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From cytology to histology: diagnosis of a relapsed mediastinal lymphoma by endobronchial ultrasound transbronchial histological needle

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Abstract

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is highly accurate in diagnosing mediastinal lymphadenopathies of lung cancer and benign disorders, with the advantage that it is a minimally invasive technique, unlike open surgery and mediastinoscopy. However, the diagnostic accuracy of EBUS-TBNA for the diagnosis of lymphoma in patients with mediastinal lymphadenopathy is not well defined. The lack of tissue architecture obtained by cytological needles decreases the diagnostic accuracy for diagnosis and subtyping of de novo and relapsed mediastinal lymphomas. We present the first described case in the literature of an anaplastic large cell lymphoma relapsed, diagnosed on tissue fragments obtained by EBUS-TBNA with the particularity of using a histological needle.

Introduction

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a safe minimally invasive diagnostic modality with a high yield for the diagnosis of mediastinal and/or hilar adenopathy as well as for lesions adjacent to the airways [1]. Few studies have examined the effectiveness of EBUS-TBNA in evaluating patients with current or previously diagnosed lymphoma, but in the majority of these cases, the lack of a histologic sample makes it difficult to obtain a diagnosis. We present the first described case in the literature of an anaplastic large cell lymphoma relapsed, diagnosed on tissue fragments obtained by EBUS-TBNA with the particularity of using a histological needle.

Case Report

A 73-year-old woman was referred to our hospital in November 2011 because of a right mandibular and submaxillary swelling. Submaxilectomy and cervical adenectomy were performed. The biopsy revealed an anaplastic large cell lymphoma. After six cycles of cyclophosphamide, hydroxyl-doxorubicin, oncovin, and prednisone therapy, complete remission was accomplished on April 2012. The patient remained on *follow-up* visits twice a year in the Hematology service. In December 2014, a whole body computed tomography (CT) scan was performed. The CT scan showed a right lower paratracheal lymph node (4R) of 17 mm in diameter with no other findings of interest (Fig. 1A). The patient did not show symptoms at this

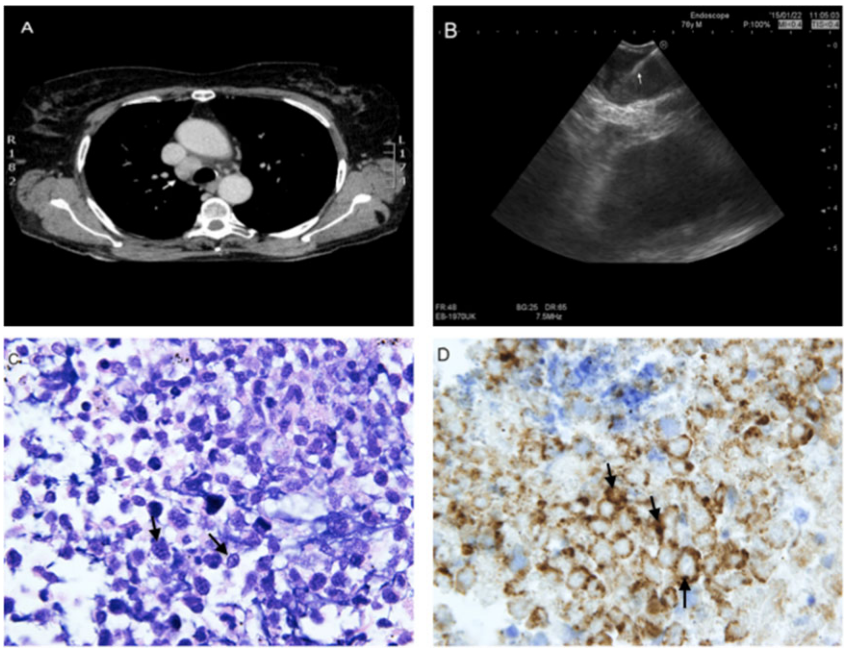

Figure 1. (A) A chest computed tomography showing an enlarged lower paratracheal lymphadenopathy. (B) Endobronchial ultrasound-guided transbronchial needle aspiration of the lower paratracheal lymph node (Station 4R; white arrow points to the sampling needle inside the lower paratracheal lymph node). (C) Large lymphocytes with atypia showing hyperchromatic nuclei with an irregular shape (black arrows pointing large lymphocytes with hyperchromatic nuclei). Mitosis and apoptosis were present (Cell Block, H/E X 1000). (D) Vast majority of atypical lymphocytes with CD30-positive cells (black arrow pointing CD30-positive cell) (Peroxidase ×1000).

time. In addition, no abnormal findings were seen in laboratory examinations including complete blood count and biochemistry.

In January 2015, EBUS-TBNA was performed. Conventional flexible bronchoscopy was first conducted to examine the tracheobronchial tree. Thereafter, EBUS was performed at 7.5 MHz (EBUS, EB-1970UK, Linear-Array; Pentax Medical, Akishima-shi, Tokyo, Japan) and a dedicated ultrasound scanner (HI VISION Avius, Hitachi Medical, Tokyo, Japan) was used for image processing. The EBUS-TBNA procedure was performed using the new 22-gauge histological needle (EchoTip ProCore; Cook Medical, Bloomington, IN, USA) (Fig. 2B). The lymph node was localized at 4R station (Fig. 1B) and also recorded using color Doppler imaging (Fig. 1C). A minimum of three passes were performed (Figs. 1D and 2A); the initial aspirated material was placed on glass slides and air-dried, alcohol-fixed smears were prepared, and the remaining material was placed in a formalin solution to prepare a cell block for histological evaluation and immunohistochemistry. From this material, there were tissue fragments (Fig. 2C) on which the pathologist was able to perform histological analysis and immunohistochemical tests clearly confirming relapsed anaplastic large cell lymphoma (CD30+). Flow cytometric analysis also showed tumor cells strongly positive for CD30. After the diagnosis was made, the patient initiated chemotherapy treatment.

Discussion

In recent years, EBUS-TBNA, which is a minimally invasive technique, has become an increasingly used diagnostic aid in the differentiation of mediastinal lymphadenopathy. However, the lack of tissue architecture obtained by cytological fine needle aspiration (FNA) samples decreases the diagnostic accuracy for diagnosis and subtyping of de novo and relapsed mediastinal lymphomas. In the case of mediastinal lymphadenopathy and a suspicion of lymphoma, a surgical biopsy is the preferred diagnostic approach, however, mediastinoscopy is a more invasive procedure with more associated complications when directed compared with endoscopic ultrasound techniques [2]. Several authors have emphasized the use of low-volume tissue samples by EBUS-TBNA. The role of EBUS-TBNA in a lymphoma diagnosis is, therefore, of uncertain value in cases of marginal zone and follicular lymphoma [3].

Prior 2007, there were no studies regarding EBUS-TBNA in patients with mediastinal adenopathy secondary to lymphoma. Kennedy et al. retrospectively reviewed their clinical experience examining the clinical use of EBUS-TBNA in patients with mediastinal lymphadenopathy secondary to suspected lymphoma [4]. In their report, they presented 25 patients in whom lymphoma was suspected based on prior history or clinical presentation. They obtained adequate

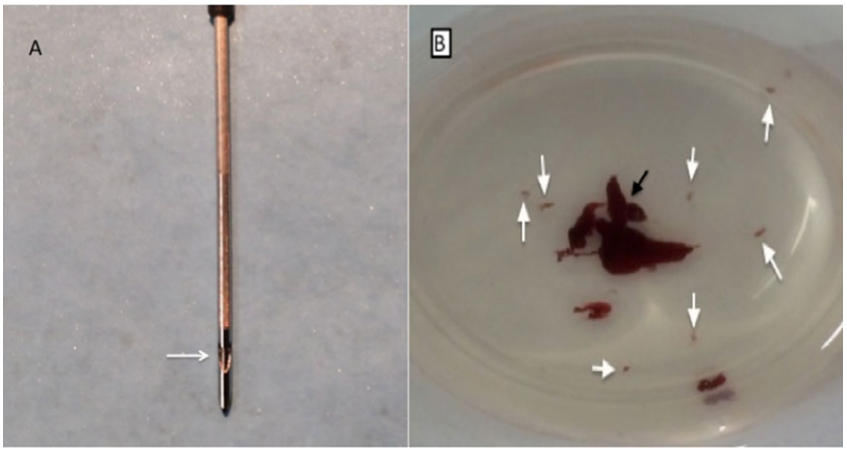

Figure 2. (A) EchoTip ProCore-Cook Medical, 22-EBUS-P-C (white arrow points the lateral shaft where the histological sample is obtained). (B) Tissue samples obtained from the histological needle (white arrows); black arrow points to a large blood clot also obtained from the sample.

lymph node tissue samples in 24 patients and identified lymphoma in 10 patients and benign disease in 14 patients. The sensitivity, specificity, positive predictive value, and negative predictive value were 90%, 100%, 100%, and 92.6%, respectively. Although their work suggested the potential of EBUS-TBNA in the diagnosis process of lymphoma, the role of EBUS-TBNA has not yet been well defined because of the limitation of sample yield.

The recently developed 22-gauge EBUS-TBNA ProCore histological needle may overcome limitations in comparison with the use of cytological needles in the diagnosis of lymphoma, especially in relapsed mediastinal lymphoma as seen in our case. Regarding EBUS-TBNA in the assessment of patients with relapsed lymphoma, it is recognized that repeat mediastinoscopy or mediastinoscopy after mediastinal radiotherapy is associated with reduced sensitivity and increased rate of major complications, thus EBUS-TBNA offers a safer and effective alternative to the more invasive mediastinoscopy.

The 22-gauge histological ProCore needle is currently available for real-time EBUS-TBNA and it is plausible that this additional histological sampling could improve the yield and sensitivity of EBUS-TBNA in patients with lymphoma. The specific needle sizes/types used in performing endoscopic ultrasound (EUS)-FNA vary [5]. The High Definition ProCore is a 22-gauge beveled needle allowing for core biopsy along with aspiration material. Witt et al. compared this needle with a standard 22-gauge needle. They reported that the beveled EUS needle affords similar cytologic interpretability, adequacy, diagnostic accuracy, and amount of cell block material as a standard needle. There was a statistically significant trend toward fewer passes to achieve adequacy with the beveled EUS-FNA needle. In this study, they concluded that the EUS-FNA needle with a lateral bevel is a diagnostically similar alternative to standard endoscopy needles, the possibility that this beveled needle may improve per pass adequacy requires further verification [5].

Remediastinoscopy is considered to be a difficult procedure because of peritracheal adhesions and fibrotic changes after induction chemotherapy and radiotherapy; because of this feature, most thoracic surgeons consider this technique unsafe. We consider that after chemotherapy or radiotherapy, given the risk of fibrosis or necrosis, EBUS should be preferred for evaluating the recurrence of lymphoma, especially now that we finally can obtain histological samples. There is also a 25-gauge histological ProCore needle available; in our case, we decided to select the 22-gauge needle in an attempt to obtain a larger histological sample.

Although more experience is needed, histological samples obtained by EBUS-TBNA could play a major role in the diagnosis of lymphomas and their relapses.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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