

Demographic, Clinic, Radiologic, and Histopathologic Pattern of Patient with Mediastinal Mass who Died during Treatment at Cipto Mangunkusumo Hospital Jakarta

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ABSTRACT

Many diseases can arise or involve the mediastinum. These diseases are primary tumor, metastase, cyst, or acute or chronic infection. Mediastinal mass is often challenging to diagnose that standard of diagnosis and treatment plan are needed. Increasing patient risk, deciding when to do aggressive treatment will lead to better outcome in decreasing morbidity and mortality rate. Nowadays, demographic, clinic, radiologic, and histopathologic pattern of patient with mediastinal mass who died during treatment at Cipto Mangunkusumo hospital have not been reported yet.

Aim: to obtain demographic, clinic, radiologic, and histopathologic pattern of patient with mediastinal mass who died during treatment at Cipto Mangunkusumo hospital in the last ten years.

Methods: this is a descriptive cross-sectional study. The study was conducted between the months of April 2010 - July 2010 by collecting and studying the medical records of patient with mediastinal mass diagnosed during January 2000 - December 2009 at Cipto Mangunkusumo hospital then being processed by SPSS program version 16.0.

Results: there were 201 patients diagnosed having mediastinal mass in Cipto Mangunkusumo hospital during these last ten years. Eighty eight medical records were not found so there were 113 samples studied. Forty five samples (39.8%) of 113 samples died during treatment at hospital.

Conclusion: there were few differences in demographic, clinic, radiologic, and histopathologic pattern of patient with mediastinal mass who died during treatment at Cipto Mangunkusumo hospital compared to other studies. Mortality rate during treatment is high. Appropriate diagnosis in early stadium is necessary in order to decrease morbidity and mortality rate and achieve a better patient outcome.

Keywords: mediastinal mass, mortality, superior cava vein syndrome

ABSTRAK

Banyak penyakit dapat timbul atau melibatkan mediastinum. Penyakit-penyakit tersebut adalah tumor primer, metastase, kista, dan infeksi akut atau kronis. Mendiagnosis massa mediastinum seringkali menjadi tantangan mengingat diperlukan standar diagnosis dan rencana perawatan. Meningkatkan risiko pasien dan memutuskan kapan harus melakukan perawatan agresif akan memberikan hasil akhir yang lebih baik dalam menurunkan angka kesakitan dan kematian. Saat ini, pola demografi, klinik, radiologi, dan histopatologi pasien dengan massa mediastinum yang meninggal selama perawatan di RS Cipto Mangunkusumo belum dilaporkan.

Tujuan: mendapatkan pola demografi, klinik, radiologi, dan histopatologi pasien dengan massa mediastinum yang meninggal selama perawatan di RS Cipto Mangunkusumo dalam kurun waktu sepuluh tahun terakhir.

Metode: penelitian ini merupakan studi *cross-sectional* deskriptif. Penelitian dilakukan antara April 2010 sampai Juli 2010 dengan mengumpulkan dan mempelajari catatan medis pasien dengan massa mediastinum yang didiagnosis selama Januari 2000 sampai Desember 2009 di RS Cipto Mangunkusumo, kemudian diproses dengan program SPSS versi 16.0.

Hasil: terdapat 201 pasien yang didiagnosis memiliki massa mediastinum di RS Cipto Mangunkusumo selama sepuluh

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tahun terakhir. Delapan puluh delapan catatan medis tidak ditemukan sehingga hanya ada 113 sampel yang diteliti. Empat puluh lima sampel (39,8%) dari 113 sampel meninggal selama perawatan di rumah sakit.

Kesimpulan: ada sedikit perbedaan dalam pola demografi, klinik, radiologi, dan histopatologi pasien dengan massa mediastinum yang meninggal selama pengobatan di RSCipto Mangunkusumo dibandingkan dengan penelitian lain. Tingkat kematian selama pengobatan tinggi. Diagnosis yang tepat pada stadium dini sangat diperlukan untuk menurunkan angka kesakitan serta angka kematian dan pasien memperoleh hasil akhir yang lebih baik.

Kata kunci: massa mediastinum, kematian, sindrom vena cava superior

INTRODUCTION

There are many diseases related to mediastinum. These diseases are primary tumor, metastase, cyst, or acute or chronic infection. Mediastinal mass is mass that is found in mediastinum; a space between both lungs. Mediastinum space is limited and cannot be extended so if there is a mass there, it will compress other nearby organs then lead to critical and dangerous situation.¹⁻³ In a study of 400 patients by Davis et al., most of them was mediastinal tumor. Lymphoma, thymoma and teratoma were the most common types of tumor found. Sixty two patients showed symptoms while being diagnosed. Clinical symptoms were more common in malignant lesions (85%) while 75% patients with anteroposterior mediastinal mass showed symptoms.⁴⁻⁶ From literature, risk factors that are related to morbidity and mortality rate in patient having mediastinal mass are infections, pulmonal emergency, cardiovascular emergency and neuro emergency.¹⁻³

Many patients came in emergency setting because of late or missed diagnosis. Patients usually already had alternative treatment outside the hospital. These conditions lead to prolong and delay in diagnostic procedure and treatment plan and make them even harder to do. When compared with the literature in foreign countries, data of patients with mediastinal mass in Indonesia is few. The purpose of this study was to obtain demographic, clinical, radiologic and histopathologic pattern of patient with mediastinal mass who died during treatment at Cipto Mangunkusumo hospital in the past 10 years so it can help the clinician to perform risk stratification of patients with high risk mortality in order to do an optimal treatment.

MATERIAL AND METHOD

Research design used was a descriptive cross-sectional study. Data was obtained from medical records of patients. The study was conducted between the months of April 2010 - July 2010 by collecting and studying the medical records of patient with mediastinal mass diagnosed during January 2000 - December 2009 at Cipto Mangunkusumo hospital, Jakarta. Sampling is done by tracing and recording of all patient's medical record. Data that has been collected then processed using SPSS program version 16.0. Data will be presented in the form of text, tables and pictures as appropriate.

RESULTS

There were 31 male samples (68.9%) and 14 female (31.1%) studied. Based on educational level, it was obtained that 3 patients (6.7%) graduated from high school, 2 patients graduated from junior high school (4.4%), 2 patients graduated from elementary school (4.4%), while 37 patients (82.2%) show no data. Sundanese is the highest type of ethnic group consisting 10 cases (22.2%), followed by the Javanese (8.9%), Batak (4.4%), Betawi (4.4%), Padang (2.2%) and the rest 21 samples (46.6%) show no data. The highest number from age group is 18-60 years by 28 patients (62.2%). There was one sample (2.2%) who was a child and 44 samples (97.8%) were adults. This result can be seen in table 3 and 4.

Table 1: Demographic patterns of patients with mediastinal mass

| Characteristics | N | % |
|--------------------|----|------|
| Gender | | |
| Male | 31 | 68.9 |
| Female | 14 | 31.1 |
| Education Level | | |
| No data | 37 | 82.2 |
| Illiteracy | 1 | 2.2 |
| Elementary school | 2 | 4.4 |
| Junior high school | 2 | 4.4 |
| Senior high school | 3 | 6.7 |
| Bachelor | 0 | 0 |
| Graduate | 0 | 0 |
| Ethnic group | | |
| No data | 21 | 46.7 |
| Javanese | 4 | 8.9 |
| Betawinese | 2 | 4.4 |
| Sundanese | 10 | 22.2 |
| Bataknese | 2 | 4.4 |
| Padang | 1 | 2.2 |
| Others | 5 | 11.1 |

Table 2: Age prevalence of patients with mediastinal mass

| Age | N | % |
|---------------|----|------|
| < 18 years | 1 | 2.2 |
| 18 – 60 years | 28 | 62.2 |
| > 60 years | 16 | 35.6 |

In Table 3 and 4, there were clinical variations of patient with mediastinal mass who died during treatment at Cipto Mangunkusumo hospital. Clinical sign and symptom were assessed when patients firstly diagnosed in hospital. Clinical symptom is subjective complaint while clinical sign is objective abnormalities or complications found during physical examination.

Table 3: Clinical symptoms in patients with mediastinal mass

| Clinical symptoms | N | % |
|--------------------------|----|------|
| Respiration symptoms | | |
| Cough | 40 | 88.9 |
| Dyspnea | 38 | 84.4 |
| Chest pain | 12 | 26.7 |
| Wheezing | 2 | 4.4 |
| Non respiration syndrome | | |
| Losing weight | 31 | 68.9 |
| Fever | 20 | 44.4 |
| Fatigue | 12 | 26.7 |
| Night sweating | 15 | 33.3 |
| Hoarse voice | 5 | 11.1 |
| No symptoms | 0 | 0 |

Clinical symptoms were found in all patients (100%). Respiratory complaints were the most commonly found at the beginning of clinical presentation. These complaints include 40 samples with cough (88.9%), shortness of breath (84.4%), chest pain (26.7%) and two patients with wheezing (4.4%). Non-respiratory complaints found were 31 samples (68.9%) with weight loss, followed by 20 samples (44.4%) with fever, 15 samples (33.3%) with night sweats, hoarseness (11.1%) and 12 patients (26.7%) with fatigue. These results can be seen in Table 3.

There were 34 samples (75.6%) studied had wet crackles and 24 samples (53.3%) with superior cava vein syndrome (SCVS) followed by lymphadenopathy (48.8%), pleural effusion (42.2%), myasthenia gravis (8.9%) and wheezing (4.4%), shown in table 4.

All 45 patients underwent chest x-ray examination, while results of thoracic CT scans were obtained in 24 patients (53.3%). Twenty one patients (46.7%) who were not checked for thoracic CT scans remain included in this study because clinical condition data and

pathology examination were present. On radiographic examination, normal image obtained as much as one case (2.2%). Based on the radiographic location, highest number of mass found at superior mediastinum (31.1%) and right mediastinum (28.9%), whereas based on the location in thoracic CT scan was found at anterosuperior (42.2%) and 7 cases (15.6%) at media area.

Table 4: Clinical signs in patients with mediastinal mass

| Physical Examination | N | % |
|----------------------|----|------|
| Lymphadenopathy | | |
| Colli | 9 | 20 |
| Supraclavicular | 11 | 24.4 |
| Axilla | 1 | 2.2 |
| Inguinal | 1 | 2.2 |
| Ronchi | | |
| Wet | 34 | 75.6 |
| Dry | 0 | 0 |
| Wheezing | 2 | 4.4 |
| SCVS | 24 | 53.3 |
| Pleural effusion | 19 | 42.2 |
| Myasthenia gravis | 4 | 8.9 |

Table 5: Rontgen thorax appearances in patients with mediastinal mass

| Appearances | N | % |
|-----------------------|----|------|
| Normal | 1 | 2.2 |
| Location | | |
| Superior mediastinum | 14 | 31.1 |
| Right mediastinum | 13 | 28.9 |
| Left mediastinum | 2 | 4.4 |
| Hilus | 4 | 8.9 |
| Lung | 2 | 4.4 |
| Edge | | |
| Clear | 15 | 33.3 |
| Irregular | 1 | 2.2 |
| Homogen consolidation | | |
| Mediastinum | 29 | 64.4 |
| Paru | 18 | 40 |
| Trachea deviation | 9 | 20 |
| Calcification | 3 | 6.7 |
| Pleura effusion | 19 | 42.2 |
| Metastase nodule | 1 | 2.2 |
| No mass | 2 | 4.4 |

On x-ray examination, 15 cases (33.3%) showed a clear mass edge, 29 samples (64.4%) showed homogen consolidation which 18 samples (40.0%) of it were in the lung. Nine samples (20%) had trachea deviation, calcification (6.7%) and pleural effusion (42.2%). This can be seen in tables 5 and 6.

Table 6: Thorax CT scan found in patient with mediastinal mass

| Thorax CT scan | N | % |
|---------------------|----|------|
| Location | | |
| Anterosuperior | 19 | 42.2 |
| Anteroinferior | 0 | 0 |
| Media | 7 | 15.6 |
| Posterosuperior | 1 | 2.2 |
| Posteroinferior | 0 | 0 |
| Edge | | |
| Clear | 17 | 37.8 |
| Iregular | 4 | 8.9 |
| Density/consistency | | |
| Solid | 21 | 46.7 |
| Cystic | 0 | 0 |
| Lymph enlargement | 10 | 22.2 |
| No CT scan examined | 21 | 46.7 |

Mediastinal tumor (35.6%) was the most common found followed by mediastinal thyroid (2.2%), other mediastinal mass (2.2%) and 27 samples (60.0%) were undiagnosed.

Table 7: Mediastinal mass found based on histopathologic examination

| Mediastinal mass | N | % |
|------------------|----|------|
| Tumor | 16 | 35.6 |
| Thyroid | 1 | 2.2 |
| Cyst | 0 | 0 |
| Lymphadenopathy | 0 | 0 |
| Others | 1 | 2.2 |
| Undiagnosed | 27 | 60 |

Table 8 shows different types of mediastinal tumors based on histopathological examination. Carcinoma (other mediastinal tumors) (15.6%) was the most common mediastinal tumor found followed by thymoma and teratoma (11.1% each), thymic carcinomas (6.7%), lymphoma (2.2%) and 60% samples were undiagnosed.

Table 8: Mediastinal tumor found based on histopathologic examination

| Mediastinal tumor | N | % |
|---------------------------|----|------|
| Tymoma | 5 | 11.1 |
| Lymphoma | 1 | 2.2 |
| Seminoma | 0 | 0 |
| Teratoma | 5 | 11.1 |
| Neurogenic tumor | 0 | 0 |
| Other mediastinal tumor : | | |
| Thymic carcinoma | 3 | 6.7 |
| Carcinoma | 7 | 15.6 |
| Others | 1 | 2.2 |
| Undiagnosed | 27 | 60 |

DISCUSSION

In this study, mortality rate while in hospital care obtained by 45 samples (39.8%), of which 16 samples (35.6%) were diagnosed having mediastinal tumor and a total of 27 patients (60.0%) were undiagnosed. This is because many patients came in emergency setting because of late or missed diagnosis, presence of comorbid diseases and financial problems that lead to optimal diagnostic procedures and treatment were prolonged, delayed, or undone. Researchers did not find the proportion of mediastinal mass mortality data of patients during treatment in other studies (both within and outside Indonesia).

Patient with mediastinal mass who died during treatment was more common in males (31 samples, 68.9%). Gender is not a predilection towards mediastinal mass. This result is similar with Júnior study conducted by Júnior RS et al.⁷ that collect data from 114 patients which result was 61 samples (53.5%) were women. A study by Vaziri M et al.⁸ of 105 samples showed 65 (62%) of them were male.

While most age group was between 18-60 years (62.2%), this result is not much different from study conducted by Nelson TG et al.⁹ which showed most age group range between 18-45 years (75%) and Júnior study by RS et al.⁷ which showed most age group range between 20-49 years (50%). Based on level of education, the majority of samples (3 samples, 6.7%) completed high school and Sundanese is the largest (10 samples, 22.2%) ethnic type found. Researchers did not find the proportion data of mortality rate in patient with mediastinal mass during treatment at hospital that is based on gender, age group, education level and ethnic in other studies (both within and outside Indonesia). These results suggest that mortality rate during treatment is determined more by stage of disease at an advanced stage where diagnostic and treatment procedures to be prolonged or delayed.

In this study, all patients 45 (100.0%) gave a complaint at diagnosis. Complaints arise when lesion is associated with malignancy.^{7,10,11} Ninety five percent of asymptomatic mediastinal masses are benign lesions and 50% of symptomatic lesions are malignant. In long-term condition, asymptomatic mass may become symptomatic.¹¹ In this study, percentage of systemic symptoms equal to non-respiratory symptoms. Respiratory symptoms may be due to late diagnosis and referral because of systemic or non-respiratory complains, as reported by Vaziri et al.⁸ Systemic or non-respiratory signs

and symptoms occurring are due to release of hormones, antibodies and inflammatory cytokines.¹² In many studies, the presence of systemic signs and symptoms in patients with mediastinal mass is in accordance with malignancy.^{11,13,15}

Wet crackles (34 samples, 75.6%) and lymphadenopathy (22 samples, 48.8%) are signs being most found on physical examination. Researchers did not find the percentage data of patients having wet crackles in other studies. Supraclavicular lymphadenopathy was found in 11 samples (24.4%). This result is similar from study conducted by Adegboye VO et al. showing 27 samples (33.3%) with lymphadenopathy and by Dubashi et al. showing 21.9% patients with supraclavicular lymphadenopathy.^{11,16} The presence of lymphadenopathy is associated with malignancy, mentioned in study by Ochicha O et al. In his study of 356 samples, Ochicha O found that tuberculosis lymphadenopathy (30%), lymphoma (24%) and metastatic malignancy (19%) as most common causes of lymphadenopathy, whereas the study by Ellison E et al. in 309 patients with supraclavicular lymphadenopathy showed 55% of samples due to malignancy (47% metastatic and 8% lymphoma) and a total of 39 samples due to micobacterial infection.^{17,18}

A wide range of complications can present in mediastinal mass cases. These complications related to suppression and mass invasion into surrounding organs or due to systemic reactions caused by the presence of the mass.¹⁰ In this study, highest number of complication obtained was SCVS (24 samples, 53.3%). This result are not much different from study by Dubashi et al. (28%) and Adegboye VO et al. (19 samples, 23.5%) but higher than study by Bastos P et al.¹³ (7%) and Vaziri et al. (10%). SCVS is mentioned to be associated with the presence of malignancy or mediastinal tumor.^{8,11,16} Some studies that relate SVCS with malignancy were conducted by Chen JC et al. which obtained lung cancer (19 samples, 75%), mediastinal tumor (20%), metastatic solid tumor (5%) and by Pratama S obtaining 25 samples (27.1%) with tumor of the mediastinum as a cause of SVCS.^{11,12} Pleural effusion is present in 19 patients (42.2%). This result is higher than a study by Dubashi et al. (20%) and by Vaziri et al. (13 samples, 12%).^{8,16} Pleural effusion is associated with malignancy and its presence means worse prognosis.

Myasthenia gravis was found in 4 patients (8.9%) diagnosed by physical examination and Harvey-Masland test. Myasthenia gravis is a

common complication found in patients with mediastinal masses and occurs in 30-50% of patients with thymoma (mediastinal tumor). Inversely, 15% of patients with myasthenia gravis also suffer thymoma. For this reason, patients who were clinically suspected thymoma should have serum levels of antiacetylcholine reseptor antibody checked or Harvey-Masland test done to rule out presence of myasthenia gravis before surgery, even in patient showing no symptoms of myasthenia gravis.¹² In this study, samples were examined by Harvey-Masland test which gave positive results not only in patients with thymoma (results not shown). This result may change the approach of treatment.

On x-ray examination, a total of one sample (2.2%) had normal impression and two samples (4.4%) had undetectable mass. This can be caused by CT scan has advantage over x-ray in detecting mediastinal mass, determining the location and characteristics of the mass. In one study involving six patients with myasthenia gravis, Thoracic CT scan could detect the presence of thymoma in all patients while chest x-ray could only detect 5.²⁰ CT scan can be an alternative modal to evaluate in a person with a suspicion of a mediastinal abnormality and normal impression on chest x-ray examination.²¹ Pleural effusion was present in 19 cases (42.2%) based on radiographic examination. Invasive thymoma often involves the pleura or pericardium. Presence of metastasis to the pleura or pericardial effusion is then likely a thymoma. However, some anterior mediastinal masses include: lymphoma, thymic carcinoma and malignant germinal cell tumor could also show metastasis to pleura or pericardial. Pleural or pericardial effusion in radiological examination are often associated with acute airway obstruction.²³

On examination of the thoracic CT scan, mediastinal mass found in this study was most common at anterosuperior (19 samples, 42.2%). Similar results were obtained in the study by Davis et al. (54%), Júnior RS et al. (57.8%), Vaziri et al. (65%), Dubashi et al. (93.6%), Bastos et al. (58%), Adegboye VO et al. (63.8%) and Shrivastava CP et al. (72%).^{7,8,10,11,13,16,24} Anterosuperior causes most symptoms found in diagnosis. This is caused by lesions in the anterosuperior mediastinum often compressed or invaded airway causing airway obstruction.²⁵ In this study no further evaluation is conducted.

Mediastinal tumors (16 samples, 35.6%) were the most type of mediastinal mass obtained. This result together with the study by Davis et al., Júnior RS et al., Vaziri et al., Nelson TG et al., Dubashi et al., Takeda S et al., Bastos et al., Adegboye VO et al., Kim KR et al. and Shrivastava CP et al. showed similarity in most type of mediastinal mass which is mediastinal tumor.^{7,8,9,10,11,13,15,16,24,26} In this study, carcinoma (15.6%) is a type of tumor of the mediastinum being most found. This is in contrast to the study by Davis et al. (17%), Júnior RS et al. (35.1%), Pratama S (37.8%), Dubashi et al. (39%), Bastos et al. (31%), and Shrivastava CP et al. (31%) that showed thymoma as the most common type found.^{7,10,13,16,24} Whereas studies by Vaziri et al. (31.5%), Nelson TG et al. (29 in 141 samples), Adegboye VO et al. (21.9%) showed mediastinal lymphoma and Kim KR et al. (28.4%) found germinal cell tumor of the mediastinum was the most tumor types found.^{8,9,11,15} Mediastinal tumor should be considered firstly while having initial assessment in patient with mediastinal mass.²⁷ Assessment of other factors associated with increased morbidity and mortality during treatment can be done by stratify patient's risk in order to achieve optimal outcomes.

CONCLUSION

Limitations of the study is a retrospective study that retrieves data from secondary source; patient's medical record. Completeness and reliability of data depends on doctor assessing the patient at that time. Some of anamnesis, physical examination and other investigations are not always listed in medical records.

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