



# Random skin biopsy for diagnosis of intravascular large B-cell lymphoma in a patient with hypoxemia and normal lung imaging

Athiphat Banjongjit, MD,<sup>a</sup> Kanokphorn Chiratikarnwong, MD,<sup>a</sup> Pirun Saelue, MD,<sup>a</sup> Siripan Sangmala, MD,<sup>a</sup> Sauvarat Auepemkiate, MD,<sup>b</sup> and Kanita Kayasut, MD<sup>b</sup>  
Songkhla, Thailand

**Key words:** anemia; hypoxemia; intravascular large B-cell lymphoma; splenomegaly; thrombocytopenia.

Intravascular large B-cell lymphoma (IVLBCL) is a very rare type of non-Hodgkin lymphoma in which tumor cells proliferate within the lumina of small blood vessels, particularly within capillaries, causing clinical symptoms.<sup>1</sup> The clinical presentation of IVLBCL differs among geographic areas. For example, Asians more commonly present with fever, hepatosplenomegaly, thrombocytopenia, bone marrow involvement, and hemophagocytic syndrome and only rarely with central nervous system involvement or cutaneous lesions, which are more often seen in western populations.<sup>1,2</sup> IVLBCL presenting as hypoxemia with no abnormal findings on chest computed tomography is rare, and only a few cases have been reported in which the disease was diagnosed by pulmonary microvascular cytology, open lung biopsy, or random transbronchial lung biopsy.<sup>3-6</sup> There are a few reports suggesting the usefulness of the random or blind skin biopsy from normal-appearing skin for diagnosis of intravascular lymphoma.<sup>7,8</sup>

## CASE REPORT

A previously healthy 63-year-old woman presented to her local hospital with a 1-month history of dyspnea on exertion without coughing and anorexia. She had lost 10 kg of weight in 2 months. She reported no orthopnea or fever. During the next 2 weeks after presentation, her symptoms gradually worsened until she felt dyspnea with even minimal

### Abbreviation used:

IVLBCL: intravascular large B-cell lymphoma

activity, and an intermittent low-grade fever developed. Her body temperature was in the range of 38°C to 39°C. A complete blood count showed a white blood cell count of  $6.0 \times 10^3/\mu\text{L}$  with 73% neutrophils and 10% lymphocytes; hemoglobin level of 9.9 g/dL; platelet count of  $85 \times 10^3/\mu\text{L}$ ; direct Coombs test 1+ and indirect Coombs test negative. A chest radiograph showed minimal left pleural effusion. Pneumonia and Evans syndrome were diagnosed. Ceftriaxone and dexamethasone were administered, but her symptoms did not improve, and she was referred to our hospital. On examination, her body temperature was 38°C, her oxygen saturation while breathing room air was 85%, which improved to 96% when she was given 10 L of oxygen by mask with reservoir bag. The breath sounds were clear and equal bilaterally. The abdomen was soft and liver span was 7 cm by percussion, with no splenic dullness. Skin lesions were not seen. A complete blood count showed a white blood cell count of  $5.9 \times 10^3/\mu\text{L}$  with 97% neutrophils and 1% lymphocytes; hemoglobin level of 8.3 g/dL; platelet count of  $17 \times 10^3/\mu\text{L}$ ; lactate dehydrogenase level of 1,576 U/L; and negative direct Coombs test. A chest radiograph was normal without the minimal left

From the Department of Internal Medicine, Faculty of Medicine<sup>a</sup> and the Department of Pathology,<sup>b</sup> Prince of Songkla University, Hat Yai.

Funding sources: None.

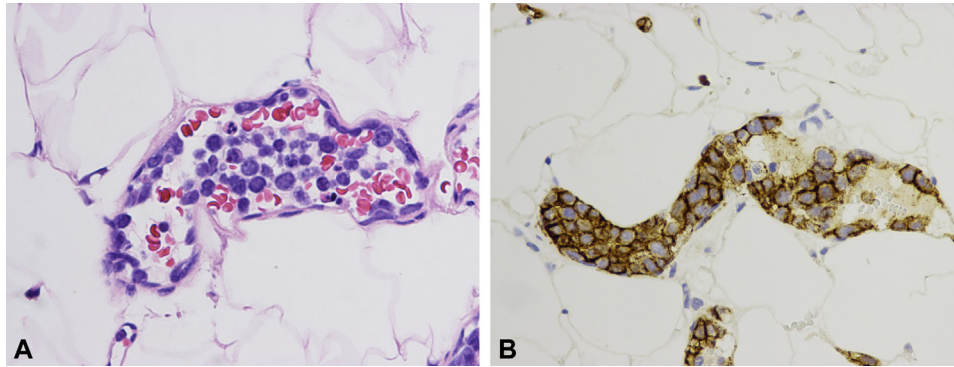
Conflicts of interest: None declared.

Correspondence to: Athiphat Banjongjit, MD, Department of Medicine, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand. E-mail: [athiphat\\_b@hotmail.com](mailto:athiphat_b@hotmail.com).

JAAD Case Reports 2018;4:149-51.  
2352-5126

© 2017 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jidcr.2017.11.013>



**Fig 1.** Punch biopsy results from the abdomen. **A**, Intravascular large lymphoid cells. **B**, CD20<sup>+</sup> tumor cells. (A, Hematoxylin-eosin stain; B, immunohistochemical stain.)

pleural effusion reported by the previous hospital. Computed tomography pulmonary angiography showed no pulmonary embolisms. A ventilation/perfusion scan was normal. High-resolution computed tomography of the chest was also done and showed only a nonspecific nodule at the apical segment of the right upper lobe and bilateral pleural effusion. A whole-abdomen computed tomography scan showed mild hepatomegaly without focal lesions, splenomegaly with multiple capsular base wedge-shaped hypodense parenchyma on venous phase, patent splenic artery and its branches with partial thrombosis of the splenic vein, and no enlarged nodes. Because she had a 2-week history of intermittent fever and 1-month history of progressive dyspnea without lung lesions on imaging (computed tomography pulmonary angiography, high-resolution computed tomography of the chest, ventilation/perfusion scan) that could explain the degree of hypoxemia, along with hepatosplenomegaly, splenic infarction, anemia and thrombocytopenia with high lactate dehydrogenase, malignant lymphomas, including IVLBCL, were considered. A bone marrow biopsy result was normal. According to a previous study,<sup>7</sup> a random skin biopsy performed on an arm, forearm, abdomen, or thigh can be a useful diagnostic tool in patients suspected of IVBCL. We performed random skin biopsies at 2 sites, the abdomen and left thigh, and immunohistochemical stains were done. The specimen from the abdomen showed intravascular large atypical lymphoid cells (CD20<sup>+</sup>, CD3<sup>-</sup>) infiltrating the deep dermis and subcutaneous tissue (Fig 1), which were also seen but less clearly in the specimen from the left thigh. IVLBCL was diagnosed. Chemotherapy was prescribed, but before it began she had severe *Klebsiella pneumoniae* sepsis with multiple organ failure and died.

## DISCUSSION

IVLBCL is a challenging diagnosis. Patients commonly present with fever of unknown origin and are investigated extensively before a diagnosis can be made, and more than half of IVLBCL cases are not diagnosed until autopsy.<sup>7</sup> Cutaneous lesions have been described in 39% of patients with IVLBCL and are most often found on the thighs (41%), followed by the legs (35%), trunk (31%), arms (15%), and buttocks (7.5%). The most common skin manifestations of IVLBCL are irregularly shaped subcutaneous nodules and indurated plaques of variable size.<sup>9</sup> Most Asian patients have no cutaneous lesions.<sup>10</sup> Even if no skin lesions are present, a random skin biopsy is a useful tool for the diagnosis of IVLBCL because it can detect tumor cells within intradermal and subcutaneous vessels. Herein, we present a case of IVLBCL that presented with hypoxemia without obvious lung lesions. To date, only a few such cases have been reported in which the patients presented with fever and hypoxemia with normal lung imaging, with IVLBCL eventually diagnosed by pulmonary microvascular cytology, open lung biopsy, or random transbronchial lung biopsy.<sup>3-6</sup> In our case, we used random skin biopsies to diagnose IVLBCL. A bone marrow biopsy was normal despite anemia and thrombocytopenia.

If IVLBCL is considered a possible diagnosis in a patient with hypoxemia, a random skin biopsy can be useful in facilitating early diagnosis and therapy. It is a less invasive procedure than a lung biopsy and can also detect tumor cells.

We thank David Patterson, an English teacher and editor with the Office of International Relations of the Faculty of Medicine, Prince of Songkla University, for help with preparation of this manuscript.

**REFERENCES**

1. Liu C, Lai N, Zhou Y, et al. Intravascular large B-cell lymphoma confirmed by lung biopsy. *Int J Clin Exp Pathol.* 2014;7:6301-6306.
2. Orwat DE, Batalis NI. Intravascular large B-cell lymphoma. *Arch Pathol Lab Med.* 2012;136:333-338.
3. Demirer T, Dail DH, Aboulafia DM. Four varied cases of intravascular lymphomatosis and a literature review. *Cancer.* 1994;73:1738-1745.
4. Martusewicz-Boros M, Wiatr E, Radzikowska E, et al. Pulmonary intravascular large B-cell lymphoma as a cause of severe hypoxemia. *J Clin Oncol.* 2007;25:2137-2139.
5. Yamakawa H, Yoshida M, Yabe M, et al. Useful strategy of pulmonary microvascular cytology in the early diagnosis of intravascular large B-cell lymphoma in a patient with hypoxemia: a case report and literature review. *Intern Med.* 2015;54:1403-1406.
6. Kaku N, Seki M, Doi S, et al. A case of intravascular large B-cell lymphoma (IVLBCL) with no abnormal findings on chest computed tomography diagnosed by random transbronchial lung biopsy. *Intern Med.* 2010;49:2697-2701.
7. Pongpudpunth M, Rattanakaemakorn P, Fleischer AB. Usefulness of random skin biopsy as a diagnostic tool of intravascular lymphoma presenting with fever of unknown origin. *Am J Dermatopathol.* 2015;37:686-690.
8. Asada N, Odawara J, Kimura SI, et al. Use of random skin biopsy for diagnosis of intravascular lymphoma. *Mayo Clin Proc.* 2007;82:1525-1527.
9. Pongpairoj K, Rerknimitr P, Wititsuwannakul J. Eruptive telangiectasia in a patient with fever and haemophagocytic syndrome. *Clin Exp Dermatol.* 2016;41:696-698.
10. Sitthinamsuwan P, Chinthammitr Y, Pattanaprichakul P, et al. Random skin biopsy in the diagnosis of intravascular lymphoma. *J Cutan Pathol.* 2017;44:729-733.