Table 1*). Subcutaneous emphysema (33%) was the most common sign (*Table 1*). The presence or absence of a Hamman sign was reported in 13 of the patients in our case series, with ten of those positive for a Hamman sign (*Table 1*). Five of the patients had imaging reads with "trace" or "tiny" pneumothorax. However, on retrospective review, four had "pseudopneumothorax"

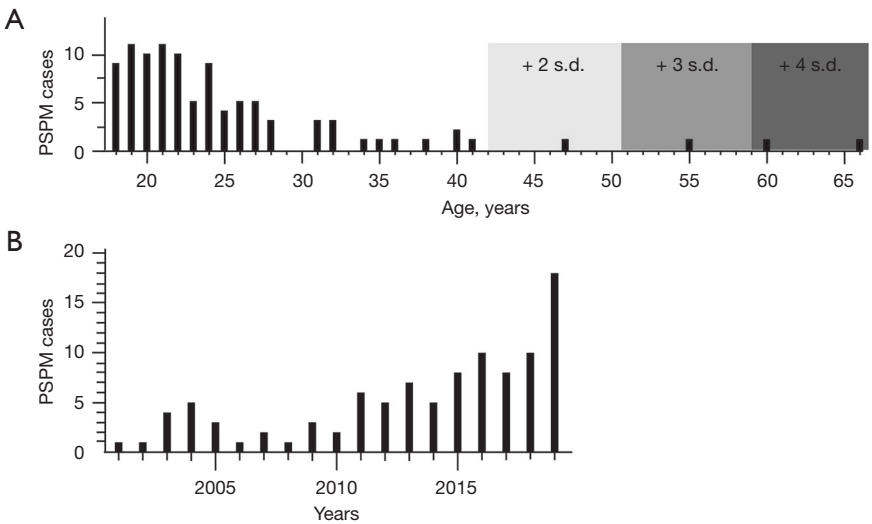

Figure 1 Age over 40 is rare for PSPM patients. (A) Distribution of PSPM patients by age. Shaded boxes indicate standard deviations above the mean. (B) Number of PSPM cases by year, range, 1–18. PSPM, primary spontaneous pneumomediastinum.

Table 2 Vitals and laboratory data

Vital signs and laboratory data	Percent (%)
Fever (>38 ℃)	0
Tachycardia (>100 bpm)	31
Hypotension (systolic blood pressure <90 mmHg)	0
Tachypnea (>20 breaths per minute)	12
Hypoxia (oxygen saturation <90%)	0
Leukocytosis (WBC >11)	30

Bpm, beats per minute; WBC, white blood cell count (cells per 10^9/L).

Table 3 Diagnostic evaluation

Study	Percent [N]
PSPM diagnosed by CXR	94% [98]
CT performed	66% [100]
CXR negative, CT positive PSPM	6% [98]
Effusions on CXR	0% [98]
Effusions on CT	0% [66]
Esophagram	44% [100]
EGD	0% [100]
Bronchoscopy	5% [100]

PSPM, primary spontaneous pneumomediastinum; CXR, chest X-ray; CT, computed tomography; EGD, esophagogastroduodenoscopy.

with a collection of gas superficial to the parietal pleura rather than being intra-thoracic (Figure S1A,S1B). Only one patient had a true pneumothorax.

Vital signs and laboratory values

We evaluated the vital signs and laboratory values of patients upon presentation. Interestingly, no patient presented with fever (*Table 2*). Tachycardia was documented in 31% of patients (*Table 2*). No patients presented with hypotension (*Table 2*). The mean systolic, diastolic, and mean arterial blood pressure (MAP) at presentation were normal (Table S1). Tachypnea was found in 12% of the patients, but none had hypoxia (*Table 2*). Leukocytosis was present in 30% of the patients (*Table 2*). Mean laboratory values at presentation for hemoglobin (14.6), platelet count [346], and creatinine (0.95) were normal (Table S1).

Imaging

A diagnosis of pneumomediastinum was made by CXR in 94% of patients. However, 66 patients underwent CT of the chest, and 64 patients underwent CT after CXR (*Table 3*). Despite a concerted review of the imaging reports and notes, we could not reliably determine the exact indications for most of the CT scans performed after CXR identified pneumomediastinum. In two cases, the reason for subsequent CT was to evaluate for pulmonary embolus. In six cases, the

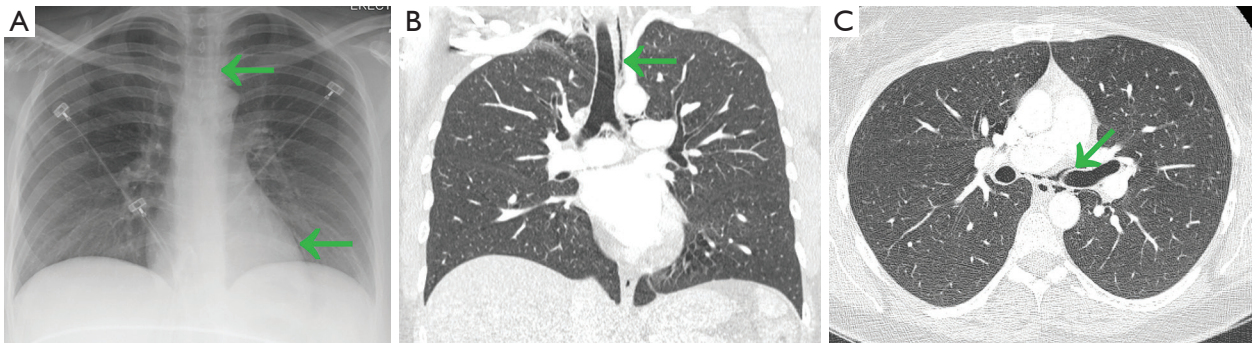

Figure 2 Subtle pneumomediastinum identified on CXR after review of CT imaging. (A) CXR demonstrating initially unrecognized pneumomediastinum. Arrows indicate pneumomediastinum gas identified retrospectively. (B) Representative axial view from CT chest of the same patient. Pneumomediastinum is indicated by arrow. (C) Representative coronal view from CT chest of the same patient. Arrow indicates pneumomediastinum. CXR, chest radiograph; CT, computed tomography.

Table 4 Management of PSPM patients

Management	Percent [N]
Transfers	27% [100]
Transfer for perforation concern	79% [27]
Thoracostomy	0% [100]
Antibiotics	25% [100]
Admission	57% [100]
LOS (days), mean ± SD	2.3±1 [57]

PSPM, primary spontaneous pneumomediastinum; LOS, length of stay; SD, standard deviation.

diagnosis of pneumomediastinum was not made by CXR, but was made on subsequent CT (*Table 3*). Three of those cases had subtle pneumomediastinum evident on our retrospective review of the initial CXR (*Figure 2A-2C*). In two other cases, chest CT was the first imaging obtained and the diagnosis was established by CT. We previously reported no pleural effusion in three earlier case series that included 104 patients (3,18-20). We reviewed both CXR and CT images and reports for pleural effusion in this series. Only one patient was reported to have small pleural effusions on CXR, but no effusion was found on our retrospective review of the CXR (Figure S2). No pleural effusion was found in the 66 patients who did undergo chest CT (*Table 3*).

Esophagography and other diagnostic procedures

Previously, we found that esophagrams are performed on approximately 36% of PSPM patients, presumably because of concern for esophageal perforation (3). In this study, 44 patients (44%) underwent fluoroscopic esophagography (*Table 3*). Twenty-four patients (24%) reported a history of retching or emesis. Of these, 16 (67%) underwent esophagography. Surprisingly, twenty-eight (28%) of patients in our series underwent esophagography without a history of retching or emesis. None of our patients underwent an esophagogastroduodenoscopy (EGD) and only five (5%) underwent bronchoscopy (*Table 3*).

Hospital transfers

Based on our own anecdotal experience, we suspected a high rate of hospital transfers for patients with PSPM due to concern for esophageal perforation. Frequently this is due to the inability to perform, or interpret, esophagography at the referring institution (JD Maloney, personal communication 2018). To our knowledge, there are no reported data regarding transfer rates for PSPM. We found twenty-seven (27%) patients who were transferred from referring facilities; either to our emergency department for triage or as direct admissions (*Table 4*). Of the nineteen transfers where a reason for transfer could clearly be identified, fifteen (79%) were for concern for esophageal perforation.

Admissions and management

In this series, the admission rate was 57% with a mean LOS of 2.3±1 days (*Table 4*). No patients required pleural drain placement for pneumothorax (*Table 4*). Antibiotics were administered in 25% of patients (*Table 4*). Due to limitations

of the electronic medical record and the retrospective nature of our study, we were unable to determine the duration or durations of the antibiotic regimens. Taken together, these results further demonstrate the resource-intensive care dedicated to PSPM patients.

Discussion

PSPM can be difficult to distinguish from spontaneous esophageal perforation (Boerhaave syndrome) due to a shared constellation of history, signs, and symptoms combined with a poor understanding of basic vital signs, laboratory values, and imaging findings of PSPM. Although not well quantified previously, this diagnostic uncertainty leads to extensive resource utilization to exclude esophageal perforation. Most of our understanding of PSPM comes from small case series (average 28 patients), with 47 patients in the largest previous report (3,21). This study includes 100 PSPM patients and has the expected limitations associated with retrospective studies. Limitations include the retrospective study design with possible selection bias as well as potential for variable definitions of clinical parameters on the patient and electronic medical record levels. Our data may also be confounded by the fact that some patients presented directly to our institution whereas others were transferred after varying durations from presentation and possible interventions at other institutions. In addition, capture of transfer utilization and indications are also limited by the reporting at the electronic medical record level.

Our study demographics correlate well with prior studies (3,4). Notably, we establish that age over 40 was rare. This is an important finding because in a systematic review of 33 case series including 1,452 esophageal perforation patients, Hasimoto *et al.* found a mean age at presentation of 55.2 years (22). While Boerhaave syndrome cannot be excluded based on age alone, age is clearly a key variable that differs between these two patient populations.

This study cohort provides the first robust data set inclusive of presenting vital signs and laboratory values of PSPM patients. Nearly one-third of patients in our series had tachycardia. We conclude that tachycardia is common in PSPM patients. The absence of fever in our cohort differs from six prior series that had an average rate of 18.8%±10.3% (8,11-13,19,23). However, one study defined fever as a temperature over 38 ℃, one as a temperature over 37.2 ℃, and no definition was reported in four studies. We conclude that the incidence of fever in PSPM needs further study, but is likely uncommon. The prevalence of leukocytosis in our series (31%) is similar to that reported in seven prior case series (30.8%), further validating leukocytosis as a common finding in PSPM cases (8,9,11,16,18,19). We conclude that tachycardia and leukocytosis remain important clinical parameters to consider in patients with possible esophageal rupture, but they are also common in PSPM patients.

Both CXR and CT are adequate to diagnose pneumomediastinum, but they are not able to adequately discriminate between PSPM and esophageal perforation (3). We now know that pleural effusions are rare in PSPM (3,18,19,20). By contrast, ~10–30% of Boerhaave syndrome patients have pleural effusions (20,22). These results greatly expand our understanding of imaging findings of PSPM patients. We conclude that pleural effusions are rare in PSPM and should raise concern for esophageal perforation in patients with pneumomediastinum and a history of retching or emesis.

When suspicion of esophageal perforation is high, esophagography remains the reference standard for diagnosis of esophageal perforation (24). Our results confirm that nearly half of all PSPM patients undergo barium esophagram to rule out esophageal perforation. Unfortunately, in our experience, many centers are unable to perform fluoroscopic esophagram urgently due to staffing or facility limitations. A growing body of evidence has shown that a contrast CT esophagram has a sensitivity and negative predictive value that is equivalent to fluoroscopic esophagram in patients with esophageal perforation (25). This modality should be considered in the workup of patients with pneumomediastinum and a history of retching, emesis, or both. Our finding that 27% of esophagrams were performed on patients with no history of retching or emesis highlights the question of which patients should undergo esophagram. Our results also show that concern for esophageal perforation drives nearly all inter-hospital transfers of PSPM patients.

Finally, our results provide a clearer view of the high level of resource utilization dedicated to PSPM. This included frequent inter-hospital transfers and diagnostic testing due to concern for esophageal perforation in PSPM patients. Most of these patients are admitted for multiple days, and many of them are treated with antibiotics.

Conclusions

PSPM patients frequently present in their twenties with chest pain, tachycardia, subcutaneous emphysema, and leukocytosis. Approximately 25% of PSPM patients

have a history of retching or emesis; it is these patients that must be distinguished from those with Boerhaave syndrome. Esophagram is rarely indicated and observation is appropriate in patients under age 40 with a known precipitating event or risk factors for PSPM (e.g., asthma, smoking) if they have no history of retching, emesis, or esophageal disease. Fever, pleural effusion, and age over 40 are rare with PSPM and should raise concern for esophageal perforation in a patient with a history of retching or emesis. More frequent use of CT esophagography in patients where concern for esophageal rupture persists may reassure the evaluating providers and decrease unnecessary patient transfers.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-1136/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-1136/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-1136/coif). DPM has received financial remuneration for consulting services from Atricure and Cook Medical, and for advisory board participation from Lung Bioengineering and Atricure. DPM has grant funding from Ethicon. None of these conflicts have any relevance to the content of this manuscript. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Institutional Review Board (IRB) approval was deemed unnecessary by institutional review board of the University of Wisconsin Health and consent was waived for this retrospective analysis.

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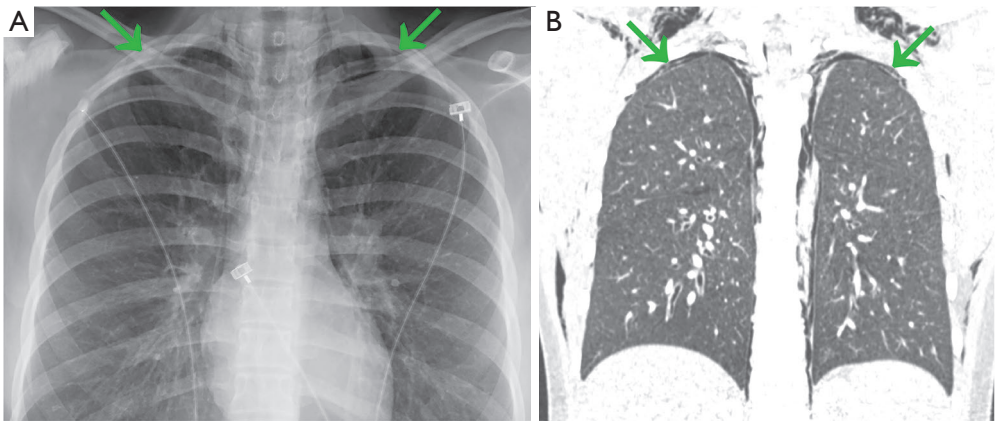

Figure S1 Pseudopneumothorax in patients with PSPM. (A) CXR chest demonstrating pseudopneumothorax in a patient with PSPM. Note the gas under the parietal pleura (green arrows). (B) CT chest demonstrating pseudopneumothorax (green arrows) in the series.

Table S1 Vitals and laboratory data

	N=100
Vital Signs Data	
Temperature (°C)	36.8±0.4
Heart rate (bpm)	90.1±21
Mean systolic blood pressure (mmHg)	128.8±16.4
Mean diastolic blood pressure (mmHg)	74.6±12.7
Mean MAP (mmHg)	92.5±13.1
Respiratory rate (breaths per minute)	18.7 ± 3.8
SpO2 (% oxygen saturation)	97.5 ± 2.3
Laboratory Data	
WBC ($\times 10^9$/L)	12±5.6
Hgb (g/dL)	14.6±1.9
PLT ($\times 10^9$/L)	346±86
Cr (mg/dL)	0.95±0.32

Data are listed as mean ± standard deviation of the mean.

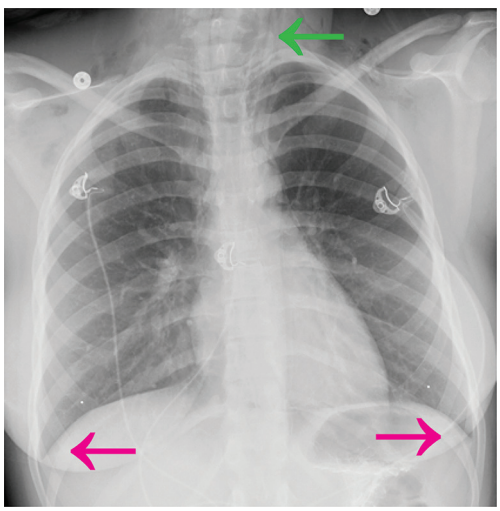

Figure S2 Absence of pleural effusion on CXR of the single patient with reported trace pleural effusions. CXR of the single patient with pneumomediastinum (green arrow) and reported trace pleural effusions. No effusion was found on retrospective review. Pink arrows indicate crisp costophrenic angles with no pleural effusion.

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