

# Starry sky sign: A prevalent sonographic finding in mediastinal tuberculous lymph nodes

Ibrahim Onur Alici, Nilgün Yılmaz Demirci<sup>1</sup>, Aydın Yılmaz<sup>2</sup>, Jale Karakaya<sup>3</sup>, Yurdanur Erdoğan<sup>2</sup>

Chest Physician, Lung Transplantation Center, Türkiye Yüksek İhtisas Training and Research Hospital, <sup>1</sup>Chest Physician, Department of Pulmonology, Gazi University, Ankara, <sup>2</sup>Associate Professor for Pulmonology, Department of Pulmonology, Atatürk Chest Diseases and Thoracic Surgery Education and Research Hospital, Ankara, <sup>3</sup>Doctor of Philosophy, Department of Biostatistics, Hacettepe University, Ankara, Turkey

## ABSTRACT

**Background and Objectives:** We report a prevalent finding in tuberculous lymphadenitis (TL): Starry sky sign, hyperechoic foci without acoustic shadows over a hypoechoic background. **Materials and Methods:** We retrospectively searched the database for a possible relationship of starry sky sign with a specific diagnosis and also the prevalence and accuracy of the finding. **Results:** Starry sky sign was found in 16 of 31 tuberculous lymph nodes, while none of other lymph nodes (1,015 lymph nodes) exhibited this finding; giving a sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of 51.6%, 100%, 100%, 98.5%, and 98.5%, respectively. **Conclusion:** Bacteriologic and histologic findings are gold standard in the diagnosis of tuberculosis, but this finding may guide the bronchoscopist in choosing the more pathologic node within a station and increase the diagnostic yield as it may relate to actively dividing mycobacteria.

**Key words:** Endobronchial ultrasound, mediastinum, tuberculosis

## INTRODUCTION

Mediastinal lymph nodes are frequently involved in a number of diseases. Of these diseases, tuberculosis is one of the prevalent diseases in our country, despite aggressive control programs. In our institution, we perform endobronchial ultrasound (EBUS) in patients with mediastinal lymph node enlargement. During the procedures, we noticed an interesting finding in very limited number of the lymph nodes: Multiple hyperechoic foci without an acoustic shadow over a hypoechoic background which will be called as “starry sky sign” [Figure 1]. Thus, we searched the entire

database in order to find out the relationship of the sign with a specific diagnosis and also, the prevalence and the relevance of the finding.

## MATERIALS AND METHODS

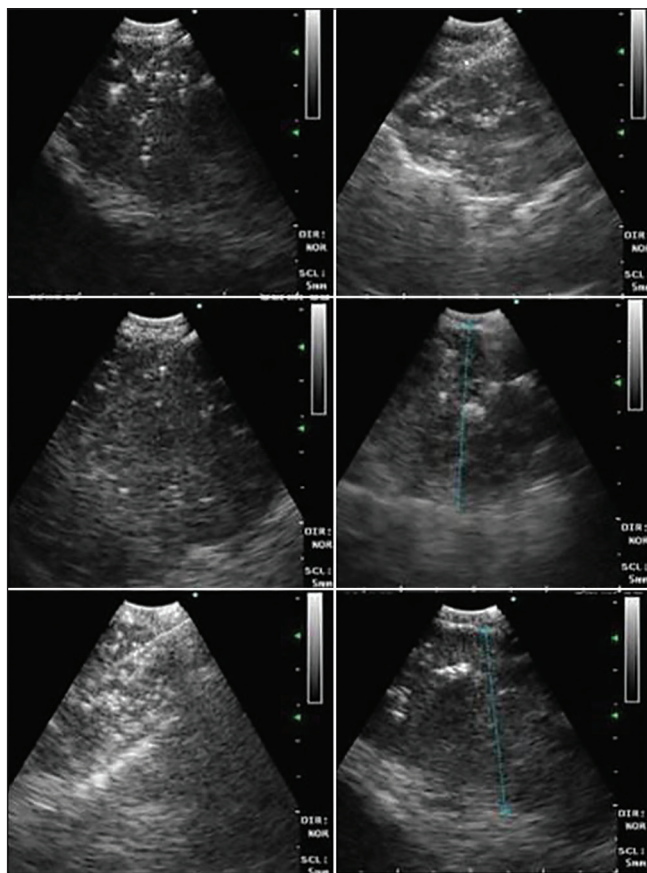
We performed a retrospective analysis of patients who underwent EBUS for the diagnosis of mediastinal lymph nodes detected on computed tomography and specifically the patients who have diagnosed as tuberculous lymphadenitis (TL) with radiological, bacteriological, cytological, or surgical work up. The study was done at a single institution between May 2010 and October 2011. Technical procedures and materials were given elsewhere.<sup>[1]</sup> All images and available video files were retrospectively reviewed by three authors (IOA, NYD, and AY) who came to a consensus, and they were blinded to the results of EBUS-transbronchial needle aspirations (EBUS-TBNA). This analysis was approved by the Ethical Committee

Access this article online	
Quick Response Code: 	Website: <a href="http://www.eusjournal.com">www.eusjournal.com</a>
	DOI: 10.4103/2303-9027.163004

## Address for correspondence

Dr. Ibrahim Onur Alici, E-mail: [ioalici@hotmail.com](mailto:ioalici@hotmail.com)

Received: 2014-09-30; Accepted: 2015-01-18



**Figure 1.** Some examples of sonographic appearances of tuberculous lymph nodes. Note the “starry sky sign”, hyperechoic foci without acoustic shadowing over a hypoechoic background in the lymph nodes

of Atatürk Chest Diseases and Thoracic Surgery Education and Research Hospital (190712/03d).

## RESULTS

In total, we performed EBUS-TBNA in 451 patients with various indications and of which, 13 patients were TL, giving a prevalence of 2.8% in this selected population. A total of 31 lymph nodes were evaluated in the cases with TL (2.38 lymph nodes per patient). The mean age was  $41 \pm 19$  years. Fifty-three percent of the patients (7/13) were male. The mean short axis length of the nodes was  $17.92 \pm 7.42$  mm. On average, we did 3.1 aspirations per lymph node to prepare smears and cell blocks. The mean time of the procedures was  $18.3 \pm 6.1$  min. The presence of the starry sky sign was evaluated in 1,015 lymph nodes of various etiologies other than TL. Of which, 195 lymph nodes were affected by sarcoidosis, 313 lymph nodes with malignancy, and 507 lymph nodes with other etiologies like normal lymph nodes, anthracosis, lymphoma, etc.

Starry sky sign was found in 16 of 31 (51.6%) tuberculous lymph nodes (those 16 lymph nodes were sampled from 7/13 patients with TL), while none of the remaining 1,015 nodes exhibited this finding. Thus, we reached a sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of 51.6%, 100%, 100%, 98.5%, and 98.5% for tuberculosis, respectively.

## DISCUSSION

Not surprisingly, with its capabilities, EBUS can play a role in the diagnosis of intrathoracic lymphadenopathy. Apart from malignancies, granulomatous diseases are one of the main indications for EBUS. There are many reliable data about the diagnostic yield of EBUS in tuberculosis. Navani *et al.*, studied the utility of EBUS-TBNA in patients with tuberculous intrathoracic lymphadenopathies and found that EBUS-TBNA was diagnostic of TB in 146 of 156 patients (94%, 95% confidence interval (CI) 88-97%).<sup>[2]</sup> In another retrospective analysis, Hassan *et al.*, reported the accuracy, sensitivity, specificity, PPV, and NPV of EBUS-TBNA in 19 patients with intrathoracic isolated lymphadenopathy related to tuberculosis (in 24 patients suspected of tuberculosis) as 79%, 95%, 100%, 100%, and 80%, respectively.<sup>[3]</sup>

The value of ultrasound in tuberculous lymphadenopathy is commonly studied in cervical lymph nodes. Khanna *et al.*, investigated the usefulness of sonography in differentiating cervical lymphadenopathy related to tuberculosis, lymphoma, and metastases.<sup>[4]</sup> They found that the ultrasonographic features of tuberculous lymph nodes were multiplicity, a fusion tendency of adjacent nodes, and a hypoechoic center with posterior enhancement. Additionally, they highlighted a common finding, strong internal echoes, which resembled calcification, in 52 of 62 patients (84%). Gupta *et al.*, reported the value of imaging modalities (USG and CT) in 27 patients with tuberculous cervical lymphadenopathy. Sonography revealed hypoechoic (100%) and necrotic (100%) lymph nodes and other features, including sharp margins (70.4%), hilum (22.2%), abnormal surrounding tissue (85.2%), matting (37%), calcification (29.6%) and posterior enhancement (22.2%).<sup>[5]</sup> Haber *et al.*, investigated sonographic findings in children with cervical lymph nodes related to atypical mycobacteria. In this study, the authors stated that sonography revealed ovoid lymph nodes with distinct margins

showing strong echoes in four of 12 patients (33%).<sup>[6]</sup> There have also been studies on abdominal tuberculosis. In one study on imaging features, Pereira *et al.*, stated that lymph nodes form discrete or matted conglomerated masses, showing central hypoechoic areas.<sup>[7]</sup> In another study, Malik and Saxena reported that of 37 patients with TL, most were hypoechoic, five (13.5%) had a hypoechoic central region and peripherally located echogenic regions, and two (5%) showed calcification.<sup>[8]</sup>

With the introduction of old imaging modalities into new areas, researchers continue to provide reasonable answers to many questions. We used to know the appearance of tuberculous lymph nodes on CT images, with low resolution and little information. In a recent study from Germany, Fritscher-Ravens *et al.*, investigated the utility of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) in differentiating tuberculosis from sarcoidosis. They enrolled 72 patients with mediastinal lymphadenopathy; including 30 cases of sarcoidosis and 28 cases of tuberculosis (other cases included malignancy, abscess, and benign lymph nodes). They found that tuberculous lymph nodes were smaller than sarcoid nodes. Tuberculosis-related nodes were isoechoic to moderately hypoechoic and nonhomogeneous, and some showed hyperechoic areas without acoustic shadowing (nine of 28 patients, 32.1%). Seven of them (25.0%) exhibited acoustic shadows representing inactive calcified foci.<sup>[9]</sup> The most recent study have been reported by Dhooria *et al.*<sup>[10]</sup> They analyzed 165 patients (118 sarcoidosis and 47 tuberculosis) and 358 lymph node stations (270 sarcoidosis and 88 tuberculosis). Shape, margin, and presence of central hilar structure did not differ between groups; but in contrast, tuberculous lymph nodes were significantly more heterogeneous and exhibited coagulation necrosis sign. In multivariate analysis, heterogeneous echotexture and positive tuberculin skin test were the only independent predictors for the diagnosis of tuberculosis.

Finally, in a relevant study, Rana *et al.*, reported a series of 42 patients with enlarged mediastinal lymphadenopathies, of whom 22 had tubercular lymph nodes. Hyperechoic foci in the lymph nodes were detected in 77.2% of the tubercular mediastinal lymphadenopathies and 5% of the patients with nontubercular lymphadenopathy ( $P = 0.00$ ).<sup>[11]</sup> In our series, a “starry sky sign”, which may represent granulomatous foci within the lymph nodes was detected in 51.6% of the patients with TL. This result was less

than other studies, but there was confusion regarding acoustic shadows. We have only included images without shadows to differentiate them from calcification. Additionally, we highlight the high accuracy of this finding (none of the sarcoid, malignant, or normal lymph nodes showed this finding). Seven patients showed the finding and six of them were culture positive for *Mycobacterium tuberculosis*. So this may show the correlation of the finding with high bacillus load within the node.

Main strength of this paper is giving a very prevalent and relatively specific finding, starry sky sign, in tuberculous lymph nodes. This is, in particular, a very important finding as it does not present in any other diseases (like malignancy) in the study population, but remains suspicious until will be correlated in the future studies. There are certain limitations in the study. First, it is a retrospective analysis. Secondly, some investigators have performed the procedures and later, visual evaluations. Many other studies were conducted in the same manner, but actually this is not a great weakness as the data were evaluated blinded to the diagnoses.

Some other studies have reported the sonographic features as a diagnostic tool, but we still believe that these features may only guide the bronchoscopist in choosing more pathologic node in a particular station as they are usually exhibited in malignant disease. Microbiological and histological findings are the gold standard for the diagnosis of tuberculosis. This finding, of course, does not offer any diagnostic value, but may give additional information for choosing an affected lymph node. Choosing the more pathologic node within the same station may spare time and increase diagnostic yield. The starry sky sign should be investigated in other databases including various diseases and the true prevalence should be documented.

## ACKNOWLEDGMENTS

Ibrahim Onur ALICI is the guarantor of the content of this manuscript. Ibrahim Onur Alici, Nilgün Yılmaz Demirci, and Aydın Yılmaz together made EBUS interventions, involved in data collection, review of the EBUS images, and wrote the manuscript. Jale Karakaya made statistical analyses and Yurdanur Erdoğan participated in the data collection, clinical judgments, and writing of the manuscript. The work was done in Atatürk Chest Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey. There are no conflicts of interest and authors did not use any kind of funding and there are no other contributors.

## REFERENCES

1. Alici IO, Demirci NY, Yilmaz A, *et al.* The combination of cytological smears and cell blocks on endobronchial ultrasound-guided transbronchial needle aspirates allows a higher diagnostic yield. *Virchows Arch* 2013;462:323-7.
2. Navani N, Molyneaux PL, Breen RA, *et al.* Utility of endobronchial ultrasound-guided transbronchial needle aspiration in patients with tuberculous intrathoracic lymphadenopathy: A multicentre study. *Thorax* 2011;66:889-93.
3. Hassan T, McLaughlin AM, O'Connell F, *et al.* EBUS-TBNA performs well in the diagnosis of isolated thoracic tuberculous lymphadenopathy. *Am J Respir Crit Care Med* 2011;183:136-7.
4. Khanna R, Sharma AD, Khanna S, *et al.* Usefulness of ultrasonography for the evaluation of cervical lymphadenopathy. *World J Surg Oncol* 2011;9:29.
5. Gupta KB, Kumar A, Sen R, *et al.* Role of ultrasonography and computed tomography in complicated cases of tuberculous cervical lymphadenitis. *Indian J Tuberc* 2007;54:71-8.
6. Haber HP, Warmann SW, Fuchs J. Cervical atypical mycobacterial lymphadenitis in childhood: Findings on sonography. *Ultraschall Med* 2006;27:462-6.
7. Pereira JM, Madureira AJ, Vieira A, *et al.* Abdominal tuberculosis: Imaging features. *Eur J Radiol* 2005;55:173-80.
8. Malik A, Saxena NC. Ultrasound in abdominal tuberculosis. *Abdom Imaging* 2003;28:574-9.
9. Fritscher-Ravens A, Ghanbari A, Topalidis T, *et al.* Granulomatous mediastinal adenopathy: Can endoscopic ultrasound-guided fine-needle aspiration differentiate between tuberculosis and sarcoidosis? *Endoscopy* 2011;43:955-61.
10. Dhoria S, Agarwal R, Aggarwal AN, *et al.* Differentiating tuberculous from sarcoidosis by sonographic characteristics of lymph nodes on endobronchial ultrasonography: A study of 165 patients. *J Thorac Cardiovasc Surg* 2014;148:662-7.
11. Rana SS, Bhasin DK, Singh K. Letters to the editor. *Endoscopy* 2012;44:106-7.

**How to cite this article:** Alici IO, Demirci NY, Yilmaz A, Karakaya J, Erdogan Y. Starry sky sign: A prevalent sonographic finding in mediastinal tuberculous lymph nodes. *Endosc Ultrasound* 2015;4:225-8.

**Source of Support:** Nil. **Conflicts of Interest:** None declared.