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ORIGINAL ARTICLE

A novel diagnostic tool for hyaline vascular Castleman disease versus lymphoma based on contrast-enhanced computed tomography in neck mass

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Abstract

Background: Castleman disease and lymphoma each have a distinct treatment plan; however, they share the same features on contrast-enhanced computed tomography.

Methods: To assess the quantitative outcomes of Castleman disease versus lymphoma using contrast-enhanced computed tomography based on Hounsfield units (HU). We retrospectively reviewed eight patients with unicentric Castleman disease and 30 patients with lymphoma based on pathological diagnosis at China Medical University Hospital between 2015 and 2020. Preoperative computed tomography with contrast scans was reviewed, and the HU of each tumor were measured.

Results: This study included eight patients with unicentric Castleman disease (four men and four women; mean age, 33 years) and 25 patients with lymphoma (11 men and 14 women; mean age, 53 years). There was no significant difference in heterogeneity between the two diseases (0.161 ± 0.052 vs 0.239 ± 0.063, $p = 0.22$); however, enhancement in Castleman disease was higher than that in lymphoma (126.40 ± 31.90 vs 74.19 ± 7.11, $p < 0.001$), providing a very good diagnostic tool (cutoff point at 88.5–91.3, sensitivity 0.86/specificity 0.88). Furthermore, we found a highly linear relationship in Castleman disease, which was not noted in lymphoma.

Conclusion: The value of HU provides a good diagnostic tool for the differential diagnosis of Castleman disease versus lymphoma in the neck lymph nodes. Considering the linear relationship in Castleman disease, an increasingly accurate differential diagnosis can be made.

Keywords: Castleman disease; Computed tomography; Lymphoma

1. INTRODUCTION

Castleman disease is a lymphoproliferative disorder first reported by Dr. Benjamin Castleman in 1954. It is also known as giant lymph node hyperplasia or angiofollicular lymph node hyperplasia. Although the etiology of Castleman disease remains unclear, the disease is classified into two subtypes, unicentric and multicentric,[1,2] with the former being more prevalent. Unicentric Castleman disease is characterized by a painless mass over the mediastinum, axillary, and cervical lymph nodes and nonspecific clinical presentations,[3] with radiographic features that demonstrate intense homogeneous enhancement following contrast on CT (CT).[4–6] However, lymphomas share the same features of intense homogeneous enhancement on CT.[7,8] One retrospective study found significantly higher Hounsfield units (HU) in patients with Castleman disease than in patients with lymphoma.[9] However, the HU of a tumor may be affected by several factors, including the timing of image capture and dose and distribution of contrast. In addition, no quantitative research has been conducted on the homogeneity of both the diseases. Therefore, this study aimed to perform quantitative research on the imaging findings of Castleman disease versus lymphoma.

2. METHODS

This study was approved by the Institutional Review Board of China Medical University and Hospital (Taichung, Taiwan). The requirement for informed consent was waived owing to the retrospective nature of the study. We retrospectively reviewed eight patients with unicentric Castleman disease and 30 patients with lymphoma based on pathological diagnosis by curative resection or excisional biopsy of the neck mass at China Medical University and Hospital between 2015 and 2020. Patients were excluded if they did not undergo preoperative CT with contrast scan completion, which ultimately led us to exclude one patient with unicentric Castleman disease and five patients with lymphoma.

Head-and-neck CT was performed using a GE Optima CT660 CT scanner (64-slice). Omnipaque was administered intravenously

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Table 1

Characteristics of patients with Castleman disease

	Age	Gender	Histology	Symptoms	Lab	Location	Treatment
1	27	F	Hyaline vascular	NECK mass	Normal	Level II	Surgery
2[a]	46	M	Hyaline vascular	Neck mass	Normal	Level III	Surgery
3	28	F	Hyaline vascular	Neck mass	Normal	Parotid	Surgery
4	10	M	Hyaline vascular	Neck mass	Normal	Level III–Va	Surgery
5	57	F	Hyaline vascular	Neck mass	Normal	Level IV	Surgery
6	21	F	Hyaline vascular	Neck mass	Normal	Level II–III	Surgery
7	33	M	Hyaline vascular	Neck mass	Normal	Level I	Surgery
8	42	M	Hyaline vascular	Neck mass	Normal	level Ib	surgery

[a]Excluded due to a lack of preoperative CT scan data.

at a rate of 2 mL per second for 40 mL, and then 1.5 mL per second for 60 mL. Postcontrast imaging was taken at the 50th second after contrast infusion. Image data were analyzed using the INFINITT PACS (Picture Archiving and Communication System) at our institution. In our study, the HU of each tumor were measured, and the mean HU was defined as the index of enhancement of a tumor, while the relative standard deviation, which is the ratio of the standard deviation to the mean, was considered to be related to heterogeneity. As for factors that may influence the HU of a tumor, such as the timing of image capture and dose and distribution of contrast, the mean HU over the tumor should be adjusted by the HU of the external carotid artery (ECA), which is the main arterial supplement to the neck mass. We prefer the ECA to the muscle because the former is more homogenous than the latter and is easier to standardize.

3. RESULTS

3.1. Patient demographics

In this study, we finally included seven patients with unicentric Castleman disease and 25 patients with lymphoma. The characteristics of the patients with Castleman disease are summarized in Table 1. The patients comprised four men and four women, ranging in age from 10–57 years (mean age, 33 years). Histology of the neck mass showed that all were hyaline vascular types. Patients presented with no specific symptoms except for a neck mass, and laboratory data revealed no abnormalities. The locations of the neck masses ranged from levels I to V and in the parotid region. All patients underwent surgical intervention, and no recurrence was noted.

Regarding lymphoma, this study included 25 patients, comprising 11 men and 14 women, ranging in age from 8–79 years (mean age, 53 years). The neck mass histology is summarized in Table 2, which demonstrates that follicular lymphoma accounts for the largest proportion (32%), while diffuse large B-cell lymphoma accounts for the second largest proportion (28%).

Table 2

Characteristics of patients with lymphoma

	Age	Gender	Histology
1	18	F	Nodular sclerosis classical Hodgkin lymphoma
2	56	F	Peripheral T-cell lymphoma, not otherwise specified
3	72	F	Small lymphocytic lymphoma with large cell transformation
4	54	F	Follicular lymphoma
5	69	M	Follicular lymphoma
6	58	M	Diffuse large B-cell lymphoma
7	51	M	Follicular lymphoma
8	8	F	T-lymphoblastic leukemia/lymphoma
9	59	F	Diffuse large B-cell, nongerminal center type
10	42	F	Diffuse large B-cell, nongerminal center type
11	45	M	Peripheral T-cell lymphoma, not otherwise specified
12	63	M	Diffuse large B-cell lymphoma, germinal center type
13	59	M	Diffuse large B-cell lymphoma, nongerminal center type
14	62	F	Diffuse large B-cell, nongerminal center type
15	65	M	Nodal marginal zone lymphoma
16	59	F	Follicular lymphoma
17	69	F	Follicular lymphoma
18	41	F	Lennert lymphoma
19	48	M	Follicular lymphoma
20	62	F	Follicular lymphoma
21	79	M	Diffuse large B-cell, nongerminal center type
22	60	F	Mantle cell lymphoma
23	50	M	Follicular lymphoma
24	48	F	Classical Hodgkin's lymphoma
25	31	M	Mixed cellularity classical Hodgkin lymphoma

3.2. Heterogeneity

In our study, the index of heterogeneity was defined by the relative standard deviation. The mean heterogeneity index (Fig. 1) of lymphoma (0.239 ± 0.063) was higher than that of Castleman disease (0.161 ± 0.052); however, the difference was not significant (p = 0.22). If we used the index of heterogeneity as a diagnostic tool, the area under the curve (AUC) of the receiver operating characteristic curve (ROC) was 0.695, indicating a barely satisfactory diagnostic tool. The cutoff point was 0.19, with a sensitivity 0.86 and specificity of 0.56.

3.3. Enhancement

In our study, we considered the index of enhancement to be related to the mean HU value of the tumor. The enhancement index was significantly higher in Castleman disease (126.40 ± 31.90) than that of lymphoma (74.19 ± 7.11). Using the index of enhancement as a diagnostic tool, the AUC of the ROC was 0.95 (Fig. 1), which indicates an excellent diagnostic tool. The cutoff point was approximately 88.5–91.3, with a sensitivity of 0.86 and specificity of 0.88.

Regarding the factors that may influence the HU of a tumor, such as the timing of image capture and dose and distribution of contrast, the mean HU over the tumor should be adjusted by the HU of the ECA, which is the main arterial supplement to the neck mass.

To confirm the relationship between the HU of a tumor and the HU of the ECA, we used simple regression analysis through least-squares estimation and related techniques. The coefficient of determination (R^2) demonstrated a highly linear correlation in Castleman disease (R^2 = 0.804), while a linear correlation was absent in lymphoma. Analysis of variance (ANOVA) revealed a significant linear correlation in Castleman disease (F = 17.495, p < 0.05); however, no significant correlation was observed in lymphoma (F = 0.409, p = 0.529).

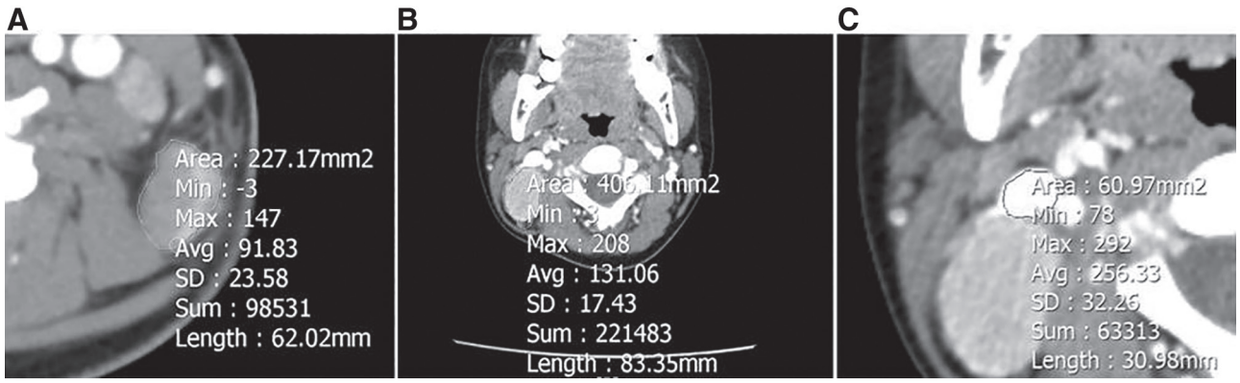

Fig. 1 Manual measurement of (A) lymphoma, (B) Castleman disease, and (C) ECA. ECA = external carotid artery.

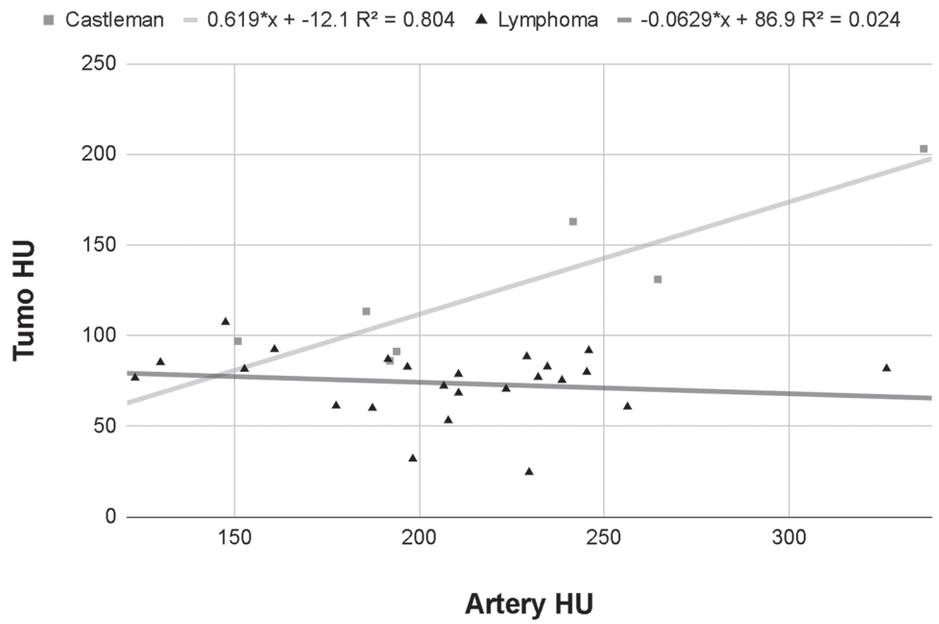

Fig. 2 Relationship between the HU of tumors and arteries. HU = Hounsfield units.

4. DISCUSSION

In our study, the clinical presentation of Castleman disease was nonspecific, except for the neck mass; laboratory data revealed no abnormalities. Additionally, we found no specific distribution of age, sex, or location of the neck mass.

For imaging findings, heterogeneity was higher in lymphoma than in Castleman disease; however, this difference was not significant. In other words, CD is more homogeneous in contrast-enhanced CT imaging findings, but this would not serve as a good diagnostic tool for distinguishing lymphoma. In contrast, Castleman disease displayed higher enhancement than lymphoma, which could make it a good diagnostic tool with a cutoff point around 88.5–91.3. Li et al[9] reached a similar conclusion in their comparative study, which indicated a cutoff value of 92.5 HU.

Considering the factors that affect tumor enhancement, we further considered the HU of the ipsilateral ECA as an adjustment factor. Drawing the chart of tumor HU and ECA HU, we found a highly linear relationship in Castleman disease, but no specific relationship in lymphoma. This finding is promising, as no other study has yet described it. It may be a good diagnostic tool if a linear relationship can be confirmed in a larger study.

The different relationships between Castleman disease and lymphoma may be related to the pathological characteristics of the two diseases. Unicentric Castleman disease is usually of the hyaline vascular type, which represents high vascularity,[10] and the HU of the tumor is thus highly related to the HU of the ECA.[11] In contrast, lymphoma does not share the same presentation; therefore, tumor HU is less related to ECA HU.

The linear relationship of Castleman disease can make a clear differentiation at the cutoff point of 200 ECA HU and 100 tumor HU. With an ECA HU greater than 200, when the tumor HU is higher than 100, Castleman disease has a high probability. Otherwise, the condition is more likely to be diagnosed as lymphoma. However, differentiating between the two diseases when the ECA HU is less than 200 is difficult; therefore, a biopsy is usually needed.

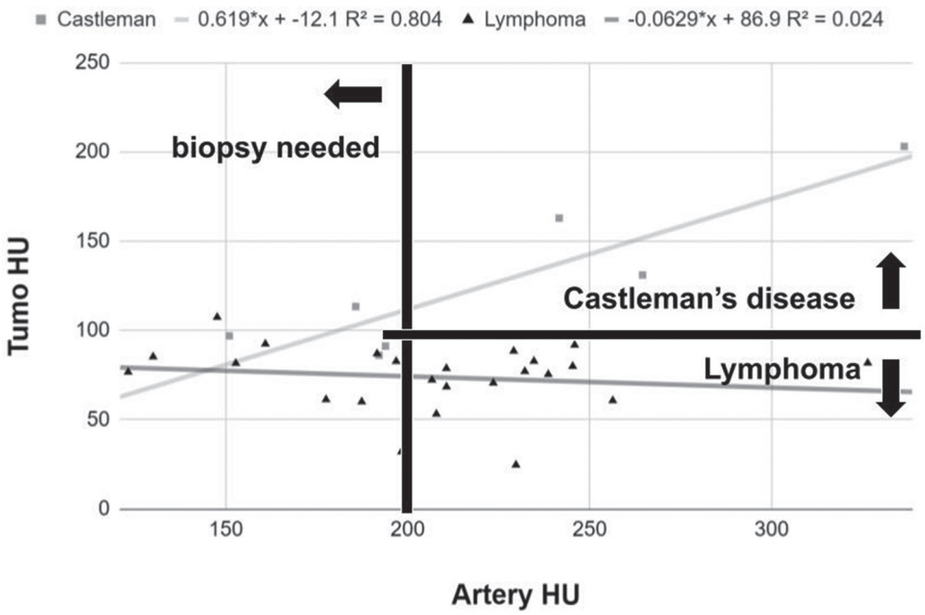

Fig. 3 Diagnostic tool made by the relationship between the HU of tumors and arteries. HU = Hounsfield units.

This study has several limitations. First, the sample size was too small to determine whether the findings are universal. Second, the range of tumors on CT imaging was determined by visual assessment, which may have produced errors and bias. Third, the reason for the wide range of ECA HUs is not clear and may have influenced the accuracy of quantization. Fourth, the relationship between the HU of tumors and arteries has not been previously described and thus may require more discussion and consensus. Finally, in most of our cases, we used only postcontrast imaging, and there was no noncontrast imaging in our data. Therefore, subtraction imaging could not be analyzed in our study, which is a limitation.

In conclusion in this study, we found that the heterogeneity of tumors on contrast-enhanced CT was not a good diagnostic tool. However, enhancement of the tumor is a good diagnostic tool, and we observed a highly linear relationship between the HU of Castleman disease and ECA. If confirmed in a large-scale study, this relationship can be a promising diagnostic tool for differentiating Castleman disease from lymphoma before performing a biopsy.

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