CT Imaging Characteristics Correlated with Overall Survival Time in Patients with AIDS-Related non-Hodgkin’s Lymphoma

Xueqin Li  
Capital Medical University Youan Hospital

Ziang Pan  
Peking Union Medical College Hospital

Meizhu Zheng  
Tianjin Third Central Hospital

Tianli Hu  
Guangzhou Eighth People's Hospital

Xing Wang  
Capital Medical University Youan Hospital

Li Li  
Capital Medical University Youan Hospital

Wen Ye  
Shanghai Public Health Clinical Center

Dongmei Jiang  
Tianjin First Central Hospital

Song Liu  
Tianjin First Central Hospital

Ruowei Tang  
Tianjin First Central Hospital

Ziyu Qi  
Tianjin First Central Hospital

Wen Shen  
Tianjin First Central Hospital

Jinxin Liu  
Guangzhou Eighth People's Hospital

Yuxin Shi  
Shanghai Public Health Clinical Center

Shuang Xia  
Tianjin First Central Hospital

Hongjun Li (lihongjun00113@126.com)
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Abstract

Background CT can provide useful information for treatment regimens and prognosis prediction of patients with AIDS-related non-Hodgkin's lymphoma (AR-NHL). It is necessary to investigate the prediction of CT imaging and clinical characteristics for overall survival (OS) in patients with AR-NHL.

Methods Data of 121 AR-NHL patients [median age: 41 (range 22-78), 112 male] between July 2012 and November 2019 were retrospectively reviewed. Patients were divided into two groups by median OS time and data were compared between two groups. K-M survival analysis and Cox proportional hazards regression analysis were used to determine the prognostic risk factors for OS.

Results The median OS time was 17 months. In the K-M survival analysis, presence of extracapsular infiltration (p=0.032), necrosis (p=0.005), CD4 ≤ 100 cells/µL (p=0.020), period from finding mass to admission ≤1 month (p=0.013), without chemotherapy (p<0.001), liver involved (p<0.001), gastrointestinal tract involved (p=0.015) and mediastinal or hilar lymph nodes involved (p=0.022) were associated with shorter OS. In the multivariate Cox regression analysis, liver involved (HR=2.48, 95%CI 1.45–4.25, P=0.001), mediastinal or hilar lymph nodes involved (HR=1.70, 95%CI 1.02–2.83, P=0.042), necrosis in lesion (HR=2.02, 95%CI 1.21–3.36, P=0.007) and CD4 ≤ 100 cells/µL (HR=2.66, 95%CI 1.42–4.98, P=0.002) were independently risk factors for shorter OS. Chemotherapy (HR=0.48, 95%CI 0.26–0.89, P=0.020) was independently protective factor for shorter OS. The predictive models based on Cox regression has good discrimination (Harrell's C-index=0.716) and good calibration (Hosmer-Lemeshow test, p=0.620).

Conclusion When the tumor had necrosis and extracapsular infiltration, involvement of mediastinal or hilar lymph nodes, liver, gastrointestinal tract in CT images, the overall prognosis was poor. And intensive chemotherapy regimens and more frequent follow-up should be considered.

1. Background

Acquired immune deficiency syndrome (AIDS)-related non-Hodgkin's lymphoma (AR-NHL), is a high-risk factor for morbidity and mortality in patients with AIDS (1,2). Although the incidence of AIDS-related tumors has decreased with the advent of highly active antiretroviral therapy (HAART), the occurrence rate of AR-NHL appears to be stable (3,4). So early diagnosis and evaluation are extremely important for treatment and prognosis.

HAART, chemotherapy, CD4 count, HIV RNA levels, Ann Arbor stage, lactate dehydrogenase (LDH) levels, international prognostic index (IPI) score, and age are key predictors of survival in AR-NHL patients in previous studies (5–7). However, few studies investigated the significance of imaging characteristics for the prediction of prognosis and survival, Novel imaging modalities for assessing lymphoma can provide useful information for treatment regimens and prediction of patients' prognoses. With the advancement of imaging technology such as CT, MR and PET/CT, radiologic techniques play an increasingly essential role in detecting lesion and evaluating disease (8–10). CT can find the enlargement of lymph nodes and
infiltration of extranodal organs, guide biopsy and observe early relapse through follow-up (11,12). MR has similar efficacy of detecting the space occupying effect with CT. Although MR is superior to diagnosis primary central nervous system lymphoma and lymphoma in skeletal muscular system, cases involved there are relatively rare (13). PET/CT can assess lymphoma stage, grade of malignancy and evaluate treatment response (14), but sometimes PET/CT is difficult to differentiate lymphoma from active inflammatory lesion or other lesions in brain and its utilization is limited due to various economic and social factors in some developing countries (15). So it is very pragmatic to assess the AR-NHL and determine the predictive factors via CT.

We hypothesized that there would be imaging differences in CT between patients with different overall survival (OS). The first purpose of the study was to find imaging and clinical factors indicated shorter OS. Second, we aimed to build a predictive model for the OS of AR-NHL based on clinical and imaging parameters.

2. Methods

2.1. Patients

The study was conducted under an approval by the Institutional Review Board. In this multi-center retrospective study, information of 181 patients with AIDS-related lymphoma from three tertiary infectious disease hospitals were reviewed and their clinical and imaging data were analyzed between July 2012 and November 2019. The diagnosis of HIV infection was based on the standards of centers for disease control and prevention of the USA. The diagnosis of lymphoma was based on puncture biopsy (163 patients), endoscopic biopsy (6 patients), and operation specimens (12 patients). All intervention and treatment were processed according to NCCN Clinical Practice Guidelines in Oncology: non-Hodgkin's lymphomas (16–18). If the patients were in stable conditions, they were followed up once every three months in the first year, once every six months in the second year and once every year in the third year and beyond. Patients were followed up at any time if disease progression and deterioration occurred. OS was chosen as the end point. OS was measured from the lymphoma diagnosis until last follow-up or death from any cause. Follow-up was continued until November, 2019.

2.2. Inclusion and exclusion criteria

Patients eligible for this study were (a) Age > 18 years. (b) With history of HIV-infection (c) With definite pathologically confirmed diffuse large B-cell lymphoma (DLBCL) or Burkitt's lymphoma (BL)(19) (d) With available clinical and CT imaging data before any clinical intervention. Patients with Hodgkin's lymphoma (HL, n = 5), indolent B-cell NHL (n = 4), and T-cell NHL (n = 7) or lacking a specific pathological type (n = 13) were excluded. One patient younger than 18 years of age and two patients with severe artifacts in the CT images were also excluded. 28 patients who were lost to follow-up were also excluded from the study. Through follow-up, the median OS time was 17 months (range, 0.5–60 months). 121 patients [median age: 41 (range 22–78), 112 male] were finally included in our research and they were subdivided into two groups in accordance with OS time. Group1 included patients with OS time ≤ median
OS time (61 patients) and group 2 included those with OS time median OS time (60 patients). Figure 1 shows flow chart of patient inclusion and exclusion criteria.

2.3. CT image acquisition and interpretation
All examinations were imaged with Philips iCT 256 (Philips; Amsterdam, Netherlands), 39 patients accepted contract-enhanced CT scan via intravenous contrast materials. The CT protocols was as follows: tube voltage, 120 kV; automatic tube current, 30–300 mA; rotation time, 0.75 s; collimation, 0.625 mm; pitch, 0.945; matrix, 512*512; section thickness, 5 mm; breath hold at full inspiration. The images were transmitted to the workstation and picture achieving and communication systems (PACS) for multiplanar reconstruction and post-processing. All images (both axial CT images and multiplanar reconstruction images) were reviewed by three radiologists (Doctor A with 22 years’ experience, B with 7 years’ experience and C with 10 years’ experience) blinded to clinical and laboratory data. Three estimators assessed the CT features independently. After separate evaluations, any divergences were resolved by discussion or consultation from a specialist in infectious imaging (Doctor D with 33 years’ experience), eventually reviewed by Doctor E for consistency analysis.

2.4. Data Analysis
The baseline data were recorded, including age, sex, pathological types, clinical manifestations, time from detecting positive HIV-antibodies to admission, time from initial mass discovery to admission, Ann Arbor stages, laboratory test results, treatment situations for each group.

Regarding the different sites of intranodal involvement, we subdivided the lesions into groups of axillary lymph nodes, cervical lymph nodes, mediastinal or hilar lymph nodes, abdominal pelvic and peritoneal lymph nodes, retroperitoneal lymph nodes, and inguinal lymph nodes. For the extranodal sites, involvement of the gastrointestinal tract, urinary system organs, liver, lung, pancreas or spleen were evaluated.

A detailed evaluation of the individual maximal lesion were analyzed including the following characteristics: diameters greater than or less than 5 cm; shape of the lesion (circular/irregular); fusion tendency; presence of extracapsular infiltration; evidence of necrosis; attenuation (hyper/iso/hypo); and texture (homogeneous/heterogeneous) in plain scans and contrast-enhanced behavior (including texture and the degree of enhancement, the CT value increased by 0–20 Hu for poor enhancement, 20–50 Hu for moderate enhancement, greater than 50 Hu for severe enhancement) in enhanced scans.

2.5. Statistical analysis
The imaging findings were tested for agreement using the Kappa test. If the Kappa value was less than 0.4, the consistency of the diagnostic findings was poor. If the Kappa value was greater than 0.75, then the diagnostic findings were considered to be sufficiently consistent.

Continuous variables of parameters were tested for normal distribution using the Kolmogorov–Smirnov method. If the data fitted a normal distribution, mean ± standard deviation (SD) and the t-test were used to check for differences between the two group. If the data were not normally distributed, then the median
(IQR) and Mann-Whitney U test were used. The chi-square test and Fisher’s exact test were used to compare categorical variables.

The univariate analysis of a Kaplan-Meier analysis model was fitted to determine the significant prognostic factors for OS in all patients. If P values of prognostic factors were less than 0.1, they were tested in a multivariate Cox proportional hazard model for independence of association and factors showing significant impact in the multivariate analysis were expressed via forest graph. Proportional hazards assumption was assessed through visual inspection of (log-log) plots of log cumulative hazard against time. A predictive model was developed for AR-NHL using Cox regression and illustrated by nomogram. The accuracy of predictions was assessed by estimating the model’s discrimination measured by the Harrell’s Concordance index (C-index). The C-index is the probability that for two patients chosen at random, the patient who had the event first had a higher probability of having the event according to the model. C-index = 0.50 represents agreement by chance; C-index = 1.0 represents perfect discrimination (20). The calibration of the nomogram was evaluated by the Hosmer-Lemeshow test. All statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). The figures were created using GraphPad Prism 7 (GraphPad Software; San Diego, CA, USA) and R software (version 4.0.1; http://www.r-project.org, with package of “rms”). The significance level was set at P < 0.05.

3. Results

3.1. Patient demographic data

Table 1 shows the demographic data of patients in each group. The median time from diagnosis of HIV to admission in group 1 was 9(2–36) months, which was statistically longer than that of group 2 [1.5(0.5–12) months, p = 0.007; Table 1]. 80% (48/60) of the patients with OS time > median OS time accepted chemotherapy vs. only 57.4% (35/61) of the patients with OS ≤ median OS time, which was a significant difference (P = 0.007). The CD4 count of patients with OS time ≤ median OS time was lower than the other group [157 (55–280) v 212 (130–375), p = 0.050]. Other laboratory results, such as WBC, NEUT, and lymphocytes, revealed no statistical differences between two groups. There was significant difference in Ann Arbor stage between two groups (p = 0.007).
Table 1. Demographic data of patients with AR-NHL

| Characteristic                      | Group 1 (n=61) | Group 2 (n=60) | P     |
|-------------------------------------|----------------|----------------|-------|
| Age (years)                         | 41 (35-50)     | 40 (33-53)     | 0.590*|
| Sex                                 |                |                | 0.710†|
| Male                                | 57 (93.4)      | 55 (91.7)      |       |
| Female                              | 4 (6.6)        | 5 (8.3)        |       |
| Pathology                           |                |                | 0.295†|
| DLBCL                               | 45 (73.8)      | 39 (65.0)      |       |
| BL                                  | 16 (26.2)      | 21 (35.0)      |       |
| Time of finding HIV (months)§       |                |                | 0.007*|
| Median (IQR)                        | 9(2-36)        | 1.5(0.5-12)    |       |
| Time of finding mass (months)‖      |                |                | 0.069*|
| Median (IQR)                        | 3(1-5)         | 1(1-3.5)       |       |
| HAART                               |                |                | 0.645†|
| Administered                        | 30 (49.2)      | 27 (45.0)      |       |
| Not administered                    | 31 (50.8)      | 33 (55.0)      |       |
| Chemotherapy                        |                |                | 0.007†|
| Administered                        | 35 (57.4)      | 48 (80.0)      |       |
| Not administered                    | 26 (42.6)      | 12 (20.0)      |       |
| B symptom                           |                |                | 0.188†|
| Positive                            | 12 (19.7)      | 18 (30.0)      |       |
| Negative                            | 49 (80.3)      | 42 (70.0)      |       |
| CD4 count (cells/µL)¶              | 157 (55-280)   | 212 (130-375)  | 0.050*|
| WBC, ×10⁹¶                         | 6.11 (3.97-7.44)| 5.29 (4.56-6.60)| 0.355*|
| NEUT, %¶                           | 66 (58-75)     | 69 (59-79)     | 0.439*|
| Lymphocytes, %¶                     | 24 (18-32)     | 23 (13-31)     | 0.340*|
| Ann Arbor Stage                     |                |                | 0.007†|
| 1                                   | 13 (21.3)      | 24 (40.0)      |       |
| 2                                   | 18 (29.5)      | 18 (30.0)      |       |
| 3                                   | 9 (14.8)       | 12 (20.0)      |       |
Group 1: Shorter than or equal to median OS, Group 2: Longer than median OS. Data are mean (SD), median (IQR) or n (%). Abbreviation: AR-NHL, AIDS-related non-Hodgkin’s lymphoma; DLBCL, diffuse large B-cell lymphoma; BL, Burkitt’s lymphoma; HAART, highly active antiretroviral therapy;

* Mann-Whitney U test; † Chi-square test; ‡ Fisher’s exact test; § period from HIV diagnosis to admission (months), there were 9 patients in group 1 and 8 patients in group 2 who did not find HIV until they went to the hospital; ‖ period from finding the mass to admission (months), there were 13 patients in group 1 and 11 patients in group 2 who did not find the mass themselves; ¶ there were 2 missing data in group 1 and 1 missing data in group 2.

3.2. Comparison of CT imaging characteristics

There was good agreement among the three doctors in evaluating the CT imaging characteristics (Kappa value 0.778–0.998, Table S1). There were significant differences in the involvement situations of inguinal lymph nodes [1.6% (1/61) vs 11.7% (7/60), p = 0.026; Fig. 2a], gastrointestinal tract [44.3% (27/61) vs 21.7% (13/60), p = 0.008; Fig. 2b], mediastinal or hilar lymph nodes [27.9% (17/61) vs 11.7% (7/60), p = 0.025; Fig. 2cd] (Table 2) between two groups. Extracapsular infiltration [63.9% (39/61) vs 38.3% (23/60), p = 0.005; Fig. 2e] and necrosis [42.6% (25/61) vs 23.3% (14/60), p = 0.024; Fig. 2f] were more common seen in patients of group 1 (Table 3).
Table 2. Differences of Involved sites between the two groups

| Sites Involvements                        | Group 1 (n=61) | Group 2 (n=60) | P     |
|-------------------------------------------|----------------|----------------|-------|
|                                           | n (%)          | n (%)          |       |
| Axillary lymph nodes                      | 0.101          |                |       |
| Involved                                  | 26 (42.6)      | 17 (28.3)      |       |
| Uninvolved                                | 35 (57.4)      | 43 (71.7)      |       |
| Cervical lymph nodes                      | 0.454          |                |       |
| Involved                                  | 10 (16.4)      | 7 (11.7)       |       |
| Uninvolved                                | 51 (83.6)      | 53 (88.3)      |       |
| Abdominal pelvic and peritoneal lymph nodes| 0.809          |                |       |
| Involved                                  | 8 (13.1)       | 7 (11.7)       |       |
| Uninvolved                                | 53 (86.9)      | 53 (88.3)      |       |
| Retroperitoneal lymph nodes               | 0.592          |                |       |
| Involved                                  | 8 (13.1)       | 6 (10.0)       |       |
| Uninvolved                                | 53 (86.9)      | 54 (90.0)      |       |
| Inguinal lymph nodes                      | 0.026          |                |       |
| Involved                                  | 1 (1.6)        | 7 (11.7)       |       |
| Uninvolved                                | 60 (98.4)      | 53 (88.3)      |       |
| Gastrointestinal tract                    | 0.008          |                |       |
| Involved                                  | 27 (44.3)      | 13 (21.7)      |       |
| Uninvolved                                | 34 (55.7)      | 47 (78.3)      |       |
| Urinary system organs                     | 0.774          |                |       |
| Involved                                  | 6 (9.8)        | 5 (8.3)        |       |
| Uninvolved                                | 55 (90.2)      | 55 (91.7)      |       |
| Liver                                     | 0.001          |                |       |
| Involved                                  | 21 (34.4)      | 6 (10.0)       |       |
| Uninvolved                                | 40 (65.6)      | 54 (90.0)      |       |
| Lung                                      | 0.596          |                |       |
| Involved                                  | 9 (14.8)       | 11 (18.3)      |       |
| Uninvolved                                | 52 (85.2)      | 49 (81.7)      |       |
| Mediastinal/hilar lymph nodes             | 0.025          |                |       |
| Involved                                  | 17 (27.9)      | 7 (11.7)       |       |
| Uninvolved                                | 44 (72.1)      | 53 (88.3)      |       |
|                | Group 1 | Group 2 |
|----------------|---------|---------|
| **Involved**   | 9 (14.8)| 7 (11.7)|
| **Uninvolved** | 52 (85.2)| 53 (88.3)|

Group1: Shorter than or equal to median OS, Group2: Longer than median OS. Data are n (%).
Table 3. Imaging characteristics of patients in the two groups

| Characteristic                        | Group 1 (n=61) | Group 2 (n=60) | P  |
|---------------------------------------|----------------|----------------|----|
|                                       | n (%)          | n (%)          |    |
| Diameter of focus, max                |                |                | 0.653† |
| <5mm                                  | 27 (44.3)      | 29 (48.3)      |    |
| ≥5mm                                  | 34 (55.7)      | 31 (51.7)      |    |
| Shape                                 |                |                | 0.526† |
| Irregular                             | 40 (65.6)      | 36 (60.0)      |    |
| Circular                              | 21 (34.4)      | 24 (40.0)      |    |
| Fusion tendency                       |                |                | 0.955† |
| With                                  | 44 (72.1)      | 43 (71.7)      |    |
| Without                               | 17 (27.9)      | 17 (28.3)      |    |
| Extracapsular infiltration            |                |                | 0.005† |
| With                                  | 39 (63.9)      | 23 (38.3)      |    |
| Without                               | 22 (36.1)      | 37 (61.7)      |    |
| Necrosis                              |                |                | 0.024† |
| With                                  | 25 (42.6)      | 14 (23.3)      |    |
| Without                               | 35 (57.4)      | 46 (76.7)      |    |
| Texture                               |                |                | 0.066† |
| Homogeneous                           | 18 (29.5)      | 27 (45.0)      |    |
| Heterogeneous                         | 43 (70.5)      | 33 (55.0)      |    |
| Attenuation                           |                |                | 0.105‡ |
| Hypoattenuation                       | 16 (26.2)      | 7 (11.7)       |    |
| Isoattenuation                        | 43 (70.5)      | 52 (86.7)      |    |
| Hyperattenuation                      | 2 (3.3)        | 1 (1.7)        |    |
| Enhancement scan texture *            |                |                | 0.635† |
| Homogeneous                           | 5 (22.7)       | 5 (29.4)       |    |
| Heterogeneous                         | 17 (77.3)      | 12 (70.6)      |    |
| Enhancement degree *                  |                |                | 0.501† |
| Mild                                  | 14 (63.6)      | 9 (52.9)       |    |
| Moderate                              | 8 (36.4)       | 8 (47.1)       |    |

Group 1: Shorter than or equal to median OS, Group 2: Longer than median OS. Data are n
*(%) *There were 22 patients in group1 and 17 patients in group 2 accepted enhanced CT scan; †Chi-square test; ‡Fisher’s exact test.

### 3.3. Prognostic factors for OS

In the univariate K-M survival analysis (Figure S1; Table S2-4), in the K-M survival analysis, presence of extracapsular infiltration [median OS (months): 12 v 24, p = 0.032], necrosis (8.75 v 22, p = 0.005), CD4 ≤ 100 cells/μL (8 v 21.5, p = 0.020), period from finding mass to admission>1 month (11 v 23, p = 0.013), without chemotherapy (7 v 23, p<0.001), liver involved (7 v 22.5, p<0.001), gastrointestinal tract involved (11 v 23, p = 0.015) and mediastinal or hilar lymph nodes involved (9.5 v 21, p = 0.022) were associated with shorter OS. In the multivariate Cox regression analysis (Fig. 3; Supplemental Table 2–4), the parameters of liver involved (HR = 2.48, 95%CI 1.45–4.25, P = 0.001), mediastinal or hilar lymph nodes involved (HR = 1.70, 95%CI 1.02–2.83, P = 0.042), necrosis in lesion (HR = 2.02, 95%CI 1.21–3.36, P = 0.007) and CD4 ≤ 100 cells/μL (HR = 2.66, 95%CI 1.42–4.98, P = 0.002) were independently risk factors for shorter OS. Chemotherapy (HR = 0.48, 95%CI 0.26–0.89, P = 0.020) was independently protective factor for shorter OS.

The predictive models based on Cox regression and illustrated by nomogram (Fig. 4) indicated the probability of 1-year, 2-year, 3-year overall survival in patients with AR-NHL. The Harrell’s C-index was 0.716 that showed relative good discrimination. The Hosmer-Lemeshow test demonstrated a p = 0.620>0.05, indicating no departure from a good fit. Probability of survival at 1, 2, 3 years are obtained by drawing a vertical line from the “total points” axis straight down to the outcome axes. The total number of points for each patient is obtained by summing the points for each of the individual factors in the nomogram. In the predictive model, chemotherapy weights most, treated with chemotherapy can increase 100 points for total points, then followed by liver involved free (add 82 points), CD4 counts>100 cells/μL (add 69 points), mediastinal or hilar lymph nodes involved free (add 58 points) and without necrosis (add 50 points). For instance, a AR-NHL patient with liver involved (0 point), without mediastinal or hilar lymph nodes involved (58 points), CD4 counts 125 cells/μL (69 points), with tumor necrosis (0 point), treated with chemotherapy (100 points), the total points is 227 points. This patient is predicted to have a 58% probability of surviving 1 year, 40% probability of surviving 2 years and 31% probability of surviving 3 years (Fig. 5).

### 4. Discussion

There were three important findings in current study. First, presence of extracapsular infiltration, necrosis, CD4 ≤ 100 cells/μL, period from finding mass to admission>1 month, without chemotherapy, liver involved, gastrointestinal tract involved and mediastinal or hilar lymph nodes involved were associated with shorter OS. Second, liver involved, mediastinal or hilar lymph nodes involved, necrosis in lesion, CD4 ≤ 100 cells/μL and treatment without chemotherapy were independently risk factors for shorter OS. Third,
chemotherapy weights most in the new predictive model for AR-NHL, then followed by liver involved, CD4 counts>100 cells/µL, mediastinal or hilar lymph nodes involved and necrosis. If the total points<295, three-year overall survival probability might<50%.

Imaging plays an important role in the detection and evaluation of AR-NHL lesions (8,10,12). CT of the head and neck, chest, abdomen, and pelvis is a critical staging modality recommended by the National Comprehensive Cancer Network guidelines (18). Necrosis shows hypoattenuation without enhancement in CT images. The potential mechanism of necrosis in lymphoma is the occlusion of the supplying hilar artery by the tumor (compression or invasion) in addition to lymphatic flow obstruction (21,22). Previous study indicated HIV(-) NHL patients with necrosis had significantly higher Ann Arbor stages, greater IPI, and higher serum LDH levels than those without necrosis but in Kaplan-Meier survival analysis, no statistically significant difference was noted for necrosis (23). Our study focused on AR-NHL patients and necrosis was an independent risk factor. Although the pathogenesis of AR-NHL necrosis remains unclear, it can be speculated that it indicates aggressive tumor growth with an apparent tendency for treatment resistance. Extracapsular infiltration was common in Kikuchi's disease (24). On CT it corresponds to periadenitis pathologically. It is caused by infiltration of inflammatory cells and karyorrhectic debris, which is the destructive fragmentation of the nucleus of dying histiocytes and plasmacytoid monocytes around the lymph node. So lymph node capsule may be broken by inflammation (24). However, it could also be observed in malignant lymphadenopathy with extracapsular extension such as lymphoma and metastasis (25). The invasion of tumor cells may be a potential mechanism of extracapsular infiltration and may correlate with poor prognosis. Natural killer (NK) cells play an important role in growth and infiltration of lymphoma cells, and activated NK cells could be a promising immunotherapeutic tool against lymphoma cells either alone or in combination with conventional therapy (26).

AR-NHLs are usually B-cell, high-grade, and poorly differentiated lymphomas (27). Extranodal sites involvement are common, the liver is the second most common site of abdominal involvement after the gastrointestinal tract with an incidence ranging from 26–45%. HIV (+) patients have a higher relative incidence of NHL than HIV (-) patients (28). HIV (+) patients are also more likely to have HCV, and vice versa. Persons with HCV have an almost two-fold greater risk of NHL, in addition, higher prevalence of HCV is associated with hepatocellular carcinoma (29). Hence, further differentiation via imaging examinations for hepatic mass in HIV (+) patients is necessary even though NHL has been diagnosed. Previous study indicated primary mediastinal large B-cell lymphoma (PMBCL), represents 10% of all DLBCL, were predictive of inferior OS and inferior PFS (30). This special tumour derives froma medullary thymic B cell and are composed of large cells expressing pan B-cell markers, but are negative for surface immunoglobulin (31). Compared with CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) regimen, rituximab and its use with intensified chemotherapy such as R-Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin and dexamethasone) and R-EPOCH (etoposide, prednisone, vincristine cyclophosphamide, doxorubicin) might improve the response rate and survival outcome for patients with mediastinal NHL, especially for PMBCL (30–32).
Epstein-Barr virus probably cause AR-NHL. Erwan P, et al. found responses of EBV-specific memory CD4 T-cell declined during HIV infection; latent antigen Epstein-Barr nuclear antigen 1 (EBNA1)-specific CD4 T-cells were lost before diagnosis of AR-NHL. Loss of EBNA1-specific CD4 T-cell immunity might lead progression to NHL (33). Although Mercy G, et al. Found AR-BL incidence declined at low CD4 counts, suggesting functional CD4 lymphocytes may be required for BL to develop (34), we consider lower CD4 counts reflect more severe immunodeficiency which is likely to cause opportunistic infections and other malignant tumors for patients with AR-NHL.

For patients have factors correlated with shorter OS time, intensive chemotherapy should be considered. Intensive chemotherapy is relative safe and effective in AIDS non-Hodgkin's lymphoma (35). Chemotherapy and concomitant HAART for AIDS-related NHL does not cause prolonged suppression of lymphocyte subsets. On the contrary, chemotherapy can increase the counts of CD4, CD8, CD19 and CD56 cell populations, which provide reassurance regarding the long-term consequences of chemotherapy in these individuals (36). Even for advanced AR-BL 70% patients achieved complete response by intensive chemotherapy regimen (LMB86), less than 10% patients occurred treatment-related deaths severe bone marrow toxicity should be concerned (37). Despite the chemotherapy treatment-related toxicity and mortality, standard chemotherapy remains the first line treatment for patients with AR-NHL.

Our study has several limitations. First, it is a retrospective study with a limited number of patients. The small number of cases in some categories may influence the stability of risk estimation. Second, we analyzed clinical and imaging data of AR-DLBCL and AR-BL together although no significant difference in pathology classifications between two groups was found in current study. Other limitations include shorter follow-up time and potential selection bias. Prospective investigations with larger samples, focus on certain pathological type should be designed in order to find more predictive factors for prognoses of AR-NHL patients.

5. Conclusion

CT is essential and pragmatic to assess AR-NHL patient’s condition. Intensive chemotherapy regimens and more frequent follow-up should be considered for patients with characteristics including lower CD4 counts, necrosis and extracapsular infiltration in lesion, vital sites like mediastinal or hilar lymph nodes, liver, gastrointestinal tract involved.

Abbreviations

CT=computed tomography
AIDS=acquired immune deficiency syndrome
NHL=non-Hodgkin's lymphoma
AR-NHL=AIDS-related non-Hodgkin’s lymphoma
OS=overall survival
HAART=highly active antiretroviral therapy
IPI=international prognostic index
LDH=lactate dehydrogenase

Declarations

Ethics approval and consent to participate: Institutional Review Board approval of You’an Hospital Affiliated of Capital Medical University was obtained. The consent to participate was waived.

Consent for publication: Not applicable.

Availability of supporting data: Not applicable.

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