PRIMARY DIFFUSE LARGE B-CELL LYMPHOMA PRESENTING AS A CHEST WALL MASS: A CASE REPORT

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Chest wall lymphoma is a rare entity and often confused with the more common sarcoma. We report a case of diffuse large B-cell non-Hodgkin lymphoma patient presented with a sole chest wall mass. Chest computed tomography revealed an abnormal mass with well-defined borders below the pectoralis major muscle with contrast enhancement. The excisional biopsy revealed diffuse large B-cell non-Hodgkin lymphoma, confirmed by immunohistochemistry. The patient was then treated with six cycles of R-CHOP and achieved complete response. She is currently free from malignancy for 12 months after treatment. This paper illustrates the rarity of this entity, the need for distinguishing it from sarcoma, and briefly reviews its current management

Keywords: DLBCL, soft tissue lymphoma, chest wall lymphoma.

I. INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma.[1] About 30% of all cases present with extranodal sites involvement.[1] Of which, primary soft tissue lymphoma is rarely encountered clinically. Indeed, among 7,000 malignant lymphomas seen at Mayo Clinic over ten years, Travis et al. found only eight cases (0.11%) of stage IAE extranodal malignant lymphoma presented as a soft tissue mass.[2] Moreover, this rare disease is often misdiagnosed with the more common soft tissue sarcoma.[3,4] These two diagnoses differ in treatment and prognosis, requiring thorough evaluation. Here we report a case of chest wall lymphoma and emphasize the need for differential diagnosis between lymphoma and sarcoma, and review the literature of its current management.

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II. CASE PRESENTATION

A 59-year-old female with no significant past medical history presented at the outpatient clinic of Hanoi Medical University Hospital because of an abnormal right chest wall mass. This mass doubled in size for over two months according to her report. She was generally in good health and reported no constitutional symptoms such as fever, weight loss, or night sweats. Clinical examination of the right chest wall revealed a firm and immobile tumor about 70x110 millimeters in size, medially to the right axillary region. Palpation of the right axillary region showed no abnormal lymph nodes. The overlying skin was intact and showed no signs of inflammation. In addition, no abnormal peripheral lymph nodes were detected at other sites.

Chest computed tomography revealed an abnormal mass with well-defined borders below the pectoralis major muscle with contrast enhancement, and no abnormal lymph nodes detected (**Figure 1**).

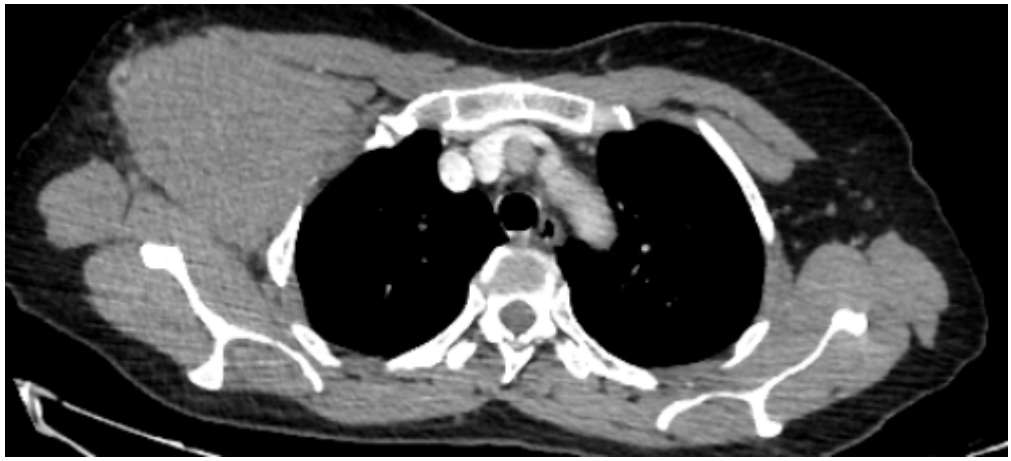

Figure 1. Soft tissue tumor at presentation

Core biopsy was then performed at the outpatient clinic, and its result was suggestive of lymphoma (**Figure 2A**). However, due to the rarity of soft tissue lymphoma, we decided to perform an excisional biopsy to obtain more specimens for a definitive conclusion. This second histopathological result was consistent with non-Hodgkin lymphoma, confirmed by immunohistochemistry with positive staining for CD20, Bcl6, MUM1, Bcl2, cMYC, Ki67 (95%), and negative staining for CD3, CD5, and CD10. (**Figure 2B&3**). These two results led to a final diagnosis of non-germinal center diffuse large B cell non-Hodgkin lyphoma.

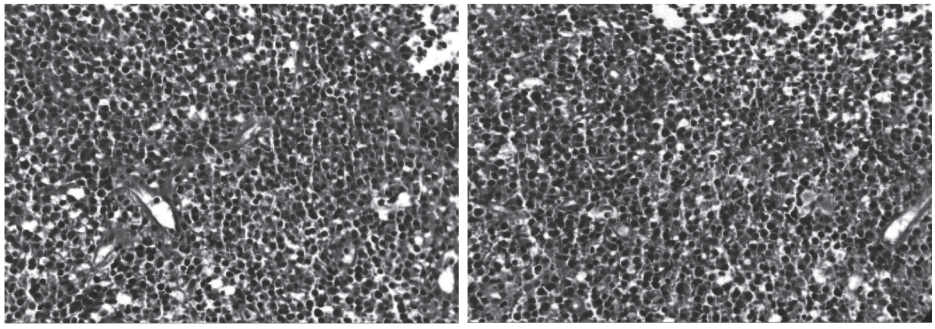

Figure 2. (A) Histopathological image of the tumor by core biopsy
(B) Histopathological image of the tumor by excisional biopsy

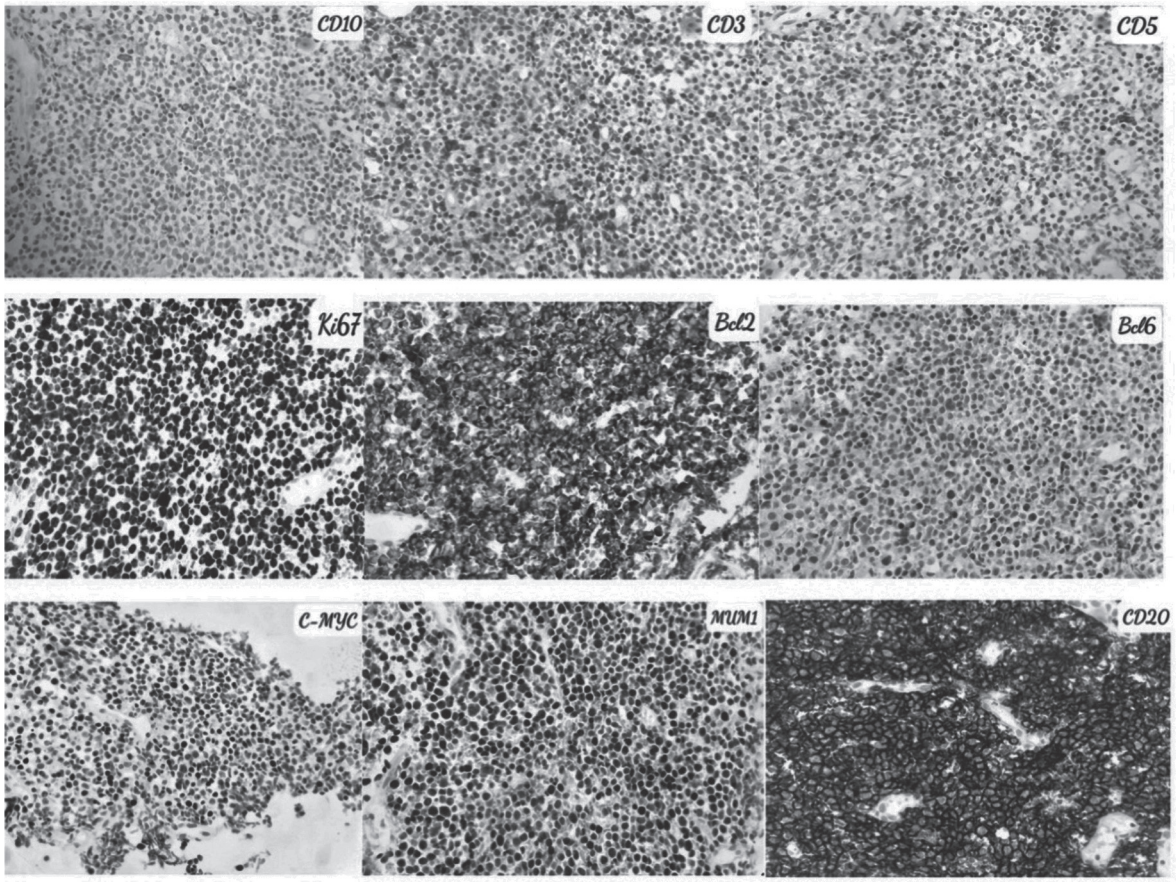

Figure 3. Immunohistochemistry results of chest wall tumor

Additional CT scan of the abdomen and pelvis and bone marrow biopsy was performed, showing no other malignancy signs. Thus, she was diagnosed as stage IAE, non-germinal center, diffuse large B-cell non-Hodgkin's lymphoma.

She was treated with six cycles of the R-CHOP regimen with curative intent. PET/CT was performed after chemotherapy and showed a complete response (**Figure 4**). Adjuvant radiotherapy was then indicated but the patient declined for fear of radiation-related toxicities. She is free from malignancy for 12 months after treatment.

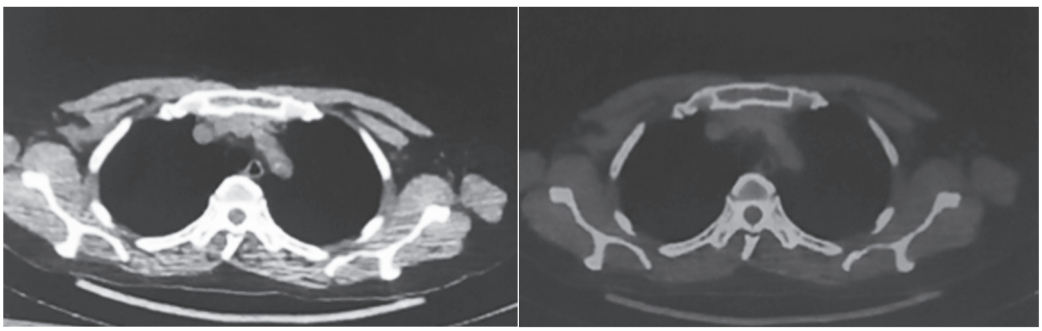

Figure 4. PET/CT scanning after treatment

III. DISCUSSION

Primary chest wall tumors arise from muscle, fat, blood vessel, nerve sheath, cartilage, or bone, the most common primary malignant tumors are sarcomas. The main treatment for this entity is complete resection with or without chest wall reconstruction.[3] In contrast, primary lymphoma of the chest wall is quite rare, and the cornerstone of treatment is chemotherapy. Specifically, the overall rate of soft tissue lymphoma is estimated to occur in 0.1% of all lymphomas.[4] The soft tissue is involved mainly by direct spreading from affected lymph nodes and/or metastatic hematogenous dissemination.[5] Indeed, in a case series of 356 lymphoma patients involving soft tissue, only 19 patients had no evidence of lymph node and skin involvement (5.3%).[6] Thus, our case with primary lymphoma presented with a solitary chest wall lesion is quite rare. This is the first case in Vietnam describing this rare entity to the best of our knowledge.

A biopsy of the tumor was the most critical evaluation of essential diagnosis. In this case, an initial clinical diagnosis of sarcoma was suggestive due to the characteristics of the tumor on imaging plus no abnormal lymph nodes and the frequency of this entity. However, surprisingly, the excisional biopsy results and IHC revealed a non-Hodgkin lymphoma. This would raise the awareness of thorough consideration before coming to a definitive diagnosis.

DLBCL is the most common type of B-cells non-Hodgkin lymphoma, constituting about 30-40% of all cases.[1] Most reported DLBCLs of the chest wall are pyothorax-associated lymphomas (PALs) - tumors that develop in the pleural cavity of patients after more than 20-year history of pyothorax resulting from an artificial pneumothorax for the treatment of pulmonary tuberculosis or tuberculous pleuritis.[7,8] They are also strongly associated with the latent form of the Epstein-Barr virus. Cytokines released at the site of chronic inflammation may trigger a local immunosuppressive environment.[7] Another reported mechanism is trauma to the thorax. Our patient had no history of chronic pyothorax or chest wall trauma, thus differentiating her case from other previous cases reported.

Concerning treatment options, the R-CHOP regimen is the current standard treatment for diffuse large B-cell lymphoma, CD 20 (+) in general, according to the NCCN guideline.[9] In a study of 16 soft tissue lymphoma patients, the response rate in 11 patients with DBLCL subtype after the first-line chemotherapy (CHOP, R-CHOP) was 66% (7 complete responses, 1 partial response). Overall survival and 5-year progression-free survivals were 43% and 39%, respectively.[4] Regarding the ideal number of chemotherapy cycles, a phase III, international, randomized trial (GOYA trial) has shown no added benefit in progression-free survival of eight versus six cycles of CHOP when combined with rituximab in previously untreated diffuse large B-cell lymphoma patients.[10] Furthermore, the incidence of grade 3-5 adverse events and any grade infections was markedly higher in participants receiving 8 cycles of CHOP versus 6 cycles.[10] Thus, the six cycles schedule has become the standard of care, replacing the eight cycles schedule. Our patient was treated with six cycles of the R-CHOP regimen and achieved a complete response. In general, lymphoma patients with bulky disease (tumor > 10 cm) like our patient would benefit from adjuvant radiation after achieving a complete response with chemotherapy. The results of an open-labeled trial of 258 bulky lymphoma patients showed that patients who received radiotherapy had significantly higher 5-year-progression-free survival (87%) than those who

did not (control group - 45%, $p < 0.001$).[11] In our case, we intended to give the patient adjuvant radiotherapy, but she refused it for fear of radiation-induced second cancers.

Given the rarity of this disease, it remains controversial whether patients with lymphoma located only in the chest wall should undergo surgical resection. Hsu *et al*. reported a series of three patients who had isolated chest-wall lymphoma treated with surgical resection and adjuvant chemotherapy. No recurrence or metastasis was noted during their follow-up period.[12] In another report of one Chinese woman with chest wall lymphoma involving the cartilages, complete resection followed by chemotherapy was performed. She remained disease-free for more than one year after treatment.[13] However, in all of these cases, patients were managed with chemotherapy after surgery. Thus, the role of additional surgery compared to standard chemotherapy alone remains uncertain, especially in the era of Rituximab, a highly effective monoclonal antibody targeting CD-20.

IV. CONCLUSION

Primary chest wall lymphoma is a rare disease, but it does happen. Physician should be aware of this diagnosis since it could be easily confused with the more common sarcoma. Open biopsy may be necessary to achieve adequate specimen for the histopathologic interpretation and immunohistochemical staining. R-CHOP regimen is preferred as first-line therapy with a high complete response rate. Further studies need to clarify the role of complete resection of the primary tumor with or without adjuvant chemotherapy.

CONSENT

The patient gave written informed consent to publish this manuscript and the accompanying images.

REFERENCE

1. Li S, Young KH, Medeiros LJ. Diffuse large B-cell lymphoma. *Pathology (Phila)*. 2018; 50(1): 74-87. doi:10.1016/j.pathol.2017.09.006.

2. Travis WD, Banks PM, Reiman HM. Primary extranodal soft tissue lymphoma of the extremities. *Am J Surg Pathol*. 1987; 11(5): 359-366. doi:10.1097/00000478-198705000-00004.

3. Bellini A, Ferrigno P, Comacchio GM, et al. Primary malignant chest wall tumors: surgical management and factors predicting survival. *Curr Chall Thorac Surg*. 2019; 1(0). doi: 10.21037/ccts.2019.11.08.

4. Derenzini E, Casadei B, Pellegrini C, Argnani L, Pileri S, Zinzani PL. Non-Hodgkin Lymphomas Presenting as Soft Tissue Masses: A Single Center Experience and Meta-Analysis of the Published Series. *Clin Lymphoma Myeloma Leuk*. 2013; 13(3): 258-265. doi:10.1016/j.clml.2012.10.003.

5. Lanham GR, Weiss SW, Enzinger FM. Malignant lymphoma. A study of 75 cases presenting in soft tissue. *Am J Surg Pathol*. 1989;13(1):1-10.

6. Salamao DR, Nascimento AG, Lloyd RV, Chen MG, Habermann TM, Strickler JG. Lymphoma in soft tissue: a clinicopathologic study of 19 cases. *Hum Pathol*. 1996; 27(3): 253-257. doi:10.1016/s0046-8177(96)90065-9

7. Aozasa K, Takakuwa T, Nakatsuka S ichi. Pyothorax-associated lymphoma: a lymphoma developing in chronic inflammation. *Adv Anat Pathol*. 2005; 12(6): 324-331. doi:10.1097/01.pap.0000194627.50878.02.

8. Nakatsuka SI, Yao M, Hoshida Y, Yamamoto S, Iuchi K, Aozasa K. Pyothorax-associated lymphoma: a review of 106 cases. *J Clin Oncol Off J Am Soc Clin Oncol*. 2002;20(20):4255-4260. doi:10.1200/JCO.2002.09.021.

9. Zelenetz, Andrew D., et al. NCCN Guidelines® Insights: B-Cell Lymphomas, Version 5.2021: Featured Updates to the NCCN Guidelines. *Journal of the National Comprehensive Cancer Network*. 2021; 19.11(2): 1218-1230.

10. Sehn, Laurie H., et al. No added benefit of eight versus six cycles of CHOP when combined with rituximab in previously untreated diffuse large B-cell lymphoma patients: results from the international phase III GOYA study. *Blood.* 2018; 132:783. doi: 10.1182/blood-2018-99-116845

11. Aviles, Agustin, et al. Role of radiotherapy in diffuse large B-cell lymphoma in advanced stages on complete response after administration of cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab. *Precision Radiation Oncology*. 2019; 3.3:100-104. doi: 10.1002/pro6.1071

12. Hsu PK, Hsu HS, Li AFY, et al. Non-Hodgkin's Lymphoma Presenting as a Large Chest Wall Mass. *Ann Thorac Surg*. 2006; 81(4): 1214-1218. doi:10.1016/j.athoracsur.2005.11.044

13. Qiu X, Liu Y, Qiao Y, et al. Primary diffuse large B-cell lymphoma of the chest wall: a case report. *World J Surg Oncol*. 2014; 12(1): 104. doi:10.1186/1477-7819-12-104