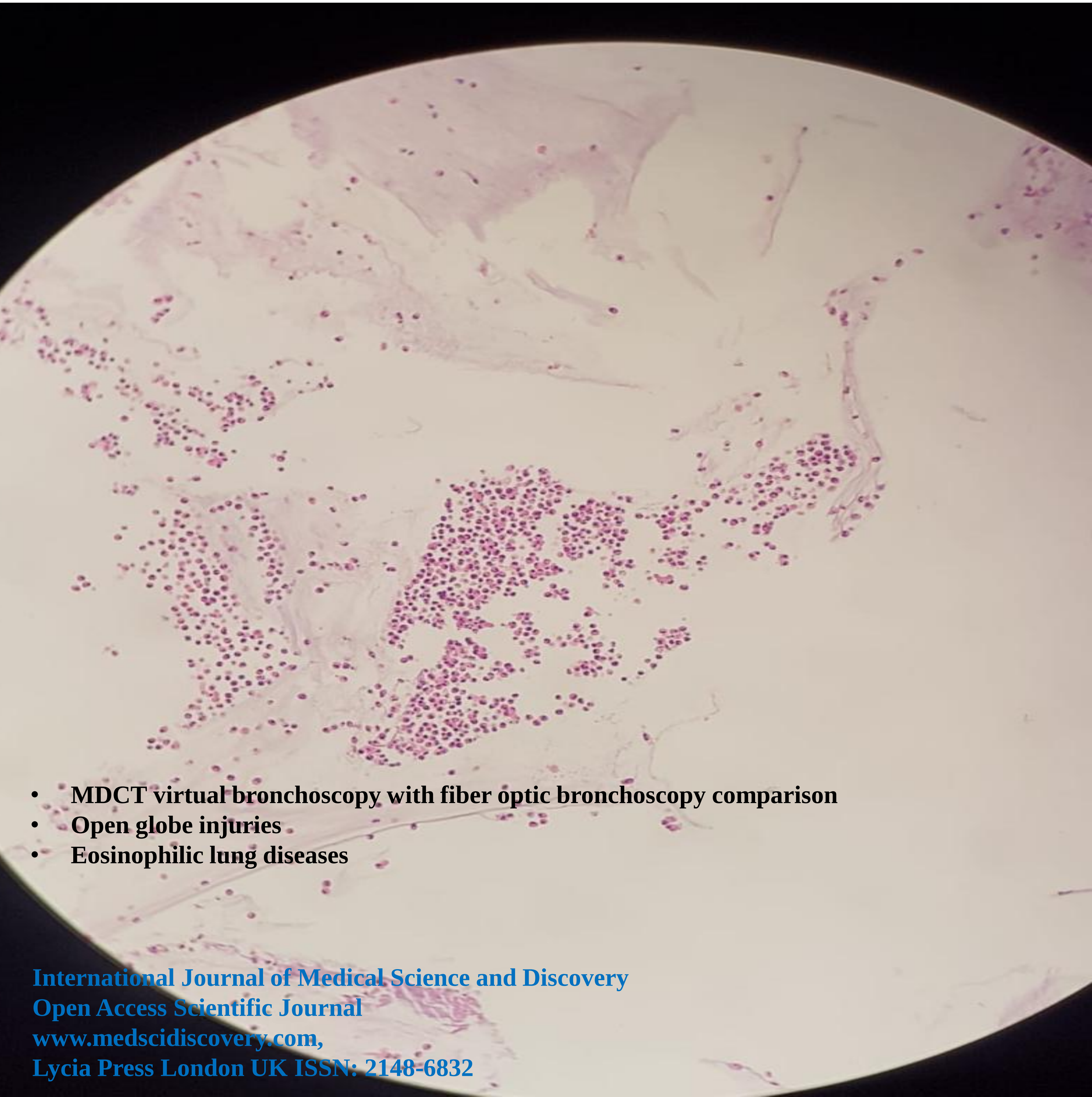
August 2019, Vol 6, No 8

MSD

Medical Science & Discovery



- MDCT virtual bronchoscopy with fiber optic bronchoscopy comparison
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ISSN: 2148-6832 (Print) E-ISSN: 2148-6832 (Online)

Category: Multi Disciplinary Health Science Journal

Abbreviated key title: Med. Sci. Discov.

Frequency: Monthly

Review System: Double Blind Peer Review

Circulation: Globally, Online, Printed

Article Processing Charge (APC): Free

Editor-in-Chief: Assoc. Prof. Dr. Dr. Ahmad Rajabzadeh, Anatomical Department of lorestan, University of Medical Sciences, Tabriz, Iran

Established: 30.04.2014

Web address: www.medscidiscovery.com; http://dergipark.ulakbim.gov.tr/msd

E-mail : editor [at] medscidiscovery.com

Phone : +44 020 3289 9294

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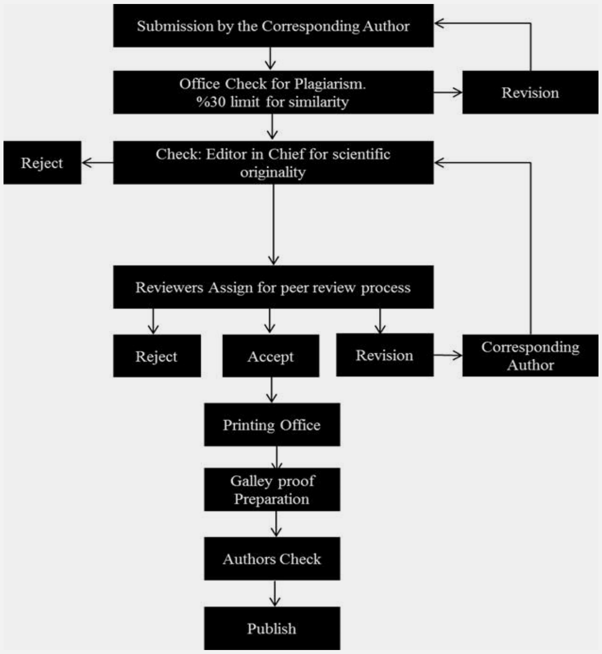

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Medical Science and Discovery, August 2019, Vol.6, No.8

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MSD

Medical Science and Discovery
2019; 6(8):136-44

Research Article Doi: 10.17546/msd.584332

In the evaluation of tracheobronchial lesions, MDCT virtual bronchoscopy with fiber optic bronchoscopy comparison

Zeyni Unverdi[1*], Resat Kervancioglu[2], Sena Unverdi[1], Mehmet Sait Menzilcioglu[2]

Abstract

Objective: The aim of this study is compare multislice CT VB and FOB to assess tracheobronchial lesions with multislace CT VB.

Material and Methods: In the period between September 2012 and August 2013 found indications for bronchoscopy and the total of 44 patients underwent FOB and FOB MDCT-SB were included in the study to be evaluated. All patients underwent VB and/or FOB. In both methods, tracheobronchial tree were divided into 18 separate segments. FOB virtual bronchoscopic findings as the gold standard method to assess the results were considered. Accordingly, positive and negative predictive values of MDCT for VB, sensitivity, selectivity and specificity values were calculated.

Results: Patient ages 1 and 79 (mean: 53 ± 16) of the patients ranged from 7 (16%) female and 37 (84%) were men. In FOB 16 narrowing, 9 congestion, four external compression, 11 mucosal abnormalities were found and in the VB 12 narrowing, 16 obstruction, 8 external compression detected. None of the 11 mucosal findings in the FOB could not be determined in VB. Patients detect in FOB 25 cases were detected in VB; two patients with lesions on the FOB, although not detected in the VB (false negative). In 14 cases both FOB and endoluminal lesion was detected in the VB. FOB lesions not seen in the VB lesion in 5 cases (false positive). According to these values, sensitivity 92%, specificity 73%, positive predictive value (PPV) of 82%, negative predictive value (NPV) 87%, Accuracy: 84%, respectively.

Conclusion: Both mucosal biopsies should not be made to give details because of disadvantages such as virtual bronchoscopy fob is not an alternative for the moment. However tracheobronchial tumor research, interventional bronchoscopic procedures and biopsy guidance, foreign body aspiration of the initial assessment, tracheal injury is evaluation and treatment planning, obstructive lesions of the distal show, stenosis evaluation of endobronchial abnormalities characterization and postoperative follow-up issues of virtual bronchoscopy, constantly evolving detector technology and software when placed through the right indications for routine use will take time, we believe that the rightful place.

Keywords: Virtual bronchoscopy, Fiberoptic bronchoscopy, MSCT, Tracheobrochial pathologies

Introduction

The term virtual endoscopy (VE) refers to the use of computer software for the construction of realistic mucosal surface and intraluminal images of hollow organs. The earliest studies in this field date back to 1994 when Vining et al. carried out a virtual colonoscopy [1], while in 1996, the same researchers published the results of their studies into virtual bronchoscopy (VB) [2] and virtual cystoscopy [3]. The term VB refers to the computer-aided construction and examination of endoscopic images of the tracheobronchial tree using volumetric data obtained from scans of the thoracic cavity with a thin-slice spiral or multi-slice computed tomography (MSCT), similar to that used in fiberoptic bronchoscopy (FOB).

Assessments made from multiplanar images and a three-dimensional perception facilitates control over anatomical structures. Images of higher quality have been acquired with the introduction of MSCT, which was first introduced in 2000 and became rapidly widespread due to the avoidance of the disadvantages associated with spiral CT such as motion artifacts and time loss. The present study evaluates the success, limitations, advantages and disadvantages of MSCT-VB in demonstrating tracheobronchial system pathologies, and makes a comparison of fiberoptic bronchoscopy and VB in terms of diagnostic accuracy and success in the evaluation of tracheobronchial lesions.

Received 29-06-2019 **Accepted** 16-08-2019 **Available Online** 17-08-2019 **Published** 30-08-2019
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Material and Methods

After obtaining the approval of the relevant ethics committee (Gaziantep University Ethics Committee) and written informed consent from all subjects, a total of 44 cases who were scheduled to undergo bronchoscopy and FOB were evaluated using MSCT and VB between September 2012 and August 2013.

For VB, the tracheobronchial system was scanned using a 64-detector (VCT XTe Light Speed, General Electric, Milwaukee, USA) MSCT in the axial plane with a slice thickness of 0.625 mm. The detector was configured with a collimation of 64x0.625 mm, a table rotation speed of 0.65 sec, 120 Kv, 120 mAs, a FOV of 25–50 mm and 1 pitch. Less than 1 cc of a contrast agent per body weight of the patient was injected intravenously as a bolus to the patients using a pump. Volumetric scanning was completed within 10 sec on average in a single breath, although this differed from patient to patient.

All axial images, with a slice thickness of 0.625 mm, were evaluated in the workstation. The virtual bronchoscopic images acquired using thoracic VCAR software in the navigation mode were evaluated by simultaneously displaying the images with axial, coronal, sagittal and curve MPR images on two screens, split into four and five quadrants. In the virtual bronchoscopic evaluation, the intraluminal appearance of the two main bronchi and segmental and subsegmental branches of the bronchi were examined starting from the proximal to the trachea, as in aFOB.

While advancing in the tracheobronchial tree, the images in the two planes were used to evaluate the localization, luminal wall and extraluminal structures. When needed, the three-dimensional external bronchial simulations were used to evaluate any lesions that extended beyond the tracheobronchial wall.

All patients underwent FOB with an Olympus bronchoscope, model LTF, type 160. The interval between the FOB and VB in each patient was a maximum of three days. The biopsy specimens obtained during FOB were evaluated by experienced pathologists (image 1).

Statistical Analysis

FOB examinations are considered the optimum approach for the evaluation of VB results. Accordingly, true positive, true negative, false positive, false negative, specificity, sensitivity and accuracy values were calculated for MSCT-VB, with IBM SPSS software v15.0 used for the statistical analysis.

Results

Included in the study were 44 patients in which FOB and MSCT-VB were performed independently. The mean age of the patients was 53±16 years with a range of 1–79 years;seven patients (16%) were female and 37 patients (84%) were male.

A total of 43 patients underwent bronchoalveolar lavage and a fine needle aspiration biopsy or histopathological sampling using surgical or radiological methods. The histopathological examinations revealed benign lesions in 12 patients (non-specific), squamous cell carcinoma in nine patients, adenocarcinoma in seven patients, small cell lung cancer in four patients, bronchiolitis obliterans with organized pneumonia (BOOP) in one patient, NSCLC-NOS in one patient, inflammatory myofibroblastic tumor in one patient, hydatid cyst in one patient, malignant epithelial tumor in one patient, malignant mesothelioma in one patient, granulomatous lesion (sarcodiosis or tuberculosis) in one patient and tuberculosis in one patient. The histopathological results of the patients are presented in Table 1.

Considering the trachea, two main bronchi and 18 segments in the lungs, a total of 968 areas in 44 patients were evaluated with FOB and VB. The rate of endoluminal lesions detected by VB was 4.4% and the rate of endoluminal lesions detected by FOB was 4.1%.

In terms of endobronchial lesions, FOB identified 16 stenoses, nine obstructions, four external compressions and 11 mucosal findings, whereas VB identified 12 stenoses, 16 obstructions and eight external compressions. None of the 11 mucosal findings on FOB were detected on VB. The distribution of the endobronchial lesions detected by both FOB and VB is presented in Table 2.

The localizations of the endobronchial lesions detected on VB and FOB are presented in Table 3. No significant difference was detected in diagnostic accuracy for the central and segmental branches in the virtual bronchoscopic evaluation ($P<0.05$).

In the comparison of FOB and VB, considering FOB as the optimum approach, 23 cases in which a lesion was detected on FOB were also detected on VB, whereas VB was unable to detect two cases in which FOB identified a lesion (false negative). FOB and VB identified no endoluminal lesions in 14 cases. VB revealed a lesion in five cases in which FOB did not identify any lesions (false positive). The comparison of diagnostic accuracy is shown in Figure 1 and Table 4; accordingly, sensitivity was 92%, specificity was 73%, positive predictive value (PPV) was 82%, negative predictive value (NPV) was 87% and accuracy was 84%.

Image 1 : A mass lesion that completely obstructs the left lower lobe bronchus by externally compressing it. FOB (A,B), 3D (C) , coronal (D) and VB (E,F) images.

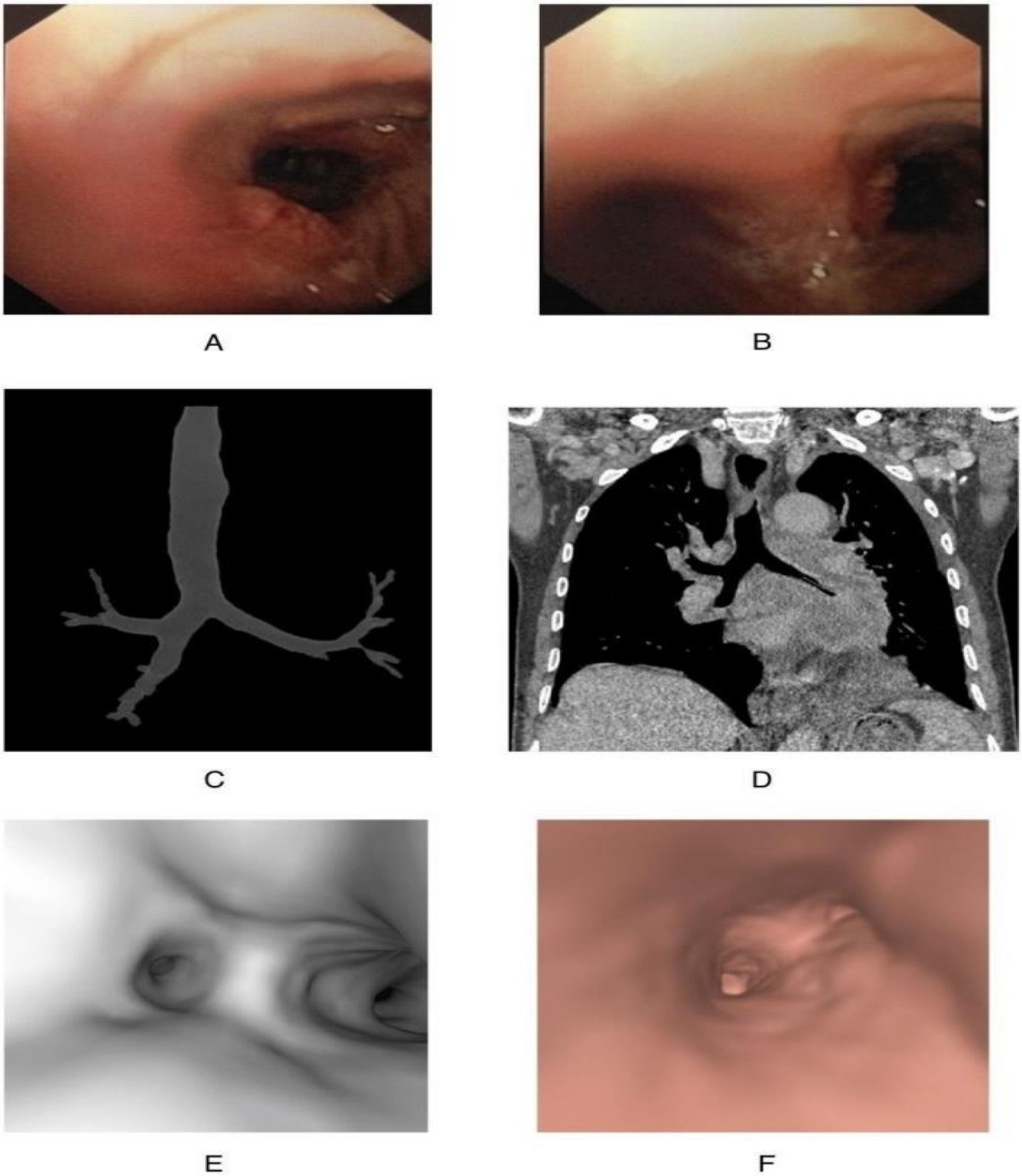

Table 1: Distribution of histopathological results of the cases.

Histopathology	Case Number
Benign (non-specific)	12
Squamous cell carcinoma	9
Adenocarcinoma	7
SCLC	4
Chronic inflammation	4
NSCLC -NOS	1
Malignant epithelial tumor	1
Malignant mesothelioma	1
Granulomatous lesion (sarcoidosis /tbc?)	1
Tuberculosis	1
Hydatid cyst	1
BOOP	1
Inflammatory myofibroblastic tumor	1
No biopsy	1

Table 2: Distribution of endobronchial lesions detected on FOB and VB.

	Stenosis	Occlusion	External Compression	Mucosal Finding
FOB	16	9	4	11
VB	12	16	8	0

Table 3: Distribution of the localization of endobronchial lesions detected on FOB and VB.

		Lesion distribution according to FOB				
		Trachea	Main Bronchus	Lober bronchus	Segmental Bronchus	No Lesion
Lesion distribution according to VB	Trachea	3				
	Main Bronchus		4	1		
	Lober bronchus			5		3
	Segmental Bronchus			1	12	2
	No Lesion		1	1		14

Table 4. Evaluation of the diagnostic accuracy of the findings detected on VB.

	VB (+)	VB (-)	Total
FOB (+)	23 (TP)	2 (YN)	25
FOB (-)	5 (FP)	14 (TN)	19
Total	28	16	44

TP: True Positive, FN: False Negative, FP: False Positive, FN: False Negative

Discussion

prompted the researcher to investigate alternative diagnostic methods. FOB is a similarly invasive diagnostic method, andalthough rare, complications may occur during the procedure. Bronchoscopy using alternative and noninvasive methods has become a popular topic in recent years, and has raised the interest of the imaging industry, resulting in a shift toward the pursuit of methods that take advantage of the advances in the computer, medical engineering and software fields. The emergence and development of the idea of VB, which dates back to the mid-1990s, was a result of technical advances and the pursuit of alternative methods [2, 3, 4]. At that time it became possible to transfer and process volumetric data on conventional axial images of tissue obtained to date through spiral or multi-slice CT systems on a separate computer. This allowed multiplanar reformatted images and virtual endoscopic images to be acquired. The direct visualization of the airways through FOB and the opportunity to obtain a biopsy instantly from the desired localization, however, have preserved the importance of this procedure, with has thus retained its value as the optimum approach. The availability of other diagnostic and therapeutic procedures, such as concurrent bronchial lavage, and obtaining culture material and removing existing foreign bodies can be regarded as other advantages of this method. There has been no change, however, in the invasiveness of the procedure, the need for sedation or the intolerance of some patients, even when performed with more flexible fiber optic catheters than a rigid bronchoscope [5, 6].

Although VB is performed using computer software, the experience of the operator is an important concern, as the region or localization of the lesion cannot be evaluated if orientation to the area is poor. VB should have a place in such evaluations, considering that it can be performed on existing CT images of the lungs, and the fact that it does not require a separate examination or patient preparation. Aside from clinical indications, VB can also be used for training and research purposes, with VB images similar to those of FOB being attained that can be used to teach and learn anatomical details of the tracheobronchial tree. VB allows chest disease specialists to practice, and permits an easier and more effective performance of a more invasive FOB if interpreted earlier [2, 7, 8].

Patients undergo 15–20 minutes of preparation for anesthesia before a conventional bronchoscopy, although the evaluation of more complicated cases may even require general anesthesia.

In terms of complications, VB is more advantageous than FOB. Unnecessary FOB examinations must be avoided, particularly in pediatric cases in whom complication rates can be as high as 7%. Haliloğlu et al. reported that unnecessary FOBs can be avoided through the use of VB [9]. Various retrospective studies have reported mortality rates of 0.008–0.04%, major complication rates of 0.05–3.4% and minor complication rates of a little below 10% [10, 11]. A prospective study, on the other hand, reported a mortality rate of 0.44%, a major complication rate of 1.65% (such as severe hemorrhage, respiratory arrest, pneumonia, pneumothorax and severe airway obstruction) and a minor complication rate of 6.5% [12]. No complication was reported among the cases that underwent FOB in the present study.

Virtual bronchoscopic images can also be obtained using helical CT scans, although such images have a low spatial resolution and a prolonged acquisition time, and the very slow reconstruction also makes their use inconvenient. The introduction of multi-slice CT into practice has reduced the entire examination time to 15–20 seconds and the slice thickness to 0.5–1 mm, and so the resolution of three-dimensional imaging has increased. According to Lacasse et al. [13], an examination with a collimation of 3 mm and a slice interval of 1.5 mm lacks sufficient accuracy for the investigation of endoluminal lesions. The use of MSCT images has also increased diagnostic accuracy, while the use of faster computers with higher processing capacities has allowed the acquisition of virtual bronchoscopic and other reconstructed images in a short period of time [14]. A virtual bronchoscopy is more advantageous than FOB in terms of the total examination time, althougha reduced procedural time can be regarded as a trivial advantage considering the time saved for the patient and physician and the lack of any increase in diagnostic accuracy. The reconstruction of images and virtual examinations after image acquisition depends on the radiologist, and the time spent on these procedures can vary considerably. The printing and saving of images and video images acquired through multidisciplinary works in hospitals lacking PACS, making them available to the clinician and then archiving them all require additional time. The time spent for VB is, on average, 15 minutes according to Wever et al. [15]. The time required for the reconstruction and examination of VB images ranged between 15 and 20 minutes in the present study, although this varied from one patient to another. The procedural time has decreased over time; although it does not seem likely that it will be further reduced in the near future. There have been studies attempting to reduce examination times through the provision of panoramic images or the use of developed automatic lesion detection software. It can currently be argued that VB is among the routine practices considering the time spent by a radiologist on VB.

One of the most significant differences between FOB and VB is that FOB is a dynamic procedure, which comes with its own advantages and disadvantages. Factors such as inspiration and expiration during FOB, cough reflex and continuous secretions that can be challenging for the clinician during the procedure are of no concern during VB. The procedure can be repeated any number of times in a VB, and there are no secretions that impair visibility. The images can be tracked from proximal to distal, and also from distal to proximal, allowing the visualization of endoluminal lesions from multiple perspectives. VB, however, lacks many of the important diagnostic advantages that come with FOB. The first of these is the inability with VB to observe the response of airways to respiratory movements and cough reflexes. A clinician can clearly observe the enlargement and narrowing of airways during FOB, as well as segmental bronchial openings that open and close and the movements of cartilage and mucosal tissues. Irregular changes in the diameter of the trachea of different types that are diagnostic for tracheomalacia, diverticula and herniation's, and that become visible during inspiration, and movements of pedunculated lesions and their extensions can also be recognized during FOB. There is no opportunity to observe such movements in VB. In a study of 45 cases with a mean age of 4.4 years, Heyer et al. [16] reported an NPV of 54.5%, and attributed this low rate to five patients with tracheomalacia/bronchomalacia in the patient group. They reported in the study that CT images acquired during inspiration would not be diagnostic for tracheomalacia, but that a diagnosis could be established through a biphasic investigation on VB during inspiration and expiration. Secretions and mucous plugs may be misdiagnosed as mass lesions, and such conditions are the most common cause of false positive results in VB [9]. Secretions and coagulum were mistaken for stenosis in five patients in VB, being later identified as secretion and coagulum. The appearance of air-foam in the left bronchus was thought to be associated with secretions. Mucous plugs can be aspirated and the lumen or orifices can be opened during FOB. Furthermore, foreign bodies can be removed upon detection, while invirtual bronchoscopy, it is not possible to recognize such bodies or remove them through aspiration.

Virtual bronchoscopic images must be correlated with conventional images and multiplanar reformatted images to reduce false positive results and to avoid mistakes. In a study of 18 patients, Bernhardt et al. [6] found no significant difference between axial, MPR and VB images in the detection, localization and identification of the severity of stenosis, and recommended the combined use of images. Finkelstein et al. [17] reported a sensitivity of 82% and a specificity of 100% for VB, but identified no significant difference in terms of diagnostic accuracy when compared to high-resolution thoracic computed tomography scans in cancer patients. That said, the results from both methods were superior to axial images. Konen et al. [18] suggested that VBmakes no contribution to cross-sectional images. Summers et al. [30] suggested that orientation would be better if VB is performed together with axial, coronal and sagittal imaging. Minghui et al. [19] found that the examination of MPR and VB images yielded higher sensitivity than that of FOB, and the same researchers suggested that this combination would be advantageous in terms of demonstrating the outer extensions of endoluminal lesions. Ferretti et al. [20] also stated that combined evaluations would increase diagnostic efficacy. Based on all the above findings, it would seem that conventional images must be combined with MPR and VB images, given that they cover each other's deficiencies and direct the radiologist to the correct diagnosis in patients with a suspected airway pathology. In our study, two screens were used while evaluating the VB images, with the correlation with MPR images investigated on the second screen. As mentioned in literature, the authors of the present study suggest that an evaluation of VB images in combination with axial and MPR images would increase diagnostic accuracy in the detection and grading of lesions.

The sensitivity of the method used for the detection of intraluminal lesions is related to the size of the lesion in VB, which can easily detect 5mm or larger endobronchial lesions. One study reported a sensitivity of 47–88% and a specificity of 48–89% in a patient group with lesions measuring 3–10 mm, while sensitivity and specificity rates increased by 20% and 34% respectively in lesions measuring 5–10 mm [21]. A 2-mm red nodule at the level of the vocal cord detected on FOB in patient number 9 could not be identified in VB, despite a repeat examination.

VB has increasing use in the grading of benign and malignant airway lesions, with high accuracy rates reported in the measurement of the depth and length of obstructive tracheobronchial lesions. Burke et al. [22] reported an excellent level of correlation between VB and FOB in the evaluation of the contours and shape of the stenotic segment. The present study found only a 10% difference in the rates of stenosis and lumen on VB and FOB. In 2002, Hoppe et al. [5] evaluated 200 bronchial segments using a 4-slice-MSCT with 2-mm collimation in a series of 20 patients. Their study reported high accuracy for MSCT in the evaluation of tracheobronchial lesions (accuracy in VB: 98%, accuracy in axial images: 96%; accuracy in coronal MPR images: 96%; accuracy in sagittal MPR images: 96.5%). The same study also reported that VB images have same diagnostic value as FOB in the evaluation of stenosis ($r=0.91$), as well as the superiority of VB over other CT imaging methods in a semi-quantitative evaluation of stenotic segments. In another study by Hoppe et al. [23] comparing FOB and VB using a 4-slice MSCT and 1-mm collimation, VB was reported to have an accuracy of 95.5% in the evaluation of both central and segmental airway stenoses. Their study also reported that VB led to a higher number of false positive results in the segmental bronchi than in the central bronchia; and that VB has a positive predictive value of 40.9% in segmental branches and a positive predictive value of 84.4% in the central airways. Lacasse et al. [13] stated that a 3-mm collimation and a 1.5-mm slice interval could overlook 32% of lobar and segmental lesions,but that further studies of MSCT could increase the sensitivity and specificity. The present study compared central and segmental airway stenoses using statistical methods, and found no significant difference in the diagnostic accuracy of VB ($P<0.05$). This can be attributed to the use of a 64-slice device with a lower collimation and higher resolution, as this allows the completion of the procedure using a single-breath-hold technique that minimizes respiratory artifacts. Finkelstein et al. [24] reported a sensitivity of 90% for VB in endobronchial lesions, a rate of 100% in obstructive lesions and a rate of 16% in mucosal lesions. In a collective analysis, sensitivity and specificity were reported to be 83% and 100%, respectively. In a study evaluating stenoses in tracheobronchial carcinomas, Rapp-Bernhardt et al. [6] reported a sensitivity of 94% and a specificity of 99.7% for VB. Liewald et al. [25] reported similar characteristics for VB and FOB in their evaluation of obstructive lesions. Table 8 summarizes the success rates in the identification of endoluminal lesions reported by various studies comparing VB and FOB in literature. Consistent with previous studies, the present study reports a sensitivity of

92%, a specificity of 73%, a positive predictive value (PPV) of 82%, a negative predictive value (NPV) of 87%, and an accuracy of 84%.

Some studies in literature have suggested that VB is as effective as FOB in identifying stenosis associated with a mass lesion, but that VB is not able to identify small infiltrations and to differentiate between complete and partial obstructions [26, 27]. The present study also found that VB can show severe stenosis as an occlusion. FOB identified 16 stenoses, nine obstructions and four external compressions, whereas VB identified 12 stenoses, 16 obstructions and eight external compressions. We believe that a simultaneous evaluation of VB images with MPR and axial images may reduce such failures. VB provides accurate information about the lumen diameter and the length of the stenotic segment, and such information is required for endobronchial procedures such as accurate stent placement, laser photocoagulation, brachytherapy and endobronchial cryotherapy [28, 17, 22, 29]. VB and three-dimensional images allow for the identification of the general appearance of the tracheobronchial tree and the delineation of the relationship between the lesion/stenosis and the surrounding pathological and normal tissues. VB can be beneficial in postoperative follow-up forthe evaluation of the percentage of the remaining stenosis in the bronchial tree, the position of the stenosis and stent permeability [28, 26, 30]. It is also a useful noninvasive method for the evaluation of the suture line following organ transplantation, lobectomy and pneumectomy. McAdams et al. [28] showed that VB provides better results than axial CT images in the evaluation of the recipient's bronchial anastomosis following lung transplantation.

Obstructive lesions are one condition in which VB is superior to FOB. The clinician cannot pass beyond an obstructive lesion during FOB, and so the status of the more distal parts of the airway will remain uncertain. VB is not subject to such limitations and can easily pass beyond an obstructive lesion [28, 22, 25, 26]. The obstruction of distal parts of the tracheobronchial tree by secretion and blood prevents evaluation of these parts by VB, although this can be overcome through an examination of three-dimensional images together with axial images [26]. Bernhardt et al. [31] used VB to evaluate the parts distal to an obstructive lesion in five patients, and found no additional lesions. In our study, the distal parts of mass lesions that completely obstruct the lumen could not be evaluated in the “VB navigation mode”, as the distal parts in all cases were filled with fluid (case numbers 6, 9, 17, 24 and 41). This problem was overcome, however, through the simultaneous examination of three-dimensional images together with axial and MPR images. No significant tracheobronchial lesion that would alter the statistical analysis was detected in any of these cases, although the need to delineate the airways that cannot be examined on FOB due to the presence of obstructive lesions seems to be one of the indications rendering VB inevitable. A clinician may proceed with a pathological diagnosis by carrying out a cellular sampling through bronchial lavage or biopsy, while VB offers no such opportunity. In addition, endoluminal surfaces are coded by a homogeneous single color tone in VB, making the identification of mucosal color changes, superficial lesions and infiltrative extensions, vascularity, fragility and other details all of which can be observed during FOB, impossible. Lesions such as blood clots, mucus, tumors and foreign bodies, being coded by the same color tone, also reduce the selectivity of VB [9, 6, 19, 26]. It is a striking finding that VB showed normal results in 11 cases who were found to have a mucosal lesion on FOB. It can therefore be clearly expressed that VB is unable to identify mucosal changes and lesions. Furthermore, mucus, secretion and purulent fluid in five cases analyzed with VB led to false positive diagnoses of “lesion”. Studies in literature mention “inability to detect mucosal lesions” and “inability to perform biopsy” as the most significant disadvantages of VB [17, 32, 33]. The authors of the present manuscript believe that VB should not be considered as an alternative to FOB, due to the inability to obtain a biopsy and to observe mucosal details.

Blind mediastinal lymph node biopsies with FOB have low sensitivity, particularly if the lesion has caused no change in the bronchial tree. The success rate is 72% for lesions that are observed during examination and only 36% if the lesion cannot be observed [34]. Whether or not a biopsy is performed will depend on estimations if a lesion cannot be detected and bronchial mucosa is normal, and this is the cause of rare false positive biopsies and a vast number of false negative biopsies [35]. A high rate of false negative biopsy results causes a delay in the staging and initiation of appropriate therapy, and thus leads to further interventional procedures [36]. Performing the procedure under the guidance of axial, coronal and sagittal reformatted images combined with VB images would be useful in determining the localization of the most appropriate biopsy site for lesions that are not causing bronchial distortion or mucosal changes [29, 36]. VB also aids the FOB operator in accessing the lesion and finding the most appropriate passageway, and can increase the effectiveness of a transbronchial biopsy in peripheral pulmonary lesions. McAdams et al. [28] reported a sensitivity rate of as high as 88% for transbronchial fine needle aspiration biopsiesof the mediastinal and hilar lymph nodes under the guidance of VB in the detection of malignancy. Shinagawa et al. [37] reported the effectiveness of transbronchial biopsy using an ultra-thin bronchoscope guided by VB navigation in the diagnosis of peripheral pulmonary lesions smaller than 20 mm. Furthermore, biopsies of mediastinal lymph nodes smaller than 1.5 cm under the guidance of VB can be useful in increasing the accuracy of the results [36].

Conventional CT findings are also evaluated during VB, during which parenchymal findings, pleural thickening and effusions, pathologies of the thoracic wall and bones, pathologies of the abdominal structures that fall into the view of the examination, neck and thyroid pathologies, mediastinal pathologies and associated compressions-invasions, and vascular pathologies along with endobronchial lesions can be easily recognized. At the same time, when the mass lesions observed on VB are correlated with MPR images, the relationship with the surrounding tissues, the invasion findings and eligibility for surgical resection can be evaluated. Bernhardt et al. [6] proposed VB as a useful method in the evaluation of mass invasion and staging when VB images are evaluated with axial and MPR images. Hoppe et al. [23] stated that axial and MPR images evaluated together with VB images yield similar sensitivity and specificity to VB, referring to it is a useful approach to the evaluation of mediastinal lymph nodes, and demonstrating their relationship with the surrounding tissue. In the present study, a mass lesion identified on VB was found to have invaded and narrowed the right pulmonary artery in one patient; A mass lesion in the upper lobe of the right lung in another patient extended into the spinal canal after eroding and destroying the upper thoracic vertebra and the neighboring ribs; and a mass lesion in another patient invaded the pericardium and mediastinal mass; while also invading most of the mediastinal vascular structures. The use of MSCT in examinations offers significant advantages. For example, it is highly possible to convert reconstruction algorithms into HRCT algorithms as thin slices are scanned with the spiral method. This allows soft tissue and bone tissue findings, while avoiding both interstitial findings and partial volume artifacts. Another advantage of a thin-slice examination is that it allows the three-dimensional reconstruction of the pulmonary nodules, thereby providing more detailed information about the nodule and allowing the more reliable follow-up of the nodule. Additional findings beyond the tracheobronchial tree were detected in most of the patients in the present study (Table 3).

VB is a useful and noninvasive means of evaluating foreign body aspirations and congenital airway anomalies in both pediatric and adult patients [15]. In their study, Konen et al. [18] reported that VB could be useful in the evaluation of the tracheobronchial tree for airway stenosis and compressive pathologies in pediatric patients. Tracheal stenosis was detected,the intermediary bronchi could not be observed, and the right upper, middle and lower lobes branched from the main bronchus in one patient in the present study, while another patient was found to have a medial accessory segmental bronchus in the left inferior lobe.

When compared to FOB, VB offers the advantages of being non-invasive, requires no anesthesia or sedation, can be repeated a number of times, permits imaging from different angles, allows investigations for tracheobronchial tumors, permits access beyond obstructive lesions that cannot be observed on FOB, has a high sensitivity rate, offers the ability to show additional lesions and findings in the bronchial tree together with axial and MPR images, thereby aiding in the evaluation of lesions for operability, and allows the characterization of anomalies in the tracheobronchial structure.

As of this time, however, VB does not seem to be an alternative to FOB due to such associated disadvantages such as the inability to perform a biopsy, the low sensitivity in detecting lesions smaller than 5 mm, the inability to detect mucosal infiltration, the relatively low specificity rate when compared to high sensitivity rates, and the inability to offer real-time evaluation.

Conclusion

The authors of the present manuscript believe that VB will find the place it deserves in routine use in time with the continued development of detector technologies and software, given its ability to guide interventional bronchoscopic procedures and biopsies, to aid in the initial evaluation and planning of treatment in foreign body aspirations, and to provide the clinician with the opportunity of practicing before following up tracheobronchial lesions with FOB.

Acknowledgements: None

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: **ZU, RK, SU, MSM**; Research concept and design, Patient examinations, Research the literature, preparation of the article **MSM;** Revision of the article.

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OPEN ACCESS JOURNAL ISSN: 2148-6832

MSD

Medical Science and Discovery
2019; 6(8):145-9

Research Article Doi: 10.17546/msd.591318

The effect of injury type and location on the prognosis of the patients with open globe injuries

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Abstract

Objective: Investigation of the effect of the globe injury site and the globe injury type on the postoperative results in the patients with a relatively softer open globe injury (OGI) was aimed.

Methods: Medical records of the patients with OGI due to blunt or penetrating trauma were analyzed retrospectively. The patient cohort was divided into laceration and rupture groups. The location of injury was evaluated in zones (I-II-III). Presence and type of the complication (cataract, retinal detachment, etc.) were evaluated. Final best corrected visual acuity (BCVA) was evaluated as the primary outcome measure.

Results: Seventy eyes of 70 patients with OGI were included in the study. While 58 eyes (82.9%) had lacerations, 12 eyes (17.1%) had ruptures. Among the 52 patients with lacerations for whom there was an available BCVA data, 13 (25%) patients showed no change, 32 (61.5%) showed an increase, and 7 (13.5%) showed a decrease in BCVA. Among the 11 patients with ruptures, 2 (18.2%) patients showed no change and 9 (81.8%) showed an increase in BCVA. A complication was observed in 23 (44.2%) patients with laceration and 4 (33.3%) patients with rupture (p: 0.474). No difference was detected in terms of the complication rate between the patients having a different zone of injury. However, final BCVA was lower in those with Zone III injury in comparison to those with Zone II injury (p: 0.028).

Conclusion: Although the injury type was thought to have an effect on the final BCVA of the patients with OGI, no difference was detected between the patients with laceration and rupture. Zone III injuries resulted in lower preoperative BCVA values. However, despite a significant difference between Zone II and III injuries, no significant difference was observed in terms of the final BCVA between the patients with Zone I and those with Zone III injuries.

Keywords: open globe injury; injury location; laceration; rupture; penetrating trauma

Introduction

Ocular traumas are one of the most common ophthalmological emergencies and can cause globe injuries with varying severities. The type of trauma (mechanical, thermal, and chemical) is important in the prognosis of the globe injury. Mechanical traumas can cause lacerations (with a sharp object) or ruptures (caused by a blunt object) leading to open or closed globe injuries. In case of a full-thickness injury within the wall of the globe (cornea and sclera), it is called open globe injury, whereas partial-thickness injury is observed in case of a closed globe injury. In case of an open globe injury, the patient should be surgically managed urgently by primary closure of the wound. Because of a full-thickness injury, post-traumatic complication rates are higher in comparison to closed globe injuries (1,2).

Thus, open globe injuries possess a higher risk of blindness in comparison to closed globe injuries. Globe injuries are among the most common risk factors for unilateral blindness and most of them are preventable. According to the World Health Organization (WHO), approximately 1.6 million blind people, 2.3 million people with bilateral low vision, and almost 19 million people with unilateral blindness or low vision from injuries were observed (3).

Numerous studies have been conduced to predict the prognosis of patients with open globe injuries (4–6). Risk factors to show poor prognosis were reported including but not limited to age, preoperative visual acuity (VA), mechanism of injury, location and extent of damage (zone of injury), afferent pupillary defect, time lapse between the injury and surgery, presence of complications such as

Received 12-07-2019 **Accepted** 04-08-2019 **Available Online** 17-08-2019 **Published** 30-08-2019
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traumatic cataract, severe intraocular hemorrhage, choroidal damage etc., presence of endophthalmitis (5,7–10). Although some studies linked the blunt trauma to a poor prognosis, Schmidt et al. showed that patients with penetrating trauma resulted in a worse final VA (11). To investigate this conflict, the effect of different injury mechanisms on the final VA should be studied.

In this study, investigation of the effect of the globe injury site and the globe injury type on the postoperative results in the patients with a relatively softer open globe injury was aimed.

Methods

The patients who were referred to the Department of Ophthalmology in Cerrahpasa Medical Faculty with open globe injury due to blunt or penetrating trauma between 2010 - 2018 were analyzed retrospectively. Since it was a retrospective study, it was not necessary to obtain informed consent from the patients. The study has been carried out in accordance with the Declaration of Helsinki.

Only the patients with mechanical injuries were included in the study. The patients with caustic injuries or thermal injuries were excluded from the study. The patients with coexisting injuries other than globe injury such as the eyelid, orbital, and optic nerve injuries were also excluded from the study. Additionally, military or terror-related injuries were excluded from the study to create a group of patients with softer injuries. Then the patient cohort was divided into two groups; laceration (1) secondary to penetrating trauma and rupture (2) secondary to blunt trauma according to Birmingham Eye Trauma Terminology (12).

The age, gender, preoperative and final best corrected visual acuity (BCVA) testing with the logarithm of the minimum angle of resolution (logMAR) measurements, presence of complication and type of complication (formation of traumatic cataract, retinal detachment, vitreous hemorrhage, posterior synechia, peripheral anterior synechia) were recorded for all patients. The patients were categorized according to their best corrected visual acuity (BCVA) into three groups; (1) increased BCVA, (2) decreased BCVA, and (3) no change in BCVA. The patients with no light perception were excluded from the statistical analysis of logMAR equivalent of BCVA.

Repair of the perforated area with primary suturing was performed for seventy eyes of 70 patients included in the study. Detailed slit-lamp and funduscopic examination were done for all of the patients. B-scan ultrasonography was performed to reveal the posterior segment pathologies for the patients who had a pathology preventing the visualization of the posterior segment. Phacoemulsification and intraocular lens implantation were performed for patients with traumatic cataract who were thought to benefit from cataract surgery in terms of an increase in the BCVA.

Additionally, the location of injury was determined according to the Ocular Trauma Classification Group (2). Injuries located to the cornea and limbus were defined as Zone I injuries. Zone II injuries involved the anterior 5 mm of the sclera (not extending into the retina). Zone III injuries involved full-thickness scleral defects more posterior than 5 mm from the limbus.

Statistical analysis

A chi-square or Fisher test was utilized to compare the ratios. A Mann Whitney U test was used to compare the means of the independent groups. Kruskal Wallis test was used for the comparison of multiple independent groups and a Mann Whitney U test with Bonferroni correction was utilized for post hoc analysis. p value below 0.05 was considered statistically significant. SPSS (version 21.0) software was used in all statistical analyses.

Results

Seventy eyes of 70 patients with open globe injury were included in the study. While 58 eyes (82.9%) had lacerations, 12 eyes (17.1%) had ruptures. The mean age of the patients with lacerations were 28.7±20.7 (3-82) years and it was 37.2±20.3 (2-74) years for the patients with ruptures. While 41 (70.7%) of 58 patients with lacerations were male and 17 (29.3%) were female, 9 (75%) of 12 patients with ruptures were male and 3 (25%) were female. The groups were homogenous in terms of age and gender (p: 0.17 and p: 0.534). The mean duration of follow up for the patients with laceration was 29.3±10.6 months (12-60 months) and it was 29.8±7.4 months (15-39 months) for the patients with rupture (p: 0.75). The most common complications observed in our patient cohort were traumatic cataract (21.5%), retinal detachment (10.0%), and vitreous hemorrhage (5.7%).

Among the 52 patients with lacerations for whom there was an available BCVA data, 13 (25%) patients showed no change in BCVA, 32 (61.5%) showed an increase in BCVA, and 7 (13.5%) showed a decrease in BCVA. Among the 11 patients with ruptures for whom there was an available BCVA data, 2 (18.2%) patients showed no change in BCVA and 9 (81.8%) showed an increase in BCVA. A total of 7 patients were children without verbal communication or patients with mental retardation whose BCVA data were not available. When both groups were compared, no significant difference was detected in terms of increase, decrease or no change in BCVA (p: 0.328). The mean BCVA of the patients with laceration was 2.03±1.13 before the operation and changed to 1.33±1.3 after the follow-up. The mean BCVA of the patients with rupture was 2.17±1.06 before the operation and changed to 0.66±0.77 after the follow-up. No significant difference was observed between the groups in terms of the BCVA before the operation and final BCVA (p: 0.67 and p: 0.38, respectively). When the patients were compared according to the injury type in terms of the frequency of complications secondary to the perforation (traumatic cataract, retinal detachment, vitreous hemorrhage, posterior synechia, peripheral anterior synechia), complication was observed in 23 (44.2%) patients with laceration and 4 (33.3%) patients with rupture (p: 0.474).

When the patients were evaluated in terms of the anatomical location of the perforation 29 patients (41.4%) had Zone I injury, 19 patients (27.1%) had Zone II injury, and 22 patients (31.4%) had Zone III injury. Comparison of the patients according to the perforation location in terms of the change in BCVA is shown in Table 3. While the mean preoperative BCVA of the patients with Zone I injury was 1.82±0.97, it was 1.64±1.36 for those with Zone II injury, and 2.67±0.81 for those with Zone III injury (p: 0.01). Comparison of the groups with post hoc Mann Whitney U test resulted in a significant difference between Zone I-III and Zone II-III (p: 0.025 and p: 0.026, respectively). While the mean final BCVA of the patients with Zone I injury was 1.07±1.13, it was 0.81±1.26 for those with Zone II injury, and 1.97±1.24 for those with Zone III injury (p: 0.021). Comparison of the groups with post hoc Mann Whitney U test resulted in a significant difference between the patients with Zone II and Zone III injuries (p: 0.028). However, when these groups were compared in terms of the complication rate, no significant difference was detected (p: 0.14) (Table 4).

Table 1. The relationship between the injury type and the change in best corrected visual acuity

	Best Corrected Visual Acuity			
Injury type	**No change**	**Increased**	**Decreased**	**Total**
Laceration	13	32	7	52
Rupture	2	9	0	11
Total	15	41	7	63

Table 2. Relationship between the injury type and the rate of complication

	Complication		
Injury type	**Absent**	**Present**	**Total**
Laceration	35	23	58
Rupture	8	4	12
Total	43	27	70

Table 3. The relationship between the zone of injury and the change in best corrected visual acuity

	Best Corrected Visual Acuity			
Zone of injury	**No change**	**Increased**	**Decreased**	**Total**
Zone I	3	19	4	26
Zone II	7	9	0	16
Zone III	5	13	3	21
Total	15	41	7	63

Table 4. Relationship between the zone of injury and the rate of complication

	Complication		
Zone of injury	**Absent**	**Present**	**Total**
Zone I	21	8	29
Zone II	12	7	19
Zone III	10	12	22
Total	43	27	70

Discussion

In this retrospective study, the patients were divided into two groups as lacerations due to penetrating injuries and ruptures due to blunt injuries. When the patients were compared according to the injury type of the perforation, no significant difference was detected between the groups in terms of the frequency of post-traumatic complications and change in BCVA. However, when the patients were compared in terms of the location of the injury, the patients with Zone III injury had lower final BCVA values.

Several studies investigated the risk factors affecting the final VA and various risk factors were determined. Age, preoperative VA, mechanism of injury, location and extent of damage (zone of injury), afferent pupillary defect, the time lapse between the injury and surgery, presence of complications such as traumatic cataract, severe intraocular hemorrhage, choroidal damage, etc. were among the reported risk factors (5,7–10).

Some studies reported rupture secondary to blunt trauma as a risk factor for a poor prognosis as well(7,13) and in the study by Schmidt et al., the authors showed that postoperative change in visual acuity was better in the patients with ruptures (11). Thus, the effect of the mechanism of injury on the final VA was evaluated in this study. However, no significant difference was detected between the laceration and rupture groups in terms of the final BCVA. This might be related to the similar complication rates between the groups.

The open globe injuries (OGIs) are observed more frequently in male patients. In our study, consistent with the previous studies (14, 15), 70% of the patients with penetrating injury and 75% of the patients with blunt trauma were male. Although Guven et al. reported 24.3% of bilateral OGIs (14), since no patient was injured due to terror-related reasons, no patient showed bilateral injury in our study.

The frequency of penetrating trauma was found to be higher in the previous studies as in our study. Consistent with 82.9% of penetrating trauma in our study, Agrawal et al. reported 71.4% of penetrating trauma in their study (8). Although penetrating trauma was observed more frequently and no difference was detected between the laceration and rupture groups, we observed interestingly that bottle cap was the etiological factor causing injury in 2 patients and their final VA was no light perception. Then, we hypothesized that the pressure and the proximity of the etiological factor might be related to the severity of the injury. However, further studies investigating the impact of these parameters on the prognosis are necessary.

Ocular Trauma Classification Group proposed a system for locating the OGIs to predict the prognosis of the patients. According to this system, zone III injuries were found to be related to a poor prognosis in many studies (14, 16). Consistent with the previous literature, the patients with Zone III injury showed lower final BCVA values in comparison to those with Zone II injuries. However, no difference was detected between the patients with Zone I and III injuries.

This difference can be linked to the relatively low number of patients, absence of an intraocular foreign body in our patients, and non-military etiology. In our study, change in visual acuity was evaluated with logMAR equivalent of BCVA, while in the other studies varying range of VA were used for the categorization (14). Furthermore, since corneal perforation scars on the optical axis can dramatically decrease the visual acuity in cases with Zone I injury, the classification of the location according to the zones can be an insufficient approach. Thus, a newer classification system with a special emphasis on the central or paracentral corneal location of the wound might be proposed.

After the open globe injury, the most commonly affected locations are the most vulnerable parts of the globe. For example, blunt trauma affects more commonly the sclera rather than cornea. Additionally, surgical wounds are another example of the vulnerable site of the globe during the injury. For example, in patients with a keratoplasty history, the most vulnerable site is expected to be the donor graft interface. However, in one of our patients with a history of keratoplasty, a blunt trauma interestingly caused scleral rupture. The presence of blue sclera or etiological factors such as connective tissue disorders that might cause a decreased scleral rigidity was investigated and no pathology was discovered (17). Thus, perforation through the surgical wound might not be a certain rule.

The most commonly observed complications after the open globe injury was traumatic cataract and retinal detachment in our study. Traumatic cataract was reported as the most common post-traumatic complication in most of the previous studies (18). However, contrary to the other studies (1, 18, 19), intraocular foreign body, and aphakia after initial trauma were not observed in our patients. Absence of these post-traumatic complications might also be linked to the indifference observed in our study between the patients with Zone I and Zone III injury in terms of the final BCVA.

The rate of endophthalmitis after open globe injuries has been reported between 0.9-6.7% (20–23). In our study, endophthalmitis was not observed in any of the patients. Risk factors related to an increased frequency of post-traumatic endophthalmitis have been reported as a delayed presentation (>24 hours), microbial keratitis, and lens capsule breach (21). In our study, all of the patients were operated earlier than 24 hours after the trauma and intraocular foreign body was not observed in any of the patients. Additionally, intracameral moxifloxacin was applied to all of the patients at the end of the surgery contrary to the study by Essex et al. where the authors did not apply any intracameral antibiotic to any of their patients (22). Absence of endophthalmitis in our patient cohort might be related to these differences.

Conclusion

In conclusion, our series of patients with relatively softer OGIs presenting to a tertiary referral center has shown no difference in terms of final BCVA and complication rate according to the injury type (laceration or rupture). Although the preoperative mean BCVA was lower in the patients with Zone III injury, final mean BCVA values showed no significant difference between patients with Zone I and III injuries.

No significant difference was observed in terms of the complication rates between the patients with different zone injuries. These differences might be attributed to the selection of a group of patients with relatively softer injuries. Limitations of the study were its retrospective design and the absence of the pupillary afferent defect data. Further studies are necessary to investigate more precise risk factors (especially central corneal location) for the prediction of the prognosis after open globe injuries.

Acknowledgements: None

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: **CD, BM, SS, GT, BG, UYG, OSA**; Research concept and design, Patient examinations, Research the literature, preparation of the article. Chemical Analysis**. CD;** Revision of the article.

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OPEN ACCESS JOURNAL ISSN: 2148-6832

MSD

Medical Science and Discovery
2019; 6(8):150-9

Case Report Article Doi: 10.17546/msd.564613

Evaluation and treatment of the eosinophilic lung diseases in 7 patients

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Abstract

Objective: Eosinophilic lung diseases (ELD) are a rare group of heterogeneous diseases characterized by increase of the eosinophilic ratio in the airways and lung parenchyma. We aimed to present and discuss the clinical, radiologic and pathologic features of six patients with eosinophilic lung diseases.

Conclusion: Peripheral eosinophilia with pulmonary infiltrates is diagnostic clues of eosinophilic lung diseases. Systemic corticosteroids are provided rapid control not only in symptoms but also radiological and clinical improvement of ELD.

Keywords: eosinophilic lung diseases, acute eosinophilic pneumonia, chronic eosinophilic pneumonia

Introduction

Eosinophilic lung diseases are a rare group of heterogeneous diseases characterized by increase of the eosinophilic ratio in the airways and lung parenchyma.(1) They are classified as eosinophilic lung diseases of unknown cause including simple pulmonary eosinophilia, acute eosinophilic pneumonia, chronic eosinophilic pneumonia, idiopathic hypereosinophilic syndrome and eosinophilic lung diseases of known cause; including allergic bronchopulmonary aspergillosis, bronchocentric granulomatosis, parasitic infections, drug reactions, eosinophilic vasculitis (allergic angiitis, granulomatosis (Churg-Strauss syndrome) (2). We aimed to present and discuss the clinical, radiologic and pathologic features of patients with eosinophilic lung diseases.

Material and Methods

We retrospectively evaluated the patients whom diagnosed with eosinophilic lung diseases between January 2013 and January 2018 in the Department of Pulmonary Medicine, VM Medicalpark Samsun Hospital, Samsun, Turkey. The clinical-radiological findings, performed treatments, responses to treatment, and prognoses of patients who diagnosed with eosinophilic lung diseases were retrospectively evaluated. The study was performed in accordance with the ethical principles in the Good Clinical Practice (GCP) guidelines, applicable local regulatory requirements, and the protocol was approved by local ethics review boards. All the patients read the patient information form about the study procedure and written informed consent forms were obtained.

Received 13-05-2019 **Accepted** 09-07-2019 **Available Online** 24-07-2019 **Published** 30-07-2019
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http://dx.doi.org/10.17546/msd.564613

Case 1: Atelectasis and respiratory failure due to allergic bronchopulmonary aspergillosis (ABPA) in a patients with severe asthma

A 52-year-old non-smoker female patient was referred to our Intensive Care Unit due to respiratory failure with pulmonary atelectasis, pulmonary mass and consolidations. She was suffering from severe dyspnea due to severe asthma and her asthma had not been controlled with optimal asthma treatment. Chest radiograph showed volume loss with opacity on left hemithorax and consolidations on right hemithorax (Figure 1A). Thoracic CT has indicated to left upper lobe atelectasis, interlobular septal thickening with pulmonary mass and dense consolidations on right lung (Arrow in Figure 1B). Despite suspicion of malignancy, her 3 months prior Thorax CT was better than now (Figure 1C).

We thought that severe asthma, atelectasis and respiratory failure may be caused from Allergic Bronchopulmonary Aspergillosis (ABPA). Laboratuary findings revealed that the total IgE level was 2430IU/ml. Aspergillus skin test and sputum culture for Aspergillus species were positive. The systemic corticosteroid treatment was started for diagnosis of “Severe asthma, Atelectasis and Respiratory Failure Due To Allergic Bronchopulmonary Aspergillosis (ABPA)”.

At the 2nd day of treatment atelectasis and pulmonary consolidations were rapidly improved (Figure 1B). Four weeks after the treatment, atelectasis and pulmonary consolidations were recovered and fungal cavitary lesion due to aspergillus was noted on right lung (Arrow in Figure 1D).

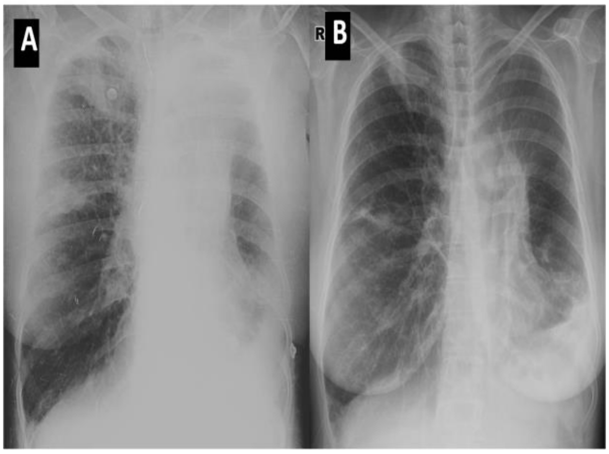

Figure 1A. Chest radiograph showed the volume loss with opacity on left hemithorax and consolidations on right hemithorax (Figure 1AA). The systemic corticosteroid treatment was started and at the 2nd day of treatment atelectasis and pulmonary consolidations were rapidly improved (Figure 1BB).

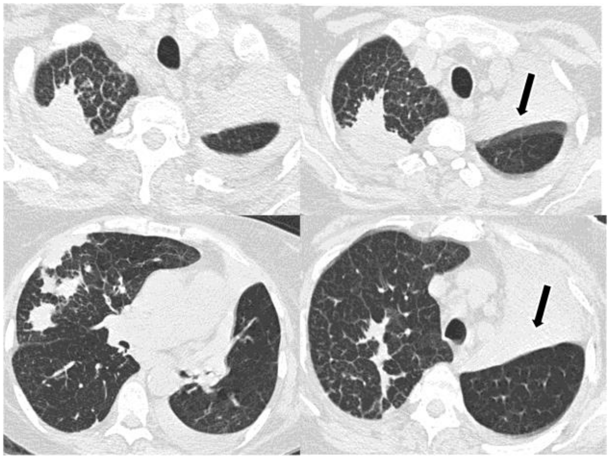

Figure 1B. Thorax CT showed the left upper lobe atelectasis, interlobular septal thickening with pulmonary mass and dense consolidations on right lung.

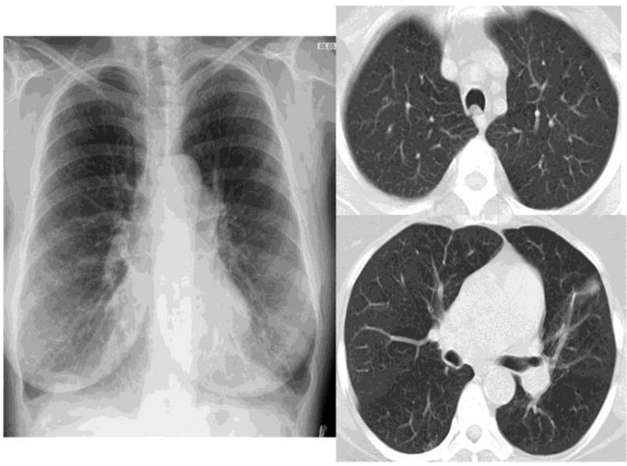

Figure 1C. Three months prior Thoracic CT findings of patient was were better than now. Due to this data, the malignancy probability removed from possibilities.

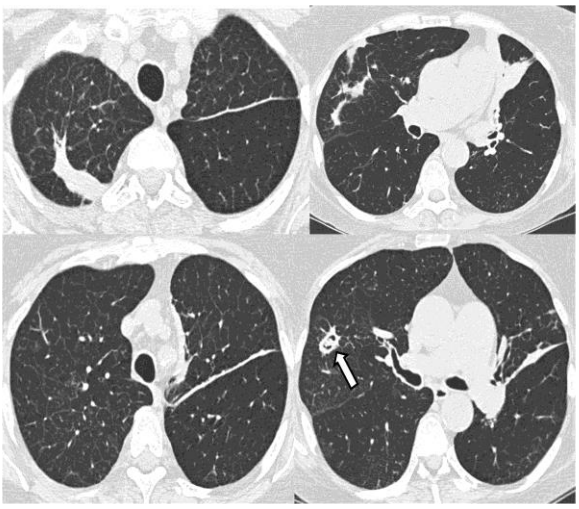

Figure 1D. Atelectasis and pulmonary consolidations were recovered and fungal cavitary lesion due to aspergillus was noted on right lung after 4 weeks of treatment.

 http://dx.doi.org/10.17546/msd.564613

Case 2: Allergic aspergillosis in an uncontrolled asthmatic patient

A 42-year-old non-smoker man with uncontrolled severe asthma was referred to our hospital. He was suffering from persistent wheezing, cough and dyspnea and his asthma had not been controlled with optimal asthma treatment. Thoracic CT performed for to definite diagnosis of "Uncontrolled Asthma" and it revealed the infiltrates on right middle lobe and peripheral cavitary lesion which includes an opacity (Figure 2A).

Laboratuary findings; Total IgE level was 6000 IU/ml and white blood cell count was 6410/uL with eosinophils of 1090/ uL (17%). Aspergillus skin test performed and it was positive. The systemic corticosteroid and itrakonazol treatments were started for the diagnosis of "Allergic Aspergillosis with Uncontrolled Asthma". After the treatment, symptoms and pulmonary lesions were improved (Figure 2B).

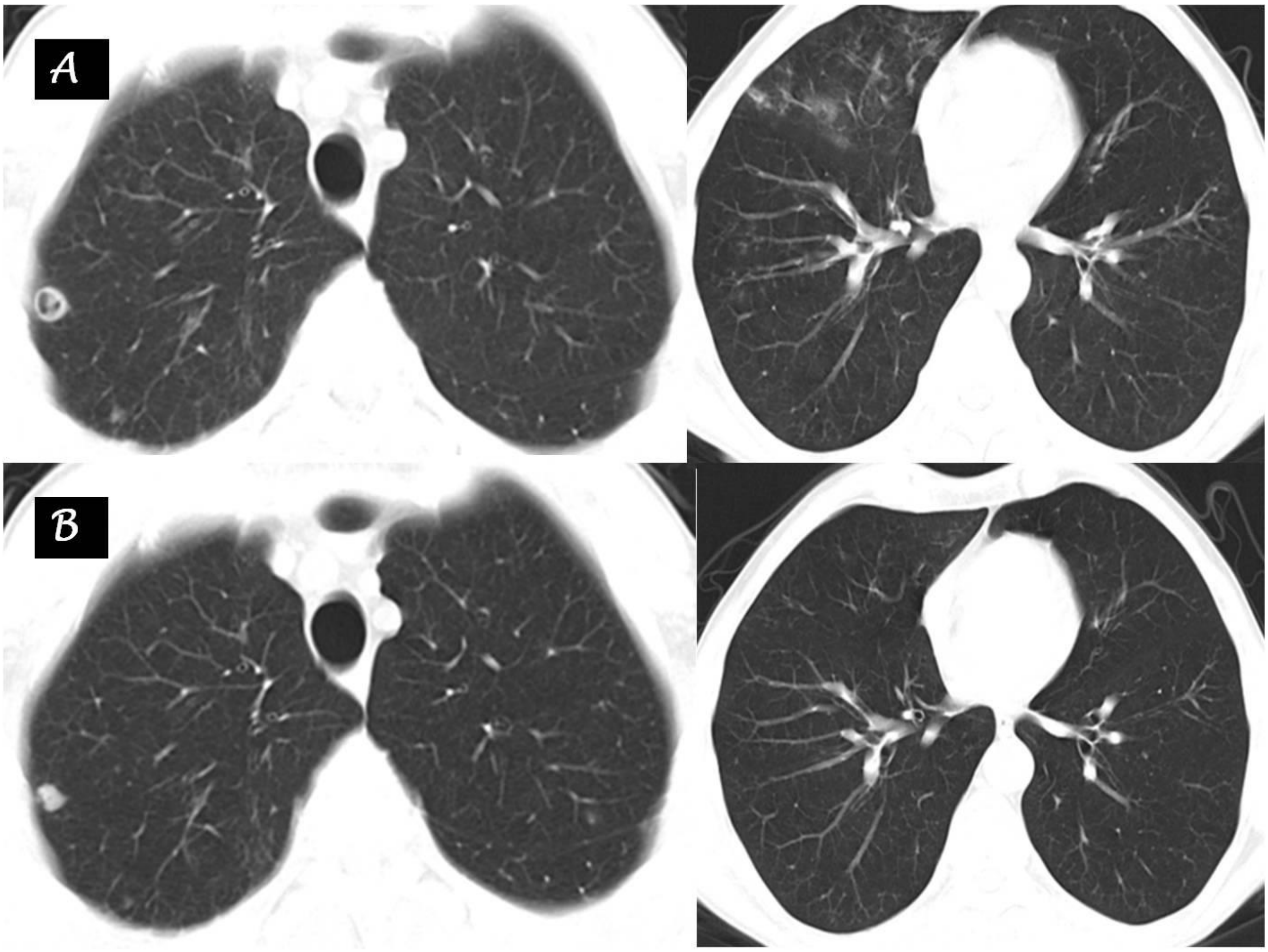

Figure 2A. Thoracic CT performed for to definite diagnosis of *"Uncontrolled Asthma"* and it revealed the infiltrates on right middle lobe and peripheral cavitary lesion which include a opacity(Figure 2AA). After the treatment, the symptoms and pulmonary lesions were improved (Figure 2BB).

Figure 2B. Thorax CT showed the left upper lobe atelectasis, innterlobular septal thickening with pulmonary mass and dense consolidations on right lung.

Case 3: Chronic Eosinophilic Pneumonia with Respiratory Failure

A 65-year-old man, referred to our Intensive Care Unit for complaints of cough, dyspnea and hypoxemic respiratory failure. Chest radiograph showed bilateral reticular infiltrates on upper fields of lung.(Figure 3A). Despite the treatment for pneumonia with levofloxacin and piperasilin/tazobactam, his radiologic features and symptoms were worsening. Thoracic CT was performed for the definitive diagnosis of "non-responding pneumonia". Thoracic CT scans demonstrated the bilateral non-segmental airspace consolidations with peripheral predominance on upper lobes of lungs which were consistent with " photographic negative shadow of pulmonary edema" (Figure 3B). Finding of photographic negative shadow of pulmonary edema was consistent with Chronic Eosinophilic Pneumonia. His white blood cell count was 24110/uL with eosinophils of 16730/ uL (69.4%). The systemic corticosteroid treatment was started for diagnosis of Chronic Eosinophilic Pneumonia with respiratory failure. After the 3 days of corticosteroid treatment, the respiratory failure and alveolar consolidations were rapidly recovered (Figure 3C).

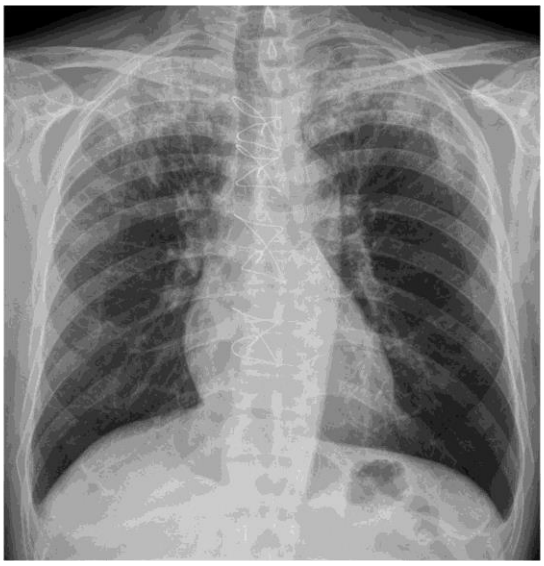

Figure 3A. Chest radiograph showed bilateral reticular infiltrates on upper fields of lung.

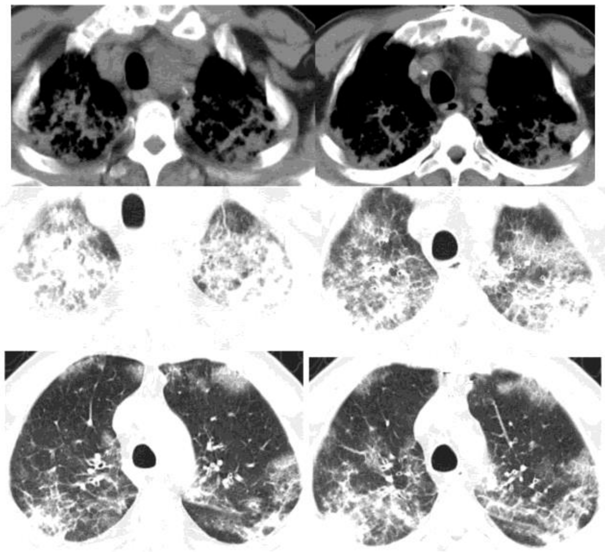

Figure 3B. Thoracic CT scans demonstrated the bilateral non-segmental airspace consolidations with peripheral predominance on upper lobes of lungs which it was consistent with " photographic negative shadow of pulmonary edema".

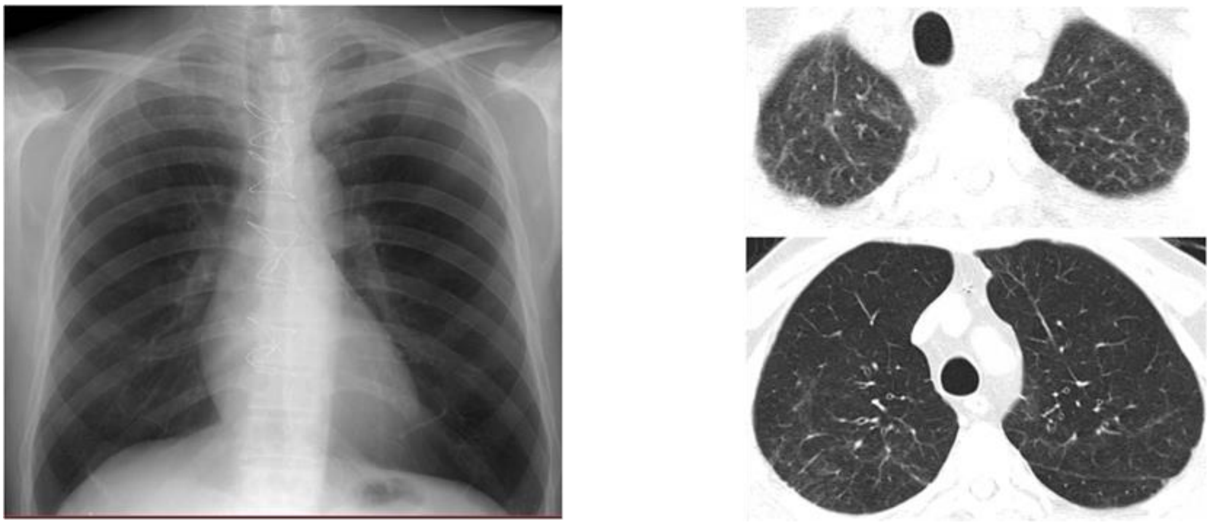

Figure 3C: After the 3 days of corticosteroid treatment, respiratory failure and alveolar consolidations were rapidly recovered

Case 4: Löffler Pneumonia

A 50-year-old non-smoker male admitted to our clinic with dry cough and dyspnea. Thorax CT revealed bilateral fleeting migratory pulmonary nodular opacities (Figure 4A). Lesions did not respond to the antibiotic treatment and malignancy was ruled out with 18 FDG PET/CT scan.

His white blood cell count was 13260 K/uL with eosinophils of 4950 K/ uL(37.3%). The systemic corticosteroid treatment was started for the diagnosis of Löffler Pneumonia and alveolar consolidations were rapidly recovered within 10 days after the corticosteroid treatment (Figure 4B).

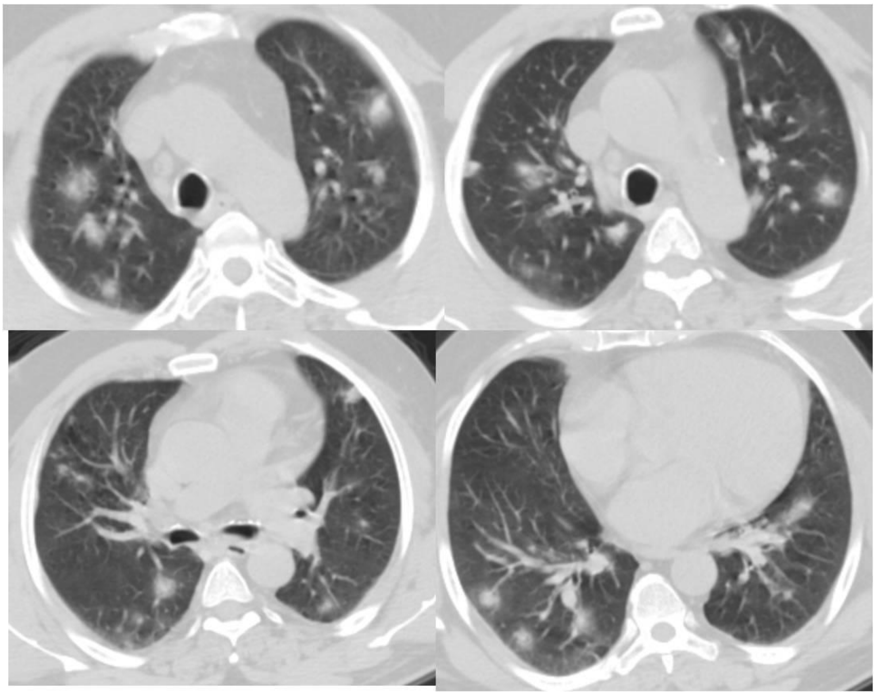

Figure 4A. Thorax CT revealed the bilateral fleeting migratory pulmonary nodular opacities.

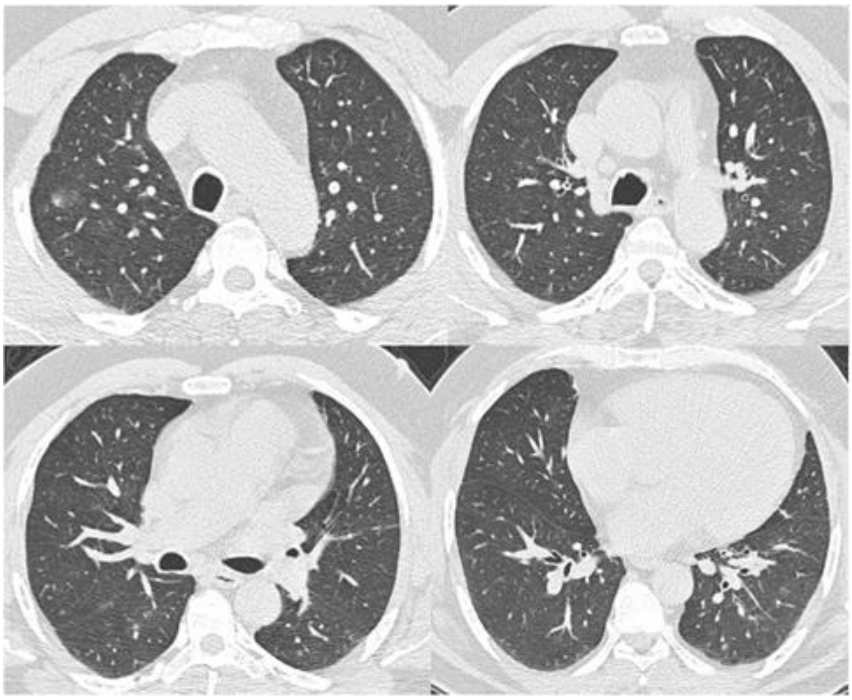

Figure 4B. The systemic corticosteroid treatment was started for diagnosis of Löffler Pneumonia and alveolar consolidations were rapidly recovered within 10 days after the treatment.

Case 5: Eosinophilic mass in a asthmatic patient

A 38 years old male admitted to the hospital with complaints of dyspnea and cough. He had diagnosis of asthma and rhoncuses were noted on chest auscultation. Chest radiography showed the plate-like atelectasis on left hemithorax. Thoracic CT scan images revealed the peribronchial mass like pulmonary lesion with atelectasis (Figure 5A).

Fiberoptic bronchoscopy was performed and there was a white colour endobronchial mass in left lower lobe bronchus. Biopsies were taken from endobronchial mass and histopathologic examination showed the eosinophilic inflammatuar infiltration(Figure 5B). After the corticosteroid treatment, pulmonary mass was fully recovered (Figure 5C).

Figure 5A. Thoracic CT scan images revealed the peribronchial mass like pulmonary lesion with atelectasis

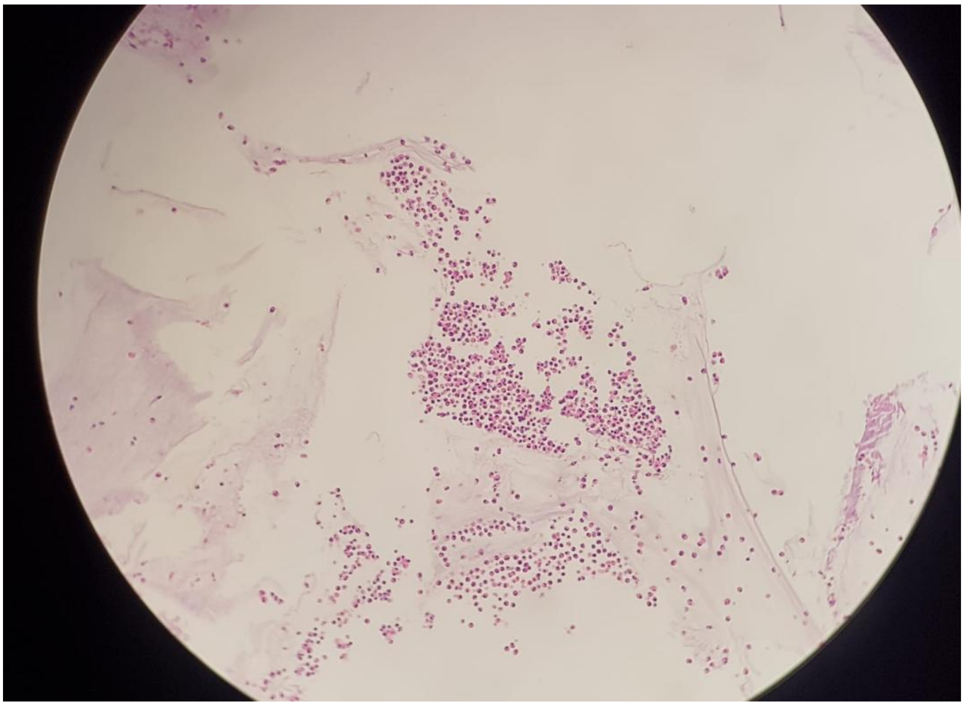

Figure 5B. The histopathologic image showing the eosinophilic infiltration.

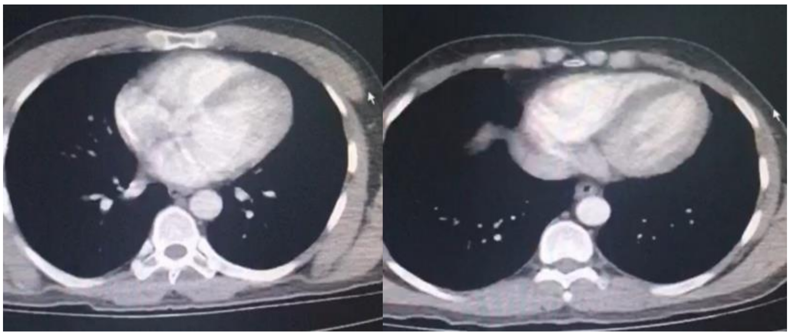

Figure 5C. After the corticosteroid treatment, pulmonary mass was fully recovered.

Case 6: Chronic Eosinophilic Pneumonia

A 54 year-old female referred to our clinic with complaints of cough, dyspnea and unresolved pneumonic infiltrations. Chest radiograph showed bilateral reticular infiltrates (Figure 6A). Thoracic CT scans demonstrated the bilateral non-segmental airspace consolidations with peripheral predominance on upper lobes of lungs which were consistent with “photographic negative shadow of pulmonary edema” (Figure 6B).

The finding of photographic negative shadow of pulmonary edema was consistent with Chronic Eosinophilic Pneumonia. His white blood cell count was 13790 K/uL with eosinophils of 5710 K/uL (41.4%) . Systemic corticosteroid treatment was started for the diagnosis of Chronic Eosinophilic Pneumonia with respiratory failure. After the corticosteroid treatment, thealveolar infiltrates were resolved (Figure 6C and 6D).

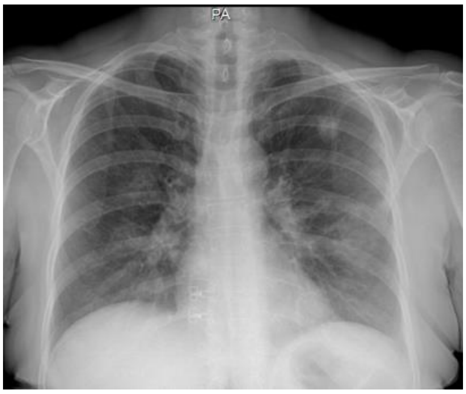

Figure 6A. Chest radiograph showed bilateral reticular infiltrates.

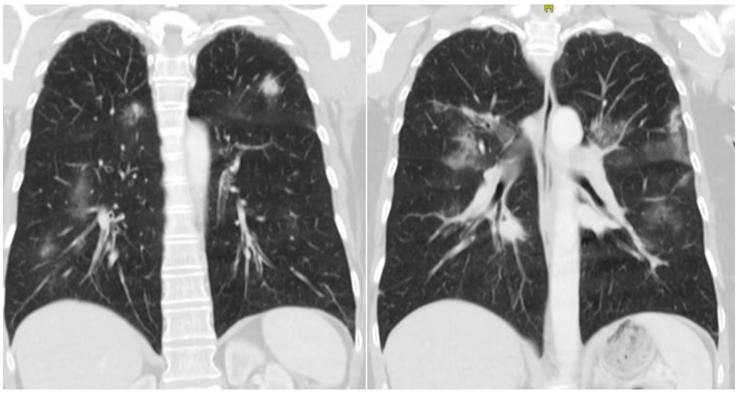

Figure 6B. Thoracic CT scans demonstrated the bilateral non-segmental airspace consolidations with peripheral predominance which it was consistent with “*photographic negative shadow of pulmonary edema*”.

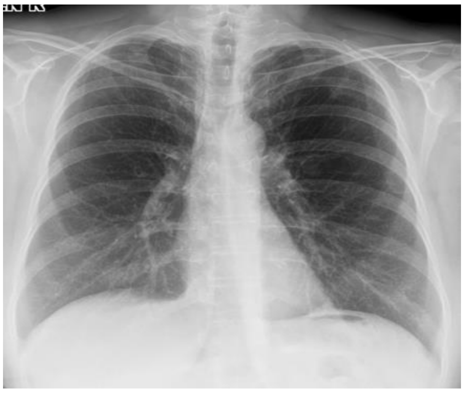

Figure 6C. Chest radiography showed that after the corticosteroid treatment, the alveolar infiltrates were completely resolved.

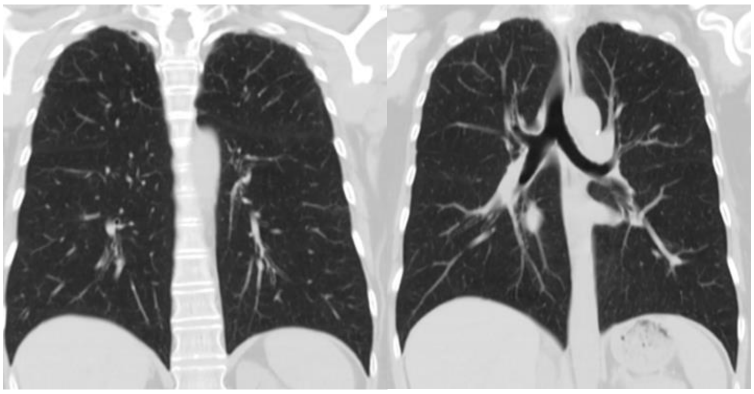

Figure 6D. Thorax CT images showed that after the corticosteroid treatment, the alveolar infiltrates were completely resolved.

Case 7: Acute Eosinophilic Pneumonia

A 32 years old male referred to ICU for ARDS. His chest radiography showed the bilateral diffuse infiltrates (Figure 7A). Thoracic CT images revealed the bilateral diffuse alveolar-interstitial infiltrates with air bronchograms(Figure 7B). He was received antipsychotic, antidepressant and antiepileptic drugs including risperidone, quetiapine, karbamazepine, valproic acid (sodium valproat) due to schizophrenia and epilepsy.

His white blood cell count was 4860 K/uL with eosinophils of 0 K/uL (0%). We suspected from Acute Eosinophilic Pneumonia caused from risperidone and it was stopped. Systemic corticosteroid treatment was started for the diagnosis of Acute Eosinophilic Pneumonia with respiratory failure. After the corticosteroid treatment, the alveolar infiltrates and respiratory were rapidly resolved (Figure 7C).

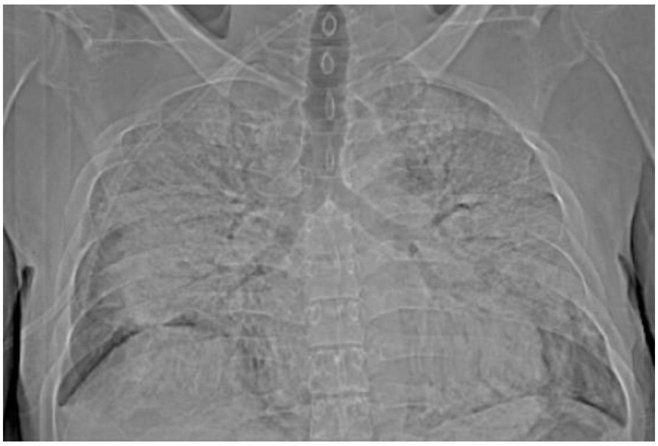

Figure 7A. Chest radiography showing the bilateral diffuse infiltrates.

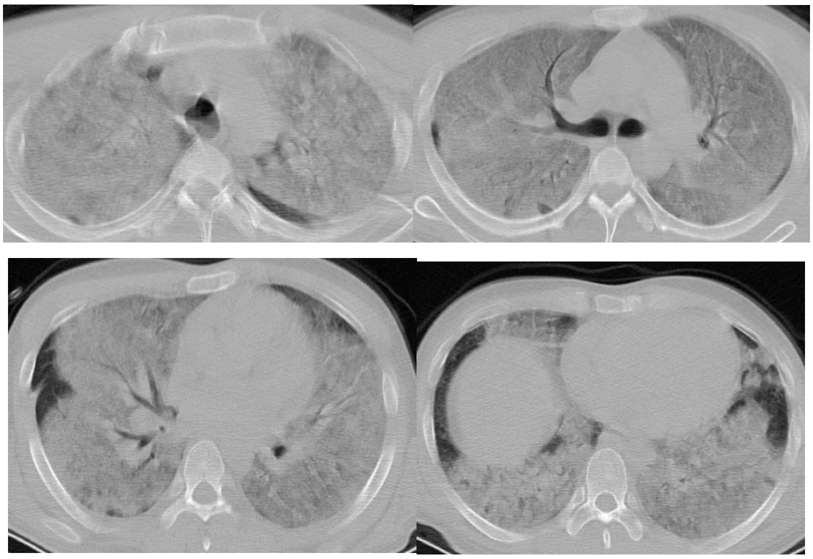

Figure 7B. Thoracic CT images showing the bilateral diffuse alveolar-interstitial infiltrates with air bronchograms.

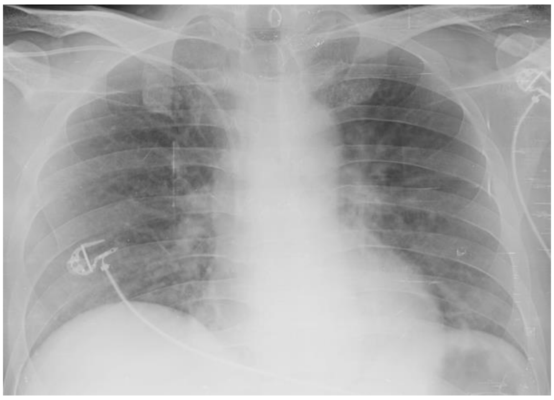

Figure 7C. After the corticosteroid treatment, alveolar infiltrates and respiratory were rapidly resolved.

Discussion

The eosinophil is a multifunctional leukocyte implicated in the pathogenesis of a wide range of inflammatory reactions. It modulates immune responses at the sites of inflammatory foci within several organ systems. Although several different normal values have been reported, normal blood generally contains 50–250 eosinophils per microliter (3,4).

Most eosinophilic lung diseases manifest with peripheral eosinophilia, although acute eosinophilic pneumonia (AEP) may not. Diagnosis is based on demonstration of opacities on chest x-ray and identification of eosinophilia (>450/µL) in peripheral blood, bronchoalveolar lavage fluid, or lung biopsy tissue.

The most valuable clinical information is derived from the patient's history and from physical examination. The duration and severity of symptoms are also of critical importance. CEP typically affects patients in their 30s or 40s, although onset in childhood has been reported. The disease has a gradual onset, with an interval of approximately four to five months between the appearance of initial symptoms and diagnosis.

Typical symptoms include a cough, fever, breathlessness, weight loss, and night sweats, as seen in our cases. Löffler syndrome, a form of eosinophilic pulmonary disease, is characterized by absent or mild respiratory symptoms(most often dry cough), fleeting migratory pulmonary opacities, and peripheral blood eosinophilia. Parasitic infections, especially Ascaris lumbricoides, may be the cause, but an identifiable etiologic agent is not found in up to one third of patients.

Treatment of Löffler syndrome may consist of corticosteroids. Pulmonary function tests can occasionally be useful in the evaluation of patients with unexplained pulmonary eosinophilia. Some eosinophilic lung diseases (Acute Eosinophilic Pneumonia (AEP), Chronic Eosinophilic Pneumonia (CEP), tropical pulmonary eosinophilia) are typically accompanied by mainly restrictive ventilatory defects, whereas others (ABPA, Churg-Strauss syndrome) typically cause mainly obstructive ventilatory defects. Bronchoalveolar Lavage (BAL) can also be very useful in the evaluation of patients with eosinophilic lung disease (10).

Normal BAL fluid consists of less than 1% eosinophils. Because some disorders are not accompanied by peripheral eosinophilia, BAL may provide the first (and, perhaps, the only) indication of an eosinophilic lung disease. Patients with eosinophilic lung disease may be identified initially on the basis of pulmonary symptoms or chest radiographic abnormalities accompanied by blood or tissue eosinophilia. Diverse and nonspecific findings may also be seen at conventional chest radiography.

Chest computed tomography (CT) demonstrates a more characteristic pattern and distribution of parenchymal opacities than chest direct radiography. Although the characteristic CT findings are often helpful, there is still a considerable overlap of CT findings among the various eosinophilic lung diseases (5,6).

Acute eosinophilic pneumonia (AEP) is a rare and life-threatening clinic condition, as seen in our 6th case. Many causes such as collagen diseases, infections, irradiation, toxins, neoplasia and a long list of drugs can be implicated in the development of AEP (7).

Antibiotics and non-steroid anti-inflammatory drugs (NSAIDs) are the most commonly reported drugs associated with AEP.

Toxins suspected of causing eosinophilic pneumonia include cigarette smoke and illicit drugs (cocaine, heroine). Drug- or toxin-induced eosinophilic pneumonia is indistinguishable from idiopathic acute or chronic eosinophilic pneumonia by clinical, radiographic, and histopathologic criteria. Diagnosis is supported by a temporal relationship to a drug or toxin. The condition usually resolves with removal of the agent and recurs with rechallenge (8).

Rizos et. al, reported the first case with risperidone-induced AEP (9). Eosinophils are exquisitely sensitive to corticosteroids and completely disappear from the bloodstream within a few hours after administration of corticosteroids. This rapid disappearance from the blood may obscure the diagnosis in patients who receive corticosteroids before the diagnostic assessment is instituted.

Conclusion

Peripheral eosinophilia with pulmonary infiltrates are diagnostic clues of eosinophilic lung diseases. Systemic corticosteroids are provides rapid control not only in symptoms but also radiological and clinical improvement.

Acknowledgements: None

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: **ÖOK, ÖMT, BÇ, İGÖ, BÇ**; Research concept and design, Patient examinations, Research the literature, preparation of the article. Chemical Analysis**. BÇ;** Revision of the article.

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Medical Science & Discovery

International Journal of
Medical Science and Discovery
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