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Case report

# A Case of Classical Hodgkin Lymphoma with Total Lymph Node Infarction

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Lymph node infarction is very rare, and is frequently associated with neoplasms, such as malignant lymphoma and non-neoplastic disease, or interventions such as fine-needle aspiration (FNA). A 76-year-old man presented with cervical lymph node swelling. Although FNA was performed, the findings were insufficient for a definitive diagnosis. Consequently, surgical biopsy of the cervical lymph node was performed, which revealed total infarction; a diagnosis of classical Hodgkin lymphoma was made later. Both lymphoma itself and FNA may cause total lymph node infarction, which makes diagnosis confusing. Therefore, it is important to repeat the biopsy rather than repeat FNA to correctly diagnose malignant lymphoma, including Hodgkin lymphoma.

**Key words:** lymph node infarction, Hodgkin lymphoma, fine-needle aspiration

## INTRODUCTION

Swollen lymph nodes have been reported to have several causes, including infection, autoimmune diseases, drug reactions, sarcoidosis, and malignancy, especially lymphoma.<sup>1</sup> Although it is important to obtain a medical history from patients, query symptoms, and perform physical examinations, histological analysis of lymph node biopsy specimens is often required to make a definitive diagnosis.

Total lymph node infarction is very rare, partly because lymph nodes are highly vascularized. Most node infarctions are accompanied by neoplastic diseases or non-neoplastic causes, including trauma, vasculitis, infection, inflammation, or occasionally, fine-needle aspiration (FNA) procedures.<sup>2,3,4</sup> Although FNA is a minimally invasive and convenient method to diagnose malignancy, it may paradoxically confound the diagnosis. Herein, we report a rare case of classical Hodgkin lymphoma with total lymph node infarction, in which the disease was self-induced or due to FNA.

## CASE REPORT

A 76-year-old man exhibited swelling on the left side of his neck, which was first observed 2 months prior to presentation. When he visited a doctor for prior stroke, he mentioned the swollen lymph node in his neck, for which we were consulted. He had no “B symptoms”, such as high fever, weight loss, night sweats, or any other symptoms or signs. He did not have any history of tuberculosis or other diseases associated with lymph node swelling. He was a heavy smoker (10 cigarettes per day for 50 years). Physical examination revealed numerous 1-cm to 2-cm swollen lymph nodes in the left neck and supraclavicular fossa region, which were immobile and elastic hard on palpation. Laboratory tests revealed a white blood cell count of  $9.1 \times 10^3/\mu\text{L}$ , a C-reactive protein level of 5.72 mg/dL, and elevation of lactate dehydrogenase (294 U/L) and soluble interleukin-2 receptor levels (3520 U/mL). Routine examinations for infectious diseases (hepatitis B and C, human immunodeficiency virus [HIV], human T-lymphotropic virus type 1 [HTLV-1], Epstein-Barr virus [EBV], and interferon-gamma releasing

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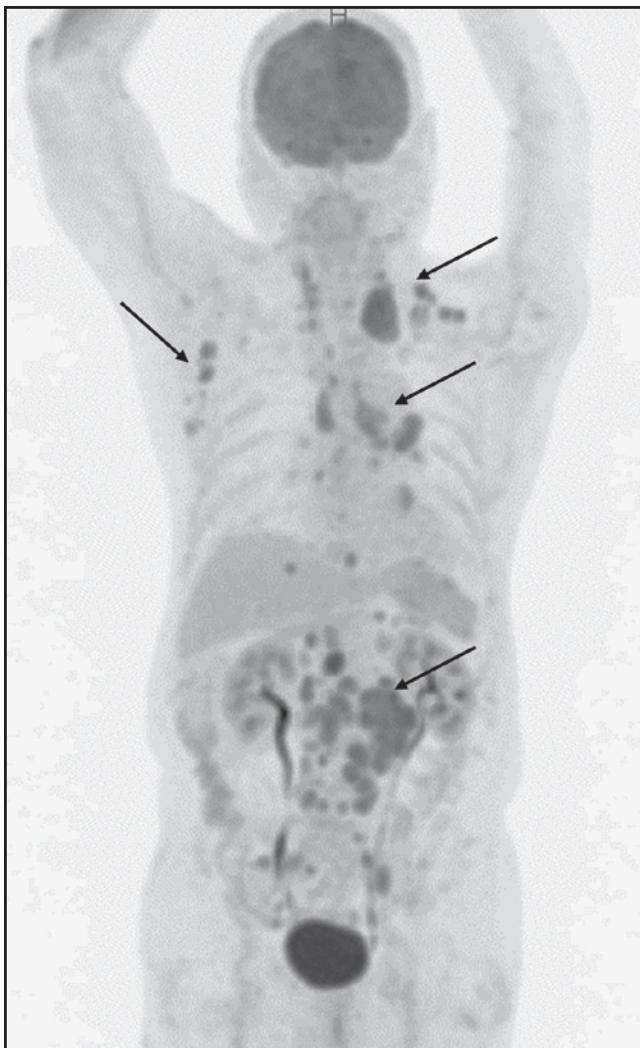
assay) all yielded negative results. Fluorodeoxyglucose positron emission tomography (FDG-PET) demonstrated abnormal uptake in the systemic lymph nodes (Figure 1). Malignant lymphoma or metastasis was highly suspected. Although FNA was performed, it was insufficient for a definitive diagnosis because there were few cells in the specimen. There was no direct indication of infarction. Therefore surgical biopsy of the lymph node in the neck was performed under local anesthesia, which revealed total lymph node infarction (Figure 2). No vasculitis, infection, or angioinvasion of tumor cells was observed. There was no evidence of malignancy; however, malignancy was suspected because of elevated lactate dehydrogenase and soluble interleukin-2 receptor levels, in addition to abnormal uptake on FDG-PET.

The patient preferred not to be treated with chemotherapy even if he had malignancy. However, if he had infection (the authors suspected tuberculosis or other infectious diseases), he would opt for treatment. Accordingly, needle biopsy instead of FNA was attempted. Histopathological examination of the specimen revealed mainly small lymphocytes, neutrophils, or eosinophils in the background,

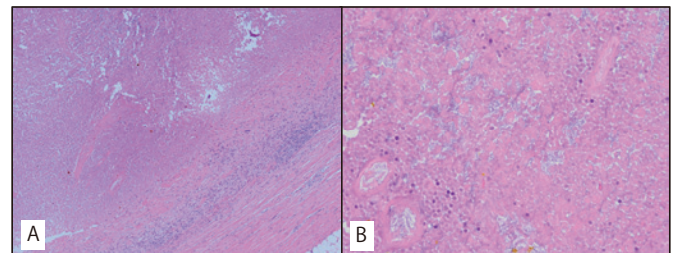
and atypical cells with large irregular nuclei or many scattered nuclei. These cells appeared to be lacunar cells and Reed-Sternberg cells, particularly known to be associated with Hodgkin lymphoma (Figure 3). On immunostaining, most of the lacunar cells and Reed-Sternberg cells were positive for CD30 and PAX5, and approximately one-half of these tumor cells were positive for CD15. These tumor cells were negative for CD3 and CD20. Large cells were positive by EBER-ISH. Small background cells were positive for CD3, but were not atypical in shape. Based on the above findings, this patient was diagnosed with nodular sclerosis classical Hodgkin lymphoma. As mentioned, he chose not to undergo chemotherapy and received only palliative care.

## DISCUSSION

Lymph node infarction is a rare pathology. A previous study reported one lymph node infarction in every 13,000 surgical biopsies.<sup>5</sup> Over a period of approximately 10 years, only 51 cases of lymph node infarction were encountered in six different histopathology departments in Switzerland, the

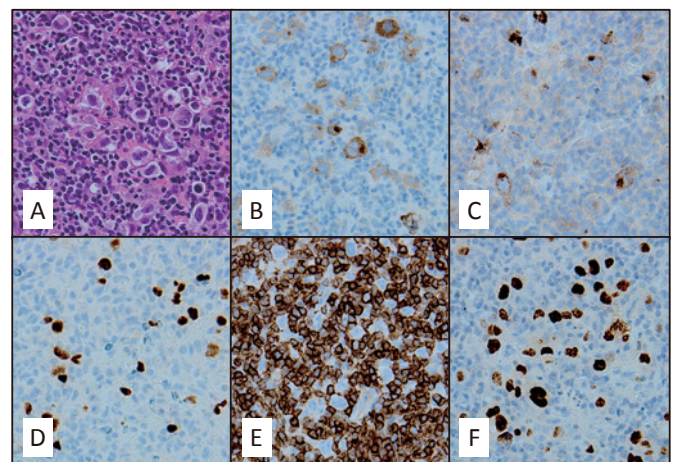


**Fig. 1.** Arrows in this figure indicate abnormal FDG-uptake in numerous swollen lymph nodes throughout the body.



**Fig. 2.** *A:* Hematoxylin and eosin (HE) staining, 4× objective *B:* HE staining, 20× objective.

A lymph node exhibiting completely coagulative necrosis, considered to be infarction, with fibrous capsule, but no granulomatous change. There was no straight needle track near the infarction. No findings suggesting vasculitis, infection, or angioinvasion of tumor cells were observed.



**Fig. 3.** *A:* HE staining *B:* CD30 staining *C:* CD15 staining *D:* PAX5 staining *E:* CD3 staining *F:* EBER in situ hybridization

A lymph node biopsy specimen containing lacunar and Reed-Sternberg cells, immunoreactive for CD30 and CD15, and positive by EBER-ISH, in a variety of inflammatory cells. The final diagnosis was classical Hodgkin lymphoma (20× objective).



United States, and England. In other reports, only 35 cases of lymph node infarction over a 20-year period were encountered at the Duke Medical Center (Durham, North Carolina, USA) and 11 cases over an eight-year period at Mount Sinai Hospital (New York, New York, USA).<sup>6,7</sup> Although the total number of biopsies performed at each hospital was not reported, lymph node infarction was rarely observed.

The etiology of lymph node infarction is diverse. It is categorized into two groups: neoplastic and non-neoplastic lesions. Neoplastic lesions are primarily associated with malignant lymphoma, especially non-Hodgkin lymphoma.<sup>2,6</sup> In bulky lesions, such as large mediastinal tumors, including lymphoma, partially infarcted lesions sometimes appear as low-density areas on computed tomography scans. However, total infarction of the superficial lymph nodes is uncommon. Lymph node infarction is often observed in diffuse large B-cell lymphoma, follicular lymphoma, and peripheral T-cell lymphoma.<sup>5,6,7,8</sup> In previous reports, lymph node infarction accompanied by Hodgkin lymphoma was rare.<sup>5,6,9</sup> Even in infarcted lymph nodes, L26 (anti-CD20 antibody) has been found to be of diagnostic value,<sup>7,8,10</sup> especially for diagnosis of B-cell lymphoma. In our case, L26 staining was negative in both the infarcted sample and in the sample that was used to diagnose Hodgkin lymphoma. Although CD30 staining was demonstrated to be useful for detecting Hodgkin/Reed-Sternberg (HRS) cells even in infarcted lesions,<sup>9</sup> CD30-positive large tumor cells, suggesting HRS cells in the infarcted sample, were not apparent. Interestingly, of 51 lymph node infarction cases, 14 were diagnosed as malignant lymphoma and the others appeared to be benign; however, six of these cases were confirmed to be malignant lymphoma in follow-up observations. Therefore, it is important that patients be followed for at least two years, even if a diagnosis of lymphoma is not initially made.<sup>5</sup> Other than malignant lymphoma, breast carcinoma, small-cell carcinoma, melanoma, pancreatic adenocarcinoma, seminoma, and squamous cell carcinoma have been reported to be causes of lymph node infarction.<sup>6</sup>

Trauma, vasculitis, infection, and inflammation also cause lymph node infarction presenting as non-neoplastic lesions.<sup>2</sup> FNA has been associated with the development of lymph node infarction by two possible causes: traumatic injury to blood or lymphatic vessels, or compression of blood vessels by internal hemorrhage following the procedure.<sup>3,4</sup> Tsang and Chan reported that among 3200 lymph node FNA procedures performed, 230 nodes had undergone subsequent excision, and of these, six exhibited infarctions, one-half of which were segmental and the others were total.<sup>3</sup> They concluded that these infarcted lymph nodes were caused by FNA. Although FNA is easy to perform and less invasive than other methods, it will not always lead to correct diagnosis in some cases, including those simply involving necrosis. In our case, we performed FNA first, suspecting metastasis of cancer to the lymph node because of our patient's long history of smoking. As a result of lymph node infarction, diagnosis took longer than expected.

There are, however, some limitations in our case. We

were unable to determine how the lymph node became infarcted. In the lymph node biopsy specimen, there was no evidence of changes caused by FNA. Furthermore, as there was no straight needle track near the infarction, classical Hodgkin lymphoma was presumed to be the cause of lymph node infarction, which is extremely rare. In the FNA sample, there were few cells, and it was speculated that the lymph node infarction was already present.

We report a very rare case of classical Hodgkin lymphoma with total lymph node infarction, which itself is an uncommon pathological finding. Although FNA is widely used for diagnosis, it is sometimes insufficient to diagnose lymphoma, which may later develop into lymph node infarction. Therefore, when total lymph node infarction is observed, internists should be aware of the importance of repeating the biopsy instead of repeating FNA to make a correct diagnosis if malignant lymphoma, including Hodgkin lymphoma, is suspected.

## CONFLICTS OF INTEREST

The authors declare no competing financial interests.

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