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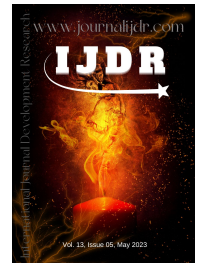
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RESEARCH ARTICLE

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A RARE CASE OF MILD SPONTANEOUS PNEUMOMEDIASTINUM ASSOCIATED WITH LOWER RESPIRATORY TRACT DISEASE WITH SPONTANEOUS REGRESSION

*¹Scaramozzino Marco Umberto, ²Sapone Giovanni, ³Levi Guido and ⁴Plastina Romeo Ubaldo

¹Director Ambulatory of Pulmonology "La Madonnina" Reggio Calabria (RC), Head of thoracic Endoscopy Tirrenia Hospital Belvedere Marittimo (CS); ²Cardiology Department Head of Nursing Polyclinic M.d.c. Reggio Calabria Italy; ³Pulmonology Department, ASST Spedali Civili Brescia, Italy, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy; ⁴MD, Radiologist in ECORAD Radiology and Ultrasound Study, Reggio Calabria (RC), Italy

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*Corresponding author:

Samuel Praveen Kumar, M.

ABSTRACT

According to Hamman's pathogenetic hypothesis, later confirmed by Macklin, the rupture of the "marginal alveoli" at the basis of the pathophysiological mechanism underlying spontaneous pneumomediastinum, would be due, among the various hypotheses, to a sudden increase in intra-alveolar pressure which can be generated by an asthmatic exacerbation. This case highlights how spontaneous pneumomediastinum can be successfully managed conservatively and how the incidence of asthmatic exacerbations secondary to lower respiratory tract infections caused by atypical bacteria is common in young sexually active and smoking populations and predisposes to the described clinical condition. The clinical case demonstrates how important it is to hypothesize the pathology when stabbing chest pain is described, to visit the pulmonologist specialist and to carry out educational campaigns against smoking and in favor of protected sex in the younger generations and to carry out primary prevention on the national territory.

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INTRODUCTION

The presence of free air within the mediastinum, that is not associated with trauma, is known as spontaneous pneumomediastinum (Ojha, 2018). The disease was originally described by Rene Laennec in 1819. The word spontaneous was introduced by Hamman later in 1939. The condition can result from an injury that leads to air leakage into the mediastinum from the lung. Spontaneous indicates that it is encountered in patients with underlying lung diseases or without any medically relevant conditions as compared to that secondary pneumothorax that results from trauma (Covantev, 2019). The pathophysiological mechanisms underlying pneumomediastinum are six:

- 1) Direct mechanism
- 2) Hamman-Macklin mechanism
- 3) Subfascial route (secondary to pneumothorax or chest wall injury)
- 4) Subserosal route:

-**Descending:** via middle cervical aponeurosis.

-**Ascending:** via retroperitoneal diaphragmatic orifices.

5) By the pleuro-mediastinal route

6) Secondary to infection by aerogenic germs.

In particular, according to Hamman's pathogenetic hypothesis, later confirmed by Macklin, the event would occur following a spontaneous pneumothorax. There is a rupture of the 'pulmonary marginal alveoli', placed in contact with the pulmonary vessels, interstitial tissue, bronchi and bronchioles, which are subjected to increased pressure stress during the event. The rupture would be due to an altered pressure gradient between the alveolus and the blood vessel or due to a sudden increase in intra-alveolar pressure (asthma crisis), Valsalva manoeuvre, vomiting, persistent coughing, deep breathing, intense exercise, Heimlich manoeuvre, abrupt reduction in pulmonary arterial flow (pulmonary embolism or altered venous return to the heart). Once the alveolus has ruptured, the air penetrates the interstitium resulting in 'interstitial emphysema' and through an 'escape route' along the perivascular sheaths at first the air reaches the

pulmonary hilum by an anterograde route, from there the air distributes either upwards or downwards, in some cases dislodging the diaphragmatic parietal pleura, in other cases passing through the mediastinal parietal pleura (pathophysiological mechanism not unanimous in the literature). A very rare eventuality described in the classification and for which it is often difficult to find a cause since the pneumomediastinal event is acute, is represented by infection with airborne germs (*Klebsiella*, *Enterobacteriaceae*, *clostridia*, etc.) especially in the post- cardiothoracic surgery (Romero, 2010). In the differential diagnosis of Pneumomediastinum causes, there is also asthma exacerbation. We hope that this case will be helpful to increase awareness among readers, and could help to identify spontaneous pneumomediastinum early in recent asthma exacerbation, as well as highlighting how such cases can be managed successfully with conservative measures in ambulatory setting.

CASE PRESENTATION

In January 2023, a 20-year-old Caucasian male came to my attention with worsening dyspnea. In the collection of anamnestic data: farm laborer, reported that in the past he had recently engaged in unprotected sexual intercourse, no use of drugs reported, no drug allergy, negative prick test performed in the past, kept farm animals (chickens and hens). Familiarity with bronchial asthma (mother) smoker of a pack of fifteen cigarettes a day, psoriasis. He reported recent episodes (December 2022) of yellowish catarrhal cough with a previous episode of cough associated with stinging chest pain, which then disappeared spontaneously.

At the outpatient visit, the patient reported only dyspnoea and an unproductive cough; he was asymptomatic due to pneumomediastinum. On physical examination of the chest there was no evidence of subcutaneous emphysema, blood pressure: 120/80mmHg, heart rate: 68 beats/minute, peripheral oxygen saturation: 98% in ambient air, diffusely harsh and soft vesicular murmur with many rhonchi in forced expiration. The patient underwent global spirometry in our center with a bronchoreversibility test visible in Table 1. It can be seen that after the administration of 400mcg of salbutamol there is a partially positive response to the bronchodilator (+10% FEV1 and +35% parameter FEF25-75 which is the expression of FVC in the small airways). Therefore I started treating the patient with a combination therapy of inhaled corticosteroids and long acting beta two agonists twice a day for 3 months combining for the first month macrolide only for six days and then doxycycline forty milligrams a day. Finally, I advised the patient to give up smoking completely. Furthermore, I advised to perform the CAT scan at three months and subsequent blood tests; as you can see in Table 2.

DISCUSSION

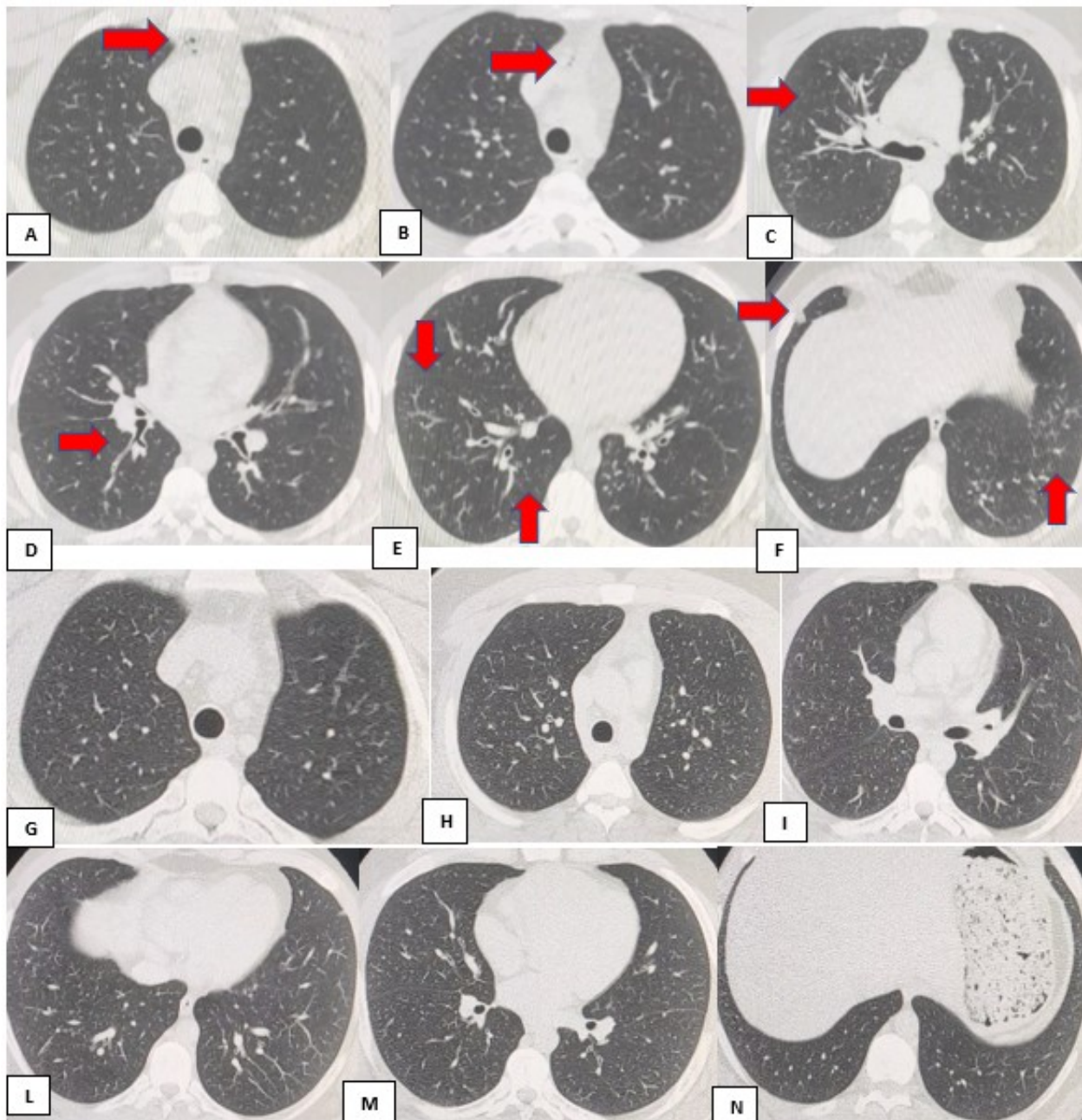
For the vast majority of patients in hospital setting with these conditions, the treatment is conservative, which includes bed rest, oxygen therapy, and adequate analgesia. Asthma is the most common chronic respiratory disease worldwide and its prevalence is increasing. Acute asthma complications are often the reason for admission to emergency healthcare service.

Table 1. Spirometry tests at time zero with broncho-reversibility test and at three months with inhaled corticosteroids and beta two agonist long acting twice day; with stability of the spirometric values compared to the volumes described during the broncho-reversibility test

	Results baseline	Results after Salbutamol 400mcg	Results three months
FVC%	102%	103% (+1%)	102% (-1%)
FEV1%	89%	98% (+10%)	97% (-1%)
FEV1/FVC%	86%	94% (+9%)	95% (+1%)
FEF ₂₅₋₇₅ %	64%	87% (+35%)	86% (-1%)
TLC%	100%	/	96%
PEF%	86%	87% (+1%)	91% (+4%)
RV%	75%	/	60%
FET (sec)	7,33 sec.	7,14 sec.	7,70 sec.
FEF ₂₅ %	80%	89% (+11%)	84% (-5%)
FEF ₅₀ %	65%	92% (+41%)	88% (-4%)
FEF ₇₅ %	58%	81% (+40%)	88% (+7%)
RV/TLC%	75%	/	62%
VC%	108%	/	108%
IC%	122%	/	119%

Tab. 2. As can be seen from the laboratory tests, despite the therapy, a weak positivity of the antibodies against *Chlamydomphila Pneumoniae* persists (IgM: 1.4). However, none of the inflammation indices is high (negative value of PCR and ESR). white blood cells normal. There is an increase in eosinophilic cells in the leukocyte count (370 cells) the latter data correlates with bronchial asthma with an eosinophilic component

Tab. 2 Blood Test at three months	Results
<i>Chlamydomphila Pneumoniae</i> IgM	1,3 AU (positive)
<i>Chlamydomphila Pneumoniae</i> IgG	<10 AU/ml (negative)
<i>Chlamydomphila Pneumoniae</i> IgA	<10 AU/ml (negative)
<i>Mycoplasma Pneumoniae</i> IgA	<10 index (negative)
<i>Mycoplasma Pneumoniae</i> IgM	0,4 index (negative)
<i>Mycoplasma Pneumoniae</i> IgG	Twenty-two index (positive)
ESR	4 mm/h
CRP	<3,30 mg/l
LDH	229 U/L
Fibrinogen	333mg/dl
Anti-Hbs	Seventy-eight mU/ml
Hemoglobin	16,2g/dl
Vitamin B12	301 pg/ml
WBC	7.470 x 10 ³ /uL
Neutrophils	3,76 x 10 ³ /uL
Eosinophils	0,37 x 10 ³ /uL
Anti-HCV	Negative
Alpha1 anti-trypsin	1,33g/l
Serum Creatinine	0,96 mg/dl
D-Dimer	0,17mg/l



A-B: Time zero chest CT scan showing areas of air bubbles within the superior mediastinal space

C: Time zero chest CT scan showing areas of bronchiolitis due to lower respiratory tract infection prevalent in the middle lobe associated with bilateral bronchial ectasia

D-E-F: Chest CT scan at time zero showing areas of bronchiolitis due to lower respiratory tract infection prevalent in lower lobes with bilateral bronchial ectasia and in the peripheral subpleural area of the right lower lobe, a subsolid nodule of about five millimeter of diameter.

G-H-I-L-M-N: Chest CT scan carried out at three months on April 2023, in the course of regular intake of inhaled corticosteroid and long-acting bronchodilator (pre-Metred Dose Inhaler with extrafine formulation) plus macrolides and doxycycline, showing complete resorption of the apical pneumomediastinum and complete regression of the previously reported bronchiolitic areas with disappearance of the right basal nodule.

Nevertheless, there are also rare complications of asthma such as spontaneous pneumomediastinum, which is often difficult to diagnose [3]. Pneumomediastinum is a rare condition, which requires differential diagnosis with several other diseases [4]. The condition is more predominant in males (57%–87%). The medical history predisposing to the development of spontaneous pneumomediastinum includes smoking in 29%–34.1% cases, asthma in 14%–21.9%, idiopathic pulmonary fibrosis in 7%, and chronic obstructive pulmonary disease in 4% [5]. Nevertheless, the condition can be associated with a variety of other diseases including the use of drugs, infections of *Pneumocystis Carinii* in HIV, perforation of the esophagus and even perforation of sigmoid diverticulum [6].

Clinical symptoms include chest pain 54%–59.5%, dyspnea 25.5%–39%, cough 32%–32.5%, subcutaneous emphysema 32%–42.9%, odynophagia 4%, neck swelling 14%, pneumothorax 7%, Hamman's sign (crunching sign over the precordial area synchronous with heartbeats) is present in approximately 20% of patients [7]. In children, cough (81%), dyspnea (75%), and chest pain (56%) are the predominant symptoms and expiratory wheezing (63%) and neck crepitus (50%) are the most common physical findings [8]. In more than a half of the cases there is no precipitating factors (51.2% of cases). Other common precipitating factors may include physical exercise in 12.2% of cases, vomiting in 9.8%, cough in 7.3%, and infection of the upper airways in 7.3% of cases [9]. The differential

diagnosis of spontaneous pneumomediastinum must include several other conditions, in particular, cardiac diseases (acute coronary syndrome, pericarditis, cardiac tamponade, pneumopericardium), lung diseases (pneumothorax, pulmonary embolism, tracheobronchial tree rupture asthma exacerbations, COPD and interstitial lung disease), musculoskeletal disorders, the Valsalva maneuver (e.g. child birth), strenuous exercise, shouting, barotrauma (diving, intubation), cocaine inhalation, and diseases of the esophagus (rupture and perforation of the esophagus, Boerhaave syndrome)[10].

CONCLUSIONS

The acute event can degenerate into pneumothorax which in some cases may require chest surgery. In the clinical case described, the prognosis was excellent as the pathology regressed spontaneously even following pharmacological therapy. It is evident from the clinical experience described and from the existing literature on the subject, that there is an association between the development of the acute event of spontaneous pneumomediastinum, bronchitic exacerbation associated with infectious bronchiolitis caused by an atypical microorganism (*Chlamydia pneumoniae*) and the diagnosis of Bronchial asthma always needs to be investigated, starting from the collection of the patient's clinical data, which can sometimes bring out interesting data on lifestyle habits and possible exposure to risk factors, potential causes of the clinical and symptomatological picture. The case is interesting to publish since rare cases of spontaneous pneumomediastinum associated with bronchial asthma emerge from the literature and spontaneously regress. The role of the pulmonologist in the management of these cases remains crucial to modify the natural clinical history of the disease. Cigarette smoking cessation and protected sexual relations represent a goal to be achieved in younger patients by sensitizing them through educational campaigns.

Corresponding author: Dr. Marco Umberto Scaramozzino, Director Ambulatory of Pulmonology "La Madonnina" Reggio Calabria (RC), Head of thoracic endoscopy Tirrenia Hospital Belvedere Marittimo (CS).

Ethics approval and consent to participate: The patient has signed informed consent for the processing of personal data and dissemination of the material for scientific research purposes within the "La madonnina" clinic.

Availability of data and material: The data that support the findings of this case report, are available from the corresponding author, MUS, upon reasonable request.

Competing interests: none to declare.

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