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Histopathology and Immunohistochemical profile of mediastinal lymphoma in Dr. Soetomo General Hospital

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Abstract--Mediastinal lymphoma is a rare tumor. Approximately 10% of primary mediastinal lymphoma occur in mediastinum. In this study we look for sex and age characteristics, histopathology and immunohistochemical profile of mediastinal lymphoma. Data were collected from the Anatomical Pathology laboratory Dr. Soetomo archives from January 2016 to August 2018. Seventeen cases of mediastinal lymphoma were found predominantly in males (76.47 %). The age range was between 17 and 64 years old. Distribution of tumor type was as follows: Non-Hodgkin's Lymphoma, B-cell type high grade (Ki67 > 30%) 17.65 % and Non-Hodgkin's Lymphoma, B-cell type low grade (Ki67 <30%) 11.76%, Non-Hodgkin's Lymphoma, T-cell type high grade 11.76%, Non-Hodgkin's Lymphoma unknown subtype 35.29%, Classical Hodgkin's Lymphoma (CHL) 17.65%, T-cell Lymphoblastic Lymphoma (T-LBL) 5.88%. Histologically, Non-Hodgkin's Lymphoma showed a diffuse pattern consisting of anaplastic lymphoid cells, pleomorphic nuclei, coarse chromatin, thin cytoplasm between fibrotic stroma and the immunohistochemistry profile showed positive for CD20 in NHL B-cell type. CD3 were positive in Peripheral T-cell Lymphoma and T-Lymphoblastic Lymphoma (T-LBL). Classical Hodgkin's Lymphoma showed large cells (reed-stenberg cells) and Hodgkin's cells dispersed between an inflammatory background, CD30 were positive in CHL cases. Tdt was positive in T-LBL cases. Samples for this study were obtained from core biopsy with

small specimens. Diagnosis of mediastinal lymphoma is challenging. Histopathology features may show similarities with other types of lymphomas, hence an immunohistochemistry profile is necessary.

Keywords---mediastinal lymphoma, histopathology, immunohistochemistry.

Introduction

Epidemiology of neoplasm of primary lymphoma in the mediastinum is heterogeneous and reflects the diversity of disease entities found in this location. About 10% of primary mediastinal tumors are lymphoma. Hodgkin's lymphoma (HL), primary mediastinal B-cell lymphoma (PMBCL) and T-lymphoblastic lymphoma (TLL) are the most common primary mediastinal lymphomas (Aggarwal et al., 2017). Diagnosis of mediastinal lymphoma tumors at Dr. Soetomo general hospital is routinely performed by involving multidiscipline experts, such as a lung expert, thoracic and cardiovascular surgeon, radiologist and anatomical pathologist. Especially in the field of anatomical pathology, the diagnosis of lymphoma tumors in mediastinum is challenging. Histopathology features may show similarities with other types of lymphomas, hence an immunohistochemistry profile is necessary. Currently a new method has begun to establish the diagnosis and to classify malignant lymphoma in the mediastinum, which is slightly invasive using a core biopsy technique. From that, histopathological examination can be done, followed by an immunohistochemistry examination.

Until now, there has been no study revealing the profile of lymphoma tumors in mediastinum at Dr. Soetomo General hospital, while the data is important for therapeutic management and epidemiological studies considering that Dr. Soetomo general hospital is a teaching hospital and also the largest referral hospital in eastern Indonesia. Based on the explanation above, the author was interested in conducting an epidemiological study of the profile of lymphoma tumors in mediastinum at Dr. Soetomo general hospital.

Method

This research design used a descriptive observational study with a cross-sectional approach because the observation was made on events that have occurred previously using secondary data. Seventeen cases were examined between January 2016 and August 2018 in the Anatomical Pathology laboratory, Dr. Soetomo General Hospital, retrospectively. The data for this study were obtained from the Anatomical Pathology archives in Dr. Soetomo General Hospital. Demographic characteristics including age, sex and subtype of histopathology results based on immunohistochemistry examination were primary variables in this study. Appropriate data were collected and grouped according to variables that have been established.

Discussion

Seventeen cases of malignant lymphoma in mediastinum were obtained. The data were analyzed according to age, sex, histopathology features and followed by immunohistochemistry examination results. Thirteen of the patients were male, four patients were female. The youngest age was 17 years old and the oldest was 64 years old with the mean age of patient being 35.88 (See Table 1).

Table 1: Percentage of lymphoma tumors in mediastinum based on sex and age of patients

Characteristic	n (Σ sample)	%
Sex		
Male	13	76,47
Female	4	23,53
Age (years)		
< 20	3	17,65
20-25	3	17,65
26-30	0	0
31-35	2	11,76
36-40	3	17,65
41-45	1	5,88
46-50	2	11,76
51-60	2	11,76
61-65	1	5,88

Profile of lymphoma tumors based on histopathological and immunohistochemical results are shown in the table below (see Table 2).

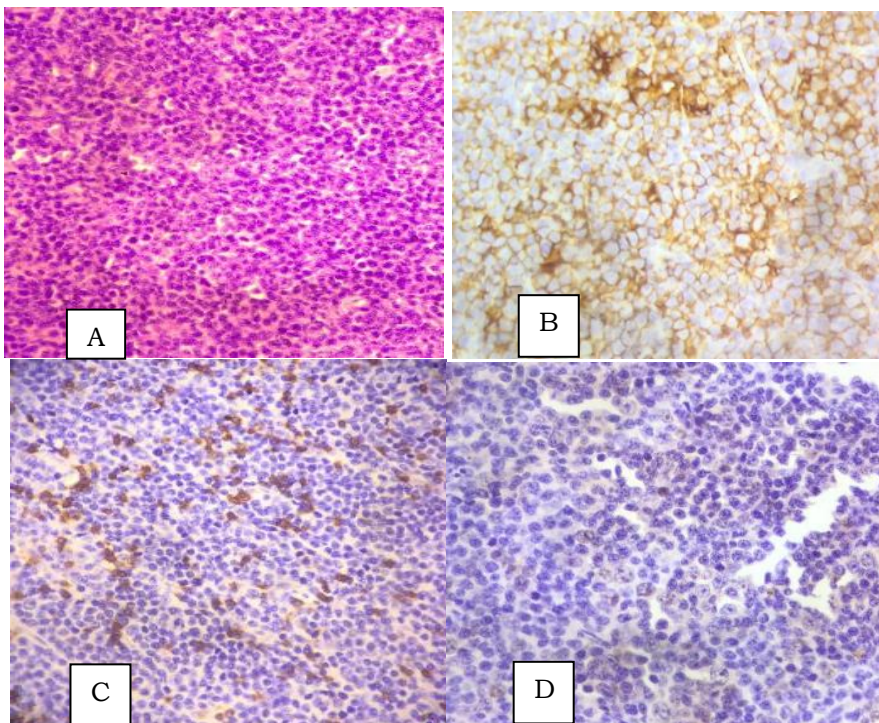
Table 2: Histopathological profile based on immunohistochemical results

Diagnosis	n	%
Non-Hodgkin's Lymphoma (NHL) B-cell type high grade	3	17.65
Non-Hodgkin's Lymphoma (NHL) B-cell type low grade	2	11.76
Non-Hodgkin's Lymphoma (NHL) unknown subtype	6	35.29
Non-Hodgkin's Lymphoma (NHL) T-cell type high grade	2	11.76
Hodgkin's Lymphoma	3	17.65
T-lymphoblastic lymphoma	1	5.88

According to the results above, there were 6 cases (35.29%) of the 17 cases lymphoma in mediastinum for which it was unknown whether they were of B or

T-cell origin. The problems were caused by no further examination being requested from the clinicians.

Histologically, Non-Hodgkin's Lymphoma shows a diffuse pattern consisting of anaplastic lymphoid cells, pleomorphic nuclei, coarse chromatin, clear and thin cytoplasm between fibrotic stroma and an immunohistochemistry profile showing positive for CD20 in Non-Hodgkin's Lymphoma B-cell type high grade and low grade (see Figure 1). Classical Hodgkin's Lymphoma showed atypical large cells (reed-stenberg cells) and Hodgkin's cells dispersed between an inflammatory background, CD30 were positive in CHL cases, PAX5 were positive in large cells, weaker than small B-lymphocyte (see Figure 3). The lymphoblasts in T-Lymphoblastic lymphoma are morphologically indistinguishable from those B-Lymphoblastic lymphoma. The normal architecture of the lymph node are involved. The tumour are consist of lymphoblasts arranged in diffuse pattern with medium-sized cells, finely granular chromatin and no evident nucleoli. The diagnosis of T-Lymphoblastic Lymphoma is made from morphologic features and immunohistochemistry staining. Tdt and CD3 were positive in T-Lymphoblastic Lymphoma (see Figure 4). Most of the samples for this study were obtained from core biopsies with a small specimen.



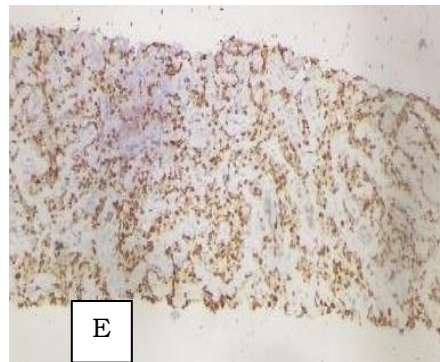


Figure 1. A. HE, NHL B-cell type low grade (400x); B. CD20+ (400x); C. CD3- (400x); D. low Ki67, 20 % (400x); E. NHL B-cell type high grade with high Ki67, 70 % (100x)

CD3 were positive in peripheral T-cell lymphoma and T-Lymphoblastic Lymphoma (T-LBL) (see Figure 2).

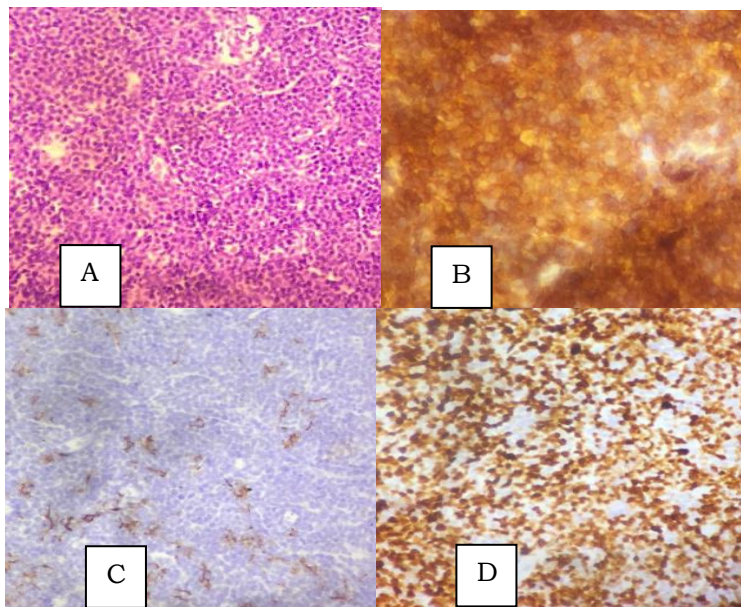


Figure 2. A. HE, NHL T-cell type high grade (400x); B. CD3+ (400x); C. CD20- (400x); D. high Ki67, 90 % (400x)

Classical Hodgkin's Lymphoma (CHL) showed large atypical cells (reed-stenberg cells) and Hodgkin's cells dispersed between an inflammatory background, CD30 were positive in CHL cases and PAX5 were positive in reed-stenberg cells and Hodgkin's cells but weaker than small B-lymphocyte (see Figure 3).

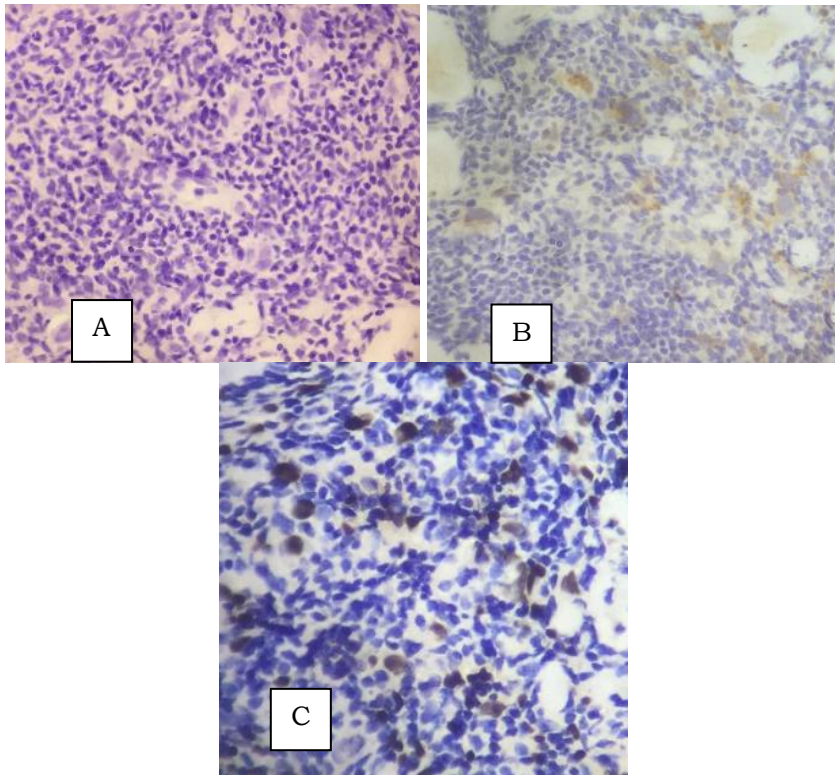


Figure 3. A. HE, Classical Hodgkin's Lymphoma (400x); B. CD30+ in large cells (400x); C. PAX5+ weak in large cells (400x).

Tdt and CD3 were positive in the T-LBL case and negative for CD20 (see Figure 4).

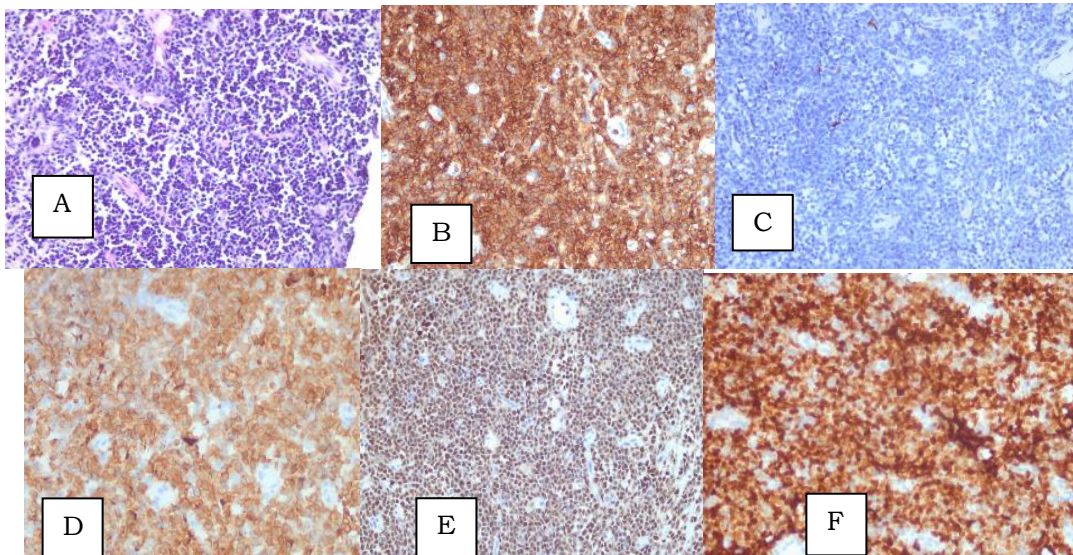


Figure 4. A. HE, T-lymphoblastic Lymphoma (400x); B. CD45+ (400x); C. CD20- (400x); D. CD3+ diffuse (400x); E. Tdt+ diffuse (400x); F. Ki67 is very high, almost stained in 100% tumor cells

Approximately, 10% of primary lymphoma tumors involve the mediastinum, meaning that mediastinal involvement is not a part of systemic disease and is largely Hodgkin's lymphoma, which is about 60% (Lee et al., 2018). Hodgkin lymphoma are divided into nodular sclerosing (most common), lymphocyte-rich, lymphocyte-depleted, and mixed-cellularity. Non-Hodgkin lymphoma (NHL) comprises 15 to 25% of primary lymphomas, the most common of which are diffuse large B-cell non-Hodgkin lymphoma, also referred to as mediastinal large cell non-Hodgkin lymphoma, and lymphoblastic non-Hodgkin lymphoma (Marino & Ascani, 2019). Other tumour that can be occurred in mediastinum is Gray Zone Lymphoma which has an intermediate picture between mediastinal large B-cells lymphoma and nodular sclerosis Hodgkin's Lymphoma (Ott, 2017). The occurrence of peripheral T-cell lymphoma (PTCL) in the mediastinum is very rare (Kakuta et al., 2017). As in this case, there was one case of Lymphoma (NHL) T-cell type high grade. This study revealed that the most cases of mediastinal lymphoma is unknown whether they were of B or T-cell origin, followed by Non-Hodgkin's Lymphoma (NHL) B-cell type high grade, Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma (NHL) B-cell type low grade, Lymphoma (NHL) T-cell type high grade and T-lymphoblastic lymphoma.

Current guidelines recommend surgical excision biopsy as the standard for diagnosis, because histopathology examination can evaluate nodal architecture, immunophenotypic and molecular analysis if needed. Those modalities can help to make diagnosis subtype of lymphoma because treatment depends on precise lymphoma subtyping (Fuso et al., 2018). Determining subtypes of primary lymphoma in mediastinum based on the WHO classification of tumours of haematopoietic and lymphoid tissues 2017, are very difficult because most of the specimens in this study were small in size so that the histomorphological architecture was difficult to analyze and no further request from the clinicians to continue immunohistochemistry staining to get a subtype of malignant lymphoma was requested more specifically.

In the current World Health Organization classification, lymphomas are distinguished, not only on the basis of tissue architecture but also on immunophenotypic, cytogenetic, and molecular features, the latter tests even being feasible on cytology samples (Swerdlow et al., 2016). In our hospital, cytogenetic and molecular examination have not been available so that we did not continue to further cytogenetic and molecular examination. Actually, gold standard diagnosis of lymphoma is excisional biopsy followed by histopathology and immunohistochemistry examination. However, excisional biopsy appears to be a more invasive procedure and need longer time to recovery and a higher risk of complications such as bleeding or infection than core-needle biopsy. Nowadays, core needle biopsy is often performed and is increasingly done by clinicians to get specimens from mediastinum (Ito et al., 2021).

Core needle biopsy appears to have a limitation in evaluating the histological architecture and in achieving enough samples for ancillary testing such as immunohistochemistry and molecular testing (Frederiksen et al., 2015; Ito et al., 2021). Other study revealed there are a number of limitations. Only patients who were suitable for biopsy underwent the procedure, and the technique (including approach and biopsy gauge) was chosen by an experienced proceduralist on a

case-by-case basis (Navin et al., 2021). The specimens for this study were taken from the Anatomical Pathology laboratory archives at Dr. Soetomo General Hospital, Surabaya, and most of specimens were obtained from core biopsy procedures due to their being minimally invasive and having minimal complication for patients.

Conclusion

Mediastinal lymphoma is a rare tumor. Seventeen cases were obtained for this study during a 2-year period. It mostly occurs in men, between the age of 17 and 64 years old. The most common type found is Non-Hodgkin's Lymphoma (NHL) unknown subtype. Diagnosis of mediastinal lymphoma is challenging. Histopathology features may show similarities with other type of lymphomas, hence an immunohistochemistry profile is necessary. The specimens should be sufficient for further ancillary testing for example immunohistochemistry staining. Communication between the clinicians, radiologist and pathologist also very important to get better samples and to solve the difficult cases. Further study is needed to improve the knowledge in diagnosis of mediastinal lymphoma based on WHO classification of haematopoietic and lymphatic tissues especially for the specimen taken from core needle biopsy.

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