

CHEST X-RAY FINDINGS AT PNEUMONIA PATIENTS WITH AND WITHOUT FUNGAL INFECTIONS AND NOT CURED AFTER ANTIBIOTIC THERAPY IN DR. SOETOMO HOSPITAL SURABAYA FROM JANUARY 2019 - SEPTEMBER 2020

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Abstract

Background: Fungal infections are often overlooked causes of community pneumonia, posing significant problems in diagnosis and treatment. The criteria for the diagnosis of fungal pneumonia are based on clinical manifestations, radiological features, and sputum culture. Definitive diagnosis based on sputum culture results takes a long time and is limited to some health center. Patients with clinical pneumonia often receive antibiotic empiric therapy which can sometimes worsen the patient's prognosis. Characteristics of lesions on chest X-rays are expected to be an easier, cheaper, and faster choice of supporting diagnostic tools.

Methods: This is a retrospective descriptive study. Researchers identified data on pneumonia patients who did not recover with antibiotic therapy who underwent chest X-ray and sputum examination. A chest X-ray was observed once without serial examination and evaluated for abnormalities in the lung, pleura, lesion site and severity category.

Results: A retrospective study of chest X-ray of the pneumonia patients who did not resolve with antibiotic therapy and sputum culture (n=200) was performed in the 15-93 year age group. It was found that the most common fungal age group was 46-55 years and males (62%). Chest X-ray images obtained are non-specific lesions on the lungs and pleura (consolidation, fibrosis, cavitation, nodulation, atelectasis, pneumothorax, pleural effusion and thickening), on the right and left sides of the thorax with mild to severe degrees. Images could not be distinguished between images without fungal (n=83) and images with fungal (n=117). In the fungal group there are several comorbidities, such as malignancy, HIV, COPD, tuberculosis, COVID 19, sepsis, stroke, hypertension, diabetes mellitus, hepatitis B, liver cirrhosis, and chronic renal failure.

Conclusion: There were no differences between the chest x-ray in pneumonia with or without fungal infection. The radiographic characteristics obtained in both groups were non-specific lesions on the lungs and pleura (consolidation, fibrosis, cavitation, nodulation, atelectasis, pneumothorax, pleural effusion and thickening), on the right and left sides of the thorax, as well as mild to severe degrees.

Keywords: pneumonia, lung infections, fungal infections, chest X-ray

1. Introduction

The frequency of pneumonia accompanied by fungal infections is increasing worldwide caused by endemic or opportunistic fungi (Di Mango, 2019; Mandanas, 2011). Endemic fungal pneumonia is a common cause of hospitalization with the patient's condition debilitating and the mortality rate is around 10%. Symptoms vary widely from asymptomatic to cause death. And what is even more surprising is that the mortality rate can reach 87% in immunocompetent patients (Hage, 2012).

Research in several hospitals in Indonesia showed the prevalence of *Pneumocystis pneumonia* was 14.5% (8 of 55 patients) in HIV/AIDS cases, while invasive pulmonary aspergillosis in the ICU was 7.7% (31 of 405 patients studied). *Candida tropicalis* and *Candida albicans* were found in patients treated at the HCU/ICU Dr.

Cipto Mangunkusomo. Research at the National Respiratory “Persahabatan” Hospital showed fungal colonization in cases of persistent asthma was found to be 44.5% (20 of 45 patients studied) (Rozaliyani, 2019; Singh; 2018).

Diagnosis of fungal pneumonia in general is still a challenge because clinical symptoms and examination results are not typical, and risk factors often go unnoticed so that the diagnosis is often made based on suspicion (Rozaliyani, 2019; Mandanas, 2011). The criteria for the diagnosis of fungal pneumonia were made based on the patient's condition, clinical and radiological features, and sputum culture examination. To determine the exact causative microorganism, a sputum culture examination is used (Wiersinga et al., 2018). Identification of various radiological manifestations of pulmonary fungal infection related to the patient's clinical and epidemiological history is very important to narrow the differential diagnosis (Di Mango, 2019).

The decision to give empirical therapy causes new problems because it has the potential to increase bacterial resistance, increase treatment costs, and side effects from drugs, which in turn worsens the patient's prognosis (Rozaliyani, 2019; H. Nightingale, G. Ambrose and M. File, 2005). Chest X-ray is expected to assist clinicians in improving the management of patients with pneumonia based on the following studies:

- Anil (April 1998 – Maret 2002), 32 patients in USA: Histoplasmosis, Coccidioidomycosis, Cryptococcosis, Blastomycosis, Paracoccidioidomycosis
- Andrew (1978-1992), 11.000 autopsy in USA: *Aspergillus spp*, *Mucor spp*, *Candida spp*
- Hage (2012) in USA: Histoplasmosis, Coccidioidomycosis, Blastomycosis
- Di Mango (2018) Brazil & Liverpool: Histoplasmosis, Coccidioidomycosis, Paracoccidioidomycosis, Blastomycosis, Sporotrichosis, Aspergillosis, Cryptococcosis
- Gurmeet Singh (Maret-September 2015), 153 patient in RSCM, Jakarta: *C. tropicalis* (44.31%), *Klebsiella pneumoniae*, *Enterococcus faecalis*.

Based on this background, researchers are interested in conducting research on the pattern of chest X-ray images in patients with pulmonary inflammation caused by fungi in patients treated in dr. Soetomo Hospital Surabaya from January 2019 to September 2020. The author hopes that knowing the characteristics of the chest radiograph in patients with fungal pneumonia can help clinicians in narrowing down differential diagnoses so as to increase the accuracy of empirical therapy in addition to waiting for culture results to be used in definitive therapy.

2. Methods

This research is descriptive research with a retrospective research design. This research was conducted at the Diagnostic Radiology Installation of the Integrated Diagnostic Center Building, Dr. Soetomo Hospital Surabaya from January 2019 to September 2020.

The study population was obtained from medical records of patients with pneumonia who had the results of a chest radiography examination and had a sputum culture examination in dr. Soetomo Hospital Surabaya from January 2019 to September 2020. With the inclusion criteria: Patients with pneumonia who have a chest radiograph and sputum culture examination result, and for the exclusion criteria do not meet the inclusion criteria.

Researchers identified medical records of patients with pneumonia or pneumonia who had the results of a chest radiography examination in dr. Hospital. Soetomo Surabaya in January 2019 – September 2020. Medical record data of patients who met the inclusion criteria, namely patients with pneumonia or pneumonia, had chest radiography results before the start of treatment and had sputum culture results, were taken as the study population. Then an evaluation of the chest radiography which includes abnormalities in the lung parenchyma was carried out by a radiology specialist and a fellow radiology fellow in the thoracic division. The observer writes down the evaluation results on the available worksheets. The data obtained were then analyzed and presented as research results.

2.1. The variables observed in this study

- Spectrum: identify patterns of lung parenchymal and pleural abnormalities on chest radiographs of patients with pneumonia with and without fungi
- Proportion: identify the proportion of chest X-ray images of patients with pneumonia that are present and without fungi based on: Demographic data, which includes gender and age, and distribution of lesions (upper, middle, and lower lobe).

2.2. Chest radiography

Chest X-ray obtained using X-ray Digital Radiography X-Ray (DRX) and Computed Radiography (CR) in the form of digital raw data made by several radiographers and read by three radiology specialists (a radiology specialist), a radiology fellow in the thoracic division, and a radiology specialist in the thoracic division) using a tool in the form of a check list table. The radiological features observed on chest radiographs are (Nambu et al., 2014; Hansell et al., 2008; Herring, 2016; Mc Loud, 2010).

2.2.1. Abnormalities in the lung parenchyma

- Ground-glass opacity: areas of hazy increased opacity of the lung parenchyma, where pulmonary bronchovascular markings are still visible (Nambu et al., 2014; Hansell et al., 2008; Mc Loud, 2010; Muller, 2007; Walker, 2019)
- Consolidation: increased lung parenchymal opacity that blurs the boundaries of the pulmonary bronchovascular pattern (Nambu et al., 2014; Hansell et al., 2008; Mc Loud, 2010; Muller, 2007; Jude et al., 2014)
- Nodules: rounded opacity, well-defined or indistinct, with a diameter of 3 cm, can be single or multiple (Nambu et al., 2014; Hansell et al., 2008; Mc Loud, 2010; Muller, 2007; Khan, 2011; Carbone, 2020; Jude et al., 2014)
- Predominant peribronchial nodules (bronchopneumonia): peribronchial nodules include centrilobular nodules with or without peribronchial consolidation (Nambu et al., 2014; Hansell et al., 2008; Li Hong Jun, 2015; Mc Loud, 2010; Gamache, 2019)
- Dominant nodule with random pattern: the presence of multiple nodules with random diffuse pattern in both lung parenchyma; occurs due to hematogenous spread or granulomatous disease; eg miliary shape (opacity, spherical shape, small profuse, measuring < 3 mm generally uniform in size, diffuse distribution) (Nambu et al., 2014; Hansell et al., 2008; Li Hong Jun, 2015; Mc Loud, 2010; Jude, 2014)
- Cavity: an air-filled cavity, appearing as a lucency within a consolidation or a nodule or mass in the lung; usually formed by expulsion or drainage of the necrotic portion of the lesion through the bronchial tree; grouped as single or multiple (Mc Loud, 2010; Usaola, 2013; Nambu et al., 2014; Hansell et al., 2008; Li Hong Jun, 2015; Gadkowski, 2008; Gafoor, 2018; Parkar, 2016; Berkowiz, 2018)
- Calcification: blotchy or nodular opacity with high density and well-defined, variable distribution (Bendayan, 2000; Mc Cloud, 2010)
- Interstitial opacities (reticular/ nodular/ reticulonodular pattern), Reticular pattern: a collection of a large number of small linear opacities that form a net-like appearance (Hansell, 2008; Mc Loud, 2010).
- Fibrosis: reticular shaped opacity (resembling a rope or stellate) with high density and rough edges (Bausas, 2017; Mc Cloud, 2010)
- Bronchiectasis: irreversible bronchial dilatation with parallel linear opacities (tram-track lines) due to bronchial dilatation and thickening of the bronchial walls, or multiple cystic lesions up to 2 cm in diameter (honeycomb appearance) in cystic bronchiectasis, or tubular density due to filled bronchi fluid

- Atelectasis: decreased lung volume characterized by increased opacity in the affected lung, accompanied by signs of retraction of fissures, bronchi, blood vessels, diaphragm, heart, or mediastinum.

2.2.2. Abnormalities in the pleura

- Pleural effusion: accumulation of fluid in the pleural cavity characterized by blunting of the phrenicocostal angle, hemithorax opacification, and meniscus sign (fluid reaches a higher position on the lateral side than the medial side of the thorax in the frontal projection) (Almeida, 2017)
- Pleural thickening (apical cap): a cap-like lesion at the lung apex, usually caused by intrapulmonary fibrosis and pleural fibrosis leading to the inferior withdrawal of the extrapleural fat layer; appears as a homogeneous opacity of soft tissue density at the lung apex (unilateral or bilateral), with a sharp or irregular inferior border, and varying thickness (up to 30 mm) (Hansel, 2010; Saito, 2019)
- Pneumothorax: the presence of air in the pleural cavity characterized by lung collapse, accompanied by a lucent area without lung tissue and visualization of the visceral pleural line.

2.2.3. Severity Category

The severity category (severity of disease) is assessed based on a modified scoring system that has been adopted from the Radiographic Assessment of Lung Edema (RALE) and Radiologic Severity Index (RSI) scoring system in which both lungs on chest radiography are divided into 6 lung fields (upper, middle, lower area for right and left lungs).

3. Results

There were 200 chest X-rays observed in this study. Researchers observed the results of existing chest X-rays and then compared them with the results of microbiological examinations, to confirm the presence of fungi in these patients.

Table 1. Basic characteristics of subjects

Age group (years)	Frequency	Percentage (%)
15 – 25	20	10
26 – 35	15	7,5
36 – 45	27	13,5
46 – 55	47	23,5
56 – 65	55	27,5
66 – 75	31	15,5
>75	5	2,5
Total	200	100

Table 2. Results of the study based on the chest radiographic images in patients with pneumonia who were present and had no fungal infection in dr. Hospital. Soetomo Surabaya in the period January 2019 to September 2020.

Chest Xray findings		With fungi		Without Fungi		p-value
		Numbers	Percentage	Numbers	Percentage	
Lung Parenchym abnormality						
1	Infiltrat/GGO (<i>Ground Glass Opacity</i>)	40	20%	48	24%	
	Location					
	- Upper zone right	10	7%	10	9,6%	0,566
	- Upper zone left	13	9,1%	5	4,8%	0,323
	- Middle zone right	25	17,5%	23	22,2%	0,386

	- Middle zone left	36	25,2%	25	24%	1,000
	- Lower zone right	33	23%	25	24%	0,892
	- Lower zone left	26	18,2%	16	15,4	0,743
2	Consolidation	74	37%	54	27%	
	Location					
	- Upper zone right	30	11,7%	18	13,2%	0,633
	- Upper zone left	23	8,9%	9	6,6%	0,139
	- Middle zone right	55	21,3%	29	21,3%	0,119
	- Middle zone left	46	17,8%	25	18,4%	0,234
	- Lower zone right	55	21,3%	32	23,5%	0,297
	- Lower zone left	49	19%	23	17%	0,056
3	Nodul	1	0,1%	1	0,6%	
	Location					
	- Upper zone right	0	0	0	0	
	- Upper zone left	0	0	1	33,3%	0,415
	- Middle zone right	1	100%	1	33,3%	1,000
	- Middle zone left	0	0	0	0	
	- Lower zone right	0	0	0	0	
	- Lower zone left	0	0	1	33,3%	0,415
4	Bronkopneumonia	8	1%	9	4,7%	
	Location					
	- Upper zone right	1	12,5%	2	8,3%	0,571
	- Upper zone left	2	25%	4	16,6%	
	- Middle zone right	2	12,5%	7	29,2%	0,035
	- Middle zone left	3	37,5%	5	21%	0,280
	- Lower zone right	0	0	2	8,3%	0,171
	- Lower zone left	0	0	4	16,6%	0,028
5	Milier	0	0	0	0	
6	Kavitas	6	3%	3	1,6%	
	Location					
	- Upper zone right	4	19%	2	25%	1,000
	- Upper zone left	3	14,5%	2	25%	1,000
	- Middle zone right	8	38%	1	12,5%	0,083
	- Middle zone left	2	9,5%	2	25%	1,000
	- Lower zone right	2	9,5%	1	12,5%	1,000
	- Lower zone left	2	9,5%	0	0	0,512
7	Calsification	0	0	2	1%	0,415
8	Fibrosis	22	11%	22	11%	0,924
	Location					
	- Upper zone right	11	16%	9	16%	1,000
	- Upper zone left	8	10%	6	11%	1,000
	- Middle zone right	16	23%	13	23%	0,850
	- Middle zone left	11	16%	7	12,5%	
	- Lower zone right	13	19%	10	18%	1,000
	- Lower zone left	11	16%	11	19,5%	0,530
9	Noduler pattern	0	0	0	0	
10	Reticular pattern	12	6%	8	3,8%	
	Location					
	- Upper zone right	2	4,5%	1	6,5%	1,000
	- Upper zone left	4	9%	3	17,7%	1,000
	- Middle zone right	12	28%	5	29,7%	0,424
	- Middle zone left	9	20%	4	25,2%	0,602
	- Lower zone right	9	20%	2	12,1%	0,127
	- Lower zone left	8	18,5%	3	8,5%	0,368

11	Reticulonodular pattern	18	9%	18	9,4%	
	Location					
	- Upper zone right	6	12,2%	3	6,4%	0,738
	- Upper zone left	3	6,1%	4	8,5%	0,452
	- Middle zone right	11	22,5%	7	14,7%	1,000
	- Middle zone left	11	22,5%	9	19,2%	0,924
	- Lower zone right	11	22,5%	15	32%	0,113
	- Lower zone left	7	14,2%	9	19,2%	0,325
12	Bronkiektasis	4	2%	2	2%	
	Location					
	- Upper zone right	2	13,3%	0	0	0,512
	- Upper zone left	3	20%	1	10%	0,453
	- Middle zone right	2	13,3%	2	20%	1,000
	- Middle zone left	6	40%	3	30%	0,738
	- Lower zone right	1	6,7%	2	20%	0,571
	- Lower zone left	1	6,7%	2	20%	0,571
13	Atelektasis	2	1%	0	0	0,143
	Location					
	- Upper zone right	4	57,1%			
	- Upper zone left	1	14,3%			1,000
	- Middle zone right	1	14,3%			1,000
	- Middle zone left	1	14,3%			1,000
	- Lower zone right	0	0			
	- Lower zone left	0	0			
14	Efusi pleura	24	26%	13	16%	
15	Pleural thickening	6	5%	4	4,8%	
16	Pneumotoraks	3	2,5%	0	0	
17	Severity index					0,769
	- Mild	40	34%	33	40%	
	- Medium	49	42%	36	43%	
	- Severe	28	24%	14	17%	

The proportion of patients with pneumonia with and without fungal infection in this study was 1: 1,5. The highest age group was 46-55 years in pneumonia with fungal infection and in pneumonia without fungal infection in the 56-65 year age group. The sex with the highest prevalence of pneumonia and no fungus was male. From the culture results, the types of fungi were *C. albican* (33.5%), *C. tropicalalis* (12%), *C. dubliniensis* (5.5%), *C. krusei* (2.5%), *C. glabrata* (2, 5%), *C. parapsilosis* (1%), *C. rugosa* (0.5%), *C. norvegensis* (0.5%), *C. fanata* (0.5%).

The most common chest X-ray images in fungal pneumonia are consolidation (37%) and the highest predilection is in the right middle & lower zone and the severity category is moderate. There was no picture of calcification, miliary and nodular pattern. Pleural abnormalities were pleural effusion (26%), pleural thickening (5%) and pneumothorax (2.5%). The chest X-ray in patients with pneumonia without fungal infection is the majority of consolidation (27%) with the most locations in the right lower zone. There was no miliary picture, atelectasis and nodular pattern and pneumothorax.

From the comparison of chest X-ray images in existing pneumonia and no fungal infection, it was found that there was no significant difference between the two. However, it should be noted that pneumonia with fungal infection has a severe severity category (24%) compared to pneumonia without fungal infection (17%)

4. Discussion

In this study, the age range of pneumonia patients observed was 15 years to 93 years, with an average of 52.41 years. Based on age group, the largest sample distribution was in the 56-65 year age group. In pneumonia

with a fungal infection, the distribution was mostly in the 46-55 age group, and in pneumonia without fungal infection in the 56-65 age group. Research from America by Tong et al., from 2008 to 2014, obtained an age range of patients with pneumonia, namely 18-64 years and a mean age of 42 years (Tong et al., 2018).

Based on the results of the sputum culture, the samples were divided into patients with pneumonia who had pneumonia and no fungal infection. The result showed that the number of patients with pneumonia who had fungal infection was 117 people and there was no fungal infection in 83 people. From the culture results, the types of fungi were *C. albican* (33.5%), *C. tropicalalis* (12%), *C. dubliniensis* (5.5%), *C. krusei* (2.5%), *C. glabrata* (2, 5%), *C. parapsilosis* (1%), *C. rugosa* (0.5%), *C. norvegenesis* (0.5%), *C. fanata* (0.5%). The proportion of patients with pneumonia with fungal infections is currently starting to increase compared to patients with pneumonia without fungal infections. This is following a study conducted by Limper et al. and Pound et al. which states that the incidence of fungal pneumonia is increasing (Limper et al., 2010; Pound et al., 2002).

At the chest radiography of pneumonia patients with a fungal infection, it was found that the most abnormal features on the chest X-ray were consolidation images of 37% of the total sample, followed by an infiltrate/GGO (ground-glass opacity) image of 20% of the total sample, and fibrosis of 11 % of the total sample, then the reticulonodular pattern is 9% of the total sample, the reticular pattern is 6% of the total sample, cavities are 3% of the total sample, bronchiectasis is 2% of the total sample, and the features of bronchopneumonia and atelectasis are 1% each. of the total sample as well as nodules (0.1%). Pleural effusion was 26% of the total sample, pleural thickening was 5% of the total sample and pneumothorax was 2.5% of the total sample.

The chest radiograph of pneumonia patients without fungal infection showed that the most abnormal features on the chest X-ray were consolidation images of 27% of the total sample, followed by an infiltrate/GGO (ground-glass opacity) image of 24% of the total sample, and fibrosis of 11 % of the total sample, then the reticulonodular pattern was 9.4% of the total sample, bronchopneumonia was 4.7%, the reticular pattern was 3.8% of the total sample, bronchiectasis was 2% of the total sample, cavities 1.6% of the total sample, calcification 1% of the total sample, and nodules of 0.6% of the total sample. Pleural effusion was 16% of the total sample and pleural thickening was 4.8% of the total sample.

5. Conclusion

There were no differences between the chest x-ray in pneumonia with or without fungal infection. The radiographic characteristics obtained in both groups were non-specific lesions on the lungs and pleura (consolidation, fibrosis, cavitation, nodulation, atelectasis, pneumothorax, pleural effusion and thickening), on the right and left sides of the thorax, as well as mild to severe degrees.

The spectrum and proportion of radiological images obtained in this study came from studies based on tertiary referral hospitals, thus allowing for different images so that further research with a wider range is needed. The fungi found from the sputum culture still allowed commensal fungi, so further research is needed to assess the patient's immune status. This study using X-rays which has limitations for evaluating several radiological features such as bronchiectasis, characterizing the size and distribution of nodules (especially small nodules) so further research is needed using more sophisticated imaging modalities such as CT scans.

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