

When is surgical resection alone appropriate treatment for pediatric nodular lymphocyte-predominant Hodgkin lymphoma?

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Abstract

The surgeon's role in the management of lymphoma is typically limited to performing biopsies for diagnosis. Most patients with lymphoma are treated with chemotherapy and/or radiation, but in rare cases, lymphoma can be primarily treated with surgery. We present a case of nodular lymphocyte-predominant Hodgkin lymphoma in a 4-year-old child with cervical adenopathy and discuss initial treatment with surgery alone. Surgery as primary treatment avoids the serious long-term sequelae of chemotherapy and radiation, and reserves those options for possible future recurrences; however, this approach should be reserved for patients with limited and low-risk disease. This case report reviews the pros and cons of treating early-stage nodular lymphocyte-predominant Hodgkin lymphoma in a pediatric patient with surgery alone.

Keywords

Hodgkin lymphoma, pediatric lymphadenopathy, surgical resection

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Introduction

Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) is an uncommon variant of Hodgkin lymphoma (HL). Pediatric patients are typically male and the majority of those affected present at the early stages of the disease with isolated cervical and axillary lymph node involvement and without B symptoms.¹ Pediatric NLPHL itself is rarely fatal with an overall survival of over 90%, and most patient deaths are related to treatment.^{2,3} While chemotherapy and/or radiation therapy are highly effective, their long-term sequelae in children including growth retardation, infertility, hypothyroidism, cardiopulmonary disease, and second primary malignancies are not inconsequential.⁴ Various studies have suggested surgical resection alone or watch-and-wait strategies as alternatives to more traditional treatment approaches.^{1,4–7} We report a case of initial surgical management of a 4-year-old boy with stage 1A NLPHL and discuss when this approach is most appropriate for the treatment of NLPHL.

Case report

A 4-year-old male presented to pediatric otolaryngology clinic with a 6-month history of right cervical lymphadenopathy without fevers, night sweats, or weight loss.

Family history was significant for HL in his father. On exam, bilateral shotty cervical lymph nodes with a prominent collection of 2-cm right level 2 lymph nodes were palpated; they were soft and non-tender without overlying skin changes. A complete blood count was normal, and mycobacteria and Lyme tests were negative. The patient underwent tonsillectomy and adenoidectomy for obstructive sleep apnea (OSA) and bilateral and symmetric tonsillar hypertrophy with a subsequent reduction in the size of his cervical nodes. At follow-up 9 months later, the nodal mass increased in size to 3 to 4 cm in diameter with prominent smaller surrounding lymph nodes. A computed tomography (CT) scan of the neck revealed a minimally enhancing 2.2 × 1.4 cm level 2 lymph node mass without areas of hypoattenuation.

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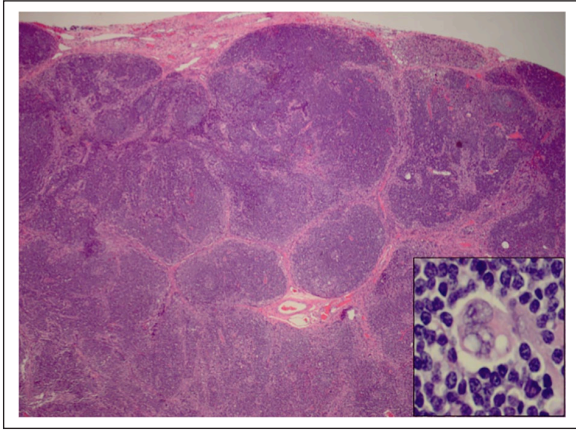


Figure 1. Lymph node involvement by nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) showing prominent nodular growth pattern (hematoxylin and eosin, 100 \times magnification). Inset is a high-magnification (400 \times) view of the characteristic cell of NLPHL, the lymphocyte-predominant (LP) or “popcorn” cell. Note the polylobulated nucleus and small, peripherally located nucleoli.

The imaging was non-specific and suggestive of an infectious or reactive process.

Because of the patient’s concerning family history and continued growth of the node, an excisional biopsy was performed. Two enlarged well-encapsulated lymph nodes measuring 4.5 \times 3.5 \times 2.5 cm and 3.5 \times 2.5 \times 2.0 cm from level 2 were excised. Flow cytometry showed no monotypic B-cell population, thereby excluding B cell-non-Hodgkin lymphoma (B-NHL) and T-lymphocytes with increased CD4⁺:CD8⁺ ratio. Histopathology revealed effacement of the lymph node architecture by a nodular infiltrate predominantly consisting of small, non-neoplastic B-cell epithelioid histiocytes and intermingled lymphocyte-predominant (LP) cells (Figure 1). The architectural pattern is consistent with the “Classic” B-cell-rich nodular type, as described by Fan et al.⁸ The immunophenotype of the neoplastic cells was CD45⁺, CD20⁺, and CD30⁻ which is typical for NLPHL (Figure 2). Because of the patient’s young age and unusual presentation, the flow cytometry results and histopathological slides were reviewed and confirmed by expert hematopathologists at Massachusetts General Hospital and Boston Children’s Hospital.

The patient was referred to the pediatric oncology service for staging and management. Functional imaging with PET (positron emission tomography)-CT revealed hypermetabolic adenopathy of the right neck cervical and supraclavicular regions, consistent with stage 1A lymphoma. The case was discussed, and pathology and imaging were reviewed at the institutional multidisciplinary pediatric tumor board and with lymphoma expert at Dana Farber Cancer Institute. They surprisingly recommended surgical treatment alone with completion lymphadenectomy. After careful consideration by the pediatric oncologist, lymphoma expert, and surgeon and review of the potential benefits and risks of surgery versus chemotherapy with the family, the patient underwent a

right-sided lymphadenectomy from levels 2 to 5 and the supraclavicular region. Histological findings confirmed NLPHL in all but one lymph node from the supraclavicular region, without evidence of transformation.

The patient was monitored closely with monthly physical examinations. At 2 months after neck dissection, he was noted to have a palpable right neck mass without fevers, night sweats, fatigue, or weight loss. PET-CT revealed hypermetabolic right supraclavicular and posterior occipital lesions. The patient underwent excisional biopsy of right supraclavicular lymph nodes and one posterior occipital node at the same time as Medi-port placement, and pathology revealed NLPHL in all nodes. Because of his short 2-month interval to recurrence and progression of his disease as well as his strong family history of lymphoma, chemotherapy was recommended over close monitoring with lymph node excisions as needed. After consultation with pediatric lymphoma experts from Dana Farber, four cycles of VAMP (vinblastine, doxorubicin (Adriamycin®), methotrexate, and prednisone) chemotherapy were begun. Radiation therapy was considered, but with no evidence for active lymphoma on PET-CT after two cycles, the patient was able to avoid neck radiation at that time.

Discussion

NLPHL is a subtype of HL with an unusually indolent, infrequently fatal course. In reviewing this case, we debated whether or not a fine needle aspiration biopsy or core biopsy could have been utilized (when the patient was under anesthesia for tonsillectomy and adenoidectomy) to obtain a diagnosis of NLPHL without violating the neck. However, diagnosis of NLPHL relies heavily on excisional biopsy because of the need for intact architecture and appropriate LP cells for diagnosis (Figures 1 and 2).^{9,10}

In the pediatric population, particular consideration is given to the late sequela of early aggressive treatment, considering both the indolent nature of NLPHL and survival outcomes approaching 100% in early-stage disease.⁶ As such, pediatric treatment protocols appropriately deviate from those used in adults by using lower doses of radiotherapy, avoiding alkylating agents, or opting for hybrid chemotherapy regimens.¹¹ However, the consequences of overtreatment are severe. Deaths in NLPHL are more frequently related to second primary malignancy than to the disease itself, and the systemic toxicities of therapy on development can be detrimental.⁶ As a result, NLPHL represents a unique clinical opportunity to spare patients the long-term sequelae of systemic chemotherapy by either reducing adjuvant treatment intensity or forgoing it completely and treating initially with surgery alone.

To date, the majority of studies assessing a “surgery first” approach to treatment of NLPHL have been retrospective studies, and have included patients with varying stages of disease and varying extents of surgical resection.^{1,4,6} Nevertheless, these studies have suggested that surgery alone represents a possible curative option for those with limited

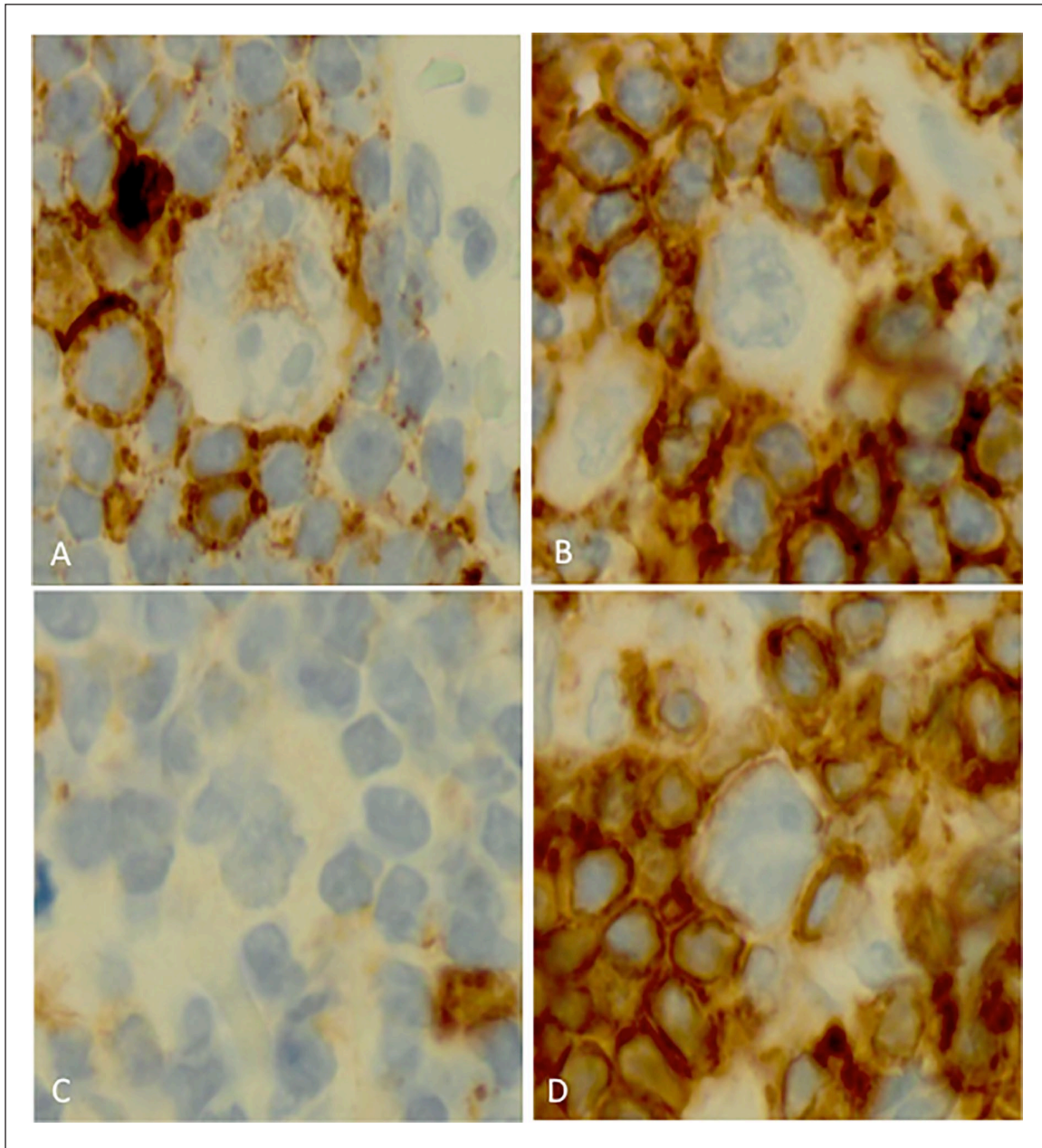


Figure 2. Immunophenotypic characterization of lymphocyte-predominant (LP) cell (400 \times magnification). The LP cell expresses CD20 (panel A) and CD45 (panel B) on the cell surface but is negative for CD30 (panel C). The immunostain for CD3 (panel D) highlights small, benign T-lymphocytes surrounding the LP and forming a characteristic rosette.

disease. Pellegrino et al.⁶ demonstrated an overall progression-free survival estimate of 57% (at 50 months) in patients treated with surgery alone, with an estimate of 67% (at 26 months) in those who achieved complete remission after surgery. The Children's Oncology group was the first to prospectively demonstrate the utility of surgical resection alone. Their study demonstrated that 75% of children with stage 1A disease can be treated with surgery alone and spared upfront chemotherapy, though the study only allowed this approach in patients with single-node involvement and total resection at diagnosis due to concern of subclinical involvement of

additional nodes in patients with more extensive disease.¹² To better understand the feasibility of applying this approach to a broader range of patients, Aldrink et al. later assessed the resectability of stage 1A disease with more than single-node involvement. Patients had a median of four nodes requiring resection, and 94% of cases were felt to be resectable with 81% (29/36 cases) surgeon agreement.¹³

The opportunity to spare a majority of children with NLPHL early exposure to cytotoxic therapy demands further investigation and awareness of the role of surgical intervention in managing pediatric NLPHL. Despite presenting with stage 1A

disease, our patient may be considered higher risk as he presented at a relatively young age with multiple involved lymph nodes and a family history of lymphoma. Here, surgery was considered an important tool to preserve his future chemotherapeutic options and reduce the risk of cervical radiation, though the patient ultimately required treatment with chemotherapy due to recurrence and progression of his disease. While there is a growing recognition for the role of surgical intervention alone in pediatric NLPHL, this case supports the notion that surgical resection alone should be restricted only to patients with complete remission according to PET/CT after nodal resection, and begs the question of whether or not patients with stage II or higher disease should be considered for this approach at all. Furthermore, future studies of risk-adapted treatment protocols in NLPHL are necessary to distinguish patient populations at highest risk of relapse, even among those with early-stage disease, single-node involvement, or other favorable prognostic features. It is important that surgical oncologists are aware of their potential therapeutic role in managing these patients and of the limited indications for this surgery-alone approach for the treatment of NLPHL.

Conclusion

The surgeon's role in the management of lymphoma is typically limited to performing biopsies for diagnosis and staging. This case of stage IA NLPHL in a 4-year-old boy treated initially with surgery alone serves as a reminder that certain types of low-grade lymphoma can be managed surgically to avoid the sequelae of chemotherapy and radiation in a young child. However, the surgery-alone approach should be reserved for patients with low-risk and limited disease. Further investigation is required to clearly define the appropriate patient population for this approach, with consideration of both the morbidities of surgical intervention and long-term toxicities of chemotherapy and radiation.

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Ethical and patient consent

The Dartmouth-Hitchcock Health (D-HH) Institutional Review Board (IRB) does not require ethical approval for reporting

individual cases or case series. Written informed consent was obtained from a legally authorized representative(s) (mother of patient) for anonymized patient information to be published in this article.

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References

1. Mauz-Körholz C, Gorde-Grosjean S, Hasenclever D, et al. Resection alone in 58 children with limited stage, lymphocyte-predominant Hodgkin lymphoma—experience from the European network group on pediatric Hodgkin lymphoma. *Cancer* 2007; 110(1): 179–185.
2. Eichenauer DA, Plütschow A, Fuchs M, et al. Long-term follow-up of patients with nodular lymphocyte-predominant Hodgkin lymphoma treated in the HD7 to HD15 trials: a report from the German Hodgkin study group. *J Clin Oncol* 2020; 38(7): 698–705.
3. Sandoval C, Venkateswaran L, Billups C, et al. Lymphocyte-predominant Hodgkin disease in children. *J Pediatr Hematol Oncol* 2002; 24(4): 269–273.
4. Murphy SB, Morgan ER, Katzenstein HM, et al. Results of little or no treatment for lymphocyte-predominant Hodgkin disease in children and adolescents. *J Pediatr Hematol Oncol* 2003; 25(9): 684–687.
5. Eichenauer DA and Engert A. How I treat nodular lymphocyte-predominant Hodgkin lymphoma. *Blood* 2020; 136(26): 2987–2993.
6. Pellegrino B, Terrier-Lacombe MJ, Oberlin O, et al. Lymphocyte-predominant Hodgkin's lymphoma in children: therapeutic abstention after initial lymph node resection—a study of the French Society of Pediatric Oncology. *J Clin Oncol* 2003; 21(15): 2948–2952.
7. Borchmann S, Joffe E, Moskowitz CH, et al. Active surveillance for nodular lymphocyte-predominant Hodgkin lymphoma. *Blood* 2019; 133(20): 2121–2129.
8. Fan Z, Natkunam Y, Bair E, et al. Characterization of variant patterns of nodular lymphocyte predominant Hodgkin lymphoma with immunohistologic and clinical correlation. *Am J Surg Pathol* 2003; 27(10): 1346–1356.
9. Roshal M, Wood BL and Fromm JR. Flow cytometric detection of the classical Hodgkin lymphoma: clinical and research applications. *Adv Hematol* 2011; 2011: 387034.
10. Bartlett NL. Treatment of nodular lymphocyte Hodgkin lymphoma: the Goldilocks principle. *J Clin Oncol* 2020; 38(7): 662–668.
11. Shankar A and Daw S. Nodular lymphocyte predominant Hodgkin lymphoma in children and adolescents: a comprehensive review of biology, clinical course and treatment options. *Br J Haematol* 2012; 159(3): 288–298.
12. Appel BE, Chen L, Buxton AB, et al. Minimal treatment of low-risk, pediatric lymphocyte-predominant Hodgkin lymphoma: a report from the children's oncology group. *J Clin Oncol* 2016; 34(20): 2372–2379.
13. Aldrink JH, Appel B, Kaplan JA, et al. Surgeon concordance in the assessment of resectability for stage IA nodular lymphocyte predominant Hodgkin lymphoma. *J Pediatr Hematol Oncol* 2018; 40(3): 246–247.