Mediastinal tumors differ in type and frequency depending on the mediastinal compartment. The tumor location, site of origin, area of existence and extension, and inner structure are extremely valuable factors in image interpretation and diagnosis. Published methods for classifying mediastinal compartments include the traditional method, Fraser and Paré method, Felson method, Heitzman method, Zylak method, and Whitten method (1). However, these approaches are confusing because of different terms and methods. In 2009 the Japanese Association for Research on the Thymus (JART) proposed a new mediastinal compartment based on transverse CT images (2), and published in the English literature in 2014 (1). They divided the mediastinum compartment into four areas: superior portion of the mediastinum, anterior mediastinum (prevascular zone), middle mediastinum (peri-tracheoesophageal zone), and posterior mediastinum (paravertebral zone). On the basis of the JART mediastinal classification, the International Thymic Malignancy Interest Group (ITMIG) proposed a three-compartment model by CT image-based classification for mediastinal compartments (3). Both classifications using CT images are useful for assessing mediastinal mass lesions and necessary for stipulating a mediastinal compartment method suited at the present time. It is necessary to be aware that the frequency distribution of mediastinal tumors is different depending on the method for subdividing the mediastinum because the mediastinal compartment is clinically important for image interpretation and diagnosis.

According to previous reports, approximately one half of all mediastinal masses occur in the anterior mediastinum, and the rest occur in the middle and posterior mediastinum (4). The common anterior mediastinal tumors are thymic epithelial tumor (thymoma, thymic carcinoma, and thymic neuroendocrine tumor), germ cell tumor (GCT), lymphoma, and thymolipoma. Thymoma is the most frequent type of tumor (4,5), accounting for 43.4% of mediastinal masses and 20–60% of anterior mediastinal masses. Thymoma affects adult patients older than 40 years of age (1,6-8). Thymic carcinoma accounts for 11.9% of mediastinal masses and 9.4–15.2% of anterior mediastinal masses (1,8). Thymic neuroendocrine tumor is rare, accounting only 2–5% of all thymic neoplasms (9). Mediastinal GCT occurs extremely often in the anterior mediastinum (1–3% of all GCTs, 10–13% of mediastinal masses, and 10–26% of anterior mediastinal masses). Furthermore, GCTs arising in the posterior mediastinum account for 3–8% of mediastinal GCTs (1,5,7-10). GCTs tend to occur frequently at a younger age (24% of anterior mediastinal masses and 19% of anterior and posterior mediastinal masses in children) (7,9,10). Intra-mediastinal goiter (3.8–10% of mediastinal masses) and parathyroid adenoma arise in the anterior compartment or superior portion of the mediastinum, but their frequency...
distributions differ according to the method of subdividing the mediastinum (4,5). Cysts (12–20% of mediastinal masses) and lymphoma frequently occur in the middle mediastinum, and approximately 90% of neurogenic tumors arise in the posterior compartment, accounting for 11–21% of mediastinal masses and 75–78.4% of posterior mediastinal masses (1,11).

Lymphoid neoplasms may occur in various regions or organs, including the mediastinal compartment. Malignant lymphoma is a common mediastinal tumor that usually occurs in the anterior mediastinum (15% of mediastinal lymphomas; 23% in adults and 12% in children) (7,9), accounting for 7.0–17.3% of anterior mediastinal masses (1,8) and 5.4% of mediastinal masses (1).

The two major types of Hodgkin's lymphoma are classical Hodgkin lymphoma (CHL) and nodular lymphocyte-predominant Hodgkin lymphoma. Of the subtypes of CHL, especially nodular sclerosis type (NSCHL) is the most frequent mediastinal lymphoma, followed by large B-cell lymphoma (LBCL) and T-lymphoblastic leukemia/lymphoma (TLL). CHL accounts for 50–70% and non-Hodgkin's lymphoma (NHL) 15–25% of mediastinal lymphoma in Western countries. Mediastinal CHL often occurs in adolescence to young adulthood (15–34 years old) (7,9,11). However, the incidence of malignant lymphoma is different in Japan and Western countries, as CHL and follicular lymphoma occur less frequently in Japan (4.41% and 6.70% of all malignant lymphomas, respectively) than in Western countries (40–45% and 11–33% of all malignant lymphomas, respectively) (12,13).

Primary mediastinal (thymic) large B-cell lymphoma (PMBL), which is diffuse large B-cell lymphoma (DLBCL) arising in the mediastinum from putative thymic B-cells, is an uncommon clinicopathological entity clearly stipulated as a diagnostic criterion for mature B-cell neoplasms by the World Health Organization (WHO) histological classification (9,14). PMBL accounts for 2–4% of NHL and 6–10% of DLBCL in Western countries (9,14,15), and 0.25–0.35% of all malignant lymphomas and 0.29–0.39% of NHL in Japan (13,16). Among children and adolescents, the frequency of PMBL is 2–5% of B-cell NHL in Western countries (17–19), and 1.0% of NHL and 2.2–2.5% of B-cell NHL in Japan (20,21).

NHL occurs at any age (median age 55 years), whereas patients with DLBCL are older (median age 64 years, range 20–92 years) and PMBL occurs in young adults (26–35 years old) (7,9,11,14,22). In addition, PMBL seems to have a better prognosis than other DLBCLs (5-year survival rate 64% for PMBL and 46% for other DLBCLs) (15,23). Thus, the clinicopathological and molecular features of PMBL are different from the other DLBCLs, and the molecular signature of PMBL is related to CHL (22,23).

The current study by Maeshima and colleagues analyzed 283 cases of anterior mediastinal tumor at a single institution, including the distribution of anterior malignant lymphoma and the frequency of PMBL (25). As previously mentioned, various types of mass lesions may occur in the mediastinum, and the frequencies of tumors are different depending on the mediastinal compartment. The first question is how the mediastinal compartment was defined, because a description of “anterior mediastinum” was vague in their study.

The crucial question is viewpoint and the method of evaluating the frequency of PMBL. Maeshima and colleagues reported that malignant lymphoma of the anterior mediastinum was diagnosed at a frequency of 27% in all anterior mediastinal masses at their hospital, with PMBL accounting for 13%, CHL 9%, TLL 2%, and other malignant lymphomas 3% of anterior mediastinal masses (25). In addition, PMBL occurred in 47%, CHL 33%, T-LBL 9%, and other malignant lymphomas 11% of all anterior mediastinal malignant lymphomas (25). The incidences were similar among newly diagnosed cases at their hospital, which were consulting cases from the other hospital. However, a report that reviewed the distribution of malignant lymphomas in Japan between 2001 and 2006 found that the incidence of PMBL was only 0.35% of all malignant lymphomas (16). Based on these results, Maeshima and colleagues suggested that the incidence of PMBL may be increasing in Japan (25), but it is difficult to compare frequencies despite different base populations. Furthermore, PMBL is a rare entity and difficult to diagnose, and it is now recognized as a rare type of B-cell malignant lymphoma. Thus, many PMBL cases must have previously been classified as B-cell malignant lymphoma. Considering this background, it is not necessarily appropriate to suggest that PMBL may be markedly increasing in Japan.

As described in the limitations, the current study by Maeshima and colleagues is a single-institution study and includes consulted cases with difficult pathological diagnoses. Therefore, bias is suggested in the PMBL cases gathered at the hospital. Moreover, diagnostic techniques,
such as immunohistochemistry, have improved, even though mediastinal tumors are sometimes difficult to diagnose, and is considered to be one factor in the increased number of PMBL cases.

PMBL often occurs at younger ages (7,9,11,14,22). Maeshima and colleagues also showed that most PMBLs occurred in patients under 40 years of age, especially for females (25). In male patients under 40 years of age with anterior mediastinal tumors, GCTs were frequent, followed by CHL and PMBL. Thymic epithelial tumors were most frequent in patients over 40 years of age. It seems that PMBL often occurs at younger ages; considering that patient age and sex may be helpful for the diagnosis of mediastinal tumors. These results are consistent with previous reports and may be useful for image interpretation and diagnosis.

There are some typos or concerns in Table 1 published by Maeshima and colleagues (25). The reference number of cited references seems to be different. In Table 1 reference 2 may be 8, and 3 is unclear. In addition, the frequencies of malignant lymphoma listed in Table 1 are comprehensive, but it is unclear and confusing because the base populations are different between the “previous reports” and their “present study”.

In summary, Maeshima and colleagues reviewed the distribution of 283 cases of anterior mediastinal masses and 76 cases of anterior mediastinal malignant lymphoma in Japan between 1997 and 2016 (25). They also analyzed the frequency of anterior mediastinal malignant lymphoma by age and sex. It is uncertain whether their results are applicable literally, but they may contribute to the diagnosis of anterior mediastinal malignant lymphoma. Further investigations using larger sample or a large number database will be necessary.

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Footnote

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References


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