

Pulmonary gas conducting interstitial pathway

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Abstract

In spite of the growing efforts oriented towards revealing different aspects of emphysema, the persistence of the emphysematous or emphysema-like changes (ELCs) is not explored yet in the open literature. In this study we demonstrate the persistence of an ELC for 22 years in a spontaneous pneumothorax (SP) patient which indicates a hitherto unknown gas supply to the ELC. For this purpose we used high resolution computed tomography (HRCT) images processed into three-dimensional (3D) geometry. By the same token, not only a long persistence but also the volume increase of this ELC between 2002 and 2010 was demonstrated. The 3D geometry visualized an aerated interstitial structure between the sites of supposed gas leakage at the wall of the third generation airways and the ELC. This potential gas conducting interstitial pathway is not a continuation and has neither the form nor the structure of a bronchus. The finding suggests that in this patient the intrabronchial gas passes through the bronchial wall and via a gas conducting interstitial pathway reaches the ELC. Despite the availability of the presently employed techniques for at least 15 years, such case and phenomenon have not been described previously. The retrieval of the patient suggests that the findings could be relevant for a considerable proportion of the population.

Keywords

Thorax, computed tomography (CT), high resolution CT, tracheobronchial tree, computer applications – 3D

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Introduction

Clinical and physiological investigations have demonstrated the irreversible progress of emphysema even after cessation of smoking (1). Emphysematous changes develop at the distal parts of the respiratory system (1). They appear on high resolution computed tomography (HRCT) as localized areas of low attenuation with thin or imperceptible walls in the pulmonary tissue of smokers. Identical radiological findings in patients who suffered from spontaneous pneumothorax (SP) but never smoked are called emphysema-like changes (ELCs) (2). Their number is strongly correlated to the number of SP events (2,3). An ELC (similarly to a SP), will be absorbed within weeks without gas supply. However, no study is available on the development and persistence of ELCs. The objective of this work was to present a case with ELC persisting for at least 22 years, being supplied with gas through an interstitial pathway.

Case report

Approval (no. 96-360) by the Stockholm Regional Ethic Committee and written consent from the patient were obtained. The patient in this case report has been retrieved from a cohort of 27 SP patients of our

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previous ELC study (2). They had at least one ELC each. None of them had ever been smokers, or suffered from obstructive pulmonary disease or alpha1antitrypsin deficiency. Twenty-four of them (including this patient) participated in our flexible fiberoptic bronchoscopic (FFB) study (4) on bilateral bronchial anomalies (4). Six of them were followed up in the radiological study of bronchial anomalies but only two had unilateral SP. One of these two patients was excluded from this report, since he had no ELC in the field of view (FOV). The other patient, who is the patient in this case report, had developed a right-sided SP in 1986. He had an ELC (approximately 20 mm in diameter) in the left middle region, first seen in 1988. This ELC was visible also in the FOV of scans from the follow-up study in 2002, but also in the CT images recorded after his right main bronchus perforation (5) (in 2007, 2009 and 2010), caused by the rupture of a proptos (6). Two different HRCT scans from 2010 demonstrated healing of his right main bronchus, but the left sided ELC was still visible 22 years after its discovery. A three-dimensional (3D) bronchial image of the ELC was reconstructed by a special segmentation technique from both the horizontal and vertical series of two-dimensional (2D) sections of a HRCT acquired in 2007. The 3D technique enables the visualization of the contour of the 2D images, neglecting all other information of the images. This allows the 3D reconstruction algorithm to show the surface of the gas in the airways, ELC and the gas conducting interstitial pathway in a much more sensitive and precise way than this can be achieved by 2D images. In our previous study (4) we used digital subtraction to remove the digital image of the peribronchial gas to demonstrate the perforation of the right main bronchus. In the present study the segmentation technique could demonstrate the density differences between both the ELC / interstitial gas conducting pathway and the pulmonary tissue. The radiological parameters for the investigations in 1988 are described in Bense et al. (2) and those from 2002–2010 are summarized in Table 1 for the readers convenience.

In order to quantify the amount of gas the volume of the ELC was determined from the HRCT images for

each examination (Table 2). Although the mean value of the density was lower than the surrounding lung tissue the difference was far less than the standard deviation and thus volume estimation by segmentation was not straightforward. However, the density of the boundary of the ELC was significantly higher and thus the interior of the ELC could be differentiated from the exterior by grayscale thresholding of the boundary and semi-automated segmentation of the interior. As a by-product of the process the air space of the ELC could be differentiated from the high density tissue. The definitions of the border of the ELC and the tails, respectively, have been defined by their imaginary contours. The volume of the ELC + tails + the non-gas content of the ELC constitute the total volume. Because of the subjectiveness of this process it was repeated several times to determine a standard error of the volume estimate which was significantly higher for older examinations with larger voxel size. The results clearly demonstrate not only the persistence, but also the increase in volume of the ELC.

The persistence of the ELC for 22 years indicates a gas supply to the ELC in this patient. Since HRCT images alone did not demonstrate any bronchial gas supply to the ELC, we applied a more sensitive technique. The HRCT images were processed mathematically for 3D geometry reconstruction (5,6) purposes to find the hypothesized gas refilling “interstitial pathway”. The reconstructed geometry is shown in Figs. 1 and 2. Fig. 2 is a 3D figure and has got “rotate” and “enlarge” functions as well. As the figures demonstrate,

Table 2. Total volumes of ELCs and their tails (aerated interstitial structure) and the volume of non-gas fraction of ELCs.

Year	Volume of ELC (mL)	Volume of tail (mL)	Volume of non-gas fraction of ELC (mL)
2002	2.12 ± 0.18	0.08 ± 0.04	0.11 ± 0.08
2007	2.76 ± 0.22	0.17 ± 0.05	0.30 ± 0.09
2010	3.38 ± 0.1	0.15 ± 0.02	0.31 ± 0.04

Table 1. Parameters of HRCT investigations from 2002, 2007, 2009, and 2010 (2010/a with GE 64 row HRCT and 2010/b with Philips Brilliant 40 row HRCT).

Date	Voxel size (mm × mm × mm)	Rows (n)	Thickness of slices (mm)	Distance between slices (mm)
2002	0.5 × 0.7 × 0.7	8	1.250	0.5
2007, 2009, and 2010a	0.63 × 0.7 × 0.7	64	0.63	0.6
2010b	0.67 × 0.34 × 0.34	40	0.67	0.33

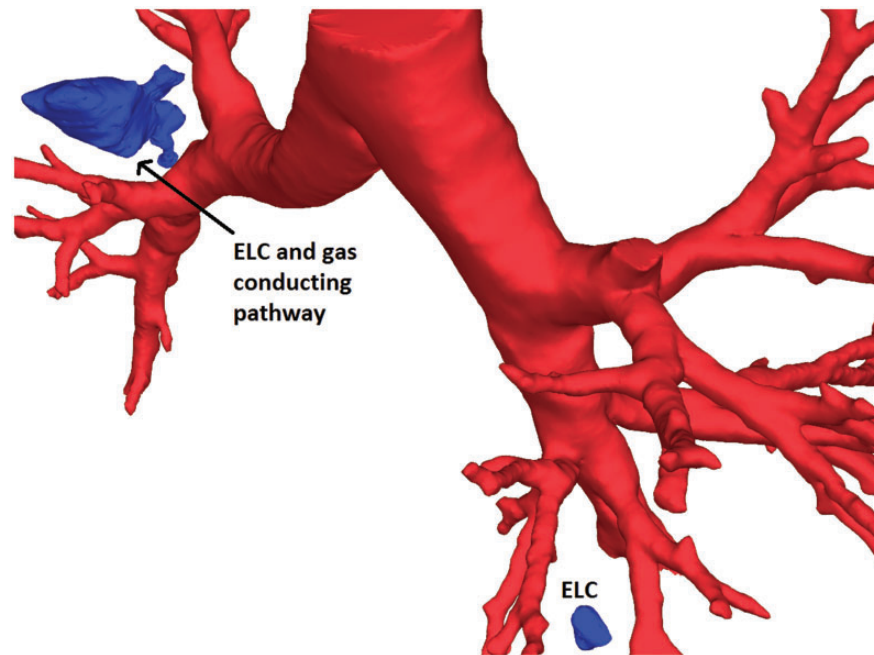


Fig. 1. The posterior view of the reconstructed geometry of the tracheobronchial tree, ELCs, and the pulmonary gas conducting “interstitial pathway” connecting the left third presegmental bronchus with the left-sided ELC. The right-to-left diameter of the trachea is 21 mm. The bronchial walls are not visualized. The right-sided ELC (4–6 mm in diameter) was not detected in the 8 mm interval between the 2 mm thick HRCT sections in 1988, but detected in every HRCT examination between 2002 and 2010.

the 3D method visualized an aerated interstitial structure (blue) with no perceptible border or form like a bronchial wall in the left lung between the third generation airway and the approximately 20 mm in diameter ELC. The two proximal tails of the aerated interstitial structure approached the visualized intrabronchial gas (2.4 and 4.4 mm distance) and were attached to the ELC. The 2.4 and 4.4 mm wide gaps between the intrabronchial gas (pink) and the aerated interstitial structure (blue) correspond to the non-visualized bronchial wall with its protuberances. Therefore, the distance between the external surface of the bronchial wall and the proximal tails of the aerated interstitial structure was virtually zero. The tails merged into a less than 2 mm wide part and then broadened until the approximately 20 mm large ELC. The measurements demonstrated the enlargement of the ELC (blue) and the aerated interstitial structure (blue) between 2002 and 2010 (Table 2).

Discussion

The gas from an ELC or SP would be absorbed within weeks unless the supplied gas replaced the absorbed one. The persistence of an ELC for 22 years proves a balance between the amounts of the supplied and the absorbed gas to/from the ELC. The volume increase of the ELC and the aerated interstitial structure even points to a ventil effect. In order to explain the origin

of the supplied gas, we hypothesize that the intrabronchial gas passes through the bronchial wall of the left third generation airway and the pulmonary parenchyma to the ELC (7).

The transparietal leakage suggests hitherto non-visualized discontinuation(s) of the layers of the anomalous bronchial wall, which may be given more consideration in the future. It may be surmised that the two point-like sites where the tails are attached to the third generation airway are “*loci minoris resistentiae*” of the bronchial wall where the intrabronchial gas leaks. The persistence of the ELC and the volume increase in both the ELC and the aerated interstitial structure suggest that the demonstrated aerated interstitial structure is a pulmonary gas conducting interstitial pathway to the ELC.

The discreet form of the interstitial gas conducting pathway indicates that the interstitial gas does not diffuse freely throughout a homogenous pulmonary tissue. Instead, the migration of gas in the pulmonary tissue/interstitium is determined by a balance of density differences of the pulmonary tissue/interstitium and a pressure gradient (7) in that. The patient’s history of SP demonstrated bronchial anomalies (4), and a bronchial perforation (5) due to the rupture of a proptos (6). This may suggest that his airways are weak due to both anomalous branching and structure.

The demonstration of the left-sided interstitial gas conducting pathway years prior to the contralateral

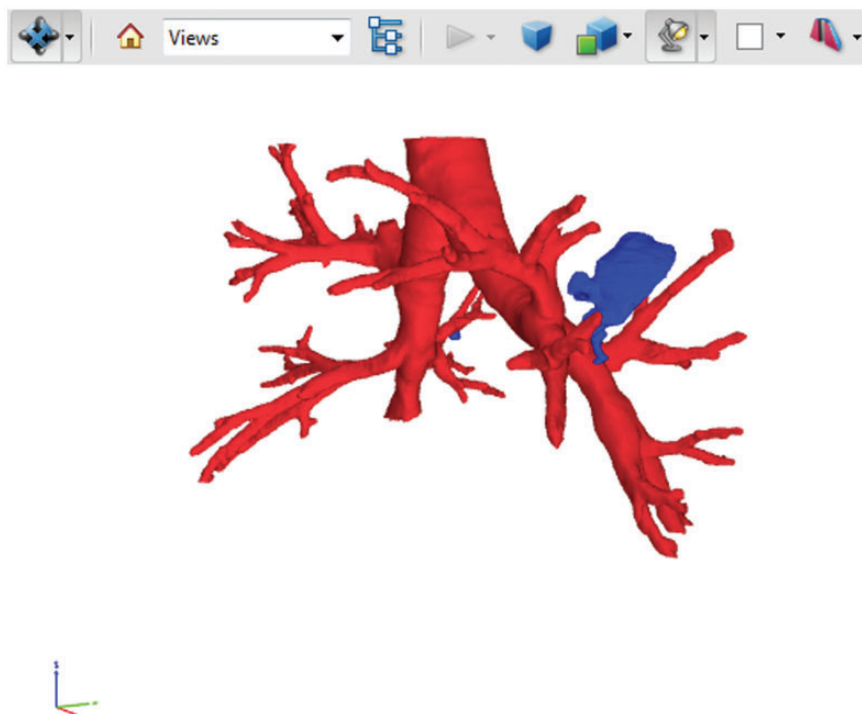


Fig. 2. The 3D image with zoom and rotate functions shows the left-sided ELC approximately 20 mm in diameter with the “gas conducting interstitial pathway” leading to the ELC (with blue). This figure shows the 3D bronchial geometry. The intrabronchial gas is visualized with pink color. The size of the right–left diameter of the trachea is 21 mm. The 3D bronchial geometry may be enlarged/ decreased and rotated to any direction with the help of the mouse/cursor. The carina is at –140 mm and the left ELC is between –133 and –163 mm of the vertical height of the axial sections. The bronchial walls are not visualized. The ELC and the pulmonary gas conducting “interstitial pathway” with tails are marked with blue color. The proximal tails of the “gas conducting interstitial pathway” are approximately 2.5–4.5 mm to the inner surface of the left third AGs. The “gas conducting interstitial pathway” is connected to the ELC by a conical intersection. This pathway is rather narrow and allows only limited streaming of gas which may explain the limited change of the volume. The second ELC (4–6 mm large, blue colored) in the right middle region remained undetected in 1988, but it was demonstrated in 2002, 2007, 2009, and 2010.

right main bronchus perforation excludes a causal relationship between them. The continuousness of bronchial pathway in emphysema is proved by morphological studies and the therapeutic efforts are based on the bronchodilating effect on the small airways. Due to the radiological limitations in visualizing the continuousness of a bronchial pathway in emphysema and to discern that from the pulmonary gas conducting interstitial pathway, we stated that gas conducting interstitial pathway has no structure, form or size of a bronchus. The central location of the ELC was an advantage for the detection of the interstitial gas conducting pathway and its contact points to the third generation airway and ELC. A small gas supplying bronchus would have been more difficult to exclude/ visualize at the periphery.

No other study has dealt with the development, central/peripheral distribution, and persistence of ELC in those who never smoked, neither with emphysematous bullae or blebs in smoker patients regarding secondary/ COPD related SP. Even though the methods used in this

investigation have been available for at least 15 years, no similar connection between an ELC and a presegmental airway has been shown. There are more than 100 papers in the available literature which state that they deal with ELC. Several of these papers describe animal studies. Some human studies are restricted to subjects who contracted different diseases. However, the denomination of ELC in these studies is deviating from our definition of ELC (2), which is not considered as a rule not even in the studies on SP. Another confusing fact is that gas filled emphysematous or ELCs are called cyst in Birt-Hogg-Dube syndrome (8) – like they were containing fluid, and no one objects this impossibility. There is no information on the smoking habits of the patients as a rule. Therefore it is impossible to discern emphysematous or emphysema-like changes (ELCs). Another item of information that is absent is the central or peripheral distribution of emphysema or ELC, which is available only in our paper on ELC (2). Only the necessary combination of persistence of the ELC, migration theory of interstitial gas, and the radiological and numerical reconstruction of the

HRCT to 3D, could demonstrate the existence of the gas conducting interstitial pathway. The results imply the possibility to find the entrance of the intrabronchial gas into the anomalous bronchial wall and seal that passage to large ELCs. That may reduce both their size and adverse effect on pulmonary structure and function. This report on the 22-year-long persistence of a central ELC and its connection to a presegmental airway via a pulmonary gas conducting interstitial pathway is the first of its kind and there is no predecessor of it to refer to.

In conclusion, we have demonstrated a persistent pulmonary gas conducting interstitial pathway between the side of a presegmental airway and a persistent ELC. This suggests the escape of the intrabronchial gas across the anomalous presegmental bronchial wall. The migration of the gas in the pulmonary tissue ought to be determined by the locally lower density of the interstitial tissue than elsewhere and the pressure gradients during inhalation. Current findings could be relevant for a considerable proportion of the population.

Declaration of conflicting interests

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