Lymphocyte-Depleted Classical Hodgkin’s Lymphoma: A Comprehensive Analysis From the German Hodgkin Study Group

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ABSTRACT

Purpose
To investigate the clinical characteristics and treatment outcome of patients with lymphocyte-depleted classical Hodgkin’s lymphoma (LDCHL) compared with other histologic subtypes of Hodgkin’s lymphoma (HL).

Patients and Methods
From a total of 12,155 evaluable patients with biopsy-proven HL treated within the German Hodgkin Study Group trials HD4 to HD15, 10,019 patients underwent central expert pathology review. Eighty-four patients with LDCHL (< 1%) were identified and confirmed. The median follow-up time was 67 months.

Results
Patients with LDCHL, compared with patients with other histologic subtypes, presented more often with advanced disease (74% v 42%, respectively; P < .001) and “B” symptoms (76% v 41%, respectively; P < .001). Other risk factors were also more frequent in patients with LDCHL. Complete remission or unconfirmed complete remission was achieved in 82% of patients with LDCHL compared with 93% of patients with other HL subtypes (P < .001), and more patients with LDCHL had progressive disease. At 5 years, progression-free survival (PFS) and overall survival (OS) were significantly lower in patients with LDCHL compared with patients with other HL subtypes (PFS, 71% v 85%, respectively; P < .001; OS, 83% v 92%, respectively; P = .0018). However, when analyzing the subgroup of patients who underwent treatment with intensified or dose-dense bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone, patients with LDCHL (n = 39) had similar outcomes when compared with patients with other subtypes of HL (n = 3,564; P = .61).

Conclusion
LDCHL has a different pattern from other HL subtypes with more clinical risk factors at initial diagnosis and significantly poorer prognosis. Patients with LDCHL should be treated with modern dose-intensive treatment strategies.

J Clin Oncol 29. © 2011 by American Society of Clinical Oncology

INTRODUCTION

Lymphocyte-depleted classical Hodgkin’s lymphoma (LDCHL) is a rare entity, accounting for less than 1% of all patients with newly diagnosed Hodgkin’s lymphoma (HL) in Western countries. Because of its rarity, little is known about clinical characteristics, course, and treatment outcome of patients with LDCHL. The WHO classification generally distinguishes between lymphocyte-predominant (LP) HL and classical HL, which has been further classified into the following four subtypes: lymphocyte rich classical (LRC), nodular sclerosing (NS), mixed cellularity (MC), and lymphocyte depleted (LD).\(^1\) Recently, other less frequent subtypes such as LRC and LP were described in more detail.\(^2,3\)

Histologically, the following two LD variants were characterized: a diffuse fibrosis variant with abundant Hodgkin’s Reed-Sternberg cells in a hypocellular background showing disordered fibrosis, rich in histiocytes but with few lymphocytes; and a reticular variant, showing numerous Hodgkin’s Reed-Sternberg cells with bizarre cytologic features (Appendix Fig A1, online only). Exact diagnosis requires immunohistochemical staining, which aids to distinguish LDCHL from other HL and non-HL (NHL) subtypes.\(^4,5,6\)
Those few patients with LD histology who are analyzed in case series or included in clinical trials generally seem to have a poorer prognosis than patients with other HL subtypes. Current multimodality treatment protocols that achieve better tumor control might have blunted the effect of histology and other historical risk factors on outcome. In contrast, results from population-based analyses suggest that morphologic groups continue to have prognostic significance, even in the modern treatment era, with a significantly poorer prognosis of MC and LD subtypes. However, no larger cohort of patients with LDCHL has been analyzed thus far, because numbers were too small for reliable conclusions. To shed more light on the clinical course of LDCHL, we revisited our database to analyze patient characteristics and treatment outcome.

**Patient Selection**

From a total of 12,155 evaluable patients with biopsy-proven HL treated within four generations of German Hodgkin Study Group (GHSG) trials (HD4 to HD15), 10,019 patients underwent central expert pathology review and were included in this analysis. Eighty-four patients (0.84%) with LDCHL and 9,935 patients with other HL histology were identified by the review board. Data were taken from the latest final or follow-up analysis (HD4 to HD12) or from the latest interim analysis (HD13 to HD15).

In most GHSG trials, patients were between 16 and 75 years of age. To be eligible for random assignment, they had to have biopsy-proven HL histology at diagnosis, a creatinine clearance more than 60 mL/min, serum aminotransferases less than 3× the upper normal limit, bilirubin less than 2 mg/dL, left ventricular ejection fraction more than 0.45, and forced expiratory volume in the first second or diffusion capacity of carbon monoxide more than 60% of predicted. Required blood cell count was defined as WBCs ≥ 3,500/μL, platelets ≥ 100,000/μL, and hemoglobin level ≥ 8 g/dL. Randomly assigned patients had to have been free of antibodies against HIV and free of active infection. All patients signed informed consent before study entry, which was based on institutional review board guidelines. All protocols were approved by the ethics committee at each participating institution and were conducted in accordance with the Declaration of Helsinki. Treatment regimens are listed in Appendix Table A1 (online only).

**Staging Procedures and Treatment**

Histopathologic diagnosis was made initially by the local pathologist who then sent paraffin block biopsy samples for central pathology review to the GHSG expert pathology panel. Diagnostic criteria for identification of LDCHL were used as described by Pileri et al. The extent of disease was assessed by chest x-ray, abdominal ultrasound, computed tomography, isotope bone scan, and bone marrow biopsy.

Patients with clinical stage I or II disease without risk factors, such as large mediastinal mass, extranodal lesions, massive spleen involvement, elevated erythrocyte sedimentation rate (ESR; ≥ 50 mm without “B” symptoms and ≥ 30 mm with B symptoms), and involvement of three or more lymph node areas, were included in studies for early favorable stages (HD4, HD7, HD10, and HD13). Patients with clinical stage I or II A disease with one or more of these risk factors and stage II B with certain risk factors only (B symptoms and/or ≥ three lymph node areas involved) were included in trials for early unfavorable stages (HD5, HD8, HD11, and HD14). Patients with clinical stage III or IV disease with the risk factors of large mediastinal mass and/or extranodal involvement and patients with clinical stage III or IV were allocated to the advanced risk group and treated accordingly (HD6, HD9, HD12, and HD15). Between the different GHSG trial generations, staging criteria were slightly altered; for example, massive spleen involvement was abolished as separate risk factor after the third generation, and age limits for patients in unfavorable and advanced stages receiving bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPP) chemotherapy were introduced (18 to 60 years). These smaller adjustments in terms of age, staging, and risk factor profile were implemented at the beginning of a new trial generation for all patients irrespective of histology. Random assignment strategies including the chemotherapeutic regimens and the amount of radiotherapy applied in GHSG trials HD4 to HD15 have been described elsewhere and are listed in Table A1. Response and relapse criteria also have been described elsewhere.

**Statistical Methods**

Statistical analyses were performed with SAS Version 9.2 (SAS Institute, Cary, NC). Differences between histologic subtypes in the distribution of demographic and clinical variables were assessed using the χ² test or Fisher’s exact test for dichotomous variables. Progression-free survival (PFS) and overall survival (OS) were estimated according to the Kaplan-Meier method and compared between groups using the log-rank test. All reported P values are two-sided. All variables found to have a P < .05 were considered significant. PFS was calculated from the date of random assignment; was defined as time until progression, relapse, or death from any cause; and was censored at the date of last information on tumor status. OS was defined from the date of random assignment until death as a result of any cause and was censored at the date of last information. Cox proportional hazards regression model was used to assess the influence of LD histology on PFS, allowing for the influences of demographic and clinical variables. These were selected for inclusion in the model using a forward stepwise procedure.

**RESULTS**

**Patient Characteristics**

In the pooled total of 16,019 patients, 84 patients with LDCHL were identified, accounting for 0.84% of all patients with HL. Interestingly, the proportion of patients with HL diagnosed from 1998 to 2008 with LD subtype varied between 0.4% and 2% per year, with decreasing tendency. Almost all patients with LDCHL were diagnosed in early unfavorable or advanced stages; only one patient was diagnosed as early favorable. The numbers of patients with LDCHL per trial are listed in Table 1.

Baseline patient demographics and clinical characteristics of patients with LD and other subtypes of HL were clearly different. Patients with LD histology, compared with patients with non-LD HL, presented more often with advanced disease (74% vs 42%, respectively; P < .001) and B symptoms (76% vs 41%, respectively; P < .001). Certain risk factors occurred more frequently in patients with LDCHL than in patients with other HL subtypes, such as large mediastinal mass (32% vs 19%, respectively; P < .001), extranodal involvement (25% vs 14%, respectively; P < .0011), high ESR (76% vs 47%, respectively; P < .001), and involvement of three or more lymph node areas (88% vs 60%, respectively; P < .001). Furthermore, newly diagnosed patients with LDCHL, compared with other patients, more often showed involvement of bone marrow (11% vs 4%, respectively; P < .0098) and liver (19% vs 4%, respectively; P < .001). Patients with LDCHL presented significantly more often with a higher International Prognostic Score (IPS; P < .001) compared with patients with non-LD HL (Table 2).

Except for the GHSG risk factor of extranodal involvement (P = .065), all described differences in baseline demographics and clinical characteristics remained consistent and significant when comparing patients with LD subtype directly with patients with NS or MC subtypes (Table 2). This ensured that the better risk profile of the patients with non-LD HL was not a result of patients with LRC or LP...
subtypes. These patients have been shown to have a better prognosis than patients with NS or MC subtypes.2,3

Response to Treatment and Causes of Death

The overall response rates were as follows. Complete remission was recorded in significantly fewer patients with LD histology compared with patients with non-LD subtypes (82% vs 93%, respectively; \( P < .001 \)). There was no further difference between NS (93%) and MC (94%) subtypes. Partial remission was documented in 4.8% of patients with LD HL and 1.3% of patients with non-LD HL, and primary progressive disease was documented in 4.8% of patients with LD HL and 3.1% of patients with non-LD HL. In total, 9% of all patients (\( n = 933 \)) died, including 20% of patients with LD, 8% with NS, and 10% with MC HL. The causes of death during the study and follow-up period included death from HL, toxicity from primary or salvage treatment or autologous transplantation, secondary malignancies, and more rare causes, such as concomitant disease with organ dysfunction, suicide, accident, and others. Deaths as a result of HL or treatment toxicity were more frequently recorded in patients with LD histology compared with all patients with NS or MC subtypes.2,3

Treatment Outcome

Median observation time for PFS was 67 months. Patients with LDCHL showed a significantly inferior PFS compared with all patients with non-LD subtype (\( P < .001 \)) and patients with NS and MC subtypes (\( P < .001; \) Fig 1). Five-year PFS rates were 71% for LDCHL (95% CI, 59.9% to 79.9%), 85% for non-LDCHL (95% CI, 83.8% to 85.3%), 85% for NS (95% CI, 84.4% to 86.4%), and 84% for MC (95% CI, 82.0% to 85.2%; \( P < .001 \)). Inferiority was also observed for OS of patients with LDCHL compared with non-LDCHL (\( P = .0018 \)) or compared with NS or MC histology (\( P < .0012; \) Fig 2). Five-year OS rates were 83% for LDCHL (95% CI, 72.3% to 89.3%), 92% for non-LDCHL (95% CI, 91.4% to 92.5%), 93% for NS (95% CI, 91.9% to 93.3%), and 91% for MC (95% CI, 89.9% to 92.4%; \( P < .001 \)).

Furthermore, log-rank test analysis stratified by early unfavorable and advanced stages continued to show inferiority in terms of PFS (\( P = .0093 \)) and OS (\( P = .019 \)) for patients with LDCHL compared with patients with non-LD subtypes. In similar stratified analyses comparing patients with LDCHL with patients with combined
NS + MC HL, the P values were .0052 for PFS and .011 for OS (data not shown).

**Risk Factors**

Multivariate analyses were performed to assess the influence of LD histology on PFS. The variables of histology (LD v NS + MC), age, sex, stage, B symptoms, and IPS and the risk factors of large mediastinal mass, extranodal involvement, high ESR, and involvement of ≥ three lymph node areas were tested in a stepwise Cox regression model, including variables with P < .05 and excluding variables with P > .10. The optimal model included the variables of age (P < .001), IPS (P < .001), stage (P < .001), ≥ three lymph node areas involved (P = .0019), large mediastinal mass (P = .030), and high ESR (P = .042). LD histology (P = .12) was not significant based on this model. Even when the model was restricted to the generally recognized clinical risk factors of stage, age, sex, and IPS, no further prognostic significance was found for the factor of LD histology (P = .16; data not shown).

### Role of Modern Chemotherapy

In a Kaplan-Meier analysis restricted to the subgroup of patients (n = 3,606) who underwent modern intensified or dose-dense treatment regimens, such as BEACOPP-escalated or BEACOPP-14 (ie, HD9 arm C, HD12, HD14 arm B, and HD15), patients with LDCHL (n = 39) no longer had an inferior PFS compared with patients with non-LD subtypes (P = .61; Fig 3). Five-year PFS rates were 83% (95% CI, 65.7% to 92.1%) for LD versus 87% (95% CI, 85.8% to 88.3%) for non-LD. OS was also not inferior (P = .55). These results are important with regard to LDCHL in advanced stages because almost all patients with LD histology treated with BEACOPP-escalated or BEACOPP-14 belonged to that risk group (n = 38). In the group of comparable patients (n = 2,260) treated without BEACOPP-escalated or BEACOPP-14, patients with LDCHL had significantly worse 5-year PFS (62%) than patients with non-LD subtypes (84%; P = .0045); OS at 5 years was also inferior for patients with LDCHL (P = .023) in this subgroup (data not shown).

**DISCUSSION**

Although the histologic and molecular features have been characterized in part, little is known about the clinical characteristics of LDCHL. The aim of this retrospective study was thus to describe the clinical features of LDCHL and to determine treatment outcome for this rare entity, accounting for 0.84% of all our patients with HL. We analyzed 10,019 patients with biopsy-proven HL from four generations of clinical trials registered in the GHSG database who had undergone central expert pathology review. The following findings emerge from this study. Compared with other HL entities, patients with LDCHL presented more often with unfavorable characteristics.

### Table 3. Response to Treatment and Causes of Death

<table>
<thead>
<tr>
<th>Response and Causes of Death</th>
<th>Review Histology</th>
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<tr>
<td></td>
<td>Non-LD (n = 9,905)</td>
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<tr>
<td>Response</td>
<td>No.</td>
</tr>
<tr>
<td>CR</td>
<td>9,247</td>
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<tr>
<td>CRu</td>
<td>4,255</td>
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<tr>
<td>PR</td>
<td>4,992</td>
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<tr>
<td>NC</td>
<td>134</td>
</tr>
<tr>
<td>PD</td>
<td>22</td>
</tr>
<tr>
<td>Known</td>
<td>309</td>
</tr>
<tr>
<td>Unknown</td>
<td>223</td>
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</table>

Causes of death:

- Hodgkin’s lymphoma: 299 (3.0) 7 (8.3) 192 (3.3) 56 (2.2)
- Toxicity of primary treatment: 85 (0.9) 3 (3.6) 41 (0.7) 30 (1.2)
- Toxicity of salvage treatment: 68 (0.7) 1 (1.2) 44 (0.7) 16 (0.6)
- Secondary malignancy: 198 (2.0) 1 (1.2) 83 (1.4) 72 (2.9)
- Other or unknown: 266 (2.7) 6 (6.0) 132 (2.2) 83 (3.4)

Abbreviations: ASCT, autologous stem-cell transplantation; CR, complete remission; CRu, complete remission unconfirmed; LD, lymphocyte depleted; MC, mixed cellularity; NC, no change; NS, nodular sclerosis; PD, progressive disease; PR, partial remission.

**Fig 1.** Progression-free survival (PFS) by histologic subtype: (A) lymphocyte depleted (LD) versus non-LD, and (B) LD versus nodular sclerosis (NS) and mixed cellularity (MC). Nos. at risk are shown at 0, 30, 60, 90, and 120 months. Error bars indicate 95% CI.

<table>
<thead>
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<th>Progression-Free Survival (proportion)</th>
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<tr>
<td>Time (months)</td>
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<tr>
<td>No. at risk</td>
</tr>
<tr>
<td>LD</td>
</tr>
<tr>
<td>NS</td>
</tr>
<tr>
<td>MC</td>
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- **A**
  - Not LD: 1.0 0.8 0.6 0.4 0.2 0.0 (P < .001)
  - LD: 1.0 0.8 0.6 0.4 0.2 0.0 (P < .001)

- **B**
  - NS: 1.0 0.8 0.6 0.4 0.2 0.0 (P < .001)
  - MC: 1.0 0.8 0.6 0.4 0.2 0.0 (P < .001)
  - LD: 1.0 0.8 0.6 0.4 0.2 0.0 (P < .001)
such as advanced stage, B symptoms, large mediastinal mass, extranodal disease, high ESR, involvement of three or more lymph node areas, and higher IPS; in addition, organ involvement of bone marrow and liver was also more frequent. Patients with LDCHL, compared with patients with other HL subtypes, had significantly poorer rates for complete remission (82% vs 93%, respectively; \( P < .001 \)), PFS (71% vs 85%, respectively; \( P < .001 \)), and OS (83% vs 92%, respectively; \( P < .001 \)). Inferiority was still significant after stratification of patients with LDCHL for early unfavorable or advanced stages according to the GHSG risk stratification. Multivariate analysis identified age (\( P < .001 \)), IPS (\( P < .001 \)), stage (\( P < .001 \)), ≥ three lymph node areas involved (\( P = .0019 \)), large mediastinal mass (\( P = .030 \)), and high ESR (\( P = .042 \)) as adverse prognostic factors for PFS. Importantly, LD histology was not identified as an independent prognostic factor. Patients with LDCHL in advanced stages treated with BEACOPP-escalated or BEACOPP-14 had similar outcome compared with patients with advanced-stage non-LDCHL, suggesting that these patients should be treated with dose-intensive treatment strategies.

The proportion of patients with newly diagnosed LDCHL in this analysis varied between 2% and 0.4% per year from 1988 to 2008 and decreased over time. The reasons are not fully understood. It is possible that the incidence of LDCHL is really slowly decreasing. In addition, most patients with LDCHL were diagnosed in advanced stages, and 10% were older than age 60 years. Because more recent GHSG trials for advanced stages (HD12 and HD15) excluded patients older than age 60 years, this might have decreased the proportion of patients with LDCHL documented in the study population. In addition, there has been a constant improvement in pathology over the last decades with more accurate definition of all HL subtypes. Before 1980, patients with aggressive NHL were sometimes misdiagnosed as having HL and classified as LD or MC subtypes. In one report, this led up to 22% of all patients with HL being originally classified as LDCHL.

So far, only small case series evaluating clinical features and prognosis of patients with LDCHL have been published. An early
report suggested a poorer prognosis for patients with LDCHL compared with patients with other HL subtypes. However, there was no difference in survival when patients with LDCHL were treated with single-agent chemotherapy in the 1960s or multiple agent chemotherapy in the 1970s.\(^2\) In 1986, Kant et al\(^2\) reviewed all patients at the National Cancer Institute who were classified as having LDCHL between 1964 and 1976. The LD subtype was confirmed in nine of the 43 patients originally diagnosed. In their series of patients with LDCHL with up-to-date diagnostics after adequate pathology review, the prognosis was not different from other histopathologic subtypes of HL. Greer et al\(^2\) performed a clinicopathologic review of 25 patients with LDCHL, which is the largest case series published so far. The clinical presentation of LDCHL was similar to our series, including more patients with B symptoms (92%), subdiaphragmatic disease (88%), bone marrow involvement (56%), and advanced-stage disease (100%). Most patients had received mechlorethamine, vincristine, procarbazine, and prednisone chemotherapy at that time, and their prognosis was poor, with a median survival time of 36 months. Other reports suggested that negative prognostic factors such as subdiaphragmatic disease or tissue eosinophilia, which were more frequently observed in LDCHL, contributed to the poorer prognosis of these patients.\(^29,30\)

What are the clinical implications of the present analysis? It is demonstrated that LD histology is associated with poorer prognostic factors and poorer overall outcome. Importantly, patients with LD histology in advanced stages have a similar prognosis to other patients with HL when treated with modern dose-intensive regimens, suggesting that the earlier impact of histology as prognostic marker has diminished with the development of more effective chemotherapy.

Thus, one of the questions raised by this analysis is whether patients with LDCHL generally should receive more intensive treatment. Our results imply that patients with LDCHL should receive a dose-intensive chemotherapy such as BEACOPP-escalated or BEACOPP-14. However, only one patient with LDCHL in early unfavorable stages was treated with BEACOPP-escalated (arm B of HD14), and only one patient with LD histology was diagnosed with an early favorable stage and subsequently treated with doxorubicin, vinblastine, bleomycin, and dacarbazine. Thus, the present data allow only conclusions on advanced-stage LDCHL. Furthermore, the recommendation for using dose-intensive treatment strategies is limited to patients with HL younger than age 60 years, because older patients are at increased risk of acute toxicity and treatment-related morbidity when treated with BEACOPP-escalated.\(^31\) Previous reports by our group on elderly patients demonstrated that better tumor control achieved with BEACOPP was offset by higher toxicity and did not translate into better outcome.\(^32,33\)

In conclusion, this series of patients with LDCHL identified differences in disease characteristics, prognostic factors, and treatment outcomes between patients with LDCHL and other HL entities. In contrast, patients with advanced-stage LDCHL younger than age 60 years have similar outcomes compared with patients with classical HL when treated with dose-intensified BEACOPP.

**REFERENCES**


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**Table A1. Study Design and Treatment Regimens of GHSG Trials**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Stage</th>
<th>Trial Design</th>
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<tbody>
<tr>
<td>HD4</td>
<td>Early favorable</td>
<td>EF 40 Gy or EF 30 Gy + IF 10 Gy</td>
</tr>
<tr>
<td>HD5</td>
<td>Early unfavorable</td>
<td>2×COPP/ABVD + EF 30 Gy (bulk 10 Gy) or 2×COPP/ABV/IMEP + EF 30 Gy (bulk 10 Gy)</td>
</tr>
<tr>
<td>HD6</td>
<td>Advanced</td>
<td>4×COPP/ABVD + IF bulk/residual mass or 4×COPP/ABV/IMEP + IF bulk/residual mass</td>
</tr>
<tr>
<td>HD7</td>
<td>Early favorable</td>
<td>EF 30 Gy (36 Gy spleen) + 10 Gy IF or 2×ABV + EF 30 Gy (36 Gy spleen) + 10 Gy IF</td>
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<tr>
<td>HD8</td>
<td>Early unfavorable</td>
<td>2×COPP/ABVD + EF 30 Gy (bulk 10 Gy) or 2×COPP/ABVD + IF 30 Gy (bulk 10 Gy)</td>
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<tr>
<td>HD9</td>
<td>Advanced</td>
<td>4×COPP/ABVD + IF bulk/residual mass or 8×BEACOPPbaseline + IF bulk/residual mass or 8×BEACOPPescalated + IF bulk/residual mass</td>
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<tr>
<td>HD10</td>
<td>Early favorable</td>
<td>4×ABVD + IF 30 Gy or 4×ABVD + IF 20 Gy or 2×ABV + IF 30 Gy or 2×ABV + IF 20 Gy</td>
</tr>
<tr>
<td>HD11</td>
<td>Early unfavorable</td>
<td>4×ABVD + IF 30 Gy or 4×ABV + IF 20 Gy or 4×BEACOPPbaseline + IF 30 Gy or 4×BEACOPPbaseline + IF 20 Gy</td>
</tr>
<tr>
<td>HD12</td>
<td>Advanced</td>
<td>8×BEACOPPescalated + RT 30 Gy bulk/residual mass or 8×BEACOPPescalated + no RT or 4×BEACOPPescalated + 4×BEACOPPbaseline + RT 30 Gy bulk/residual mass or 4×BEACOPPescalated + 4×BEACOPPbaseline + no RT</td>
</tr>
<tr>
<td>HD13</td>
<td>Early favorable</td>
<td>2×ABVD + IF 30 Gy or 2×ABV + IF 30 Gy or 2×AV + IF 30 Gy</td>
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<td>HD14</td>
<td>Early unfavorable</td>
<td>2×ABVD + IF 30 Gy or 2×BEACOPPescalated + 2×ABV + IF 30 Gy</td>
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<tr>
<td>HD15</td>
<td>Advanced</td>
<td>8×BEACOPPescalated (+ RT 30 Gy to PET-positive residual ≥2.5 cm) or 8×BEACOPPescalated (+ RT 30 Gy to PET-positive residual ≥2.5 cm) or 8×BEACOPP-14 (+ RT 30 Gy to PET-positive residual ≥2.5 cm)</td>
</tr>
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</table>

Abbreviations: ABV, doxorubicin, vinblastine, and bleomycin; ABVD, doxorubicin, vinblastine, bleomycin, and dacarbazine; BEACOPP, bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone; COPP, cyclophosphamide, vincristine, procarbazine, and prednisone; EF, extended field; GHSG, German Hodgkin Study Group; HD, Hodgkin’s disease; IF, involved field; IMEP, ifosfamide, methotrexate, and etoposide; PET, positron emission tomography; RT, radiotherapy.
Fig A1. Different histologic variants of lymphocyte-depleted classical Hodgkin’s lymphoma (LDCHL): (A) diffuse fibrosis variant of LDCHL, and (B) reticular variant of LDCHL. Images courtesy of Donald J. Innes, Jr, MD, Professor of Pathology at the University of Virginia School of Medicine, University of Virginia, Charlottesville, VA.