European Review for Medical and Pharmacological Sciences 2022; 26: 3249-3260

Non-traumatic non-cardiovascular thoracic emergencies: role of imaging

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Abstract. – Patients presenting to the emergency with thoracic symptoms could have a wide variety of causes, even if the traumatic and vascular causes are excluded. Therefore, the diagnosis is often a challenge for emergency physicians. Anamnesis, physical examination and laboratory testing need to be integrated with imaging to get a rapid diagnosis and to distinguish among the potential causes. This review discusses the role of diagnostic imaging studies in the emergency setting in patients with non-traumatic non-cardiovascular thoracic symptoms. The use of chest x-ray, bedside lung Ultrasound and Computed Tomography in the diagnosis and care of these patients have been reviewed as well as the common findings on imaging.

Key Words:
Emergency, Imaging, Computed tomography.

Introduction

Evaluating patients who present to the Emergency Department (ED) with thoracic symptoms is a challenge for clinicians. Excluding the traumatic and vascular causes, many other potential causes can lead to these conditions, such as infectious diseases, pneumothorax, or neoplasms. Although clinical history, physical examination, and the presence of risk factors are important in establishing the etiology of the symptoms, these methods need to be integrated with laboratory and radiologic testing to make a correct and prompt diagnosis[1]. In the emergency setting the first-line imaging method used is chest x-ray (CXR), capable of assessing the localization and presence of many pleural and pulmonary parenchymal alterations, as well as an evaluation of mediastinal structures. However, the main limitation of CXR is its low sensitivity[2]. Thoracic ultrasound (US) has also found its use in emergencies, given its easy availability and execution at the patient's bedside. The Bedside Lung Ultrasonography in Emergency (BLUE) protocol, proposed by Lichenstein et al[3], offers one approach to differentiate several causes of respiratory failure. However, some skill to acquire and interpret images is required[3,4]. Unenhanced and/or contrast-enhanced Computed Tomography (CT) provides detailed imaging of the respiratory system with highly sensitive and specific results, so that is often necessary for a correct diagnosis, to evaluate the cause and extent of the disease[5].

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Chest Pain

Acute chest pain represents the second leading cause of access to the ED, especially among women over 65 years of age[6,7]. About 60-80% of patients with chest pain in ED have no evidence of acute coronary syndrome so they have non-cardiac chest pain (NCCP)[8]. Among the many causes leading to NCCP, musculoskeletal, gastrointestinal (for example, gastroesophageal reflux disease or esophageal motility disorders), psychiatric, and pulmonary or mediastinal (pulmonary embolism, pneumonia, pneumothorax) disorders are detected[9]. CXR and CT imaging are crucial in recognizing pulmonary pleuro-parenchymal causes of chest pain and are also useful in recognizing musculoskeletal causes in association with specialist clinical evaluation. A frequent cause of chest pain is pneumothorax (PNX). Subjects presenting to the ED with suspicion of spontaneous pneumothorax, not caused by trauma or iatrogenic causes, are typically male, of tall stature, and low body weight. In cases where the pneumothorax is in older patients, the cause often lies in underlying pulmonary problems, especially in smokers with chronic obstructive pulmonary disease (COPD)[10-12]. Diagnosing PNX at an early stage is critical to prevent it from worsening to life-threatening conditions[13]. Chest US is a useful tool for an initial assessment of the pulmonary conditions[14], so much so that a study conducted by Ding et al[15] showed that this method has a sensitivity and specificity of 88% and 99% respectively in comparison with CXR examination in anteroposterior projection, which had 52% sensitivity and 100% specificity in the diagnosis of PNX. Characteristic signs of PNX on US examination are the absence of lung sliding and the presence of A-lines (repeated linear artifacts parallel to the pleural line)[16-19]. At CXR, pneumothorax is identified by the visualization of a pleural line separated from the chest wall causing a diaphanous area in the absence of visible parenchymal vessels (Figure 1). However, these signs can be difficult to detect, especially if PNX is small, or due to the presence of emphysema, or poor exposure of the film. Tian et al[20] proposed a computer aided diagnosis system (CAD) to assist radiologists in PNX identification via frontal CXR. Tulay et al[21] suggested oblique chest X-ray as an alternative imaging technique to identify PNX in EDs. CT is the gold standard in the evaluation and quantification of PNX, be-

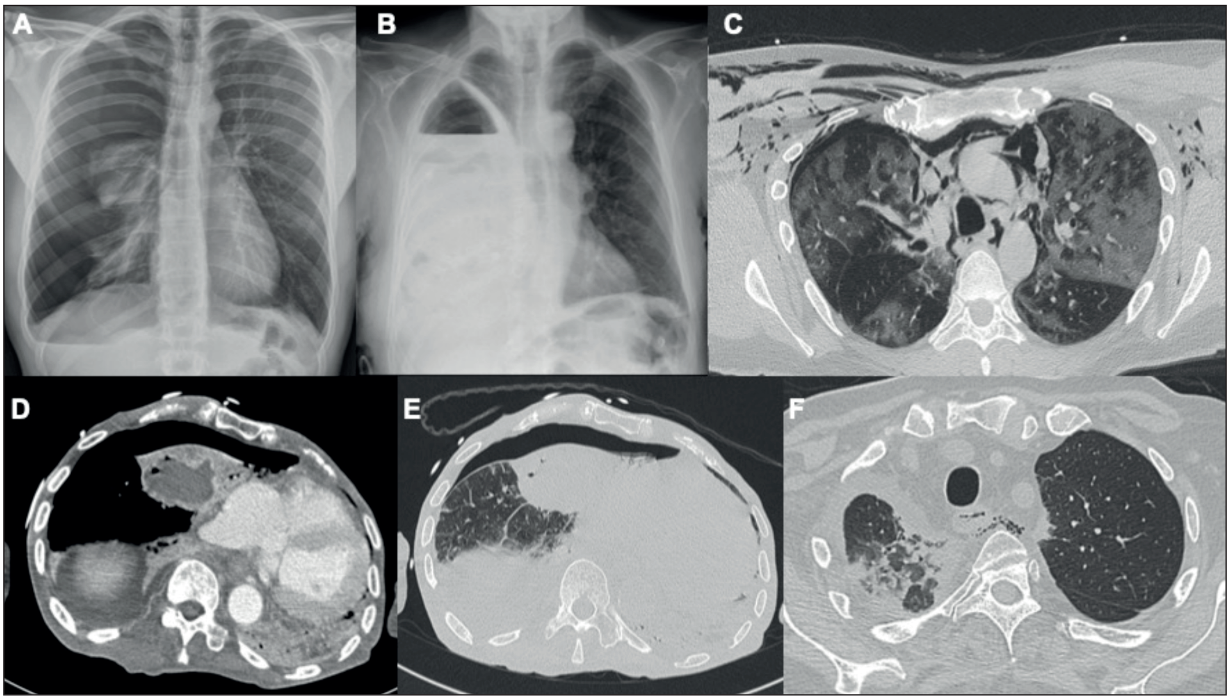

Figure 1. Chest pain. A case of pneumothorax (**A**) and pneumothorax with pleural effusion (**B**) both with compression on the mediastinal structures. **C,** A case of acute COVID-19 pneumonia with important pneumomediastinum and subcutaneous emphysema, due to barotrauma caused by cough. **D-E,** A case of pneumothorax with an associated abscess of the medium lobe. **F,** Esophageal perforation with pneumomediastinum due to esophageal lymphoma, note the aspiration pneumonia in the right lung.

ing also able to assess the presence of subpleural blebs or other associated pathology[22]. To better quantify the volume of PNX, some studies have been performed with the use of deep learning software such as the one by Röhrich et al[23] that could facilitate the therapeutic decision in these patients. In association with PNX, another entity that should be considered in the emergency setting is hemo-pneumothorax, in which hemothorax and pneumothorax occur together. Hemothorax is a complication of PNX in 3-7% of cases[24,25]. Pneumomediastinum most frequently results from perforation of organs such as the esophagus, trachea or bronchi, and lungs. The most common symptoms are chest pain and dyspnea in association with signs of subcutaneous emphysema. On CXR imaging, the characteristic sign is a diaphanous area surrounding the normal mediastinal profile. Other signs, such as the "double bronchial wall sign" or air surrounding the pulmonary artery, may also be present[26] (Figure 1). Spontaneous pneumomediastinum may be associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia. In literature, there are described cases of spontaneous pneumomediastinum with or without PNX developing in patients with COVID-19. All cases didn't undergo invasive or non-invasive positive pressure ventilation. The authors suggested that the cause could be severe diffuse alveolar damage developing the alveolar rupture resulting in interstitial emphysema up to pneumomediastinum[27].

Dyspnea

People accessing the ED with dyspnea as a symptom could have many different underlying causes most of which have a cardiac or pulmonary etiology. The most common pulmonary causes of dyspnea are exacerbation of COPD, bronchial asthma, pneumonia, pulmonary embolism. Other causes could be a reactivation of interstitial lung disease (ILD) or superimposed infection, up to the acute interstitial pneumonitis condition, which is a rare cause of progressive and worsening dyspnea with multiple pulmonary opacities in an otherwise healthy lung, which has a high mortality rate exceeding 50%[28]. CXR often represents the primary imaging modality in acute dyspnea because it can assess the presence of consolidation, PNX and pleural fluid even if it shows low sensitivity. Spirometry is the gold standard for the diagnosis of COPD. However, imaging has a role in the evaluation of patients with COPD, especially for recurrent COPD exacerbations, low response to medical therapy, or to rule out coexisting pulmonary abnormalities[29]. In the case of COPD, the most frequent CXR findings are a flattening of the diaphragmatic profile, an enlarged lung volume represented by an increased anteroposterior thoracic diameter, a verticalized cardio-mediastinal profile and an increased retrosternal air space[30]. On CT, patients with emphysema show areas with low attenuation values. To avoid intra and inter-reader variability, automated CT quantification of emphysema was proposed. Several studies found a correlation between CT densitometric analysis and clinically significant parameters such as levels of dyspnea, FEV_1, frequency of COPD exacerbations[31,32]. Coxson et al[33] proposed quantitative CT for monitoring the progression of emphysema.

In recent years the use of Transthoracic US is becoming increasingly important for its non-invasiveness and the absence of ionizing radiation. Guttikonda et al[34] proposed a multiorgan (lung-cardiac-renal and inferior vena cava) US strategy for rapid differentiation of causes of dyspnea in ED. Zanobetti et al[35], in their study on 2.683 patients presenting in ED with acute dyspnea, demonstrated that the integration of US with the standard approach can reduce the diagnostic time without significant difference in terms of sensitivity and specificity. However, high-resolution computed tomography (HRCT) remains the "gold standard" for appropriate detection, characterization, radiological diagnosis and the definition of the severity of pulmonary involvement[36,37]. The transthoracic US shows a very high negative predictive value for the interstitial syndrome. However, the presence of B-lines (hyperechoic comet-tail artefacts arising from the pleural line) is not specific for ILD, being found in many other conditions such as pneumonitis, acute respiratory distress syndrome, and atelectasis[38]. CT has a central role in the assessment of ILD. On CT examination, the presence of new areas with ground glass opacities (GGO) features, on the background of honeycombing and fibrosing-like alterations, is suggestive of ILD exacerbation[39,40]. Several CAD systems were proposed to improve CT evaluation. For example, Maldonado et al[41], using a novel software tool named CALIPER (Computer-Aided Lung Informatics for Pathology Evaluation and Rating), found that some quantified measurements were predictive of survival in idiopathic pulmonary fibrosis. Another cause of dyspnoea is tracheobronchial foreign body (TFB) aspiration, a potentially fatal cause that should be promptly evaluated because of the high possibility of airway obstruction. In the case of suspected TFB, CXR is the first-line imaging modality. It can detect the inspired material whenever it is radiopaque such as metal or teeth. However, the most frequent causes of aspiration in adults are organic materials, such as food, which are not radiopaque, raising problems in their diagnosis. Indirect signs of TBF that can be evaluated at CXR are atelectasis, air trapping, or obstructive pneumonitis. At CT evaluation, the presence of the foreign body within the bronchial lumen in association with bronchial wall thickening or parenchymal alterations such as atelectasis of the involved tract can also be demonstrated[42-44]. Another cause of dyspnoea is lung cancer. This is the leading cause of death in men and the second leading cause of death in women, especially in smokers. Chest emergencies related to this disease can be caused either by the primary tumour itself or by complications related to therapy. In particular, the tumour can cause the compression or obstruction of adjacent structures, such as superior vena cava syndrome (SVC), bronchial or tracheal obstruction, or the infiltration of vascular or lymphatic structures. There may also be indirect complications, including all systemic manifestations resulting either from the presence of the tumour or from therapy, such as pulmonary embolism, deep vein thrombosis, or pulmonary infections due to concomitant immune-compromised conditions[45,46]. Airway obstruction may be central or peripheral, extrinsic or endoluminal. CXR may be normal or show indirect signs of obstruction such as parenchymal atelectasis or deviation of bronchi or trachea. CT may more extensively evaluate the involvement of the tracheobronchial tree, properly assessing its location and extension. SVC syndrome is caused by direct obstruction of the superior vena cava by the primary tumor or by mediastinal lymphadenopathy. CT imaging after administration of intravenous contrast medium is essential to confirm the diagnosis by evaluating the presence of ab extrinsic SVC obstruction or the presence of thrombosis. Pulmonary toxicity is a common occurrence in the course of tumor therapy that despite not having significant imaging features, often manifests as diffuse alveolar damage (DAD) or organizing pneumonia (OP). DAD manifests on CT as diffuse areas of GGO, consolidations and septal thickening. Organizing pneumonia manifests as heterogeneous opacities that may be associated with pleural effusion[47-50]. The most frequent CT findings of OP are consolidations with air bronchograms, subpleural ground-glass opacities and sometimes the reversed halo sign. These pulmonary abnormalities are sometimes migratory. OP is an interstitial lung disease and can be idiopathic (known as cryptogenic organizing pneumonia) or secondary organizing pneumonia. There are several causes of secondary organizing pneumonia, such as connective-tissue diseases, infections, drugs, radiation therapy to the chest and other toxic exposures[51]. The largest case series of Radiation-Induced Organizing Pneumonia has been reported after breast radiotherapy, with an incidence ranging from 0.8% to 2.9%. However, there are also reports on Radiation-Induced Organizing Pneumonia after chest irradiation for lung cancer and thymoma. In these patients, chest CT has a central role in distinguishing OP from radiation pneumonitis[52]. Lung tumors, esophageal cancer as well as mediastinal masses including lymphoma, can cause abnormal communication between the airway and esophagus, leading to the formation of fistulas. The most affected tract is the tracheal one, but also the bronchi can be involved, mainly the left one. This communication causes the occurrence of lung infections, aspiration and cough, leading to symptoms such as dyspnea. The site and extension of the fistula can be evaluated by CT, as well as the involvement of the lung parenchyma[53,54] (Figure 2).

Hemoptysis

Hemoptysis is a manifestation of many different diseases, and prompt diagnosis is critical given the severity and high mortality of this entity. CXR is often the first imaging performed on patient admission to the ED. This imaging modality can assess the localization of the problem, evaluating the involvement of a single lobe or hemithorax. This information can be used to help in the subsequent therapeutic/diagnostic procedure[55,56]. However, several studies have shown that only in about 45% of cases the site of bleeding is identified by CXR examination alone, especially in those who have had massive hemoptysis, emphasizing that CT-angiography is necessary to correctly assess the site of bleeding and the cause, being useful in the therapeutic management of these patients[57]. CT-angiography, according to some studies conducted, such as the one of Chalumeau-Lemoine et al[58], has demonstrated equivalence to flexible bronchoscopy in localizing the source of bleeding but is more effective in determining the cause of bleeding. CT

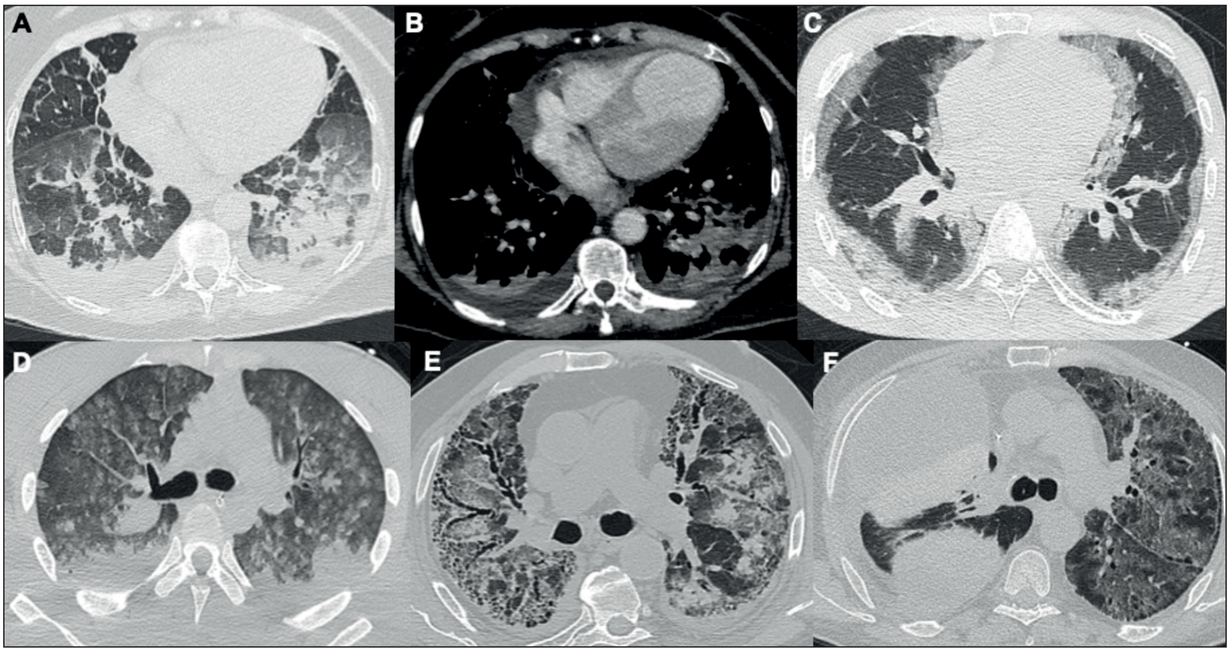

Figure 2. Dyspnea. **A-B,** A case of acute pulmonary edema caused by myocardial infarction (note in B the interventricular septum getting thinner in the apex). **C,** Acute pneumonia caused by inhalation of a drug (Crack-lung). **D,** Acute pulmonary edema due to inhalation of pool water. Finally, a case of exacerbation of an interstitial pneumonia (**E**) and drug toxicity in patient with right-lung cancer during immunotherapy (**F**).

findings suggestive for bleeding are the presence of endoluminal fluid density material in a lobar or segmental bronchus in association with areas of consolidation or GGO in the adjacent lung parenchyma, representative of alveolar haemorrhage[59]. Among the causes of hemoptysis, we mention neoplastic pathologies such as lung cancer. The highest frequency of bleeding has been found in patients with squamous cell carcinoma of the lung. The origin of the bleeding is most often a bronchial artery, while more rarely the erosion of a pulmonary artery by the tumour[60]. Necrotizing inflammatory diseases such as tuberculosis are also a cause of hemoptysis. In particular, Rasmussen's aneurysms, which are arterial pseudoaneurysms found in areas involved by inflammatory processes of tubercular nature, can cause hemoptysis, leading to sentinel bleedings that precede more important hemorrhages and need a timely diagnosis. These are visible on CT imaging as small nodularity in the walls of the tubercular cavity that show vivid enhancement[61]. Dieulafoy disease is a rare pathology, best known in organs such as the colon or the small intestine, but recently found and studied also in the bronchial system. It is characterized by the presence of submucosal dilated vessels that have a higher tendency to bleed. They are often associated with chronic inflammatory states such as chronic bronchitis and its diagnosis is essential in case biopsy is to be undertaken due to the high risk of bleeding[62] (Figure 3).

Infections

Another cause of ED access is symptomatology suspicious for pneumonia. In the last two years, the pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to an increase in hospitalizations caused by this respiratory virus. Therefore, this is currently the first diagnosis that should be excluded, but many other viruses or bacteria can cause pulmonary manifestations and have also to be recognized[63]. The most severe cases of SARS-CoV-2 have manifested as viral interstitial pneumonia that could be complicated in severe acute respiratory distress syndrome (ARDS) necessitating hospitalization to intensive care unit (ICU) and even death[64-66]. CXR is used in most Italian hospitals as first-line imaging to assess the pulmonary involvement of these patients as also recommended by the Italian Society of Radiology (SIRM)[67-70]. In these two years many studies have been conducted on what are the main features found at CXR examination, but from different studies conducted by Cozzi et al[71], as well as in the study of

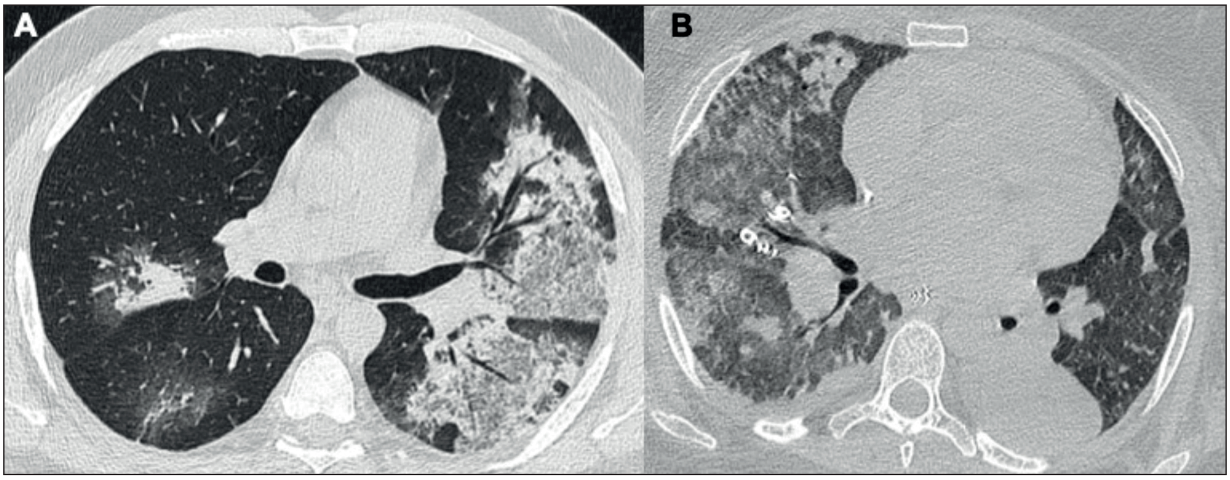

Figure 3. Hemoptysis. **A,** A case of acute bilateral alveolar hemorrhage in a patient with vasculitis, instead (**B**) is a case of Rendu-Osler disease (note the endovascular treatment with metallic coils) with active hemorrhage during bacterial lung infection.

Moroni et al[72], conducted respectively on 482 and 327 patients, it was found that the most frequently detected signs are lung consolidations, GGO, nodules and reticular-nodular opacities, with a prevalent bibasal distribution. However, given its low diagnostic sensitivity, especially in the early stages of the disease, CT is indicated in clinical suspicion of the disease with normal CXR or nonspecific signs, in case of acute complication, or after intubation (Figure 2)[73,74]. It's important to standardize CT imaging making it more useful for clinical practice, and allowing the selection of cut-offs that can also help in various therapeutic decisions. Therefore, many studies have been conducted to validate a standardized assessment of pulmonary involvement of COVID-19, such as the COVID-19 Reporting and Data System (CO-RADS) created by The Dutch Radiological Society or the Radiological Society of North America (RSNA) chest CT classification system[75-77]. In the early stages of the disease, lung imaging, also on CT, may be negative[78,79]. As Bernheim et al[80] reported in their study conducted on 121 symptomatic patients, normal CT imaging was found in 56% of patients who had symptoms arising within the previous 2 days. As the days increased, the percentage of negative CTs decreased, reaching 9% at 3-5 days and 4% at 6-12 days[80]. In particular, in the early stages of the disease, the radiological patterns most commonly encountered were bilateral, peripheral, and sub-pleural or peri-broncho-vascular areas of patchy or segmental ground-glass opacities, mainly involving the lower lobes, in association with rare areas of consolidation (Figure 2). GGOs were defined as hazy areas with slightly increased density in lungs without obscuration of bronchial and vascular margins, which may be caused by the partial displacement of air due to partial filling of airspaces or interstitial thickening [81]. In later stages, the predominant pattern is diffuse GGO, with parenchymal consolidations, interlobular septal thickening, and sometimes crazy-paving pattern (Figure 3). The late phase, before resolution, consists of diffuse consolidations[82-84]. Although artificial intelligence (AI) cannot currently be used as the first modality of detection, especially in emergencies, there is much expectation for the future regarding the role it could take in the diagnosis, quantification of parenchymal involvement and treatment of serious and complex diseases such as COVID-19 pneumonia. Indeed, since the onset of this pandemic, many studies have been conducted through the use of AI to identify, stratify, and assess the severity of pulmonary involvement on imaging through the use of specific software[85-89]. An example in this regard is the study conducted by Grassi et al[90], who tried to use AI software for quantification of pneumonia lesions to improve the management for these patients. Another study is the one conducted by Caruso et al[91], who evaluated the role of texture-based radiomics analysis in differentiating SARS-CoV-2 pneumonia from pneumonia of other etiology on Chest CT imaging. In addition to viral pneumonia, bacterial pneumonia is also important in the hospital setting. Community-acquired pneumonia (CAP) is a frequent respiratory infectious disease, caused by bacteria such as *S. Pneumoniae* and *S. Aureus*. Unlike the CXR pattern described above for viral infections, imaging of bacterial infections typically shows lobar consolidation with air bronchograms, which may be associated with pleural effusion. Segmental or lobar parenchymal consolidation with air bronchograms can also be shown on CT examination, which can more correctly assess disease burden[92]. Two other entities are aspiration pneumonitis and aspiration pneumonia. These are two different pathologies. The first one is caused by a chemical insult due to a macro-aspiration of liquids such as gastric acid or bile; this condition leads to symptomatology characterized by hypoxemia, fever and tachycardia. The second one is, instead, a bacterial infection involving the lungs, mainly sustained by anaerobes, secondary to aspiration of oropharyngeal contents or of the upper gastrointestinal tract. These predominantly involve the lower lobes of both lungs. On CXR examination they appear as an area of basal pulmonary thickening while on CT as parenchymal consolidations in the territory of the involved bronchi that may show the presence of possible endoluminal obstruction[93,94]. A pulmonary abscess is defined as an area of necrotic parenchyma leading to the formation of a cavity with air-fluid levels due to communication with the bronchial tree. Abscesses can be acute (less than 6 weeks) characterized by an abscess formation well demarcated from the surrounding parenchyma with necrotic contents, or chronic (greater than 6 weeks). Depending on the pathogenesis, the abscess may be bronchogenic, if the way of spreading is by aspiration or inhalation, or hematogenic. Some risk factors for their development are advanced age, dental infections, alcoholism, or drug abuse, malnutrition or immunocompromised states. Differential diagnosis is critical, as it may be caused by an excavating bronchial carcinoma (squamous cell or small-cell), tuberculosis, or empyema[95,96] (Figure 4).

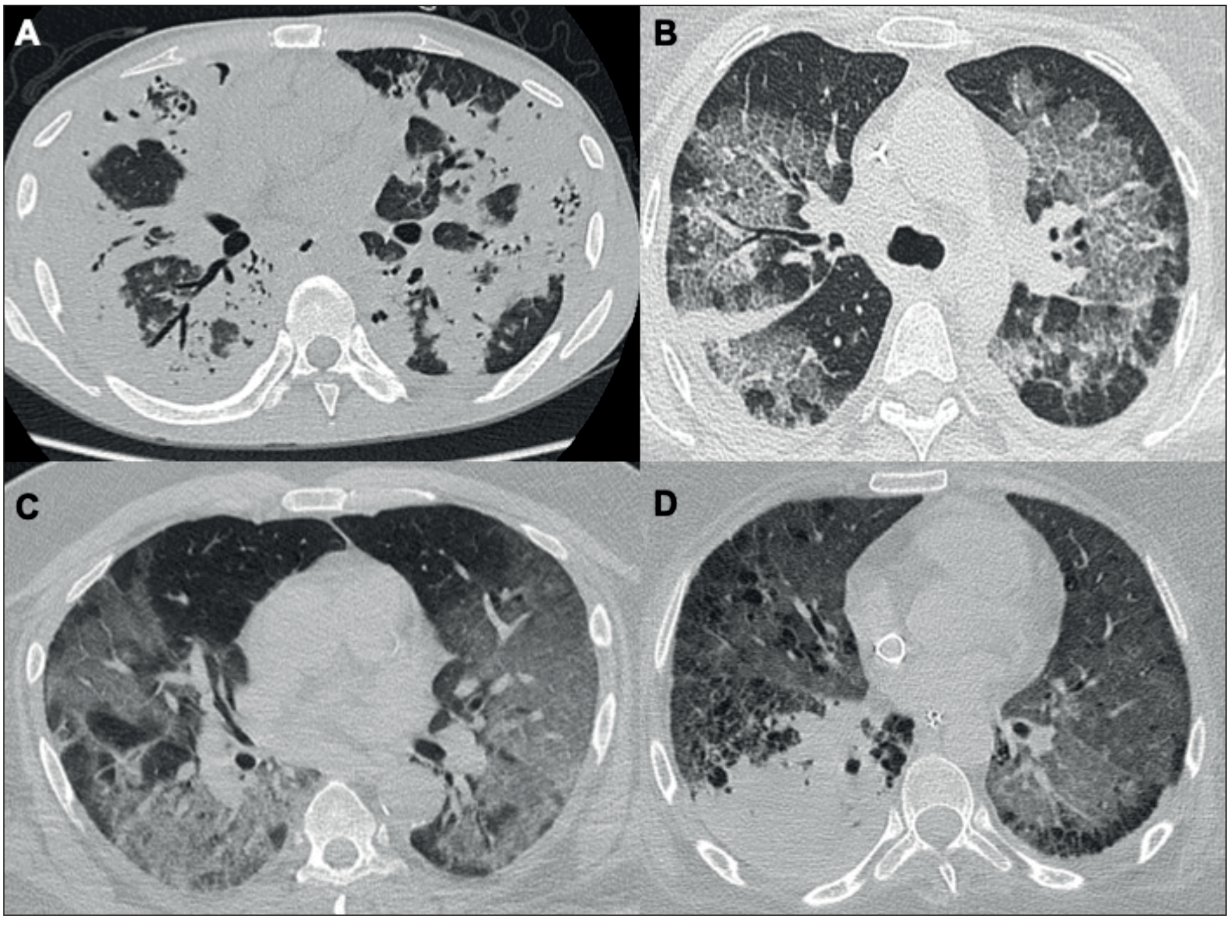

Figure 4. Infection. A case of important bilateral involvement in tuberculosis infection (**A**), a classical HRCT pattern of Pneumocystis jirovecii pneumonia in a patient with hematological malignancy (**B**) and two cases of COVID-19 pneumonia: acute interstitial pneumonia (**C**) and a lobar super-infection (**D**).

Conclusions

Imaging in non-cardiovascular and non-traumatic thoracic emergencies is essential to recognise potentially life-threatening causes that have to be promptly recognised to allow a correct and timely therapeutic decision.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Acknowledgements

The authors are grateful to Alessandra Trocino, librarian at the National Cancer Institute of Naples, Italy.

Authors' Contribution

Each author has participated sufficiently to take public responsibility for the content of the manuscript.

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